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Optically Active β-Ketoiminato Cationic Cobalt(III) Complexes: Efficient Catalysts for Enantioselective Carbonyl-Ene Reaction of Glyoxal Derivatives

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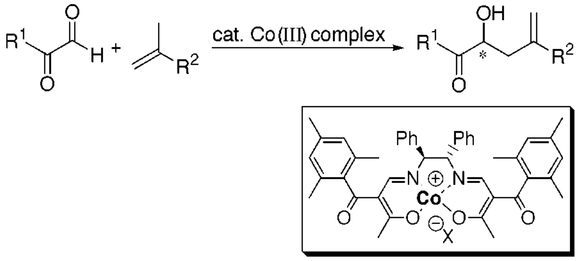
ABSTRACT



Optically active β-ketoiminato cationic cobalt(III) complexes were synthesized as effective Lewis acid catalysts for the enantioselective carbonyl-ene reaction. In the presence of a catalytic amount of cobalt(III) hexafluoroantimonate derived from the optically active 1,2-diphenyl-1,2-ethanediamine, the carbonyl-ene reaction with a variety of alkenes and glyoxal derivatives smoothly proceeded to afford the corresponding homoallylic alcohols in good-to-high yields with high enantioselectivities.

The enantioselective carbonyl-ene reaction promoted by a catalytic amount of Lewis acid is an intriguing route to some optically active homoallylic alcohols. The carbonyl-ene reaction[1] is one of the most convenient methods for carbon−carbon bond formation without any pretreatment such as enolization, and the resulting homoallylic alcohol could be further transformed into more functionalized products by taking advantage of its carbon−carbon double bond. In addition, like the Diels−Alder reaction, it is assumed that the carbonyl-ene reaction is a 6π-electron electrocyclic reaction.[2] For these reasons, a variety of metal complexes with optically active ligands have been widely investigated as Lewis acid catalysts; various centered metals, the design of chiral ligands, and their combination have been tried for achieving a high catalytic ability and high enantioselectivity in the carbonyl-ene reaction.[3]

Optically active β-ketoiminato cobalt complexes[4] derived from the corresponding 1,3-dicarbonyl compounds and optically active 1,2-diaryl-1,2-ethanediamines were also

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(1) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426 and references therein.

(2) A zwitterionic intermediate was also proposed for the Lewis acid catalyzed carbonyl-ene reaction: Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555. Snider, B. B.; Phillips, G. B. *J. Org. Chem.* **1983**, *48*, 464.

(3) Maruoka, K.; Hoshino, Y.; Shirasaka, T.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 3967. Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940. Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949. Mikami, K. *Pure Appl. Chem.* **1996**, *68*, 639. Evans, D. A.; Burgey, C. S.; Paras, N. A.; Vojkovsky, T.; Tregay, S. W. *J. Am. Chem. Soc.* **1998**, *120*, 5824. Evans, D. A.; Tregay, S. W.; Burgey, C. S.; Paras, N. A.; Vojkovsky, T. *J. Am. Chem. Soc.* **2000**, *122*, 7936. Hao, J.; Hatano, M.; Mikami, K. *Org. Lett.* **2000**, *2*, 4059. Qian, C.; Huang, T. *Tetrahedron Lett.* **1997**, *38*, 6721. Qian C.; Huang, T. *Tetrahedron: Asymmetry* **2000**, *11*, 2347. For reviews on the carbonyl-ene reaction, see: Mikami, K.; Terada, M.; Shimizu, M.; Nakai, T. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 292. Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.

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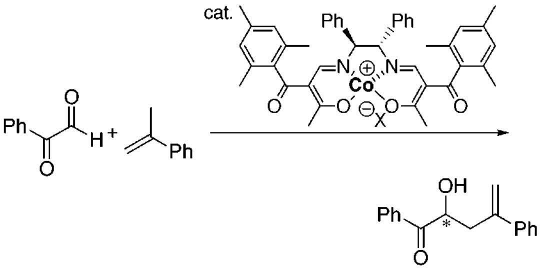
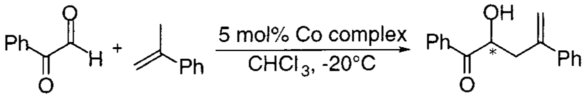
employed as effective Lewis acid catalysts for enantioselective hetero Diels−Alder reactions.[5] In the presence of 5 mol % cationic cobalt(III) complexes, the reaction of aromatic or aliphatic aldehydes with electron-rich dienes smoothly proceeded to afford the corresponding pyranone derivatives in good-to-high yields with high enantioselectivities.[6] In this communication, we report that the cationic cobalt(III) complex with the optically active β-ketoiminato ligand was efficiently employed as a Lewis acid catalyst for the enantioselective carbonyl-ene reaction of various terminal alkenes with glyoxal derivatives (eq 1).



(1)

First of all, a variety of β-ketoiminato cobalt(II) and cobalt(III) complex catalysts were examined for the asymmetric carbonyl-ene reaction of phenylglyoxal and α-methylstyrene (Table 1).[7] The cobalt(II) complex **1a** and the corresponding iodo cobalt(III) complex **1b** could scarcely catalyze the carbonyl-ene reactions (entries 1 and 2). To improve the catalytic activity of the cobalt complex, the corresponding cationic cobalt(III) complexes with various counteranions were prepared by treatment of the iodo cobalt(III) complex **1b** with the corresponding silver salts, and then they were subjected to the carbonyl-ene reaction. The cobalt(III) triflate complex **1c**, one of the most effective catalysts for the hetero Diels−Alder reaction,[6b] afforded the carbonyl-ene product in only 9% yield and with 2% ee (entry 3). The corresponding cobalt(III) tetrafluoroborate **1d** and cobalt(III) hexafluorophosphate **1e** effectively catalyzed the carbonyl-ene reaction to obtain the corresponding homoallylic alcohol in good yields with good enantioselectivities (entries 4 and 5). Screening of the counteranions revealed that the hexafluoroantimonate cobalt(III) complex **1f** could be significantly employed as a highly reactive cationic cobalt(III) complex and that the resulting homoallylic alcohol with 88% ee was afforded in 90% yield (entry 6).

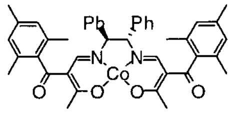
Table 1. Various Cationic Cobalt Complex Catalysts for Asymmetric Carbonyl-Ene Reaction



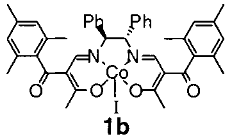
2 **3a** **4a**

Entry[a]	Catalyst	Time / hr	Yield / %[b]	Ee / %ee[c]
1	**1a**	125	trace	—
2	**1b**	125	trace	—
3	**1c**	48	9	2
4	**1d**	48	25	56
5	**1e**	48	34	69
6	**1f**	48	90	88

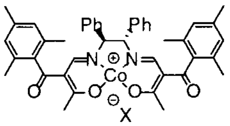
[a] Reaction conditions: cobalt catalyst, 0.025 mmol (5.0 mol%); phenylglyoxal, 1.0 mmol; and alkene, 0.5 mmol in CHCl$_3$ (2.5 mL). [b] Isolated yield. [c] Determined by HPLC analysis using Daicel Chiralcel OB-H (EtOH 2% in hexane).



1a



1b



X = OTf (**1c**)
BF$_4$(**1d**)
PF$_6$(**1e**)
SbF$_6$(**1f**)

It could be assumed that the cobalt(III) complexes in which counteranions were completely separated from the centered cobalt effectively catalyzed the present carbonyl-ene reaction as effective Lewis acids. These series of catalytic activities could be correlated to the acidity of the conjugate acid[8] of the counteranion in the cobalt(III) complexes; the cobalt(III) complex whose counteranion derived the stronger conjugate acid achieved the higher yield of the carbonyl-ene product. For instance, the carbonyl-ene product was obtained with low ee catalyzed by cobalt(III) trifluoromethanesulfonate (H_0 value[9] of trifluoromethanesulfonic acid (CF_3SO_3H), −14.1), whereas the corresponding cobalt(III) hexafluoroantimonate (H_0 value of hexafluoroantimonic acid ($HF{-}SbF_5$), −27.9) afforded the resulting homoallylic alcohol with high ee.

The highly active catalyst, cationic cobalt(III) hexafluoroantimonate complex **1f**, was successfully applied to the enantioselective carbonyl-ene reaction of various alkenes with the glyoxal derivatives (Table 2). The reaction with benzyl glyoxylate smoothly proceeded to afford the corresponding homoallylic alcohol with good enantioselectivity (entry 1). When the carbonyl-ene reaction of phenylglyoxal with α-methylstyrene was tried, the enantioselectivity of the resulting product was increased to 88% ee (entry 2). The carbonyl-ene reaction of phenylglyoxal with various alkenes was then attempted in the presence of a catalytic amount of cobalt(III) hexafluoroantimonate **1f**. The α-methylstyrenes substituted with 4-methyl and 4-fluoro smoothly reacted with phenylglyoxal to afford the corresponding homoallylic alcohols in high yields with high enantioselectivities (entries 3 and 4). The reaction of isopropenylnaphthalene was completed in 48 h, and the optical yield of the corresponding product was 89% ee (entry 5). In the presence of a catalytic

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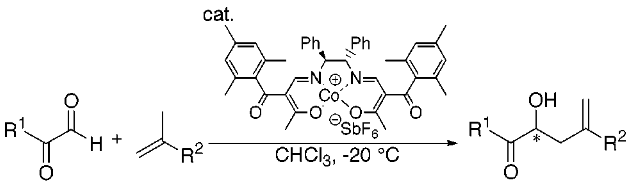
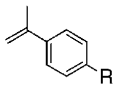
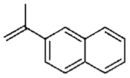
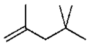
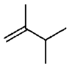
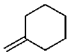
(4) The ketoiminato cobalt(II) complexes effectively catalyzed the enantioselective borohydride reductions of ketones, imines, and α,β-unsaturated carboxamides and the enantioselective cyclopropanation of styrene derivatives: Nagata, T.; Yorozu, K.; Yamada, T.; Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2145. Sugi, K. D.; Nagata, T.; Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1997**, 493. Yamada, T.; Ohtsuka, Y.; Ikeno, T. *Chem. Lett.* **1998**, 1129. Yamada, T.; Ikeno, T.; Sekino, H.; Sato, M. *Chem. Lett.* **1999**, 719. Ikeno, T.; Sato, M.; Yamada, T. *Chem. Lett.* **1999**, 1345.

(5) Yamada, T.; Kezuka, S.; Mita, T.; Ikeno, T. *Heterocycles* **2000**, *52*, 1041.

Table 2. Asymmetric Carbonyl-Ene Reaction of Various Alkenes



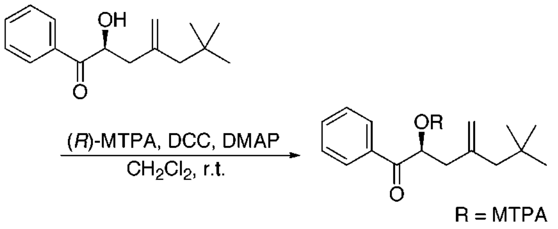
2, 5 **3a-g** **4a-g, 6a**

entry[a]	aldehyde	alkene		yield / %[b]	ee / %
1	R^1 = OBn (**5**)		R = H	90	76
2	R^1 = Ph (**2**)			90	88
3			R = F	92	88
4[c]			R = Me	70	84
5				87	89
6				81	91
7				56	84
8				75	94

[a] Reaction conditions: cobalt(III)-SbF_6 catalyst, 0.025 mmol (5.0 mol%); glyoxal, 1.0 mmol; and alkene, 0.5 mmol in $CHCl_3$ (2.5 mL). [b] Isolated yield. [c] $CHCl_3$ (5.0 mL) was used.

amount of the cobalt(III) hexafluoroantimonate complex **1f**, the carbonyl-ene reaction of 2,4,4-trimethyl-1-pentene, 2,3-dimethyl-1-butene, and methylenecyclohexane with phenylglyoxal proceeded, and the corresponding products were obtained with high enantioselectivities (entries 6, 7, and 8, respectively).[10] It should be considered that two geometric isomers could be produced; however, the regioselectivity in the present carbonyl-ene reaction was totally superior (>99:1, NMR analysis).

The absolute configuration of the obtained product was determined by NMR analysis of the corresponding MTPA esters (eq 2)[11] and it was confirmed that the homoallylic



(2)

alcohol of the (*S*)-configuration corresponding to the (*S*,*S*)-cobalt complex catalyst was obtained (Figure 1). The absolute configuration of the resulting homoallylic alcohol was in accord with the postulated mechanism for the corresponding hetero Diels–Alder reaction (Figure 2).[12]

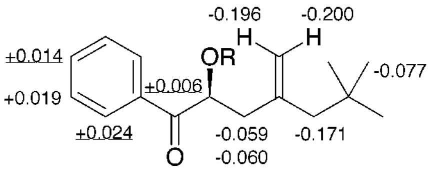


Figure 1. Values (ppm) obtained for (*R*)-MTPA esters of secondary alcohols.

In summary, the cationic cobalt(III) hexafluoroantimonate complex with an optically active *β*-ketoiminato ligand effectively catalyzed the asymmetric carbonyl-ene reaction of various alkenes with glyoxal derivatives to afford the corresponding homoallylic alcohols in high yields with high enantioselectivities.

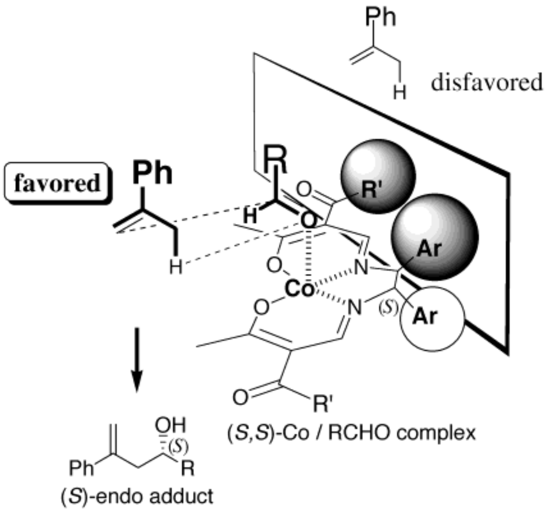


Figure 2. Reasonable explanation for the enantioselection in the carbonyl-ene reaction catalyzed by the (*S*,*S*)-cobalt complex.

Supporting Information Available: Experimental procedures and spectral data for compounds **4a–g**, and **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) (a) Kezuka, S.; Mita, T.; Ohtsuki, N.; Ikeno, T.; Yamada, T. *Chem. Lett.* **2000**, 824. (b) Kezuka, S.; Mita, T.; Ohtsuki, N.; Ikeno, T.; Yamada, T. *Bull. Chem. Soc. Jpn.*, in press.

(7) Among a number of solvents ($CHCl_3$, CH_2Cl_2, PhF, $PhCH_3$, Et_2O, CH_3CN, and hexane), $CHCl_3$ was the most suitable solvent to afford the corresponding homoallylic alcohol in high yield and with high enantioselectivity. The enantioselectivity at 0 °C was lower than that at −20 °C. Although the enantioselectivity at −40 °C was slightly improved, the reaction rate was decreased.

(8) Olah, G. A.; Prakash, G. K. S.; Sommer, J. *Superacids*; John Wiley & Sons: New York, 1985.

(9) Fabre, P. L.; Devynck, J.; Tremillon, B. *Chem. Rev.* **1982**, *82*, 591. Grondin, J.; Sagnes, R.; Commeyras, A. *Bull. Soc. Chim. Fr.* **1976**, 1779.

(10) For the present carbonyl-ene reaction, mono- and trisubstituted alkenes were not reactive enough to the glyoxal derivatives.

(11) Ohtani, I.; Kusumi, T.; Kashnan, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

(12) The absolute configuration of the resulting pyranone derivatives in the cobalt-complex-catalyzed hetero Diels–Alder reaction was explained by the semiempirical method; ref 6b.