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Enantioselective Copper Catalyzed Diels-Alder Reaction Using Chiral Quinoline-Phosphine Ligand

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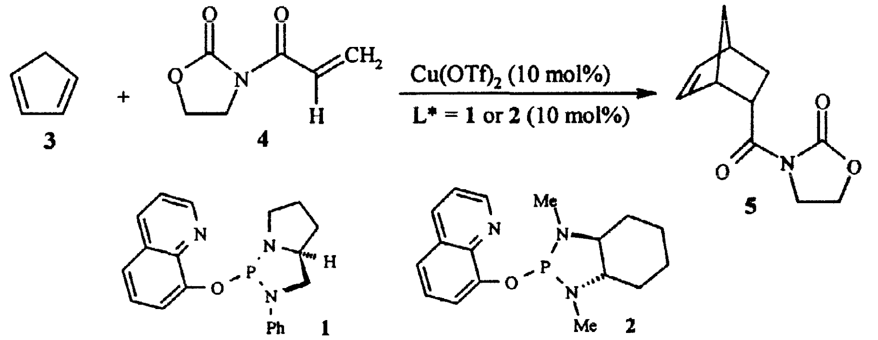
Abstract : A new chiral copper (II) catalyst was prepared from $Cu(OTf)_2$ and chiral pyridine-phosphine ligands **1-2** in dichloromethane and used in the Diels-Alder reaction of 3-acryloyl-1,3-oxazolidine-2-one with cyclopentadiene leading to enantioselectivities up to 99%.

One of the most important reaction in organic chemistry for the formation of carbon-carbon bonds is the Diels-Alder reaction and a great deal of effort has been devoted to the development of this reaction in recent years[1,2]. In this area, Evans *et al.* discovered that Cu(II) complexes of C_2 symmetric bisoxazolines are effective chiral Lewis acid catalysts[3]. On the other hand, Helmchen *et al.* have reported the first application of chiral (phosphinooxazoline)Cu(II) complexes as catalysts in the Diels-Alder reaction between cyclopentadiene and substituted N-acylamide dienophiles leading to the expected adducts in high enantiomeric excesses (ee) up to 97%[4]. Thus, compared to a N-donor ligand, phosphorus σ-donor π-acceptor ligands such as phosphino oxazolines ligands has enhanced the Lewis acidity of these complexes[4].

Recently, we described the synthesis and the use of new non symmetric chiral pyridine-phosphine ligands bearing the chirality at the phosphorus atom in palladium catalyzed asymmetric allylic alkylation and amination reactions with enantioselectivities up to 94%[5]. In this paper, we wish to report our preliminary results using such chiral ligands **1-2** in catalytic enantioselective copper Diels-Alder reaction of 3-acryloyl-1,3-oxazolidine-2-one with cyclopentadiene[6].



Scheme 1

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The chiral catalyst (10 mol% with respect to 4) was prepared by treatment of $Cu(OTf)_2$ with ligand 1 or 2 (molar ratio $L^*/Cu(II) = 1/1$) at room temperature and subsequent stirring in dry solvent for 15 minutes under an inert atmosphere. The resulting stirred colored solution (dark brown) was cooled to the desired temperature and 1 equivalent of dienophile and 5 equivalents of freshly distilled diene were added. After 24 hours, cycloadduct 5 was isolated by chromatography on silicagel column and analyzed for *endo-exo* ratio by ^1H NMR spectroscopy and ee by HPLC using a Daicel Chiralcel OD-H column[7]. The results are summarized in Table 1 :

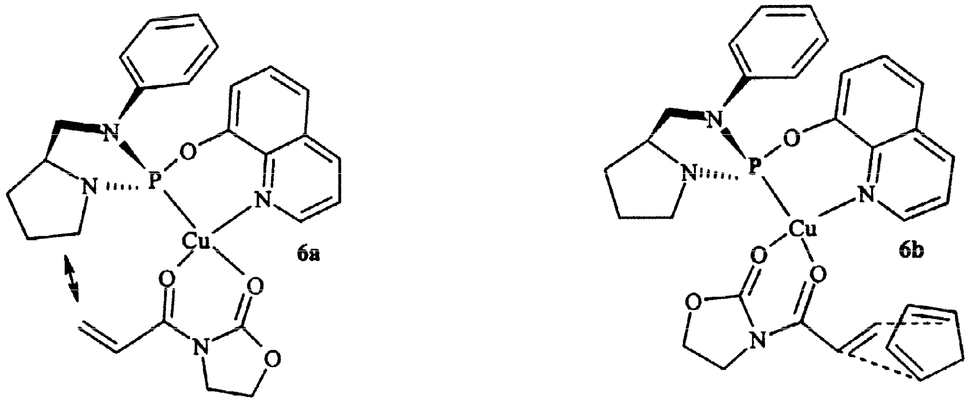
Table 1 : Asymmetric copper catalyzed Diels-Alder reaction of cyclopentadiene with N-acyloxazolidinone 4

Entry	Solvent	T (°C)	Reaction Time (h)	Conversion (%)	*Endo-exo* ratio[d]	Ee (%)[e]
1[a]	CH_2Cl_2	25	24	> 99	> 98 : 2	2
2[a]	CH_2Cl_2	0	24	> 99	> 98 : 2	56
3[a]	CH_2Cl_2	-78	24	20	> 98 : 2	76
4[a]	**CH_2Cl_2**	**-78 to r.t.**	**24**	**> 99**	**> 98 : 2**	**> 99**
5[a]	**CH_2Cl_2**	**-78 to r.t.**	**3**	**> 99**	**> 98 : 2**	**> 99**
6[a]	THF	25	24	> 99	> 98 : 2	5
7[a]	THF	-78 to r.t.	24	> 99	> 98 : 2	32
8[a]	Toluene	25	24	65	> 98 : 2	4
9[a]	Toluene	-78 to r.t.	24	0	-	-
10[a]	$CH_3CH_2NO_2$	-78 to r.t.	24	50	> 98 : 2	4
11[a]	CCl_4	-78 to r.t.	24	> 99	> 98 : 2	2
12[b]	CH_2Cl_2	-78 to r.t.	24	> 99	-	14
13[c]	CH_2Cl_2	-78 to r.t.	24	> 99	>95 : 5	36

[a] Experiments performed using 10 mol% of catalyst generated from $Cu(OTf)_2$ and ligand 1. [b] Experiment performed using 10 mol% of catalyst generated from Cu(OTf) and ligand 1. [c] Experiments performed using 10 mol% of catalyst generated from $Cu(OTf)_2$ and ligand 2. [d] The *endo-exo* ratio was determined by ^1H NMR spectroscopy on the crude product. [e] Ee determined by HPLC on a Daicel Chiralcel OD-H column (ref. 7).

We first examined the use of ligand 1 in CH_2Cl_2 at different temperatures. Lowering the reaction temperature from 25 to 0°C led to a significant increase of the ee from 2 to 56% (entries 1-2). Moreover, an experiment realized at –78°C and slowly warmed to 25°C led to the formation of only *endo* adduct with 2*S* absolute configuration in 99% ee (entries 4-5). In a second time, a wide variety of solvents were probed. Thus, whatever the experimental conditions used, the enantioselectivities are varying from 2 to 32% ee with low conversions in some cases (entries 6-11). Under the best conditions, the use of chiral Cu(I) complex led to a low enantiomeric excess (14%, entry 12). On the other hand, the use of ligand **2** led to a complete conversion but the adduct **6a** is obtained in only 36% ee (entry 13).

The steric course of these reactions can be rationalized by assuming a square planar phosphino-pyridine-Cu(II)-dienophile complex as intermediate similar to that proposed by Evans for bis(oxazoline)Cu(II) complexes. Thus, two possible isomeric square-planar complexes **6a** and **6b** may be suggested. In complex **6a**, both pyrrolidine ring and N-phenyl group led to strong steric interactions with cyclopentadiene whatever the diastereofacial approach of the dienophile. In contrast, the formation of isomer **6b** is favoured by lowering the steric interactions, the attack of the diene may occur at the *endo-Re* face of the acryloyl group leading to the formation of the observed *endo* (2*S*)-cycloadduct **5** (Figure 1).



6a

disfavoured intermediate

6b

favoured intermediate

Figure 1. Proposal concerning the steric course of the cycloaddition via a square planar Cu(II) complex.

In conclusion, we have shown that readily accessible pyridine-phosphine ligand **1** is an efficient ligand for enatioselective copper(II) catalyzed Diels-Alder reaction. Further studies including modification to dienes, dienophiles and ligands design are in progress.

References.

(1) For a review, see : (a) Kagan, H. B. ; Riant, O. *Chem. Rev.* **1992**, *92*, 1007-1019. (b) Diaz, L. C. *J. Braz. Chem. Soc.* **1997**, *8*, 289-332

(2) For other catalytic asymmetric Diels-Alder reactions, see : (a) Corey, E. J. ; Imai, N. ; Zhang, H. Y. *J. Am. Chem. Soc.* **1991**, *113*, 728-729. (b) Corey, E. J. ; Loh, T. P. *J. Am. Chem. Soc.* **1991**, *113*, 8966-8967. (c) Corey, E. J. ; Loh, T. P. ; Roper, T. D. ; Azimioara, M. D. ; Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290-

8292. (d) Corey, E. J. ; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807-6810. (e) Evans, D. A. ; Lectka, T. ; Miller, S. J. . *Tetrahedron Lett.* **1993**, *34*, 7027-7030. (f) Evans, D. A. ; Miller, S. J. ; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460-6461. (g) Pikul, S. ; Corey, E. J. *Org. Synth.* **1993**, *71*, 30. (h) Corey, E. J. ; Roper, T. D. ; Ishihara, K. ; Sarakinos, G. *Tetrahedron Lett.* **1993**, *34*, 8399-8402. (i) Kobayashi, S. ; Ishitani, H. ; Hachiya, I. ; Araki, M. *Tetrahedron* **1994**, *50*, 11623. (j) Ishihara, K. ; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 1561-1562. (k) Narasaka, K. ; Inoue, M. ; Ojada, N. *Chem. Lett.* **1986**, 1109-1112. (l) Narasaka, K. ; Inoue, M. ; Yamada, T. *Chem. Lett.* **1986**, 1967-1970. (m) Narasaka, K. ; Inoue, M. ; Yamada, T. ; Sugimori, J. ; Iwasawa, N. *Chem. Lett.* **1987**, 2409-2412. (n) Narasaka, K. ; Inoue, M. ; Sugimori, J. ; Kawaze, Y. *Chem. Lett.* **1989**, 1947-1950. (o) Narasaka, K. ; Iwasawa, N. ; Inoue, M. ; Yamada, T. ; Narashima, M. ; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340-5341.

(3) (a) Evans, D. A. ; Miller, S. J. ; Lecta, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460-6461. (b) Evans, D. A. ; Murry, J. A. ; von Matt, P. ; Norcross, R. D. ; Miller, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 798-800. (c) Johannsen, M. ; Jorgensen, K. A. *J. Org. Chem.* **1995**, *60*, 5757-5762. (d) Johannsen, M. ; Jorgensen, K. A. *Tetrahedron* **1996**, *52*, 7321-7328.

(4) Sagasser, I. ; Helmchen, G. *Tetrahedron Lett.* **1998**, *39*, 261-264.

(5) (a) Brunel, J. M. ; Constantieux, T. ; Labande, A. ; Lubatti, F. ; Buono, G. *Tetrahedron Lett.* **1997**, *38*, 5971-5974. (b) Constantieux, T. ; Brunel, J. M. ; Labande, A. ; Buono, G. *Synlett* **1998**, 49-50.

(6) **1** was prepared by exchange reaction at 110°C in 20 mL of anhydrous toluene between 163 mg of tris(dimethylamino)phosphine (1 mmole) and 176 mg of (*S*)-(+)-2-anilinomethylpyrrolidine (1 mmole) for 2 hours, followed by subsequent addition of 136 mg of hydroxyquinoleine (1 mmole). Slow crystallization in toluene afforded ligand **1** in 92% chemical yield as a white solid stable to air and moisture. Similar procedure was used in order to prepare ligand **2** (34% yield) which was purified by distillation (bp 220°C/0.05 mbar).

(7) *Typical procedure for the asymmetric Diels-Alder reaction (Table 1, entry 4).* Commercially available $Cu(OTf)_2$ (Fluka) (0.071 mmol, 26 mg) is treated with ligand **1** (0.071 mmol, 25 mg) in dichloromethane (10 mL) at room temperature for 15 minutes under an argon atmosphere. The resulting stirred dark brown solution was cooled to –78°C and N-acyl-1,3-oxazolidine-2-one (0.71 mmol, 100 mg) and freshly distilled cyclopentadiene (3.55 mmol, 235 mg) were added. The solution was slowly warmed to 25°C and stirred overnight. The reaction mixture was concentrated *in vacuo* and the crude material purified by flash chromatography affording the *endo* adduct with 2*S* absolute configuration in 75% yield (*endo*/*exo* = >98/2) and 99% ee. The ee was determined by HPLC analysis using a Daicel Chiralcel OD-H column with 10% *i*-PrOH in hexane for elution (0.5 mL/min ; retention times 37.8 min (*S*) and 41.2 min (*R*)).