Catalytic C-H Bond Activation-Asymmetric Olefin Coupling Reaction: The First Example of Asymmetric Fujiwara-Moritani Reaction Catalyzed by Chiral Palladium(II) Complexes[1]

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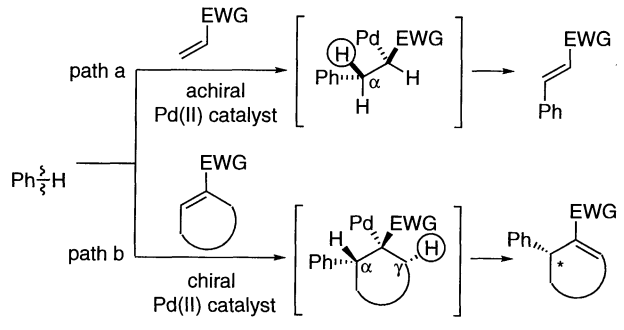
The first example of the asymmetric Fujiwara-Moritani reaction catalyzed by chiral Pd(II) complexes is reported to represent a catalytic aromatic C-H bond activation-asymmetric olefin coupling reaction.

C-H Bond activation[2] 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 to give the chiral phenyl-substituted 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 reoxidant[12] 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.

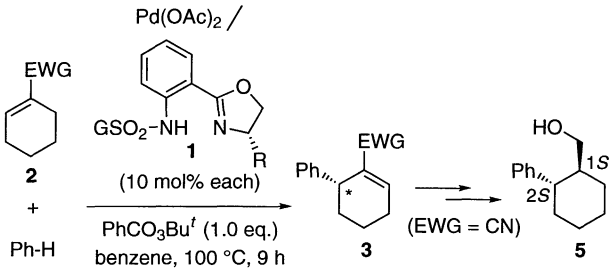
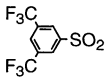


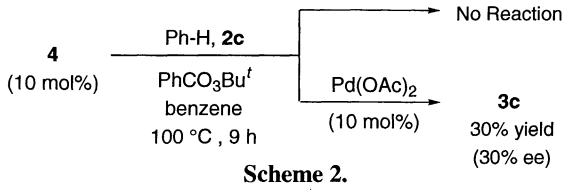
Table 1. C-H bond activation by chiral Pd(II) catalysts

Run	R	GSO_2	2 (EWG)	3	Yield /%	Ee /%
1	*i*-Pr	CF_3SO_2	**2a** (CO_2CH_3)	**3a**	33	1
2	*i*-Pr	CF_3SO_2	**2b** (NO_2)	**3b**	9	27
3	*i*-Pr	Ts[a]	**2c** (CN)	**3c**	6	40
4	*i*-Pr	CF_3SO_2	**2c**	**3c**	25	44
5	*t*-Bu	CF_3SO_2	**2c**	**3c**	15	47
6	*i*-Pr	$C_4F_9SO_2$	**2c**	**3c**	25	42
7	*i*-Pr		**2c**	**3c**	19	49

[a] T. Fujisawa, T. Ichiyanagi, 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, $GSO_2 = CF_3SO_2$) 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.



Scheme 2.

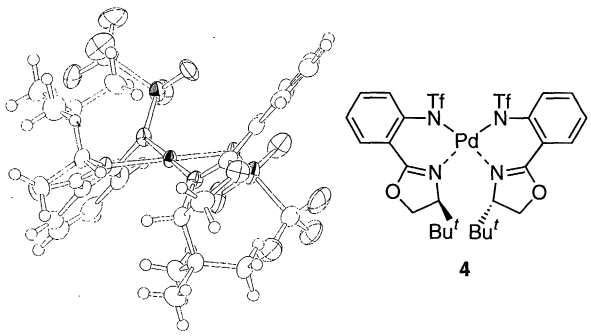


Figure 1. ORTEP drawing of **1** (R = *t*-Bu, $GSO_2 = CF_3SO_2$) / Pd(II) 2 : 1 complex (**4**).

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).

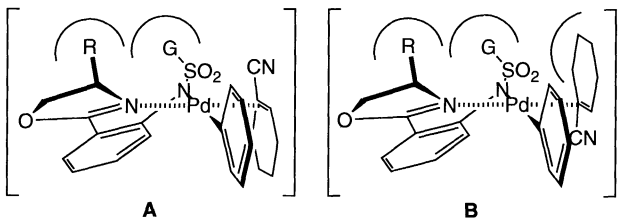


Figure 2. Transition states for the insertion process.

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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13 Crystal data for **4**: formula $C_{28}H_{32}F_6N_4O_6PdS_2$, triclinic, space group *P*1, *a* = 10.2464(9) Å, *b* = 18.260(1) Å, *c* = 10.0381(7) Å, α = 102.856(6)°, β = 108.363(6)°, γ = 84.735(6)°, *V* = 1737.3(2) Å^3, *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-Kα (λ = 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 *Rw* = 0.027.

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