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Communications

Structure and Reactivity of (η^3-Indolylmethyl)palladium Complexes Generated by the Reaction of Organopalladium Complexes with *o*-Alkenylphenyl Isocyanide

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*Summary: The reaction of methylpalladium complexes with o-alkenylphenyl isocyanides results in the successive intramolecular insertion of the alkenyl and isocyano groups followed by the 1,3-migration of hydrogen to give (η^3-indolylmethyl)palladium complexes (**4**) in good yields. Treatment of **4** with diethylamine causes nucleophilic attack at the exo methylene carbon to give 2-methyl-3-(aminomethyl)indole, whereas the reactions with HCl produce 2,3-dimethylindole derivatives.*

Cyclization via a tandem reaction of organic molecules mediated by transition-metal complexes is a powerful tool for the synthesis of heterocyclic compounds. Although several methods have been developed for the construction of an indole nucleus, indole derivatives are still fascinating targets in these synthetic reactions, due to their importance as basic units in a wide variety of biologically active natural products.[1,2] Ortho-functionalized aryl isocyanides have attracted much attention as a substrate for the synthesis of the indole framework.[3,4] Despite the high reactivity of isocyanides toward organometallic compounds,[5] there have been few reports on approaches to indole synthesis using transition-metal mediators.[6] We recently showed that the reactions of organopalladium complexes with *o*-ethynylphenyl isocyanide produce (*E*)- and (*Z*)-(indolidenemethyl)palladium complexes in good yields.[7] We describe here the formation of novel (η^3-indolylmethyl)palladium complexes from the reaction with *o*-alkenylphenyl isocyanide and their reactivity, leading to 2,3-disubstituted indole derivatives.

Treatment of complex **1a** with *o*-vinylphenyl isocyanide (**2a**)[8] at room temperature resulted in the insertion of the isocyano group of **2a** to give an iminoacyl complex

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(1) For reviews, see: (a) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113. (b) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2849. (c) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045.

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(5) For reviews, see: (a) Yamamoto, Y.; Yamazaki, H. *Coord. Chem. Rev.* **1972**, *8*, 225. (b) Treichel, P. M. *Adv. Organomet. Chem.* **1973**, *11*, 21. (c) Shingleton, E.; Oosthuizen, H. E. *Adv. Organomet. Chem.* **1983**, *22*, 209.

(6) (a) Jones, W. D.; Kosar, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 5640. (b) Hsu, G. C.; Kosar, W. P.; Jones, W. D. *Organometallics* **1994**, *13*, 385.

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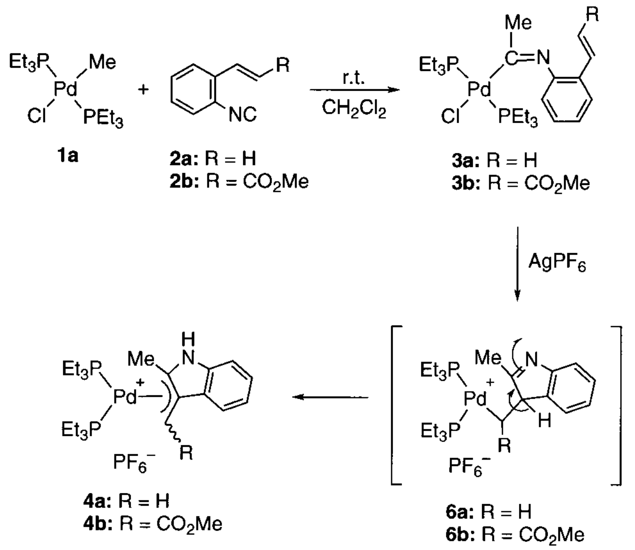
Scheme 1



(**3a**) in 86% yield (Scheme 1). Similar reaction with *o*-((methoxycarbonyl)ethenyl)phenyl isocyanide (**2b**)[3a,c] also produced an insertion product (**3b**) in 97% yield. These complexes were fully characterized by spectral analyses as well as by X-ray crystallography, as shown in Figure 1.[9]

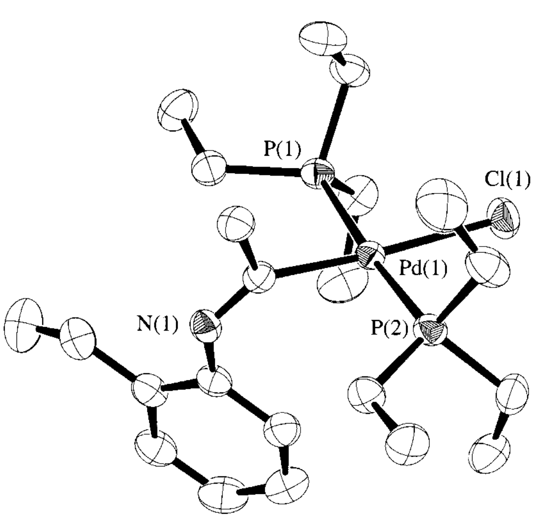


Figure 1. ORTEP drawing of **3a**. Hydrogen atoms are omitted for clarity. Bond distances and angles are included in the Supporting Information.

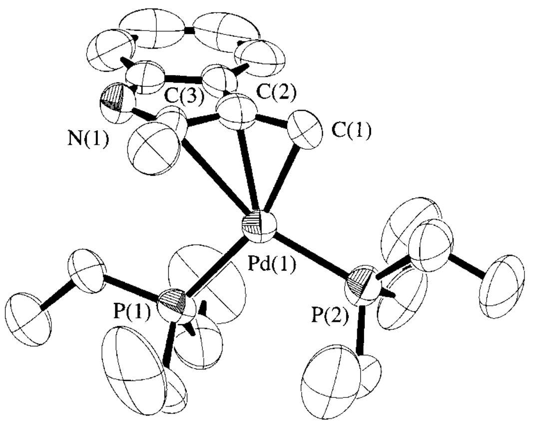
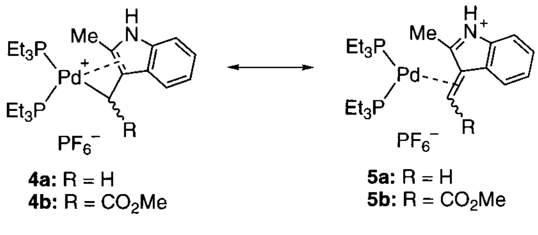


Figure 2. ORTEP drawing of **4a**. Hydrogen atoms and a counteranion are omitted for clarity. Selected bond distances (Å) and angles (deg) are as follows: Pd(1)−P(1) = 2.239(2), Pd(1)−P(2) = 2.277(3), Pd(1)−C(1) = 2.105(9), Pd(1)−C(2) = 2.189(9), Pd(1)−C(3) = 2.620(9), C(1)−C(2) = 1.42(1), C(2)−C(3) = 1.42(1); P(1)−Pd(1)−P(2) = 104.97(9), C(1)−C(2)−C(3) = 126(1).

Chart 1



No intramolecular insertion of the vinyl group took place upon heating a chloroform solution of **3a** at 45 °C, in contrast to the results with the acetylenic analogue.[7] Elevation of the reaction temperature caused decomposition of **3a** to $Pd(PEt_3)_2Cl_2$ and unidentified organic compounds. However, treatment of **3a** with $AgPF_6$ at 0 °C quantitatively gave a new palladium complex (**4a**), which was isolated in 50% yield. The ^{31}P NMR spectrum of **4a** showed two doublet signals at δ 7.1 and 29.8 with the coupling constant $J_{PP} = 29$ Hz, which is characteristic of a *cis*-bis(phosphine)palladium complex, along with a septet signal at δ −143.3 ($J_{PF} = 713$ Hz) due to the counteranion PF_6^-. In the ^1H NMR spectrum, the signals due to the vinyl protons disappeared, and two new signals assignable to those on the part derived from the vinyl group in the range of δ 2−4 along with a broad signal at δ 10.36 were observed. The IR spectrum revealed an absorption at 3304 cm^{-1}. These data are consistent with the formation of an indole skeleton produced by insertion of the vinyl group into the Pd−C bond followed by a hydrogen shift to the nitrogen atom. The structure of **4a** was unequivocally determined by an X-ray diffraction study, as shown in Figure 2, to be an η^3-indolylmethyl complex.[10] The most striking structural feature is that the Pd(1)−C(3) bond is much longer than Pd(1)−C(1) and Pd(1)−C(2). Although a similar phenomenon has often been observed in η^3-benzyl complexes,[11] the length of the Pd(1)−C(3) bond is remarkable. This may be due to the contribution of an η^2 structure (**5a**) (Chart 1), in which the formal oxidation state of the palladium atom is zero and the positive charge is located on the nitrogen atom.[12] The high stability of the indole skeleton in **4a** would be a driving force for the 1,3-hydrogen shift in the intermediate (**6a**), which was produced by intramolecular olefin insertion

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[7] Onitsuka, K.; Segawa, M.; Takahashi, S. *Organometallics* **1998**, *17*, 4335.

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[9] Crystallographic data for **3a**: formula $C_{22}H_{40}ClNP_2Pd$, fw = 522.37, monoclinic, space group $P2_1/n$ (No. 14), a = 10.8148(9) Å, b = 14.311(1) Å, c = 16.6209(8) Å, β = 98.873(5)°, V = 2541.7(2) Å^3, Z = 4, d_{calcd} = 1.365 g cm^{-3}, −70 °C, ω−2θ scan, 6° < 2θ < 55°, μ(Mo Kα) = 9.69 cm^{-1}, R (R_w) = 0.027 (0.044) for 244 parameters against 5167 reflections with $I > 3.0\sigma(I)$ out of 5833 unique reflections (R_{int} = 0.020) by full-matrix least-squares methods, GOF = 1.24.

[10] Crystallographic data for **4a**: formula $C_{22}H_{40}F_6NP_3Pd$, fw = 631.88, monoclinic, space group $P2_1/c$ (No. 14), a = 14.328(4) Å, b = 11.429(4) Å, c = 17.842(3) Å, β = 97.97(2)°, V = 2893(1) Å^3, Z = 4, d_{calcd} = 1.450 g cm^{-3}, 23 °C, ω−2θ scan, 6° < 2θ < 55°, μ(Mo Kα) = 8.57 cm^{-1}, R (R_w) = 0.059 (0.081) for 298 parameters against 2982 reflections with $I > 3.0\sigma(I)$ out of 6649 unique reflections (R_{int} = 0.048) by full-matrix least-squares methods, GOF = 1.09.

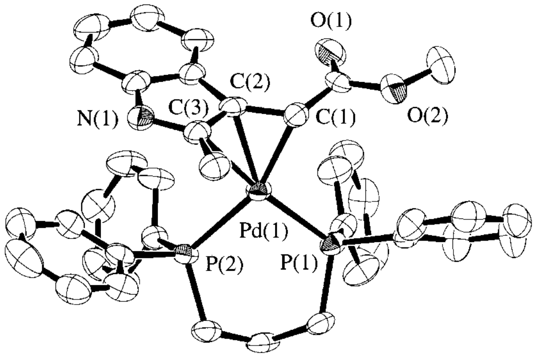
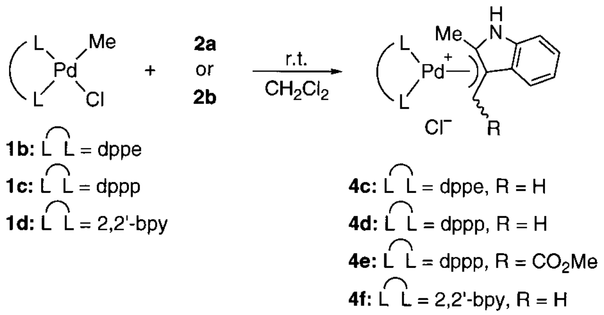


Figure 3. ORTEP drawing of *syn*-**4d**. Hydrogen atoms, solvent molecules, and a counteranion are omitted for clarity. Selected bond distances (Å) and angles (deg) are as follows: Pd(1)−P(1) = 2.278(2), Pd(1)−P(2) = 2.301(1), Pd(1)−C(1) = 2.118(4), Pd(1)−C(2) = 2.184(4), Pd(1)−C(3) = 2.713(4), C(1)−C(2) = 1.436(6), C(2)−C(3) = 1.408(6); P(1)−Pd(1)−P(2) = 94.41(4), C(1)−C(2)−C(3) = 120.9(4).

from **3a**. The η^3 coordination mode in **4a** is stable compared to that in analogous (η^3-benzyl)palladium complexes. Thus, treatment of Et_4NCl did not change the coordination mode to η^1, whereas (η^3-benzyl)palladium complexes are easily converted into η^1-benzyl complexes under similar conditions.[13] Reaction of **3b** with $AgPF_6$ also gave an η^3-indolylmethyl complex (**4b**), which consisted of two isomers, *syn*- and *anti*-**4b**, in a ratio of 71:29 as determined by ^1H and ^{31}P NMR spectra.

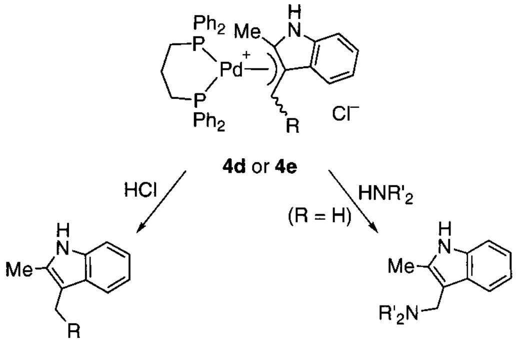
Upon treatment of complex **1b**, which has the ligand bis(diphenylphosphino)ethane (dppe), with **2a** at room temperature, both the isocyano and olefinic groups of **2a** smoothly inserted into the Pd−C bond in the absence of $AgPF_6$ to give an η^3-indolylmethyl complex (**4c**) in 76% isolated yield (Scheme 2). Reaction of complex **1c**, which has the ligand bis(diphenylphosphino)propane (dppp), also produced complex **4d**, which was isolated in 46% yield. Although a mixture of *syn*- and *anti*-**4e** was produced in a ratio of 78:22 from the reaction of complex **1c** with **2b**, the major product was isolated by recrystallization from a $CHCl_3-CH_2Cl_2$−hexane solution and was confirmed to be *syn*-**4e** by an X-ray analysis (Figure 3).[14] The Pd(1)−C(3) bond is slightly longer than the corresponding bond in **4a**, suggesting that the η^2-coordinated structure has a greater contribution, since the electron-withdrawing nature of the methoxycarbonyl group stabilizes the low oxidation state of the palladium species. The reaction of complex **1d**, which has 2,2′-bipyridine as a bidentate ligand, with **2a** smoothly proceeded to give complex **4f** in 77% yield.

Scheme 2



1b: L L = dppe
1c: L L = dppp
1d: L L = 2,2′-bpy
4c: L L = dppe, R = H
4d: L L = dppp, R = H
4e: L L = dppp, R = CO_2Me
4f: L L = 2,2′-bpy, R = H

Scheme 3



4d or **4e**

7a: R = H
7b: R = CO_2Me
8a: R′ = Et
8b: R′ = Pr

The (η^3-indolylmethyl)palladium complex **4** shows reactivities similar to those of common (η^3-allyl)palladium complexes. Complexes **4d** and **4e** underwent the quantitative cleavage of the Pd−C bond in an η^3 fashion by treatment with HCl to give 2,3-dimethylindole derivatives (**7**) in quantitative yields[15] (Scheme 3). On the other hand, the η^3-indolylmethyl group also underwent nucleophilic attack.[16] Treatment of complex **4d** with dialkylamine at room temperature selectively produced 2-methyl-3-(aminomethyl)indole derivatives (**8**) in good yields.

In summary, we have demonstrated the stoichiometric transformation of *o*-alkenylphenyl isocyanides into 2,3-disubstituted indole derivatives on a palladium atom through η^3-indolylmethyl intermediates. Further studies focused on the application of the present finding to a catalytic system are now in progress.

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Supporting Information Available: Text giving experimental details and full characterization data for all new complexes and X-ray crystallographic data for complexes **3a**, **4a**, and **4e**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM010897O

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[14] Crystallographic data for **4e**·$CHCl_3$·$2H_2O$: formula $C_{40}H_{43}Cl_4NO_4P_2Pd$, fw = 911.94, monoclinic, space group $P2_1/c$ (No. 14), $a = 15.446(3)$ Å, $b = 21.114(2)$ Å, $c = 13.115(4)$ Å, $\beta = 106.37(1)°$, $V = 4105(1)$ Å^3, $Z = 4$, $d_{calcd} = 1.475$ g cm^{-3}, −50 °C, $\omega-2\theta$ scan, $6° < 2\theta < 55°$, μ(Mo Kα) = 8.31 cm^{-1}, R (R_w) = 0.055 (0.092) for 469 parameters against 6823 reflections with $I > 3.0\sigma(I)$ out of 9410 unique reflections (R_{int} = 0.043) by full-matrix least-squares methods, GOF = 1.22.

[15] A similar reaction of [(η^3-allyl)Pd(dppp)]Cl with HCl resulted in quantitative elimination of the allyl group to give Pd(dppp)Cl_2. Rapid Pd−allyl bond cleavage has been observed in the reaction of (η^1-allyl)palladium complexes with an equimolar amount of electrophiles: Kurosawa, H.; Urabe, A.; Miki, K. Kasai, N. *Organometallics* **1986**, *5*, 2002.

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