Optically Active Cationic Cobalt(III) Complexes: Highly Efficient Catalysts for Enantioselective Hetero Diels–Alder Reaction

Satoko Kezuka, Tsuyoshi Mita, Natsuki Ohtsuki, Taketo Ikeno, and Tohru Yamada
Department of Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama 223-8522

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Optically active β-ketoiminato cobalt(III) complexes were developed for use as effective catalysts of the enantioselective hetero Diels–Alder reaction of aryl and alkyl aldehydes with 1-methoxy-[3-(*tert*-butyldimethylsilyl)oxy]-1,3-butadiene. In the presence of 5 mol% cationic cobalt(III) triflate complexes derived from optically active 1,2-bis(3,5-dimethylphenyl)-1,2-ethylenediamine, the hetero Diels–Alder reaction of *p*-nitrobenzaldehyde proceeded in 94% yield with 94% ee.

Among the various carbon–carbon bond-forming reactions, the enantioselective hetero Diels–Alder reaction has emerged as an important target in synthetic organic chemistry[1] because carbon–carbon and carbon–oxygen bonds are both formed to afford six-membered pyran derivatives in a stereoselective manner. In a previous paper, it was reported that the hetero Diels–Alder reactions of *ortho*-substituted aryl aldehydes with electron-rich dienes proceeded in the presence of a catalytic amount of the optically active β-ketoiminato[2] cobalt(II) complex to afford the corresponding dihydropyran-4-ones with moderate yields and good enantioselectivities.[3] In order to achieve high performance in the catalytic enantioselective reaction, the detailed design of the optically active β-ketoiminato complex catalysts should be required, e.g., for increasing their catalytic activities, cobalt complex catalysts of high oxygenophilicity should be developed. The corresponding cobalt(III) halides and cationic cobalt(III) complexes are expected to be employed as highly active Lewis acid catalysts. The optically active β-ketoiminato cobalt(III) iodide complexes were already prepared and their structures were determined by X-ray analysis,[4] but they have never been used for asymmetric reactions. In this communication, we would like to report that the cobalt(III) derivatives were synthesized and employed as efficient catalysts for the highly enantioselective hetero Diels–Alder reaction of aryl and alkyl aldehydes with electron-rich dienes.

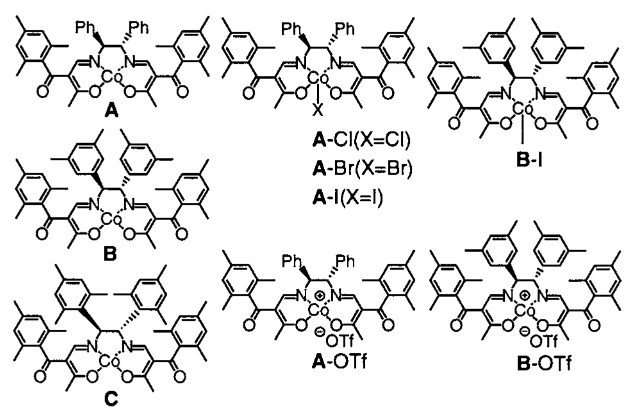
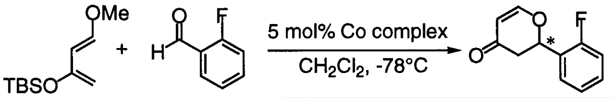


Figure 1. Various β-ketoiminato cobalt(II) and (III) complexes.

First of all, a variety of optically active β-ketoiminato cobalt complexes (Figure 1) was examined for the asymmetric hetero Diels–Alder reaction of *o*-fluorobenzaldehyde (Table 1). These complexes **A**, **B** and **C** were respectively prepared from the corresponding optically active 1,2-diaryl-1,2-ethylenediamines and 1,3-dicarbonyl compounds. When the optically active cobalt(II) complex **B** was employed as the catalyst, the yield and the enantioselectivity of the product were slightly improved compared with complex **A** (Entries 1 and 2). On the contrary, both the activity and enantioselectivity were unexpectedly decreased when complex **C** was used. For improvement of the catalytic activity, a variety of axial ligands that enhance the Lewis acidity was next examined. The cobalt(III) complex **A**-Cl was prepared by the ligand-exchange procedure[5] from the corresponding cobalt(III) acetate complex[6] and lithium chloride. The cobalt(III) complexes **A**-Br and **A**-I[7] were obtained by oxidation of the cobalt(II) complex **A** with Br_2 and I_2, respectively. In the presence of complexes **A**-Cl and **A**-Br, the optical yield of the product was rather decreased whereas the reaction smoothly proceeded (Entries 4 and 5). When the cobalt(III) complex **A**-I was employed, the reaction time was shortened and the optical yield of the product was maintained (Entry 6). Furthermore, the cationic cobalt(III) complex **A**-OTf, synthesized by treatment of the corresponding cobalt(III) complex **A**-I with AgOTf,[8] was proved to be a highly active catalyst for the hetero Diels–Alder reaction. In the presence of 5 mol% complex catalyst **A**-OTf, the reaction was completed in 12 h with 79% ee (Entry 7). The addition of MS4A to the reaction mixture improved both the yield and optical yield of the

Table 1. Various cobalt complex catalysts for the asymmetric hetero Diels-Alder reaction



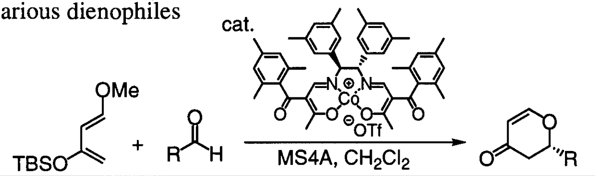
Entry[a]	Catalysts	Time / h	Yield / %[b]	Ee / %ee[c]
1	**A**	50	62	78
2	**B**	72	71	83
3	**C**	31	9	14
4	**A**-Cl	36	61	71
5	**A**-Br	36	84	73
6	**A**-I	36	87	78
7	**A**-OTf	12	92	79
8	**B**-I	24	83	81
9[d]		24	91	86
10[d]	**B**-OTf	3	89	87

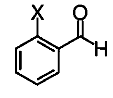
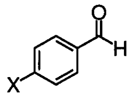
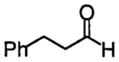
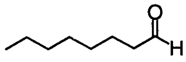
[a] Reaction Conditions: 0.025 mmol (5.0 mol%) cobalt(II) catalyst, 0.5 mmol dienophile (*o*-fluorobenzaldehyde), and 1.0 mmol diene in CH_2Cl_2 (2.5 mL). [b] Isolated yield after the treatment with CF_3COOH. [c] Determined by HPLC analysis using Daicel Chiralpak AD (IPA 1% in hexane). [d] Powdered 4 Å molecular sieves (MS4A) were added.

product, and the cationic cobalt(III) triflate complex **B**-OTf, prepared from the complex **B**-I, remarkably accelerated the hetero Diels–Alder reaction to produce the corresponding dihydropyran-4-one with high enantioselectivity (Entries 8, 9 and 10).

The highly active cationic cobalt(III) triflate complexes **A**-OTf and **B**-OTf were successfully applied as effective chiral catalysts for the enantioselective hetero Diels–Alder reaction of various aldehydes with the electron-rich diene.[9] As shown in Table 2, the hetero Diels–Alder reactions of the *o*-fluoro- and *o*-chloro-benzaldehydes proceeded smoothly to afford the corresponding dihydropyran-4-ones in high yield[10] with high enantioselectivity (Entries 1 and 2). By using the cationic cobalt(III) complex **B**-OTf as a Lewis acid catalyst, aryl aldehydes substituted by an electron-withdrawing group at the *para*-position reacted with Danishefsky's diene and was completely consumed within 7–24 h. The enantioselectivities in these reactions of the *p*-nitro-, *p*-trifluoromethyl-, and *p*-chlorobenzaldehydes were 94% ee, 91% ee, and 91% ee, respectively (Entries 3–5). The hetero Diels–Alder reaction of benzaldehyde itself also proceeded to produce the corresponding pyranone derivative in 83% yield with 90% ee[11] (Entry 6). In the presence of a catalytic amount of the cationic cobalt(III) triflate complex **A**-OTf, the hetero Diels–Alder reaction of 3-phenylpropionaldehyde and octanal smoothly proceeded to afford the corresponding dihydropyran-4-ones with high enantioselectivity (90% ee and 88% ee, Entries 7 and 8, respectively).

Table 2. The asymmetric hetero Diels-Alder reaction of various dienophiles



Entry[a]	R-CHO		Time / h	Yield / %[b]	Ee / %ee
1		X=F	3	89	87
2		X=Cl	3	81	81
3		X=NO_2	7	94	94
4		X=CF_3	7	88	91
5		X=Cl	24	81	91
6		X=H	59	83	90
7			96[c]	69	90
8			96[d]	89	88

[a]Reaction conditions: 0.025 mmol (5.0 mol%) cobalt(III)-OTf **B**-OTf catalyst, 0.5 mmol dienophile (aldehyde), 150 mg MS4A, and 1.0 mmol diene in CH_2Cl_2 (2.5 mL). [b]Isolated yield after the treatment with CF_3COOH. [c]9.0 mol% cobalt(III)-OTf complex **A**-OTf and 200 mg MS4A was employed. [d]8.0 mol% **A**-OTf was employed.

It is noted that the cationic cobalt(III) triflate complexes with optically active β-ketoiminato ligands effectively catalyzed the hetero Diels–Alder reaction of various aryl and alkyl aldehydes with Danishefsky's diene to afford the corresponding dihydropyran-4-one derivatives in high yield with high enantioselectivity. Further applications of the present cationic cobalt(III) complexes as chiral Lewis acid catalysts are in progress.

References and Notes

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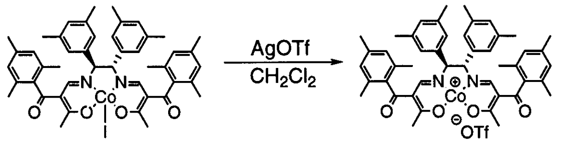
8 Preparation of cobalt(III) triflate complex: To a solution of the cobalt complex **B**-I (259.9 mg, 0.295 mmol) in dichloromethane (10.0 mL) was added AgOTf (84.4 mg, 0.329 mmol) in dichloromethane (1.0 mL). The mixture was stirred for 1.5 h and the resulting AgI was filtered off. The crude product was purified by reprecipitation from dichloromethane/hexane to afford the cationic cobalt(III) complex **B**-OTf (231.4 mg) in 87% yield as a green solid.



9 Typical procedure: To a solution of the cobalt complex **B**-OTf (22.9 mg, 5.0 mol%) in dichloromethane (0.5 mL) in the presence of molecular sieves 4A was added *p*-nitrobenzaldehyde (75.4 mg, 0.50 mmol) in dichloromethane (1.0 mL). A solution of the diene (200 µL, 0.97 mmol) in dichloromethane (1.0 mL) was then added at –78 °C. The mixture was stirred for 7 h at –78 °C, followed by treatment with trifluoroacetic acid (0.2 mL) at rt for 5 h. After neutralization with sat. $NaHCO_3$ solution, a standard workup and chromatography on silica gel afforded 2,3-dihydro-2-(4-nitrophenyl)-4*H*-pyran-4-one (102.5 mg) in 94% yield. The optical yield of the product was determined by HPLC analysis (Daicel Chiralcel OD-H, IPA 10% in hexane) to be 94% ee.

10 Aryl aldehydes with *ortho*-halide or *orhto*-alkoxide reacted with dienes faster than that with the corresponging aldehydes of *para*-substitution. A detailed study of these observations is currently under way.

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