

Catalytic C-H Bond Activation-Asymmetric Olefin Coupling Reaction: The First Example of Asymmetric Fujiwara-Moritani Reaction Catalyzed by Chiral Palladium(II) Complexes¹

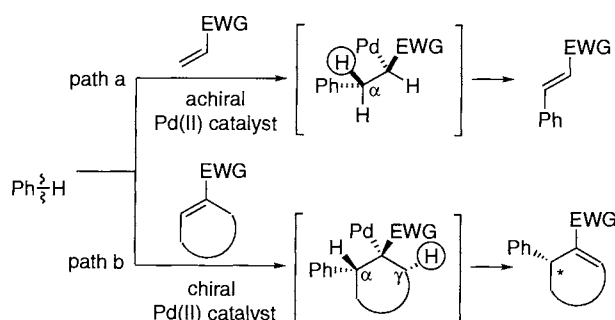
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The first example of the asymmetric Fujiwara-Moritani reaction catalyzed by chiral Pd(II) complexes is reported to represent a catalytic aromatic C-H bond activation-asymmetric olefin coupling reaction.

C-H Bond activation² and C-C bond formation are the key issues in organic synthesis. In this context, we have been developing catalytic asymmetric ene reactions;³ the ene reaction is one of the simplest ways for C-C bond formation, which converts readily available olefins with activation of an allylic C-H bond and allylic transposition of the C=C bond, into more functionalized products.⁴ The so-called "Fujiwara-Moritani" reaction has also proven to be one of the most versatile methods for activation of aromatic C-H bonds to provide a coupling product with an olefin using a catalytic amount of Pd(II) complex.⁵ However, there is no example of catalytic asymmetric version of the Fujiwara-Moritani reaction, presumably because of the inherent nature of the reaction mode that styrene-type products are formed through *syn*-β-H-elimination from α-phenyl side of the olefin insertion intermediate (Scheme 1: path a). Furthermore, as compared to the significant development of catalytic asymmetric reactions with chiral Pd(0) catalysts,⁶ catalytic asymmetric reactions by chiral Pd(II) species have so far received only little attention.⁷ Herein, we now wish to report the first example of the catalytic asymmetric Fujiwara-Moritani reaction of benzene as a coupling reaction with cyclic olefins through *syn*-β-H-elimination, however, from the opposite (γ) side to the phenyl-group (Scheme 1: path b).⁸⁻¹¹



Scheme 1.

Typical experimental procedure is as follows: Pd(OAc)₂ (0.1 mmol, 10 mol%) was mixed with chiral sulfonylamino-oxazoline ligand (**1**) (0.1 mmol, 10 mol%) in dry benzene (2 ml) and then cyclohexenecarbonitrile (**2c**) (1.0 mmol) was added to the resultant mixture. The mixture was then heated in the presence of *t*-butyl perbenzoate (1.0 mmol) as a reoxidant¹² at 100 °C with stirring for 9 h. The precipitated palladium was separated and the

mixture was poured into water. After usual work-up, chromatographic purification on silicagel gave 6-phenyl-1-cyclohexenecarbonitrile (**3c**). The enantiomeric excess of the product was determined by chiral HPLC analysis (Daicel CHIRALPAK AS, hexane : 2-propanol = 50 : 1); (*S*)- and (*R*)-**3c**: 28.9 and 31.2 min, respectively.

The representative results are summarized in Table 1. (1) Interestingly, ester substrate (**2a**) gave modest yield of the coupling product (**3a**), however, in almost racemic form. (2) In sharp contrast, nitrile **2c** afforded better enantioselectivity of product **3c**. (3) Modification of chiral ligand (**1**) with an electron withdrawing and sterically demanding highly fluorinated sulfonyl group was found to lead to the increased chemical yield and enantioselectivity.

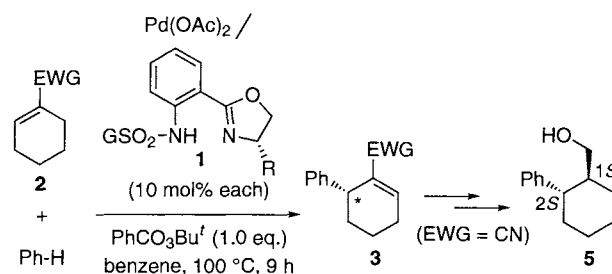


Table 1. C-H bond activation by chiral Pd(II) catalysts

Run	R	GSO ₂	2 (EWG)	3	Yield /%	Ee /%
1	<i>i</i> -Pr	CF ₃ SO ₂	2a (CO ₂ CH ₃)	3a	33	1
2	<i>i</i> -Pr	CF ₃ SO ₂	2b (NO ₂)	3b	9	27
3	<i>i</i> -Pr	Ts ^a	2c (CN)	3c	6	40
4	<i>i</i> -Pr	CF ₃ SO ₂	2c	3c	25	44
5	<i>t</i> -Bu	CF ₃ SO ₂	2c	3c	15	47
6	<i>i</i> -Pr	C ₄ F ₉ SO ₂	2c	3c	25	42
7	<i>i</i> -Pr		2c	3c	19	49

^a T. Fujisawa, T. Ichiyang, and M. Shimizu, *Tetrahedron Lett.*, **36**, 5031 (1995); J. A. Allen, G. J. Dawson, C. G. Frost, and J. M. J. Williams, *Tetrahedron*, **50**, 799 (1994).

Interesting phenomena of formation of chiral Pd(II) complexes deserve special comments; upon mixing Pd(OAc)₂ with an equimolar amount of **1** (R = *t*-Bu, GSO₂ = CF₃SO₂) in dry benzene, a crystalline Pd(II) complex (**4**) was formed. However, the use of **4** as a catalyst, no benzene-olefin coupling product **3c** was obtained. Only in the co-presence of a catalytic amount of *achiral* Pd(OAc)₂, the enantio-enriched coupling product was obtained (30% ee, 30% yield) (Scheme 2). X-Ray crystallographic analysis of the crystalline complex (**4**) showed

the 2 : 1 complex of the chiral ligand and Pd(II) species (Figure 1).¹³ Therefore, the 1 : 1 complex of the chiral ligand and Pd(II) species formed through equilibrium between **4** and Pd(OAc)₂ or *in situ* prepared from Pd(OAc)₂ with an equimolar amount of the chiral ligand could be the active catalyst species in this catalytic asymmetric Fujiwara-Moritani reaction.

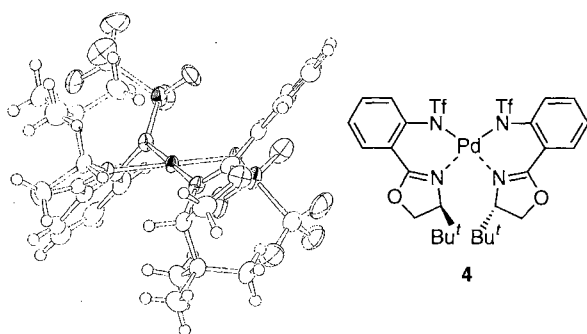
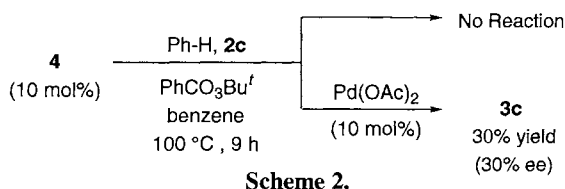


Figure 1. ORTEP drawing of **1** ($R = t\text{-Bu}$, $\text{GSO}_2 = \text{CF}_3\text{SO}_2$) / Pd(II) 2 : 1 complex (**4**).

It should be noted here that the coupling product (**3c**) has been proven to be of (*R*)-configuration after transformation to the known (1*S*,2*S*)-(2-phenylcyclohexane)methanol (**5**).¹⁴ Thus, the transition state for the key insertion process can be designated as follows: The (*S*)-oxazoline Pd(II) complex preferentially provides (*R*)-**3c** probably because the transition state **A** is more favorable than the transition state **B** with severe steric repulsion of the cyclohexene ring with the sulfonylamino (GSO_2N) and/or alkyl (*R*) groups in the oxazoline ligands (Figure 2).

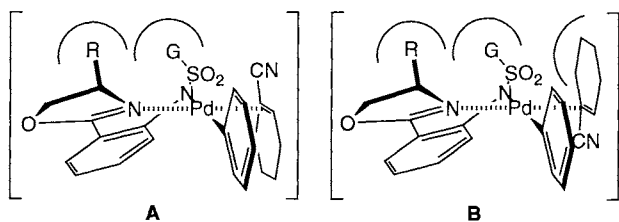


Figure 2. Transition states for the insertion process.

In conclusion, we have reported the first example of the catalytic asymmetric Fujiwara-Moritani reaction catalyzed by chiral sulfonylamino-oxazoline ligand-derived chiral Pd(II) complexes. This process exemplifies a catalytic aromatic C-H bond activation-asymmetric olefin coupling reaction.

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- Crystal data for **4**: formula $\text{C}_{28}\text{H}_{32}\text{F}_6\text{N}_4\text{O}_6\text{PdS}_2$, triclinic, space group $P1$, $a = 10.2464(9)$ Å, $b = 18.260(1)$ Å, $c = 10.0381(7)$ Å, $\alpha = 102.856(6)^\circ$, $\beta = 108.363(6)^\circ$, $\gamma = 84.735(6)^\circ$, $V = 1737.3(2)$ Å³, $Z = 2$, and $D_c = 1.539$ g cm⁻³. X-Ray diffraction data were collected on a Rigaku AFC7R diffractometer with graphite-monochromated Mo-K α ($\lambda = 0.71069$ Å) at -50°C and the structure was solved by direct methods (SIR92). All non hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 7358 observed reflections ($I > 3\sigma(I)$) and 902 variable parameters and converged to $R = 0.030$ and $R_w = 0.027$.
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