

OPTICALLY ACTIVE ALDIMINATO COBALT(II) COMPLEX CATALYST FOR ENANTIOSELECTIVE HETERO DIELS-ALDER REACTION†

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Abstract- Among various aldiminato metal complexes, the optically active cobalt(II) complex efficiently catalyzed the enantioselective hetero Diels-Alder reaction of aromatic aldehydes with 1-methoxy-[3-(*tert*-butyldimethylsilyloxy)-1,3-butadiene. In the presence of 0.5 mol% of the catalyst, the reaction smoothly proceeded and *ortho* substituents of the dienophiles that could chelate to the catalyst significantly accelerated the reaction to improve the chemical and optical yields.

The optically active aldimines derived from the corresponding 1,3-dicarbonyl compounds and optically active 1,2-diaryl-1,2-ethylenediamines have been reported to form a new class of effective ligands for catalytic enantioselective reactions; manganese(III) complexes with optically active aldiminato ligands were employed as effective catalysts for the aerobic and enantioselective epoxidation of unfunctionalized olefins¹ and asymmetric oxidation of sulfides to the corresponding optically active sulfoxides.² The corresponding cobalt(II) complexes, for example, MPAC (Figure 1), effectively catalyzed the enantioselective borohydride reduction of prochiral aryl ketones,³ phosphinyl imines,⁴ and α,β -unsaturated carboxamides.⁵ Recently, the optically active aldiminato cobalt(II) complex has also proved to be an efficient catalyst for the enantioselective cyclopropanation of styrene derivatives with diazoacetates to afford the corresponding cyclopropanecarboxylates in high yields with high enantioselectivity.⁶

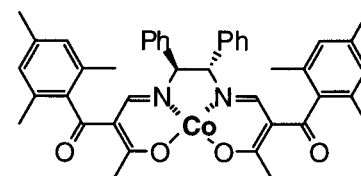


Figure 1. (*S*)-MPAC

In the course of our continuing study to develop catalytic enantioselective reactions directed to practical syntheses, the reactivities as Lewis acid catalysts of these optically active aldiminato complexes were examined using the hetero Diels-Alder reactions of various aldehydes with electron-rich dienes. Lewis acid catalysts are generally moisture-sensitive since the complexes could be inactivated by hydrolysis or since contaminants such as water and amines could coordinate the centered metal to prevent the substrate from approaching the catalyst. Therefore, absolutely anhydrous conditions or more than 10 mol% catalyst were most often required to achieve high enantioselectivities. The transition-metal complex

catalysts, particularly the pre-synthesized complexes, were expected to be one of the most promising solutions of these difficult problems. For examples of their possibilities, the copper(II)-bisoxazoline complex for the enantioselective Diels-Alder⁷ and hetero Diels-Alder⁸ reactions, and the titanium(IV)-salen complexes⁹ for enantioselective cyanohydrin were recently reported to achieve high enantioselections and high catalytic efficiencies.

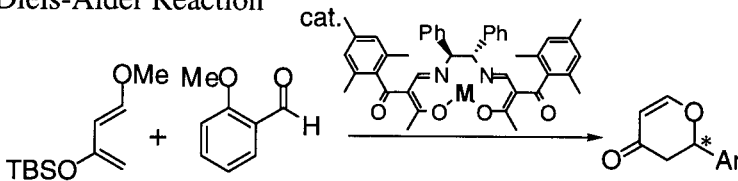
In this communication, we report that the cobalt(II) complex with the optically active aldiminato ligand was employed as an efficient catalyst for the enantioselective hetero Diels-Alder reaction of *o*-substituted arylaldehydes with Danishefsky's dienes.¹⁰

First of all, various metal complexes

with the optically active aldiminato ligand were prepared and their catalytic activities for the hetero Diels-Alder reaction were examined. In the presence of 5.0 mol% of each complex catalyst, the hetero Diels-Alder reaction of *o*-methoxybenzaldehyde with 1-methoxy-[3-(*tert*-butyldimethylsilyloxy)-1,3-butadiene was tried in dichloromethane solution below $-20\text{ }^{\circ}\text{C}$ (Table 1). After the treatment of the crude product with trifluoroacetic acid, the optical yield of the obtained dihydropyran-4-one derivative was determined by HPLC analysis (Chiralpak AD). Although titanium and aluminum complexes were often employed as effective Lewis acid catalysts, the optically active aldiminato complexes with these metals were not efficient catalysts for the present hetero Diels-Alder reaction (Entries 1 and 2). The copper(II) complexes with the bisoxazoline ligand⁸ and chromium(III) complexes with salen ligand¹¹ were reported to be effective as Lewis acid catalysts for the hetero Diels-Alder reaction, however, the corresponding aldiminato complexes were not employed (Entries 3 and 4). When the aldiminato manganese(III), nickel(II), or oxovanadium(IV) complex catalyst was subjected to the reaction, the racemic product was obtained only in low yield (Entries 5, 6 and 7). On the contrary, in the presence of a catalytic amount of the optically active aldiminato cobalt(II) complex catalyst¹² ((*S*)-MPAC), the hetero Diels-Alder reaction smoothly proceeded to afford the corresponding dihydropyran-4-one with moderate enantioselectivity (Entry 8).

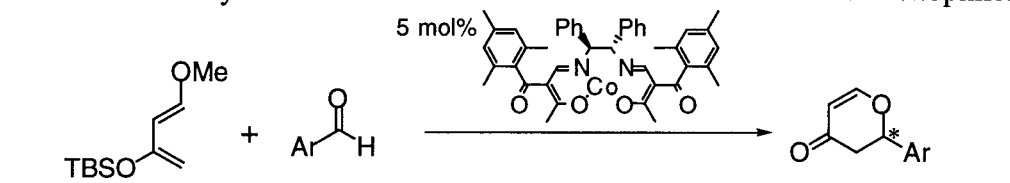
The optically active aldiminato cobalt(II) complex catalyst ((*S*)-MPAC) was applied to the hetero Diels-Alder reaction of various dienophiles with 1-methoxy-[3-(*tert*-butyldimethylsilyloxy)-1,3-butadiene

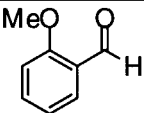
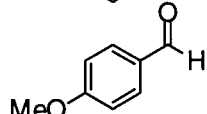
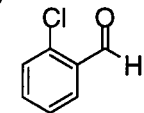
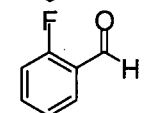
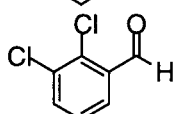
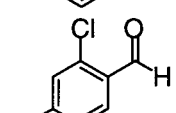
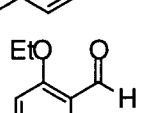
Table 1. Various Metal Complex Catalysts with Optically Active Aldiminato Ligand for Asymmetric Hetero Diels-Alder Reaction



Entry ^{a)}	Catalyst	Yield (%) ^{b)}	Ee (%) ^{c)}
1	Ti(IV)Cl ₂	23	4
2	Al(III)Cl	23	1
3	Cu(II)	trace	—
4	Cr(III)Cl	10	0
5	Mn(III)Cl	15	0
6	Ni(II)	41	0
7	V(IV)=O	32	6
8	Co(II)	80	62

a) Reaction Conditions: metal complex catalyst 0.025 mmol (5.0 mol%), dienophile 0.5 mmol, and diene 1.0 mmol at $-20\text{ }^{\circ}\text{C}$ in CH_2Cl_2 (2.5 mL). b) Ar = 2-Methoxyphenyl. Isolated yield after the treatment with CF_3COOH . c) Determined by HPLC analysis using Daicel Chiralpak AD (IPA 1% in hexane).

Table 2. The Asymmetric Hetero-Diels Alder Reaction of Various Dienophiles


Entry ^{a)}	Dienophiles	Temp / °C	Time / h	Yield (%) ^{b)}	Ee (%) ^{c)}
1		-20	55	96	62
2		rt	100	49	ND
3		-78	31	81	72
4		-78	50	62	78
5		-78	46	72	58 ^{d)}
6		-78	46	quant	53
7		-40	67	81	57

a) Reaction Conditions: cobalt(II) catalyst, (*S*)-MPAC 0.025 mmol (5.0 mol%), dienophile (arylaldehyde) 0.5 mmol, and diene 1.0 mmol in CH₂Cl₂ (2.5 mL). b) Isolated yield after the treatment with CF₃COOH. c) Determined by HPLC analysis using Daicel Chiralpak AD (IPA 1% in hexane). d) Determined by HPLC analysis using Daicel Chiralcel OD-H (IPA 5% in hexane).

(Table 2). In the presence of 5 mol% of (*S*)-MPAC, *o*-methoxybenzaldehyde smoothly reacted with the diene whereas the hetero Diels-Alder reaction of *p*-methoxybenzaldehyde proceeded very slowly (Entries 1 and 2).

These results suggest that oxygen atoms of the *o*-substituent and carbonyl group in the *o*-methoxybenzaldehyde coordinated to the cobalt(II) atom to form a rigid conformation with the six-membered chelate.^{13,14} Therefore, this coordination accelerated the reaction and fixed the transition state of the hetero Diels-Alder reaction to improve the enantioselection of the prochiral face of the carbonyl group. The reactions of the *o*-hetero-atom-substituted arylaldehydes other than the methoxyl group were also examined. Chlorine and fluorine atoms on the *o*-position were more effective for accelerating the present reaction. Even at -78 °C, the reaction of the *o*-chloro and *o*-fluorobenzaldehydes proceeded in moderate to good yield with 72% ee and 78% ee,¹⁵ respectively (Entries 3 and 4). The hetero Diels-Alder reaction of the dichlorobenzaldehydes also smoothly proceeded to afford the corresponding dihydropyran-4-ones in good yields with moderate

enantioselectivities (Entries 5 and 6). The catalytic amount of the cobalt(II) complex, (*S*)-MPAC, was examined in the hetero Diels-Alder reaction of *o*-methoxybenzaldehyde (Table 3). The smaller the catalytic amount of the complex employed, the longer the reaction time required for complete consumption of the dienophile. Whereas, regardless of the amount of complex catalyst used (0.5 – 10 mol%), the yield and enantiomeric excess of the products in each reaction were retained in the ranges of 80 – 96% yields and 57 – 62% ee, respectively.

These observations suggested that the optically active aldiminato cobalt(II) complex could possess strong catalytic activity as a Lewis acid for the hetero Diels-Alder reaction and that it would resist any reactions with moisture or contaminants even for a lower catalyst loading.

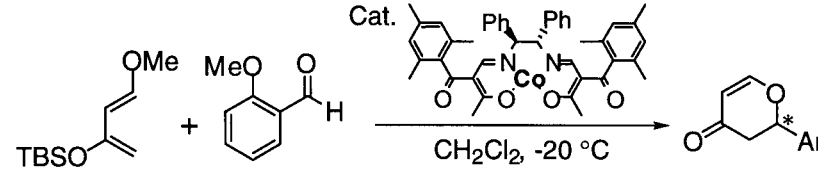
It is noted that the optically active aldiminato cobalt(II) complex effectively catalyzed the enantioselective hetero Diels-Alder reaction of *ortho*-substituted arylaldehydes with Danishefsky's diene to afford the corresponding dihydropyran-4-ones with moderate-to-high enantioselectivities. In order to achieve a higher enantioselection and higher catalyst efficiency, a rational design of the optically active aldiminato ligands is now underway.

REFERENCES AND NOTES

†Dedicated to Prof. Teruaki Mukaiyama on the occasion of his 73rd birthday.

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Table 3. Catalytic Amount of Cobalt(II) Complex



Entry ^{a)}	Cat / mol%	Time / h	Yield (%) ^{b)}	Ee (%) ^{c)}
1	10	20	89	59
2	5	55	96	62
3	2	58	88	61
4	1	71	87	57
5 ^{d)}	0.5	46	80	60

a) Reaction Conditions: catalytic amount (0.5 - 10 mol%) of (*S*)-MPAC, 2-methoxybenzaldehyde 0.5 mmol, and diene 1.0 mmol at -20°C in CH₂Cl₂ (2.5 mL). b) Ar = 2-Methoxyphenyl. Isolated yield after the treatment with CF₃COOH. c) Determined by HPLC analysis using Daicel Chiralpak AD (IPA 1% in hexane). d) 2.5 mL of solvent (CH₂Cl₂) was used for 1.0 mmol of 2-methoxybenzaldehyde.

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14. It was suggested that during the reduction of *o*-haloacetophenone derivatives, the simultaneous coordination of the carbonyl oxygen and halogen atoms to the metal atom produces a five- or six-membered chelate ring. M. Kitamura, T. Ohkuma, S. Inoue, N. Sano, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, and R. Noyori, *J. Am. Chem. Soc.*, 1988, **110**, 629; T. Yamada, K. D. Sugi, and T. Nagata, unpublished results.
15. Typical procedure: To a solution of the cobalt(II) complex (*S*)-MPAC (17.8 mg, 4.9 mol%) in dichloromethane (0.5 mL) was added *o*-fluorobenzaldehyde (65.3 mg, 0.53 mmol) in dichloromethane (1.0 mL), then cooled to $-78\text{ }^{\circ}\text{C}$. The diene (200 μL , 0.97 mmol) in dichloromethane (1.0 mL) was next added. The mixture was stirred for 50 h at $-78\text{ }^{\circ}\text{C}$, followed by treatment with trifluoroacetic acid (0.2 mL) at rt for 5 h. The reaction was quenched with sat. NaHCO_3 solution. A standard workup and chromatography on silica gel afforded 2-(2-fluorophenyl)-2,3-dihydro-4*H*-pyran-4-one (62.2 mg) in 62% yield as a yellowish oil. Optical yield of the product was determined by HPLC analysis (Daicel Chiralpak AD, IPA 1.0% in hexane) to be 78% ee.

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