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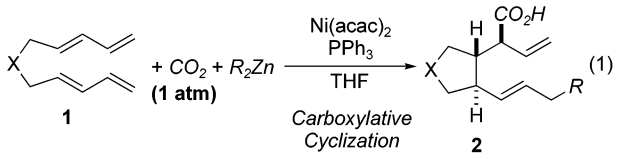
Highly Enantioselective Catalytic Carbon Dioxide Incorporation Reaction: Nickel-Catalyzed Asymmetric Carboxylative Cyclization of Bis-1,3-dienes

Masanori Takimoto, Yoichi Nakamura, Kaoru Kimura, and Miwako Mori*

Graduate School of Pharmaceutical Sciences, Hokkaido University, Hokkaido, Sapporo 060-0812, Japan

Received January 28, 2004; E-mail: mori@pharm.hokudai.ac.jp

Carbon dioxide (CO_2) is regarded as an important source of C1 due to its abundant reserve and low toxicity. Hence, the development of transition metal-catalyzed reactions for CO_2 incorporation onto organic molecules is of great importance.[1] It is especially quite challenging to develop efficient catalytic protocols that enable carbon−carbon bond formation between CO_2 and substrates in an enantioselective manner. However, such catalytic asymmetric CO_2 incorporation processes have rarely been explored[2] due to the limited number of available catalytic carbon−carbon bond-forming CO_2 incorporation reactions that can be efficiently carried out under mild conditions.[3,4] In the course of our research focused on nickel-promoted CO_2 incorporation reactions,[5] we found that $Ni(acac)_2$ and PPh_3 could catalyze the addition of CO_2 and diorganozinc to bis-1,3-diene **1** under very mild conditions (eq 1).[5c] This process was accompanied by carbocyclization of the bis-1,3-diene moiety to afford cyclic carboxylic acid **2** in a highly regio- and stereoselective manner. Here we report a transition metal-catalyzed highly enantioselective carbon−carbon bond-forming CO_2 incorporation reaction based on this carboxylative cyclization.



We first screened various chiral phosphine ligands (Chart 1) in carboxylative cyclization of **1a** using Me_2Zn. The reactions were carried out in the presence of $Ni(acac)_2$ (10 mol %), chiral phosphine ligands (10 mol % for bisphosphines or 20 mol % for monophosphines), and Me_2Zn (4.5 equiv) at room temperature under a CO_2 atmosphere (1 atm) in THF. The results are summarized in Table 1. While the reactions using common chiral ligands provided **2a**[5c] in relatively good yields, the enantioselectivities were moderate (entries 1−6). The highest enantioselectivity was achieved with the use of (*S*)-MeO-MOP as a chiral ligand.[7] The reaction of **1a** with CO_2 and Me_2Zn at room temperature in the presence of (*S*)-MeO-MOP afforded **2a** in 83% yield and 91% ee (entry 7). The reaction performed at a lower temperature (0 °C) resulted in higher enantioselectivity (93% ee) with a slight decrease in chemical yield (entry 8). The absolute configuration of a chiral center at the C-2 position of **2a**, which was obtained in this reaction, was confirmed to be *S* according to Kusumi's method for determining the absolute configuration of carboxylic acids.[8]

Encouraged by these results, asymmetric carboxylative cyclization using MeO-MOP was further investigated (Table 2). When Ph_2Zn was used as an organozinc reagent with bisdiene **1a**, phenylative cyclization proceeded in a highly enantioselective manner to afford **3a** in 81% yield and 95% ee (entry 1). In the reaction of **1a** with Et_2Zn, reductive cyclization product **5** was also obtained in 13% yield (94% ee) along with ethylative cyclization

Chart 1. Chiral Phosphine Ligands Screened for Asymmetric Carboxylative Cyclization of Bis-1,3-diene

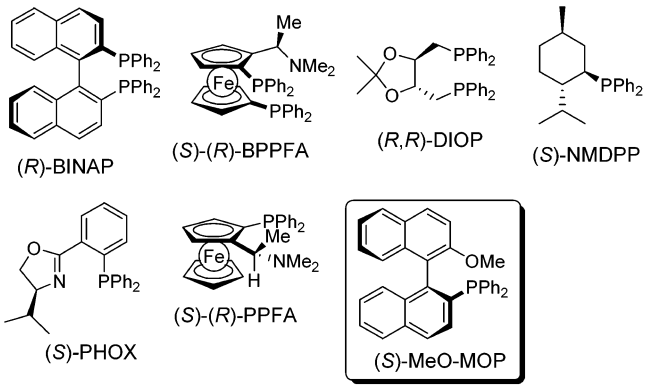
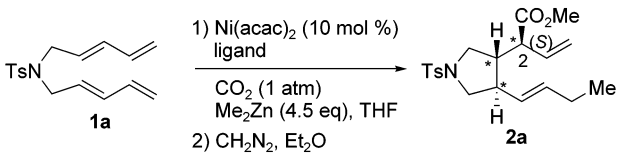


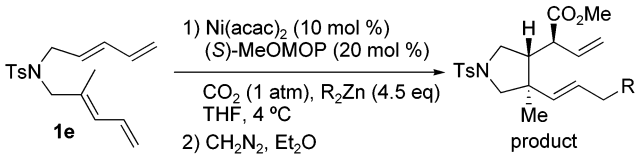
Table 1. Asymmetric Carboxylative Cyclization of **1a** Using Me_2Zn



entry	ligand (mol %)	conditions	yield, %	ee, %[a]	config.[b]
1	(*R*)-BINAP (10)	rt, 23 h	52	12	2*S*
2	(*S*)-(*R*)-BPPFA (10)	rt, 24 h	62	11	2*S*
3	(*R*,*R*)-DIOP (10)	rt, 13 h	75	55	2*R*
4	(*S*)-NMDPP (20)	rt, 15 h	67	3	2*S*
5	(*S*)-PHOX (20)	rt, 33 h	38	15	2*R*
6	(*S*)-(*R*)-PPFA (20)	rt, 24 h	66	43	2*S*
7	(*S*)-MeO-MOP (20)	rt, 4 h	83	91	2*S*
8	(*S*)-MeO-MOP (20)	0 °C, 24 h	71	93	2*S*

[a] The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column. [b] Absolute configuration of chiral center at the C-2 position.

Scheme 1. Asymmetric Carboxylative Cyclization of **1e**



R_2Zn	*time (h)*	*product (yield / ee)*
Me_2Zn	62	**2e** (R=Me, 88% / 96% ee)
Ph_2Zn	90	**3e** (R=Ph, 87% / 91% ee)

product **4a** (57% yield, 94% ee). The similarity of the enantioselectivities of **4a** and **5** suggested that these products were produced from a same intermediate. The formation of **5** was rationalized by considering a transfer of β-hydride from the ethyl group via a β-hydride elimination process.[5c] Bisdienes **1b**, **1c,** and **1d** were also

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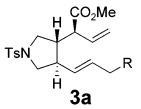
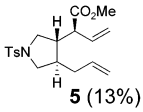
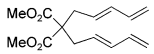
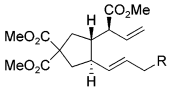
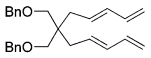
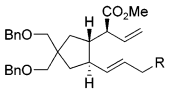
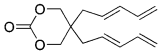
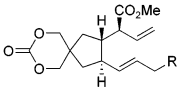
Table 2. Asymmetric Carboxylative Cyclization Using MeO-MOP[a]

entry	substrate	organozinc temp, time	product [b] (yield)	ee, %
1	**1a**	Ph_2Zn 0 °C, 19 h	 **3a** (R=Ph, 81%)	95
2	**1a**	Et_2Zn 0 °C, 8 h	**4a** (R=Et, 57%) +  **5** (13%)	94
3	 **1b**	Me_2Zn rt, 32 h	 **2b** (R=Me, 100%)	94
4	**1b**	Ph_2Zn rt, 28 h	**3b** (R=Ph, 89%)	92
5	 **1c**	Me_2Zn rt, 36 h	 **2c** (R=Me, 95%)	95
6	**1c**	Ph_2Zn 4 °C, 93 h	**3c** (R=Ph, 80%)	90
7	 **1d**	Me_2Zn rt, 17 hr	 **2d** (R = Me, 90%)	94
8	**1d**	Ph_2Zn 0 °C, 68 h	**3d** (R=Ph, 83%)	95

[a] All reactions were carried out in the presence of $Ni(acac)_2$ (10 mol %), (*S*)-MeO-MOP (20 mol %), and an organozinc reagent (4.5 equiv) under an atmosphere of CO_2 (1 atm) in THF. [b] All products were isolated as methyl esters after treatment with CH_2N_2. The absolute configurations of all products were unequivocally determined as indicated above. For details, see Supporting Information.

applicable to the asymmetric carboxylative cyclization, and the desired products having a carbocyclic five-membered ring skeleton were obtained in high yields and in high enantioselectivities (entries 3−8).

It is notable that unsymmetrical bis-1,3-diene **1e** could be used in this asymmetric carboxylation with high selectivity (Scheme 1). Methylative cyclization of **1e** in the presence of (*S*)-MeO-MOP proceeded at 4 °C with regioselective introduction of CO_2 into a less-substituted 1,3-diene moiety to afford **2e** in 88% yield and 96% ee. Phenylative cyclization of **1e** also proceeded smoothly in a regioselective manner under similar conditions to give **3e** in 87% yield and 91% ee.

In conclusion, we have developed a nickel-catalyzed asymmetric carboxylative cyclization of bis-1,3-dienes. This reaction can be carried out easily under mild conditions, and the yields and enantioselectivities are generally high. Further investigation to expand the scope of this reaction is in progress.

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Supporting Information Available: Spectral data for all new compounds, typical procedures for enantioselective carboxylations, procedures for determination of the stereochemistry, enantiomeric excess, and absolute configuration (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Reviews: Arakawa, H.; Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; DuBois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953.

(2) To the best of our knowledge, there is no report on a catalytic enantioselective carbon−carbon bond-forming CO_2 incorporation reaction, although some examples of zinc-catalyzed asymmetric alternating copolymerization of cyclohexene oxide and CO_2 have recently been reported. (a) Nozaki, K.; Nakano, K.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 11008. (b) Nakano, K.; Nozaki, K.; Hiyama, T. *J. Am. Chem. Soc.* **2003**, 125, 5501. (c) Cheng, M.; Darling, N. A.; Lobkovsky, E. B.; Coates, G. W. *Chem. Commun.* **2000**, *30*, 2007.

(3) Reviews: (a) Behr, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 661. (b) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.* **1988**, *88*, 747. (c) Leitner, W. *Coord. Chem. Rev.* **1996**, *153*, 257. (d) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27. (e) Walther, D.; Ruben, M.; Rau, S. *Coord. Chem. Rev.* **1999**, *182*, 67.

(4) Louie recently reported efficient catalytic procedure for [2 + 2 + 2] cycloaddition of diyne and CO_2 under mild conditions. Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188.

(5) (a) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895. (b) Takimoto, M.; Shimizu, K.; Mori, M. *Org. Lett.* **2001**, *3*, 3345. (c) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008. (d) Shimizu, K. Takimoto, M.; Mori, M. *Org. Lett.* **2003**, *5*, 2323. (e) Takimoto, M. Kawamura, M.; Mori, M. *Org. Lett.* **2003**, *5*, 2599. For recent examples reported from other laboratories, see ref 6 and references cited in ref 3.

(6) Saito, S.; Nakagawa, S.; Koizumi, T.; Hirayama, K.; Yamamoto, Y. *J. Org. Chem.* **1998**, *64*, 3975.

(7) For reviews on enantioselective reactions using MOP derivatives, see: (a) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354. For preparation of MeO-MOP, see: (b) Uozumi, Y.; Kawatsura, M.; Hayashi, T. *Org. Synth.* **2002**, *78*, 1. (c) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**. *58*, 1945.

(8) Nagai, Y.; Kusumi, T. *Tetrahedron Lett.* **1995**, *36*, 1853. For details, see Supporting Information.

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