Highly Enantioselective Cyclopropanation of Styrenes with Diazoacetates Catalyzed by Optically Active β-Ketoiminato Cobalt(II) Complexes

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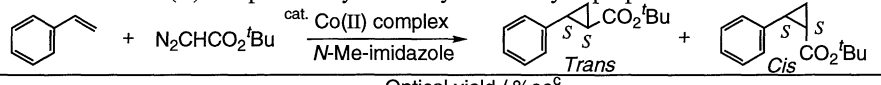
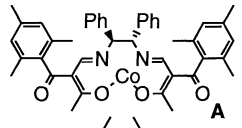
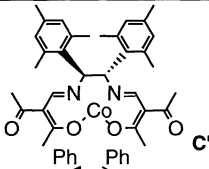
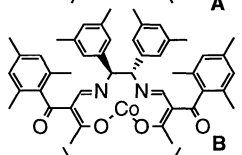
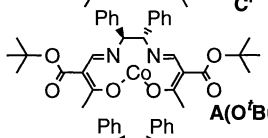
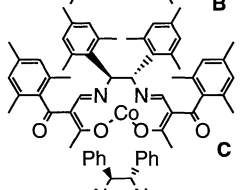
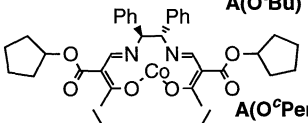
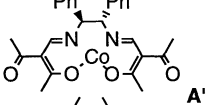
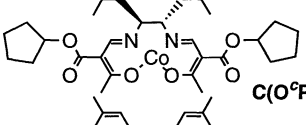
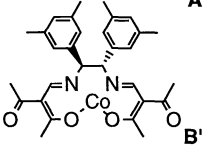
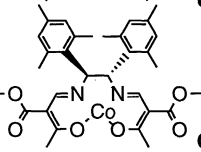
The highly enantioselective cyclopropanation of styrenes with diazoacetates was achieved using reasonably designed β-ketoiminato cobalt(II) complex catalysts. In the presence of optically active cobalt(II) complexes derived from optically active 1,2-(2,4,6-trimethylphenyl)-1,2-ethylenediamine, the cyclopropanation of styrene with methyl, ethyl, and *tert*-butyl diazoacetates proceeded to afford the corresponding cyclopropanecarboxylates with 94-96% ee.

Optically active β-ketoiminato ligands derived from various 1,3-dicarbonyl compounds and 1,2-diaryl-1,2-ethylenediamines are complexed with many varieties of metals to afford optically active β-ketoiminato complexes. It had already been reported that the optically active β-ketoiminato manganese(III) complexes catalyzed the enantioselective aerobic oxidation, and the prototype of these manganese(III) complexes was defined by X-ray structure analysis.[1] Based on their structural information, efficient ligands were rationally designed to achieve high enantioselectivity during aerobic oxidation[2] and the cobalt(II) complex catalyst was developed for the enantioselective borohydride reduction.[3] In a previous paper,[4] we reported that the optically active β-ketoiminato cobalt(II) complex **A** also catalyzed the enantioselective cyclopropanation of *tert*-butyl diazoacetate with styrene and that the presence of *N*-methylimidazole remarkably accelerated the reaction and improved both the optical and chemical yields of the product. In order to complete the enantioselectivities and diastereoselectivities (*trans*/*cis*) of the present cyclopropanation catalyzed by the cobalt(II) complex, a rational design of the optically active β-ketoiminato ligands of the cobalt(II) complexes should be required. In this communication, we report that the highly enantioselective cyclopropanations of various diazoacetaes with styrene derivatives were achieved by using the cobalt(II) complex catalysts derived from optically active 1,2-(2,4,6-trimethylphenyl)-1,2-ethylenediamine and that the corresponding cyclopropanecarboxylates were obtained with 94-96% ee.

The optically active β-ketoiminato cobalt(II) complexes **A**,[5] **B**, and **C** were prepared from the optically active 1,2-diphenyl-1,2-ethylenediamine, 1,2-(3,5-dimethylphenyl)-1,2-

Table 1. Various cobalt(II) complex catalysts for asymmetric cyclopropanation



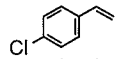
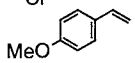
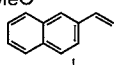
Entry[a]	Catalyst	*Trans* : *Cis*[b]	Optical yield / %ee[c] (Yield / %)[d]	Entry[a]	Catalyst	*Trans* : *Cis*[b]	Optical yield / %ee[c] (Yield / %)[d]
1[e]	 **A**	76:24	84 (94)	6	 **C'**	83:17	96 (80)
2	 **B**	75:25	85 (quant.)	7	 **A(O^{t}Bu)**	83:17	63 (94)
3	 **C**	68:32	90 (89)	8	 **A(O^{c}Pent)**	81:19	66 (quant.)
4	 **A'**	76:24	70 (quant.)	9	 **C(O^{c}Pent)**	90:10	96 (97)
5	 **B'**	78:22	61 (quant.)	10	 **C(O^{t}Bu)**	91: 9	96 (99)

[a]Reaction conditions: 5 mol% of catalyst, 5.0 mmol of styrene, 1.0 mmol of *tert*-butyl diazoacetate and 10 mol%(2.0 equiv. vs. Co(II) complex) of additive in THF at 25-40 °C under N_2 atmosphere for 2-10 h. [b]Determined by GC. [c]Optical yields of *trans*-products were determined by HPLC analysis after reduction of the isolated products into the corresponding alcohols(*Trans*: Daicel Chiralcel OD-H and/or OB-H, hexane / 2-propanol). Absolute configuration of the *trans* isomer: (+)-(*1S,2S*) corresponding to (*S*)-complex. [d]Isolated yield based on *tert*-butyl diazoacetate. [e]Reported in ref.4.

ethylenediamine, and 1,2-(2,4,6-trimethylphenyl)-1,2-ethylenediamine, respectively.[6] They were first examined in the cyclopropanation of styrene with *tert*-butyl diazoacetate (Entries 1-3 in Table 1). The cobalt(II) complexes **A** and **B** catalyzed the reaction to afford the resulting cyclopropanecarboxylates with 84-85% ee and 75-76% *trans*-selectivity, whereas complex **C** improved the optical yield of the product to 90% ee but decreased the *trans*-selectivity (68:32). The cobalt(II) complexes **A'**, **B'**, and **C'** with a smaller side chain[3](acetyl in **A'** series vs. mesitoyl in **A** series) were then subjected to the cyclopropanation (Entries 4-6). When the complex catalyst **A'** or **B'** was used, the optical yield of the product was lower than that using complex catalyst **A** or **B**. On the contrary, in the reaction catalyzed by complex **C'**,[7] the optical yield of the product was remarkably improved to 96% ee and the *trans*-selectivity was also enhanced to 83%. These observations suggested that the sterically required diamine would be effective for improving the enantioselection and that the side chain of the complexes could contribute to the *trans*-selection in the present cyclopropanation. Various cobalt(II) complexes with ester moieties on the side chains were then synthesized and tested. When complexes **A(O^{t}Bu)** and **A(O^{c}Pent)**[2] with *tert*-butyl and cyclopentyl esters were used as catalysts, the *trans*-selectivities of the product were enhanced compared to that by complex catalyst **A** (Entries 7 and 8). Finally, the cobalt(II) complexes having ester side chains and an optically active 1,2-(2,4,6-trimethyl)phenyl-1,2-ethylenediamine unit, **C(O^{c}Pent)** and **C(O^{t}Bu)**, were designed and synthesized.[8] In the presence of these complexes, the cyclopropanation was smoothly completed and the products were obtained in 96% ee with 90% *trans*-selectivity (**C(O^{c}Pent)**, Entry 9) and in 96% ee with 91% *trans*-selectivity (**C(O^{t}Bu)**, Entry 10), respectively.

The cobalt(II) complex catalysts, **C(O^{c}Pent)** and **C(O^{t}Bu)**, were successfully used for the enantioselective cyclopropanation of various diazoacetates and styrene derivatives. In the presence of 5 mol% of cobalt(II) complex **C(O^{t}Bu)**, methyl, ethyl, cyclohexyl, and *tert*-butyl diazoacetates (Entries 1-4 in Table 2) were reacted with styrene to afford the corresponding cyclopropanecarboxylates in high yield with high diastereoselectivity (82-91%) and very high enantioselectivity (92-96% ee). It was reported that the high enantiomeric and diastereomeric excesses of the products were generally achieved by using diazoacetates with bulky alkyl groups, such as menthyl,[9] dicyclohexylmethyl,[10] or 2,6-di-*tert*-butyl-4-methylphenyl[11] groups, and only a few complex catalysts that realize highly enantioselective cyclopropanation of methyl or ethyl diazoacetate were found in literature.[12] In the present cyclopropanation catalyzed by the optically active β-ketoiminato cobalt(II) complexes, the steric size of the alkyl groups in the diazoacetates had little influence on the enantioselection and even the methyl diazoacetate with styrene gave a product with 94%ee. Various styrene derivatives, *p*-chlorostyrene, *p*-methoxystyrene, and 2-vinylnaphthalene, were also converted to the corresponding cyclopropanecarboxylates in high yields with 92-96% ee (Entries 5-7) and α-methylstyrene was also transformed into the corresponding cyclopropane in 47% yield with 99% ee(for *trans* product, Entry 8).

Table 2. Various olefins and diazoacetates (N_2CHCO_2R) in asymmetric cyclopropanation

Entry[a]	Olefin	R	Catalyst	*T*: *C*[b]	Optical yield/ %ee[c] (Yield / %)[d]
1		-CH_3	**C(O^{t}Bu)**	85:15	94[e] (83)
2		-C_2H_5	**C(O^{t}Bu)**	84:16	95[e] (87)
3		-$^tC_4H_9$	**C(O^{t}Bu)**	91: 9	96[e] (99)
4			**C(O^{c}Pent)**	86:14	94[e] (94)
5		-$^tC_4H_9$	**C(O^{c}Pent)**	90:10	96[f] (93)
6			**C(O^{c}Pent)**	82:18	92[f] (85)
7			**C(O^{c}Pent)**	87:13	96[f] (95)
8			**C(O^{c}Pent)**	47:53	99[f] (47)

[a]Reaction conditions: 5 mol% of catalyst, 5.0 mmol of olefin, 1.0 mmol of diazoacetate and 10 mol%(2.0 equiv. vs. Co(II) complex) of *N*-methylimidazole in THF at 40-50 °C under N_2 atmosphere for 9-27 h. [b]*Trans* : *Cis* ratio was determined by GC. [c]Optical yields of *trans*-products were determined by HPLC analysis after reduction of the isolated products into the corresponding alcohols(*Trans*: Daicel Chiralcel OD-H and/or OB-H, hexane / 2-propanol). [d]Isolated yield based on diazoacetate. [e]Absolute configuration of the *trans* isomer was (+)-(*1S,2S*) corresponding to (*S*)-complex. [f]Absolute configurations of the *trans* isomers were not determined.

In conclusion, reasonably designed cobalt(II) complexes prepared from 1,2-(2,4,6-trimethylphenyl)-1,2-ethylenediamine and β-ketocarboxylates produced high enantioselective and *trans*-selective cyclopropanations of various diazoacetates and styrene derivatives. Further investigations into the reaction mechanism and stereoselectivities are now in progress.

References and Notes

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