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Enantioselective Diels-Alder Reactions Catalyzed by Chiral 1,1'-(2,2'-Bisacylamino)binaphthalene-Ytterbium Complex

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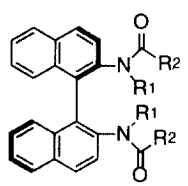
Abstract

A new axially chiral ligand, 1,1'-(2,2'-bisacylamino)binaphthalene, was found to be effective in the ytterbium-catalyzed asymmetric Diels-Alder reaction between cyclopentadiene and crotonyl-1,3-oxazolidin-2-one. The Diels-Alder reaction using 15 mol% of 1,1'-(2,2'-bisbenzoylamino)binaphthalene•Yb(OTf)3•2*i*-Pr2NEt afforded the adduct with high enantioselectivity (97% yield, endo/exo=91/9, >98% ee for the endo adduct).

Keywords: *Amides; Asymmetric reactions; Diels-Alder reaction; Lanthanides;*

Recently, great progress has been made in asymmetric synthesis, especially in catalytic asymmetric processes [1]. Of the many chiral ligands developed for preparing chiral reagents and catalysts in asymmetric synthesis, 1,1'-2,2'-binaphthol (BINOL) has been one of the most useful, and has made a considerable contribution to asymmetric synthesis [2]. Compared to the remarkable advances in organic chemistry based on BINOL, much less attention has been paid to the use of 1,1'-binaphthyl-2,2'-diamine and its derivatives in asymmetric synthesis [3-7]. In connection with our Diels-Alder strategies for the synthesis of natural products such as manzamines and dynemicin A [8-11], we particularly focused on the asymmetric Diels-Alder reaction. We report here a highly enantioselective Diels-Alder reaction using 1,1'-(2,2'-bisacylamino)binaphthalene **1** as a chiral ligand.



1: R1, R2=alkyl, aryl, etc

Figure 1. General structure of new chiral ligand.

Fine-tuning of the structure of ligands is sometimes required to improve the activity and selectivity of the catalyst. Flexibility of the ligand structure is essential for this purpose. 1,1'-(2,2'-Bisacylamino)binaphthalene (BINAMIDE) could be easily synthesized from commercially available chiral 1,1'-binaphthyl-2,2'-diamine. The general structure, shown in Figure 1, appears to show that the steric and electronic characters of R^1 and R^2 can be changed systematically to tune the character of the binding metal and also the conditions surrounding the catalytic center. We first tested the function of this ligand in the asymmetric Diels-Alder reaction of **4** or **5** with cyclopentadiene **3** using

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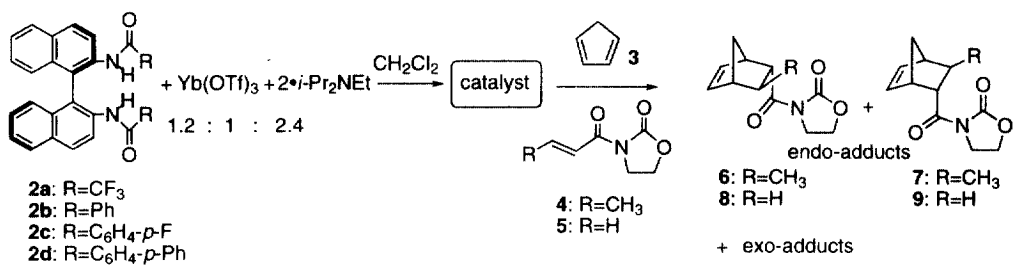
a chiral ytterbium catalyst developed by Kobayashi and co-workers [12-15].

The chiral catalyst was prepared by stirring (*R*)-1,1'-(2,2'-trifluoroacetamino)binaphthalene **2a** and ytterbium triflate [Yb(OTf)3] in the presence of diisopropylethylamine (**2a**:Yb(OTf)3:amine=1.2:1:2.4) in dichrolomethane at room temperature for 2 h under argon (Scheme 1). To this catalyst solution was added cyclopentadiene **3** and crotonyl-1,3-oxazolidin-2-one **4** at room temperature. The Diels-Alder reaction was completed in 30 min to give a mixture of adducts in 82% yield using 25 mol% of the catalyst (Table 1, run 1). Asymmetric induction was 35% ee for the endo adduct and **7** was the major enantiomer (endo/exo=85/15). Without diisopropylethylamine, the product was essentially racemic, although the **2a**-Yb(OTf)3 complex catalyzed the reaction (run 2). The reverse enantioselectivity was observed when the reaction was carried out at 0 °C. However, asymmetric induction was not improved (23% ee, run 3).



Scheme 1

Table 1 Enantioselective Ytterbium Catalyzed Diels-Alder reaction Using 1,1'-(2,2'-Bisacylamino)binaphthalene as a Chiral Ligand

run	ligand	(mol%)	temp (°C)	time (h)	yield[a] (%)	endo/exo ratio[b]	**6** ee %[c]
1	**2a**	(25)	rt	0.5	82	85/15	35[d]
2	**2a**	(25)	rt	0.5	95	88/12	0.5[e]
3	**2a**	(25)	0	4	27	>99/<1	23
4	**2b**	(25)	rt	1	77	92/8	>98
5	**2b**	(25)	0	4	95	91/9	>98
6	**2b**	(25)	0	6	95	80/20	3.3[e]
7	**2b**	(15)	0	4	97	91/9	>98
8	**2b**	(10)	0	4	64	91/9	>98
9	**2b**	(5)	0	4	26	90/10	91
10	**2c**	(25)	0	4	85	91/9	97
11	**2c**	(25)	0	4	81	85/15	0.9[e]
12	**2d**	(25)	0	4	81	93/7	>98

[a] Isolated yield except runs 4-8 and 11, in which yields were estimated by ^{1}H-NMR. [b] Determined by ^{1}H-NMR. [c] Enantiomer ratios of the endo adduct, which were determined by HPLC analysis using a chiral column (Daicel, Chiralcel OD). [d] The major product was **7**. [e] The reaction was carried out without *i*-Pr2NEt.

Next, we turned our attention to the use bisbenzoyl derivative **2b**, which was expected to have a deeper cavity around ytterbium metal than **2a**. The reaction with **2b**-Yb(OTf)3 com-

plex was carried out under the same conditions as in runs 1 and 3. Excellent asymmetric inductions [>98% ee, **6**] as well as high chemical yields were observed (runs 4 and 5).

Bis-*p*-fluorobenzoyl derivative **2c** also worked as a good ligand for this reaction (run 10). Without diisopropylethylamine, the reactions using **2b** and **2c** gave racemic products again (runs 6 and 11). A catalyst prepared using bis-*p*-phenylbenzoyl derivative **2d** showed the best selectivity with regard to both enantioselectivity and the endo/exo ratio (>98% ee, endo/exo=93/7, run 12). This shows that a sterical factor surrounding the center metal is important for achieving high enantioselectivity in this asymmetric Diels-Alder reaction.[1]

Although a presence of bulky amine, such as *cis*-1,2,6-trimethylpiperidine, was important to obtain high ee's in the asymmetric Diels-Alder reaction using chiral BINOL-Yb complex [14], diisopropylethylamine afforded the best result in this reaction. The results obtained using other amines and **2b**-Yb(OTf)$_3$ complex were as follows: triethylamine 55% yield, 95% ee (0 °C, 4h), 1,2,2,6,6,-pentamethylpiperidine 59% yield, 89% ee (0 °C, 4h), *cis*-2,6-dimethylpiperidine 29% yield, 91% ee (0 °C, 24 h), *cis*-1,2,6-trimethylpiperidine 4.1% yield (0 °C, 72 h), pyridine 53% yield, 0% ee (0 °C, 4 h, then rt, 24 h).

We briefly studied the effect of the amount of the catalyst (runs 7-9) and found that 15 mol% of **2b** could be used without decreasing either the yield or selectivity. The use of 10 and 5 mol% of **2b** still gave high ee's (>98 and 91% ee). However, the yield of the adduct decreased to 64 and 26%, respectively.

A similar Diels-Alder reaction of acryloyl-1,3-oxazolidin-2-one **5** with **3** was completed within 20 min at 0 °C, even using 15 mol% of **2b**, to give the adduct in quantitative yield, and **8** was a major enantiomer with 88% ee (99%, endo/exo=91/9). The use of 5 mol% of the catalyst was enough to complete the reaction, although the ee value was considerably low (98% yield, endo/exo=90/10, 41% ee). Changing the catalyst from **2b** to **2d** (5 mol%) greatly enhanced the enantioselectivity [99% yield, endo/exo=93/7, 76% ee for **8**]. The selectivity was not further improved when the reaction was carried out at -20 °C (97% yield, endo/exo=94/6, 69% ee).

Isolation of an active catalyst was important for determining the structure and origin of the selectivity. When *n*-hexane was added to a solution of the catalyst in dichloromethane, pale yellow precipitates appeared, which were isolated and dried *in vacuo*. The resulting powder showed the same reactivity and selectivity for the reaction of **3** with **4** (97% yield, >98% ee, endo/exo=91/9) as the catalyst prepared *in situ* (Table 1, run 5). ^{1}H-NMR spectra of the powder showed **2b** and diisopropylethylamine in a 1:2 ratio. ^{1}H and ^{13}C-NMR spectra of this catalyst showed a slight downfield shift of the signals assigned to the methine and methylene protons or carbons of diisopropylethylamine.[2] Mass spectra (FAB) of the catalyst powder showed a molecular ion at m/e 1456, which was attributed to the structure of Yb(OTf)$_3$•**2b**•[*i*-Pr$_2$NEt]$_2$•*n*-hexane. The structure of the catalyst is tentatively assumed to be as shown in Figure 2.[3,4] Further studies to elucidate the structure are underway.

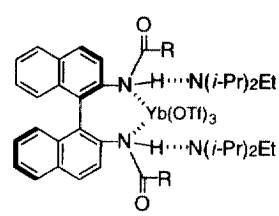


Figure 2.
A plausible catalyst strucure.

In conclusion, we have developed a new axially chiral ligand, 1,1'-(2,2'-bisacylamino)binaphthalene. This ligand was structurally simple, easily synthesized, and finely tunable. This ligand was effective in the ytterbium-catalyzed asymmetric Diels-Alder reaction. Further studies of ligands based on the structure of **1** and their application to other reactions are underway.

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Footnotes

1 Reactivity of the catalysts was also influenced by the electronic character of the acyl group in the ligand. Both the catalysts prepared using *p*-methoxybenzoyl and *p*-trifluoromethylbenzoyl derivatives of **1** were ineffective compared to **2b** or **2d** [35% (endo/exo=11/1, 61% ee) and 7% yields, after 24 h at 0 °C, respectively]. The catalyst prepared using 1,1'-(2,2'-bisacetamino)binaphthalene was also less effective (20% yield, 0% ee, rt, 24h).

2 ^{1}H and ^{13}C NMR data of the *i*-Pr_2NEt-Yb-**2b** catalyst[a]

		$(H_3C)_2\underline{CH}N$	$(\underline{H_3C})_2CHN$	$N\underline{CH_2}CH_3$	$NCH_2\underline{CH_3}$
2b + $Yb(OTf)_3$+ *i*-Pr_2NEt	^{1}H	3.62	1.39	3.11	1.42
	^{13}C	54.832	18.532, 17.151	43.037	12.384
2b + *i*-Pr_2NEt	^{1}H	3.02	1.01	2.47	1.02
	^{13}C	48.486	20.642	39.043	17.035

[a] NMR spectra were recorded in $CDCl_3$.

3 The 1,1'-bis(2,2'-*N*-benzoyl-*N*-ethylamino)binaphthalene-$Yb(OTf)_3$ complex catalyzed this reaction without presence of amine (96% yield, endo/exo=81/19, 25% ee, 0 °C, 9 h using 25 mol% catalyst). Considering the experiments shown in runs 2, 6, and 11 in table 1, this result may support the catalyst structure shown in figure 2, in which some bulky groups are located around the nitrogen atoms to create an effective asymmetric pocket.

4 The isolated catalyst showed its activity for several days when it stored under argon in a refrigerator.