ELECTRONIC EFFECT OF PROLINATE LIGAND-DIRHODIUM(II) COMPLEXES ON CATALYTIC ASYMMETRIC DIPOLAR CYCLOADDITION[1†]

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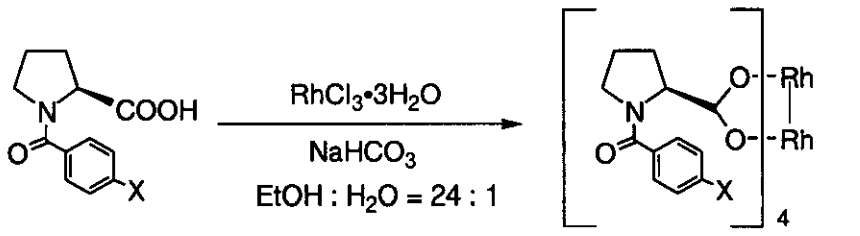
Abstract —— We prepared several efficient chiral *N*-benzoylpyrroridine-carboxylic acid ligands for dirhodium-catalyzed asymmetric dipolar cycloaddition and found that the electronic effect of the dirhodium(II) complexes influenced the catalytic activity, and the electron-poor catalysts were shown to be efficient for the reaction. Enantioselectivities of up to 98% ee were attained.

Rhodium(II) carboxylates are widely acknowledged to be the most effective catalysts for metal carbene transformations of diazo compounds.[2] Comparison of enantiocontrol in metal-carbene reactions catalyzed by representatives of dirhodium(II) catalysts defines the structural features of chiral ligands that control their selectivity. Finally, comparative reactivity and selectivity data suggest the stereoelectronic and steric factors that contribute to the effectiveness of dirhodium(II) catalysts for highly enantioselective transformations.

Scheme 1. Preparation of Dirhodium(II) Prolinate Complexes (**2a-e**)



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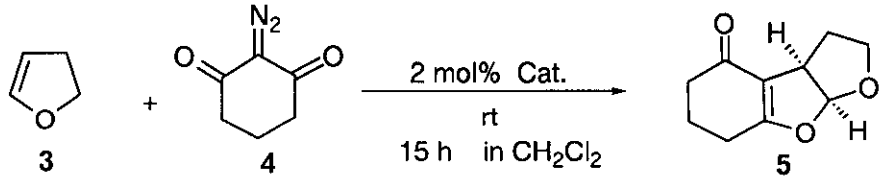
2a (X=H) **d** (X=F)
b (X=OMe) **e** ($X=CF_3$)
c ($X=NMe_2$)

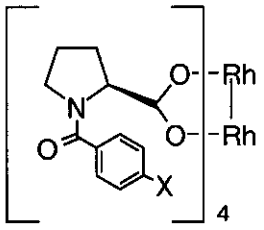
† Dedicated to the memory of the late Professor Shun-ichi Yamada.

We have already exhibited steric and electronic effects of substrates and chiral rhodium catalysts in asymmetric cyclopropanation.[3] It was found that electron-rich catalysts were efficient for asymmetric cyclopropanation. Herein we report electronic effect of chiral dirhodium(II) complexes in dipolar cycloaddition.[4] In order to design dirhodium(II) chiral carboxylate catalysts which are efficient in terms of enantioselectivity and reactivity, we prepared several chiral ligands which differ in electronic factor. That is to say, they were designed based on L-proline as a fundamental skeleton while varying the electronic factor of the *N*-substituents, which were thought to affect catalytic activity and asymmetric control. The dirhodium(II) complexes (**2a-e**) were synthesized as shown in Scheme 1.



3 **4** **5**

Table 1. Asymmetric Dipolar Cycloaddition of 2-Diazocyclohexane-1,3-dione(**4**) with 2,3-DHF(**3**) Catalyzed by Chiral Rh(II) Complexes



2a (X=H)
b (X=OMe)
c ($X=NMe_2$)
d (X=F)
e ($X=CF_3$)

Cat.	Yield (%)[a]	ee (%)[b]
2a (X=H)	36	93
2b (X=OMe)	27	98
2c ($X=NMe_2$)	No Reaction	
2d (X=F)	47	95
2e ($X=CF_3$)	66	96

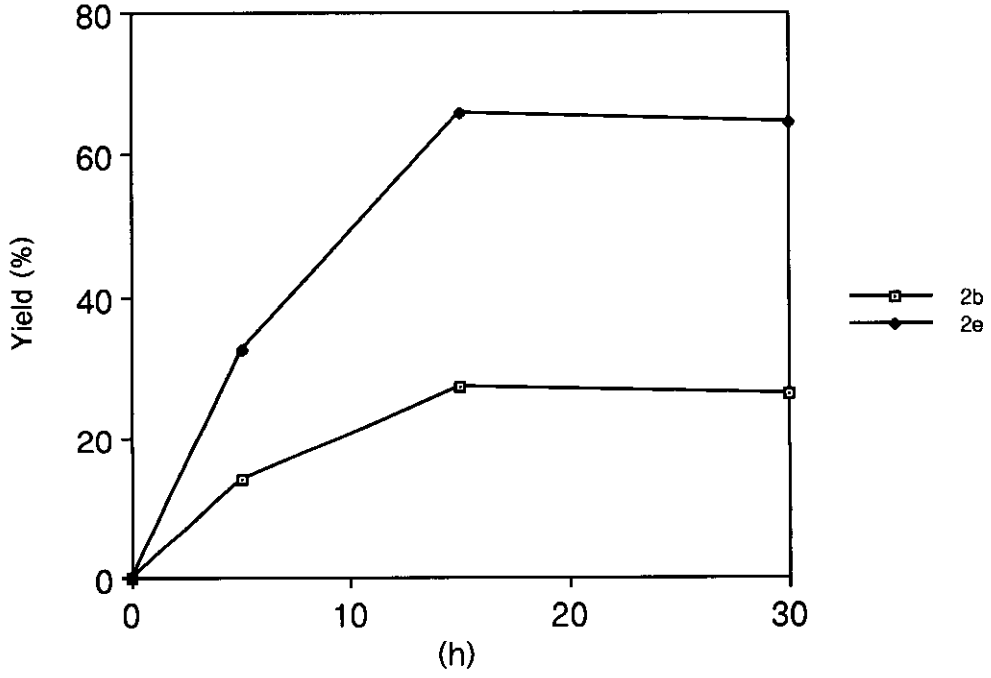
a) Determined by GC analysis.
b) By GC using Chirasil-DEX-CB.

Each *N*-benzoyl L-proline was prepared by *N*-acylation of L-proline benzyl ester hydrochloride with benzoyl chloride in the presence of *N,N*-diisopropylethylamine, followed by debenzylation by hydrogenolysis. Each dirhodium(II)-ligand complex was prepared by treating rhodium(III) chloride with the appropriate carboxylate salt in ethanol and H_2O.[5] The structures of these complexes were determined

by ^{1}H-NMR analysis and elemental analysis. So we carried out asymmetric dipolar cycloaddition of 2,3-dihydrofuran (**3**) with 2-diazocyclohexane-1,3-dione (**4**) catalyzed by **2a-e**.

Table 1 summarizes the results of asymmetric dipolar cycloaddition.[6] Yield was determined by GC analysis using *cis*-decalin as an internal standard. Enantiomeric excess in the cycloadduct (**5**) (absolute configuration not determined) was determined by GC using a chiral capillary column, Chirasil DEX-CB. As can be seen in Table 1, electron-withdrawing catalysts such as **2d** and **2e** were greatly superior to electron-rich catalysts in the case of the asymmetric dipolar cycloaddition. The reaction with **2c** barely proceeded, where the dimethylamino group probably functioned as a catalyst poison.

Figure 1. Reaction Rate of the Asymmetric Dipolar Cycloaddition



We next studied the reaction rate of the asymmetric dipolar cycloaddition catalyzed by **2b** and **2e** (Figure 1). Both the reactions stopped in 15 h, since the remaining 2-diazocyclohexane-1,3-dione (**4**) decomposed completely. Thus, introduction of further electron-withdrawing substituents to the ligands will improve the catalytic activity.

In conclusion, it was found that the electronic effect of the ligands influenced the catalytic activity in asymmetric dipolar cycloaddition with 2-diazocyclohexane-1,3-dione. Also high enantioselectivities of

up to 98% ee were attained. The products of the asymmetric dipolar cycloaddition are proposed to be key intermediates in projected synthesis of *Aspergillus* metabolites[7] as aflatoxin.

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6. A solution of 2-diazocyclohexane-1,3-dione (0.26 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise to a stirred mixture of 2,3-dihydrofuran (0.1 mL) and rhodium prolinate ($5.1x10^{-3}$ mmol) in dry CH_2Cl_2 (5 mL) under argon atmosphere. The reaction mixture was stirred for 16 h, then *cis*-decalin (9 mg) was added an internal standard for GC analysis to determine the yield. The mixture was evaporated and the residue was purified by silica gel preparative TLC to give a colorless oil. Enantiomeric excess in the cycloadduct (**5**) (absolute configuration not determined) was determined by GC using a chiral capillary column: fitted with a flame-ionization detector; carrier gas He, injection, split mode; injector temp. 200°C; retention times t_R[min], racemate (t_R 14.0 and 15.5; 170C°), Chirasil DEX-CB: 0.25 mmx25 m. ^{1}H-NMR ($CDCl_3$) δ: 6.24 (d, J=5.9 Hz, 1H), 4.04 (ddd, J=8.6, 5.9 and 4.8 Hz, 1H), 3.74-3.69 (m, 1H), 3.65 (ddd, J=5.9, 3.5 and 1.35, 1H), 2.51-2.32 (m, 4H), 2.12-1.98 (m, 4H). GCMS: m/z=180 (M^+). $[\alpha]_D^{25}$ +88.4° (98% ee) (*c* 0.4 $CHCl_3$).
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