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LETTERS

The First Tridentate Ligand for Catalytic Enantioselective Aza-Claisen Rearrangement of Allylic Imidates

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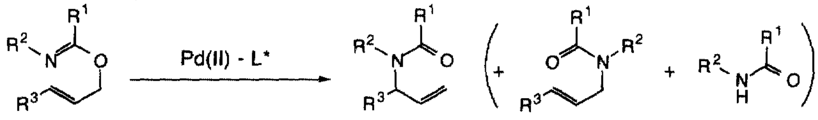
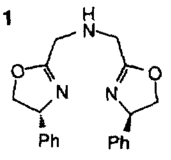
Summary: Chiral tridentate ligand ph-ambox (**1**) can form a cationic Pd(II) catalyst for the [3,3]-sigmatropic rearrangement of allylic imidates to allylic amides with ees up to 83% for one substrate.

The late transition metal-catalyzed aza-Claisen [3,3]-sigmatropic rearrangement offers convenient access to various allylic amides from the corresponding allylic alcohols.[1] However, only scattered attention has been devoted to developing efficient enantioselective catalysts for this powerful transformation. Since the first such example was recently reported by Overman, a variety of bidentate ligands bearing imine or amine functions have been tested and have given performance superior to phosphine ligands.[2] Despite these encouraging achievements, the transformation is often sluggish and complicated by side reactions. Enantiomeric excesses up to 81% have been reported but with poor yield.[2d] During the past several years, a series of chiral tridentate ligands have been developed in our laboratory, and their late transition metal complexes have been applied to facilitate various asymmetric transformations.[3] For instance, (*R*)-ph-ambox (**1**, bis[4-(*R*)-phenyloxazolin-2-yl-methyl]amine) is highly effective for the Ru-catalyzed asymmetric transfer hydrogenation of simple aryl-alkyl ketones.[3a] The ambox ligand system might also provide favorable stereoelectronic properties for catalyzing the aza-Claisen rearrangement reaction. Therefore we have examined its catalytic capability, and the preliminary results for this rearrangement catalyzed by Pd(II)-ambox complexes are presented in the Table.



	R^1	R^2	R^3
5	Ph	4-$CF_3C_6H_4$	Pr
6	Ph	4-$CF_3C_6H_4$	i-Pr
7	Ph	Ph	Pr
8	CCl_3	H	Pr

1



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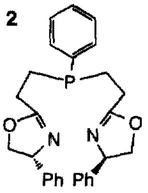

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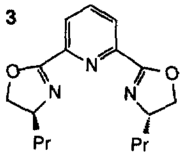

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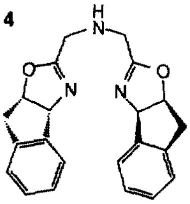

Imidate **5** was used as the model substrate in optimizing catalytic conditions. The reaction outcome turned out to be strongly dependent upon solvents (entry 3-5) and the catalyst precursor selected (entry 1-2, 8-11). Moderate gains in both yield and ee were observed at higher concentrations (entry 2/3, 6/7). Although 83% ee (71% yield) was achieved for **5**, this optimal condition was not applicable to other imidates (entry 8-12). Compared to **5**, **6** is more sterically encumbered while **7** has a less electron-withdrawing nitrogen substituent. As observed in other catalyst systems,[2] competing anti-Claisen [1,3]-rearrangement and C-O cleavage side reactions

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Table. Asymmetric Aza-Claisen Rearrangement of Allylic Imidates Catalyzed by Pd(II) Complexes[a]

Entry	Substrate	Pd (II)	Ligand	Solvent	[Substrate]/M	t	yield%[b]	ee%[c]
1	**5**	**9**	**1**	CH_2Cl_2	0.2	20 h	93	0
2	**5**	**10**	**1**	CH_2Cl_2	0.2	72 h	71[e]	83
3	**5**	**10**	**1**	CH_2Cl_2	0.1	72 h	65[e]	80
4	**5**	**10**	**1**	ClC_6H_5	0.1	72 h	0[d]	N/A
5	**5**	**10**	**1**	$CDCl_3$	0.1	72 h	0[d]	N/A
6	**5**	**10**	**1**	$ClCH_2CH_2Cl$	0.1	32 h	59[e]	79
7	**5**	**10**	**1**	$ClCH_2CH_2Cl$	0.2	48 h	76[e]	81
8	**6**	**10**	**1**	$ClCH_2CH_2Cl$	0.1	22h	1[d]	76
9	**6**	**9**	**1**	$ClCH_2CH_2Cl$	0.1	7 d	2[d]	29
10	**7**	**10**	**1**	$ClCH_2CH_2Cl$	0.2	11 d	9[d]	35
11	**7**	**9**	**1**	$ClCH_2CH_2Cl$	0.1	9 d	47[f]	66
12[g]	**8**	**10**	**1**	$ClCH_2CH_2Cl$	0.2	7 d	4[d]	13
13	**5**	**10**	**2**	$ClCH_2CH_2Cl$	0.2	72 h	0[d]	N/A
14	**5**	**10**	**3**	$ClCH_2CH_2Cl$	0.1	5 d	4[d]	55 (*S*)
15	**5**	**10**	**4**	$ClCH_2CH_2Cl$	0.2	72 h	5[f]	17

a. Reactions done at rt unless otherwise stated. **9** $PdCl_2(CH_3CN)_2/AgOTf$ (1:1); **10** $[Pd(CH_3CN)_4](BF_4)_2$; Pd(II):L*:imidate = 0.01:0.01:0.1 mmol. *b.* Isolated yield. *c.* *R* isomers dominate except for **3**; absolute configurations determined by analogy; ees determined with HPLC (Chiralpack AD; 5-10% 2-propanol in hexane). *d.* Reaction incomplete. *e.* Elimination products dominate remainder of material. *f.* Remainder of material a mixture of unreacted imidate and [1,3]-rearrangement product. *g.* ee determined by GC (γ-DEX 225).

also plagued our work, resulting in lower yields. Because palladium black was often observed during our experiments, the low yields most likely resulted from partial decomposition of the Pd(II) catalyst to Pd(0).[4] Despite the structural similarity that ligands **2-4** bear to **1** (especially for pybox **3**), they formed much poorer catalysts under the same conditions.

In conclusion, the first tridentate ligand-Pd(II) catalyzed aza-Claisen rearrangement of allyl imidates proceeded with good ee and in respectable yield for one substrate. Further stabilization of the Pd(II) catalytic species will be crucial for developing more effective and general enantioselective catalysts.

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