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# Enantioselective catalysis of Claisen rearrangement by DABNTf–Pd(II) complex

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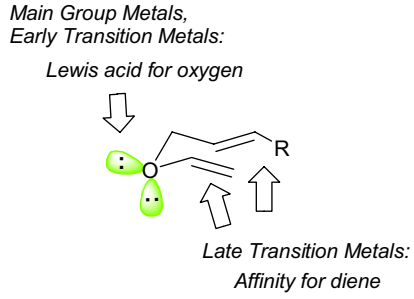
**Abstract**—Two types of palladium complexes, cationic (*R*)-BINAP–$Pd^{2+}(SbF_6^-)_2$ and neutral (*R*)-DABNTf–$Pd(CH_3CN)_2$ were examined as chiral catalysts for enantioselective Claisen rearrangement. DABNTf–$Pd(CH_3CN)_2$ complex gave high enantio- and *anti*-diastereoselectivity, and good yield. This Claisen rearrangement should proceed via six-membered boat transition state through bi-dentate coordination to the Pd catalyst.


The Claisen rearrangement of allyl vinyl ether is one of the most important carbon–carbon bond forming reactions in organic synthesis.[1] However, there are only a few examples of asymmetric catalysis of the Claisen rearrangement. Yamamoto and Maruoka reported several chiral Al complexes as equimolar reagents for the Claisen substrate.[2] Hiersemman reported Cu bis-oxazoline complexes for 2-alkoxycarbonyl substituted substrate.[3] These examples, however, require stoichiometric amounts of reagents or specific substrates, because these metal catalysts are based on the Lewis acidity to distinguish presumably two enantiotopic lone pairs on oxygen of allyl vinyl ether and because carbonyl products are strongly complexed to these oxophilic metals (Scheme 1).

In sharp contrast, the late transition metals are more coordinative to soft carbon–carbon multiple bonds rather than hard oxygen. Furthermore, bi-dentate coordination is advantageous over the weak mono-dentate coordination of γ,δ-unsaturated carbonyl product allowing the catalytic cycle. Herein we report the enantioselective catalysis of Claisen rearrangement using (*R*)-DABNTf [(*R*)-diamino-binaphthyl trifluoromethanesulfonylamide]–Pd complex.




**Scheme 1.** Two distinct models of metal catalyzed enantioselective Claisen rearrangement.

First, we examined two types of palladium complexes; cationic (*R*)-BINAP–$Pd^{2+}(SbF_6^-)_2$ and neutral (*R*)-DABNTf–$Pd(CH_3CN)_2$[4] (Scheme 2). Under the cationic conditions, the product was not obtained, presumably because of the high Lewis acidity of the BINAP–$Pd^{2+}$ complex. In contrast, using the neutral (*R*)-DABNTf–Pd complex, the reaction proceeded to give (*R*,*R*)-*anti*-**2** with high enantioselectivity (83% ee)[5] though in low yield at room temperature. This result suggests that the trifluoromethanesulfonylamide ligand DABNTf[6] is effective for the enantioselective Claisen rearrangement.

Several chiral trifluoromethanesulfonylamide ligands were then examined (Table 1). The solution of $Pd(OAc)_2$ and a chiral ligand in acetonitrile was stirred for 3 h. The Pd–trifluoromethanesulfonylamide complex was employed in situ in this screening. The substrate was added and stirred at room temperature. (*R*,*R*)-DPENTf [6c,d,7]

*Keywords*: Claisen rearrangement; Enantioselective catalysis; Palladium; DABNTf.
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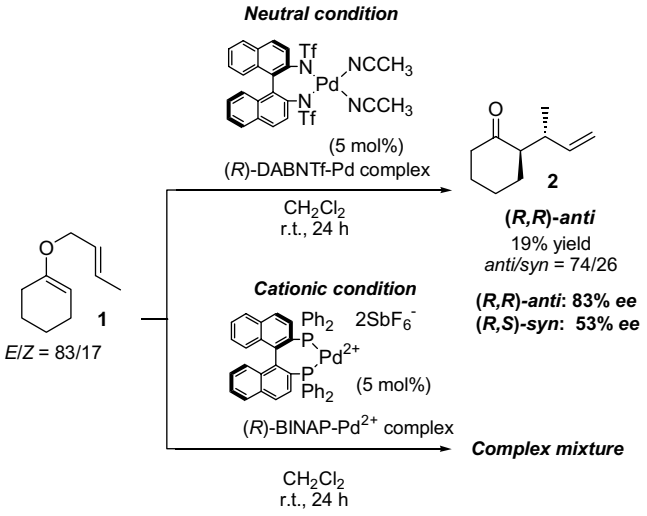



**Scheme 2.** Enantioselective Claisen rearrangement: cationic (*R*)-BINAP–$Pd^{2+}$ versus neutral (*R*)-DABNTf–Pd.

gave opposite enantiomer (*S*,*S*)-*anti*-**2** in lower yield, *anti*/*syn* diastereoselectivity, and enantioselectivity (entries 1 and 4). (*R*,*R*)-DACyTf gave the highest yield and *anti*/*syn* selectivity, but enantioselectivity was only moderate (entries 2 and 5). (*R*)-DABNTf gave the highest enantioselectivity and high *anti*/*syn* diastereoselectivity (entries 3 and 6). As a solvent, acetonitrile was better than dichloromethane, because of high *anti*/*syn* selectivity and catalyst stability therein.

Next, the reaction temperature was examined (Table 2). At higher temperature, product was obtained in high yield. The highest yield (69%) was obtained at 80 °C (entry 4). However, *anti*/*syn* selectivity and enantioselec-

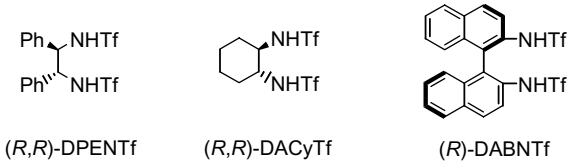
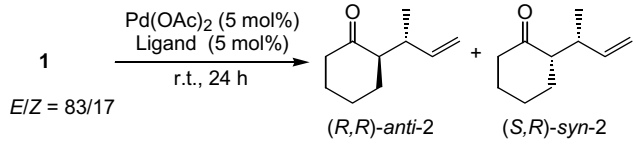


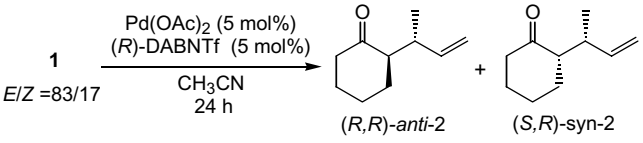

**Table 1.** Effect of trifluoromethanesulfonylamide ligands on enantioselective Claisen rearrangement




| Entry | Solv. | Ligand | Yield[a] [%] | *anti*/*syn*[b] | ee[b,c] [%] |
|---|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | (*R*,*R*)-DPENTf | 14 | 78/22 | 53/29[d] |
| 2 | | (*R*,*R*)-DACyTf | 35 | 95/5 | 60/54 |
| 3 | | (*R*)-DABNTf | 16 | 78/22 | 84/73 |
| 4 | $CH_3CN$ | (*R*,*R*)-DPENTf | 6 | 80/20 | 28/21[d] |
| 5 | | (*R*,*R*)-DACyTf | 29 | 94/6 | 63/51 |
| 6 | | (*R*)-DABNTf | 24 | 85/15 | 84/50 |

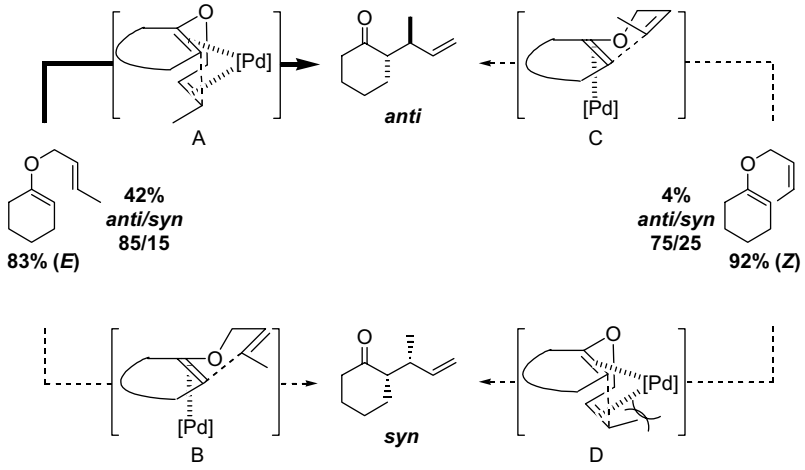
[a] Determined by $^1H$ NMR using DMF as an internal standard.
[b] Determined by GC (Cp-Chirasil-Dex CD) *anti*: 56.1 min; (*S*,*S*)-*syn*: 61.1 min; (*R*,*R*)-*syn*: 62.7 min.
[c] *anti* ee was calculated after isomerization.
[d] (*S*,*S*)-*anti* product.

**Table 2.** Temperature effect of enantioselective Claisen rearrangement




| Entry | *T* [°C] | Yield[a] [%] | *anti*/*syn*[b] | ee[c] [%] |
|---|---|---|---|---|
| 1 | −10 | 7 | 63/37 | 78/27 |
| 2 | rt | 24 | 85/15 | 84/50 |
| 3 | 40 | 42 | 85/15 | 83/57 |
| 4 | 60 | 54 | 82/18 | 81/53 |
| 5 | 80 | 69[d] | 78/22 | 77/32 |

[a] Determined by NMR.
[b] Determined by GC.
[c] *anti* ee was calculated by isomerization.
[d] Reaction time was 14 h.




**Scheme 3.** Transition states for DABNTf–Pd(II)-catalyzed enantioselective Claisen rearrangement.

tivity gradually decreased in increasing the reaction temperature (>60 °C). Therefore, the best temperature conditions were at around 40–60 °C.

In order to take a deep insight into the reaction mechanism, the effect of configuration of allyl group [(*E*) versus (*Z*)] was examined at 40 °C (Scheme 3, Table 2, entry 3). At that temperature, there is no thermal rearrangement. The stereochemical course of Claisen rearrangement can be generally predicted on the basis of conformational analysis in chair-like transition states leading (*E*)-substrate to *syn* selectivity.[1,8] However, in the DABNTf–Pd(II)-catalyzed Claisen rearrangement, (*E*)-substrate gave, in contrast, *anti*-isomer.[8] It appears that (*Z*)-substrate does not rearrange; in the case of 92% (*Z*)-ether, (*E*)-substrate gave *anti*-major product in only 4% yield.

Therefore, this reaction mechanism could be the same as that reported for our $PdCl_2(PhCN)_2$ catalysis.[8] This reaction should proceed via six-membered (*E*)-boat transition state (A) through bi-dentate coordination to the DABNTf–Pd catalyst rather than mono-dentate coordination (B). In contrast, (*Z*)-substrate did not rearrange because of steric repulsion in the (*Z*)-boat transition state (D).[9]

On the basis of our X-ray structure of (*R*)-DABNTf–Pd-(*S*)–BINAP complex,[4] the sense of enantioselectivity could be explained as follows. Because of the steric repulsion of *trans*-methyl group in the Claisen substrate and $CF_3$–$SO_2N$ in DABNTf, a six-membered boat transition state (*R*,*R*)-**A** should be favored over the enantiomeric (*S*,*S*)-**A**. Therefore, (*R*,*R*)-*anti*-**2** would be obtained (Fig. 1).

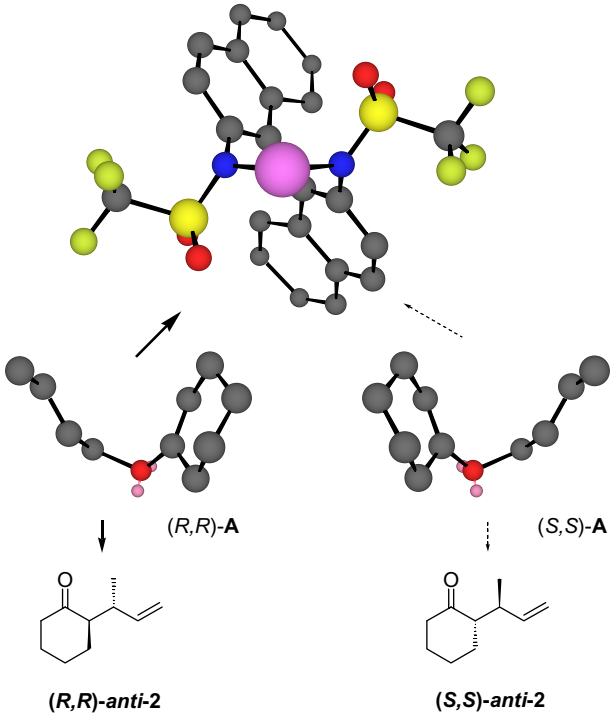



**Figure 1.** Transition state model of enantioselective Claisen rearrangement. The color of the atoms is as follows: black, carbon; blue, nitrogen; red, oxygen; green, fluorine; yellow, sulfur; purple, palladium.

In summary, we have reported enantioselective catalysis of Claisen rearrangement by DABNTf–Pd(II) complex. This Claisen rearrangement proceeds via bi-dentate boat transition state to give *anti*-isomer in high enantioselectivity and good yield.

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