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Key Process in Palladium-Catalyzed Asymmetric Transformation of Propargyl Electrophiles. Racemization of Optically Active η^1-Allenylpalladium(II)

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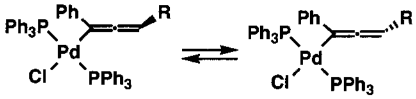
Transition metal-catalyzed asymmetric reactions are a very powerful tool for organic synthesis, where either configurational rigidity or flexibility of the organometal intermediate is often a very crucial issue for the attainment of a highly selective outcome depending on the reaction type. For instance, in palladium-catalyzed reactions of propargyl or allenyl electrophiles, quite rapid interconversion between the enantiomers of allenyl complex having a chiral axis[1] is necessary for the dynamic kinetic resolution reaction of racemic propargyl substrates,[2] while the enantiomeric stability must be high enough to avoid partial racemization of optically active propargyl substrates.[3] Here we report novel racemization of the optically active mononuclear η^1-allenylpalladium complex, a conventional intermediate in catalytic cycles, by way of the exchange of its allenyl ligand with that in the highly configurationally labile μ-η^3-allenyl/propargyldipalladium complex, a process that could occur easily under usual catalytic reaction conditions.

Optically active allenylpalladium complexes (**1a**−**c**) were prepared from the reaction of the corresponding optically active propargyl chlorides with $Pd_2(dba)_3$ and PPh_3 and the optical rotation of a solution of **1** was large enough to allow us to follow the racemization by measurement of its decrease (eq 1).[4,6]



(1)

1a: R = CH_3, **1b**: R = $^nC_5H_{11}$, **1c**: R = ^tBu

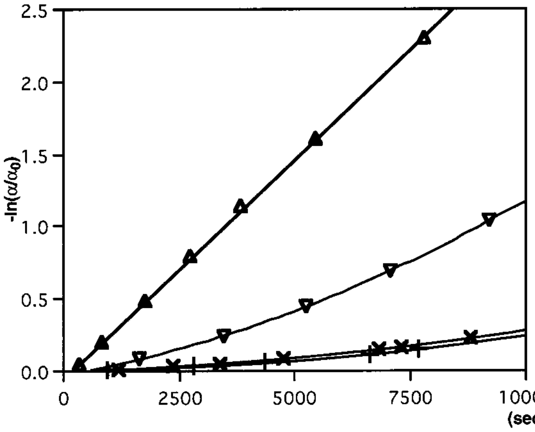
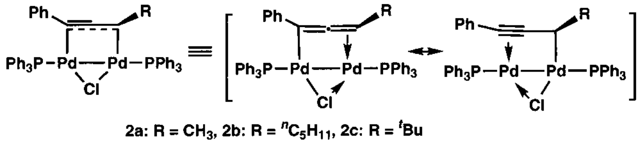
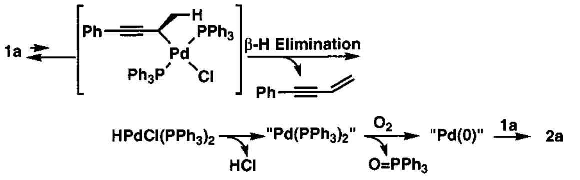


Figure 1. Racemization of **1a** at 25 °C: (▽) C_6D_6 solution prepared under air; (×) C_6D_6 solution prepared under N_2; (+) $CHCl_3$ solution prepared under N_2; (△) in the presence of 10 mol % of **2a**. $CHCl_3$ solution prepared under N_2.

Scheme 1



Scheme 2



Although very slow racemization of **1a** and **1b** was observed in a solution of oxygen-free C_6H_6 or $CHCl_3$, **1c** having no β-hydrogen was totally stable with respect to the racemization under the same conditions. The racemization of **1a** in a solution prepared under air proceeded considerably faster, somewhat in an autocatalytic manner, than in the oxygen-free solution (Figure 1).[7] These results suggest that the presence of oxygen in the solution of **1a** or **1b** having β-hydrogen leads to generation of a catalyst or mediator responsible for the racemization. The ^1H and ^{31}P NMR spectra of the residue recovered after the racemization experiment with **1a** in the C_6H_6 solution prepared under air showed the presence of **1a** (87%), $O{=}PPh_3$ (7.6%), 1-phenyl-4-buten-1-yne (6.8%), and the μ-η^3-allenyl/propargyl dinuclear complex (**2a**: R = CH_3, Scheme 1) (6.2%).

A possible path for generation of **2a** and the other minor products in the presence of oxygen is depicted in Scheme 2. First, the β-hydrogen elimination may take place in a propargyl isomer, which is assumed to lie in equilibrium with **1a**,[8] to give enyne and $HPdCl(PPh_3)_2$ and subsequently "$Pd(PPh_3)_2$" species. Then this may react with oxygen to give $O{=}PPh_3$ and PPh_3-deficient Pd(0) species, the latter of which might react further with **1a** to give **2a**.[9] The addition of 10 mol % of PPh_3 to a solution of **1a** prepared even under air suppressed the racemization of **1a**

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[1] No chiral propargyl complex has been known, since the introduction of substituents on the propagylic carbon leads to the formation of allenyl complexes exclusively.

[2] Mikami, K.; Yoshida, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 858.

[3] Elsevier, C. J.; Stehouwer, P. M.; Westmijze, H.; Vermeer, P. *J. Org. Chem.* **1983**, *48*, 1103. Elsevier, C. J.; Mooiweer, H. H.; Kleijn, H.; Vermeer, P. *Tetrahedron Lett.* **1984**, *25*, 5571. Elsevier, C. J.; Vermeer, P. *J. Org. Chem.* **1985**, *50*, 3042. Dixneuf, P.; Guyot, T.; Ness, M. D.; Roberts, S. M. *J. Chem. Soc., Chem. Commun.* **1997**, 2083. Marshall, J. A.; Wolf, M. A.; Wallace, E. M. *J. Org. Chem.* **1997**, *62*, 367. Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1998**, *63*, 3812. Marshall, J. A.; Grant, C. A. *J. Org. Chem.* **1999**, *64*, 696. Konno, T.; Tanikawa, M.; Ishihara, T.; Yamanaka, H. *Chem. Lett.* **2000**, 1360.

[4] We assumed oxidative addition occurred with inversion of configuration as previously reported.[5] However, this assumption does not affect the conclusion of the present work at all.

[5] Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716.

[6] The complex **1a** was prepared by the reaction of $Pd_2(dba)_3$ and PPh_3 with (*R*)-$PhCCCH_2(Me)Cl$ (95% ee). Yield 86%. $[\alpha]^{25}_D$ +5613° (*c* 1.34, C_6H_6). ^1H NMR ($CDCl_3$) δ 0.96 (dt, J_{HH} = 6.8 Hz, J_{PH} = 1.5 Hz, 3H), 4.04 (q, J_{HH} = 6.8 Hz, 1H), 6.75 (m, 3H), 7.15 (d, J = 6.2 Hz), 7.2−7.7 (m, 30H). ^{31}P NMR ($CDCl_3$) δ 22.83 (d, J_{PP} = 430.5 Hz), 24.66 (d, J_{PP} = 430.5 Hz). Anal. Calcd for $C_{46}H_{39}ClP_2Pd$: C, 69.44; H, 4.94. Found C, 69.24; H, 4.99. For **1b** and **1c**, see Supporting Information.

[7] Solvents were purified with the freeze−pump−thaw method and solutions were prepared in a glovebox. Thus, complex **1a** would not undergo racemization under the absolutely oxygen free condition.

[8] Recently, we reported the first reversible interconversion between propargyl and allenylplatinum complexes which occurs spontaneously or is catalyzed by Pt(0) complexes. (a) Ogoshi, S.; Fukunishi, Y.; Tsutsumi, K.; Kurosawa, H. *J. Chem. Soc., Chem. Commun.* **1995**, 2485. (b) Ogoshi, S.; Fukunishi, Y.; Tsutsumi, K.; Kurosawa, H. *Inorg. Chim. Acta* **1997**, *265*, 9. (c) Ogoshi, S.; Nishida, T.; Fukunishi, Y.; Tsutsumi, K.; Kurosawa, H. *J. Organomet. Chem.* **2001**, *620*, 190.

[9] **2a** was separately prepared from the reaction of **1** with $Pd_2(dba)_3$. See: Ogoshi, S.; Tsutsumi, K.; Ooi, M.; Kurosawa, H. *J. Am. Chem. Soc.* **1995**, *117*, 10415. Ogoshi, S.; Nishida, T.; Tsutsumi, K.; Ooi, M.; Shinagawa, T.; Akasaka, T.; Yamane, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 3223.

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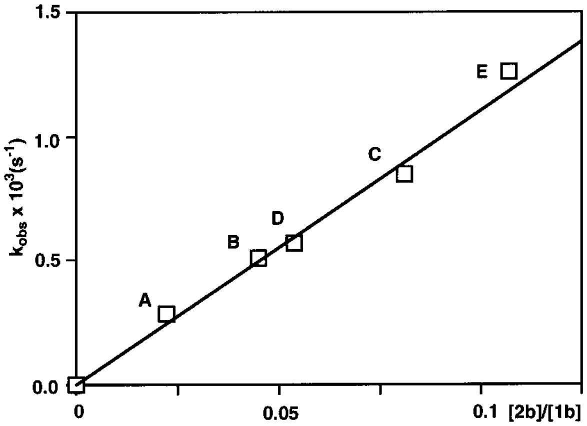


Figure 2. The plot of k_{obs} vs the ratio of [**2b**]/[**1b**]: (A) $[\mathbf{1b}]_{(A)} = 5.58 \times 10^{-3}$ M, $[\mathbf{2b}]_{(A)} = 1.25 \times 10^{-4}$ M; (B) $[\mathbf{1b}]_{(B)} = 5.58 \times 10^{-3}$ M, $[\mathbf{2b}]_{(B)} = 2.50 \times 10^{-4}$ M; (C) $[\mathbf{1b}]_{(C)} = 5.58 \times 10^{-3}$ M, $[\mathbf{2b}]_{(C)} = 4.52 \times 10^{-4}$ M; (D) $[\mathbf{1b}]_{(D)} = 8.40 \times 10^{-3}$ M, $[\mathbf{2b}]_{(D)} = 4.52 \times 10^{-4}$ M; and (E) $[\mathbf{1b}]_{(E)} = 4.21 \times 10^{-3}$ M, $[\mathbf{2b}]_{(E)} = 4.52 \times 10^{-4}$ M.

completely for 2 h, presumably owing to the role of additional PPh_3 to prevent the generation of **2a** by forming $Pd(PPh_3)_n$ (n = 3 or 4).[10] In support of this assumption, the ^{1}H and ^{31}P NMR spectra of the concentrate of the solution of **1a** and added PPh_3 which had been kept under air for 2 h showed no formation of dinuclear complex **2a**, although the production of very small amounts of $O{=}PPh_3$ and 1-phenyl-4-buten-1-yne was confirmed.

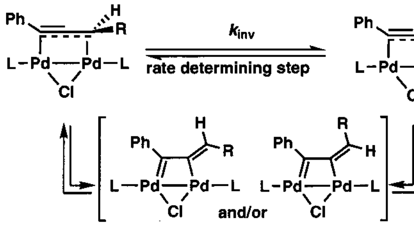
From the above results, we suspected that the dinuclear complex is the catalyst or mediator for the racemization of **1a** or **1b**. In fact, we found that addition of the dinuclear complex **2a** or **2b** accelerated the racemization of **1a** or **1b** (under N_2) in $CHCl_3$ at 25 °C efficiently; the plot of $-\ln[\alpha/\alpha_0]$ vs time gave a straight line over 3 half-lives (Figure 1) (**1a**: $k_{obs} = 3.0 \times 10^{-4}$ s^{-1} at $[\mathbf{1a}] = 1.53 \times 10^{-3}$ M and $[\mathbf{2a}] = 1.53 \times 10^{-4}$ M; **1b**: $k_{obs} = 2.5 \times 10^{-5}$ s^{-1} at $[\mathbf{1b}] = 7.59 \times 10^{-3}$ M and $[\mathbf{2b}] = 7.59 \times 10^{-4}$ M; $-d\alpha/dt = k_{obs}\alpha$). Interestingly, racemization of optically more stable complex **1c** was also accelerated by addition of the dinuclear complex **2c** ($k_{obs} = 1.1 \times 10^{-5}$ s^{-1} at $[\mathbf{1c}] = 2.19 \times 10^{-2}$ M and $[\mathbf{2c}] = 2.25 \times 10^{-3}$ M).

To understand how the dinuclear complex participates in the racemization, the rate of the decrease in the optical rotation was measured at 40 °C at several concentrations of **1b** and **2b** with [**2b**] being less than 1/10 of [**1b**].[12] The rate constant k_{obs} was linearly dependent on the concentration of **2b**, if the concentration of **1b** was kept constant (Figure 2, A−C), which suggests that **2b** might be the catalyst for the racemization. More remarkably, however, k_{obs} was linearly dependent on the inverse of the concentration of **1b**, if the concentration of **2b** was kept constant (Figure 2, C−E). This leads us to believe that the inversion of stereochemistry of the allenyl ligand does not occur simply in an association complex involving **1** and **2**; otherwise k_{obs} should be independent of the initial concentration of **1**.

We now propose the occurrence of rapid exchange of the allenyl ligand between **1** and **2** with retention of stereochemistry (Scheme 3) and rate determining inversion in the dinuclear complex **2** (Scheme 4). We confirmed by the spin saturation transfer experiment at 40 °C that the rate of allenyl group exchange between **1b** and **2b** is on the order of ^{1}H spin relaxation time (a few seconds),[13,14] which is much faster than the rate of racemization of **1b** in the presence of **2b**. This observation indicates that the allenyl transfer proceeds with the retention of stereochemistry, otherwise the observed racemization rate should have been much higher, comparable to the allenyl transfer rate. Through this transfer, the enantiomeric excess (ee) of **1b** is always equal to that of **2b**. According to the scheme, the overall rate is written as rate $= -d\{([\mathbf{1b}]_0 + [\mathbf{2b}]_0)(ee)\}/dt = 2k_{inv}[\mathbf{2b}]_0(ee)$ and thus we obtain $-d(ee)/dt = \{[\mathbf{2b}]_0/([\mathbf{1b}]_0 + [\mathbf{2b}]_0)\}(2k_{inv})(ee)$. On the other hand, since k_{obs} is determined from $-d\alpha/dt = k_{obs}\alpha$ and α can be written as α = (constant)(ee), we can obtain the equation $-d(ee)/dt = k_{obs}(ee)$.[15] Thus, the following relationship between k_{obs} and k_{inv} can be obtained, $k_{obs} = \{[\mathbf{2b}]_0/([\mathbf{1b}]_0 + [\mathbf{2b}]_0)\}2k_{inv}$, which is in accordance with Figure 2 if $[\mathbf{2b}]_0$ in the denominator is neglected.[16] The rate constant ($2k_{inv}$) for the racemization of the dinuclear complex is expected to be much larger than k_{obs}.[17] Likely candidates for such inversion in the dinuclear complex include the formation of a nonchiral μ-η^1:η^1-vinyldipalladium intermediate[18] (Scheme 4).

Scheme 3. Rapid Allenyl Transfer between **1** and **2** with Retention

Scheme 4. A Plausible Path for Inversion of Stereochemistry



By referring to the overall scheme presented here, we could give a criterion for the palladium-catalyzed asymmetric reaction of propargyl electrophiles; the generation of the dinuclear complex should be designed to meet the dynamic kinetic resolution, for example, by decreasing the amount of phosphine ligand, or be suppressed to avoid the loss of optical purity of the substrate by adding an excess amount of ligand.

Further efforts related to this problem are underway in this laboratory.

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Supporting Information Available: Procedures and spectral data for complexes **1a**−**c** and **2a**−**c**, and measurement for the decrease of optical rotation (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The reaction of $Pd(PPh_3)_4$ with mononuclear allenyl/propargylpalladium does not lead to the formation of dinuclear complex, and addition of excess PPh_3 to the dinuclear complex results in the re-formation of the mononuclear complex and $Pd(PPh_3)_n$ (n = 3 or 4).[9] In fact, $Pd(PPh_3)_4$ (10 mol %) was not effective at all in promoting racemization of **1a** and **1b** in contrast to Pd(0)-catalyzed loss of stereochemistry of η^3-allylpalladium.[11]

(11) (a) Ogoshi, S.; Kurosawa, H. *Organometallics* **1993**, *12*, 2869. (b) Kurosawa, H.; Ogoshi, S.; Chatani, N.; Kawasaki, Y.; Murai, S.; Ikeda, I. *Chem. Lett.* **1990**, 1745. (c) Granberg, K. L.; Bäckvall, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6858.

(12) Decrease of optical rotation was measured at 40 °C due to the ease of accurate temperature control for long hours.

(13) Transfer of Pd(0) from dinuclear complex to mononuclear complex can give rise to the virtual allenyl transfer between **1** and **2**.

(14) Irradiation at the resonance frequency of the allenyl proton in **2b** resulted in a decrease (1.48%) of the signal due to allenyl proton in **1b**. A similar equilibrium between mononuclear and dinuclear complexes of η^3-allylpalladium had been reported. Kurosawa, H.; Hirako, K.; Natsume, S.; Ogoshi, S.; Kanehisa, N.; Kai, Y.; Sakaki, S.; Takeuchi, K. *Organometallics* **1996**, *15*, 2089.

(15) $\alpha = \alpha_M + \alpha_D = ([\alpha_M][\mathbf{1}]_0 + [\alpha_D][\mathbf{2}]_0)ee$ ($[\alpha_M]$ and $[\alpha_D]$ being specific rotations of mononuclear and dinuclear complexes, respectively).

(16) The plot of k_{obs} vs the ratio $[\mathbf{2b}]_0/([\mathbf{1b}]_0 + [\mathbf{2b}]_0)$ also gives a straight line (slope $= 1.24 \times 10^{-2}$ s^{-1}, while that of Figure 2 is 1.11×10^{-2} s^{-1}).

(17) We could not isolate the optically active dinuclear complex due to the expected rapid inversion of the stereochemistry on Pd(I)−Pd(I) even in the configurationally most stable complex **2c** ($k_{inv} = 9.6 \times 10^{-4}$ s^{-1} at 25 °C).

(18) A μ-η^1:η^1-vinyl complex similar to this intermediate has been known. Al-Obaidi, Y. N.; Green, M.; White, N. D.; Taylor, G. E. *J. Chem. Soc., Dalton Trans.* **1982**, 319.