ChemPubSoc Europe

DOI: 10.1002/ejoc.201600338

EurJOC European Journal of Organic Chemistry

Communication

Hydrocarboxylation

Rhodium-Catalyzed Hydrocarboxylation of Olefins with Carbon Dioxide

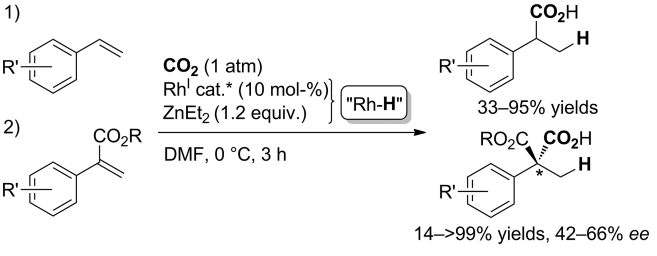
Shingo Kawashima,[a] Kohsuke Aikawa,[a] and Koichi Mikami*[a]

Dedicated to Professor Achille Umani-Ronchi on the occasion of his 80th birthday

Abstract: The catalytic hydrocarboxylation of styrenes derivatives and α,β-unsaturated carbonyl compounds with CO_2 (101.3 kPa) in the presence of an air-stable rhodium catalyst was explored. The combination of $[RhCl(cod)]_2$ (cod = cyclooctadiene) as a catalyst and diethylzinc as a hydride source allowed for effective hydrocarboxylation and provided the corresponding α-aryl carboxylic acids in moderate to excellent yields. In this catalytic process with carbon dioxide, intervention of the Rh^I–H species, which could be generated from the Rh^I catalyst and diethylzinc, was clarified. Significantly, the catalytic asymmetric hydrocarboxylation of α,β-unsaturated esters with carbon dioxide was also performed by employing a cationic rhodium complex possessing (*S*)-(–)-4,4′-bi-1,3-benzodioxole-5,5′-diylbis(diphenylphosphine) [(*S*)-SEGPHOS] as a chiral diphosphine ligand. A plausible model for asymmetric induction was proposed by determination of the absolute configuration of the product.

Introduction

The transformation of carbon dioxide as a cheap, nontoxic, and, hence, attractive C_1 source is a challenging subject in modern synthetic organic chemistry.[1] Although carbon dioxide is thermodynamically stable and of kinetically low reactivity, various transformations of carbon dioxide with homogeneous transition-metal catalysts have been reported.[1,2] In particular, the catalytic hydrocarboxylation of olefins with carbon dioxide has attracted much attention, owing to the fact that it is a direct method for the synthesis of carboxylic acid derivatives, which are important intermediates in the pharmaceutical industry.[1] For example, the employment of styrene derivatives can lead to non-steroidal anti-inflammatory[3] and anti-Alzheimer[4] drugs such as ibuprofen derivatives. However, the transition-metal-catalyzed hydrocarboxylation of olefins such as styrenes and α,β-unsaturated compounds with carbon dioxide is extremely limited to few examples for which Ni,[5,6] Fe,[7] and Co[8] complexes are used and thus remains undeveloped. Furthermore, there is no successful report on the catalytic asymmetric hydrocarboxylation of olefins with carbon dioxide. In 2004, Mori and co-workers reported a rare example of the MeO-MOP/Ni^0-catalyzed asymmetric carboxylation of bis-1,3-dienes through nucleophilic attack of a π–allyl nickel intermediate to carbon dioxide.[9] Herein, we report the rhodium-catalyzed hydrocarboxylation[10] of olefins, such as styrene derivatives and α,β-unsaturated carbonyl compounds with carbon dioxide to provide the corresponding α-aryl carboxylic acids. Significantly, it is also demonstrated that our rhodium catalyst system can be applicable to asymmetric catalysis (Scheme 1).



Scheme 1. Rh-catalyzed hydrocarboxylations of olefins with CO_2.

Results and Discussion

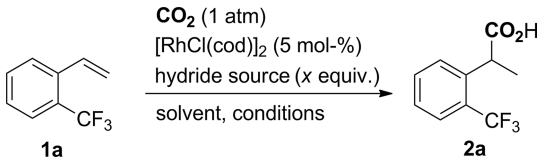
We initially examined the hydrocarboxylation of styrene derivative **1a** bearing the sterically demanding *o*-CF_3-substituent as a model substrate with diethylzinc as the hydride source in the presence of $[RhCl(cod)]_2$ (5 mol-%, cod = cyclooctadiene) under an atmosphere of carbon dioxide (1 atm = 101.3 kPa) (Table 1). Various solvents were investigated (Table 1, entries 1–7), but only a low yield (4 %) of desired carboxylated product **2a** was obtained in THF[5] at room temperature after 12 h (Table 1, entry 8). Replacement of THF with more polar dimethylacetamide (DMA) and DMF provided higher yields (Table 1, entries 9 and 10). Increasing the concentration of the reaction mixture further increased the yield, even in a catalytic fashion [turnover number (TON) = 3.3, though] at a lower reaction temperature (0 °C) and in a shorter reaction time (3 h) (Table 1, entry 11).

[a] *Department of Applied Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8552, Japan*
E-mail: mikami.k.ab@m.titech.ac.jp
www.apc.titech.ac.jp/~mikami/index-j.html

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejoc.201600338.

Other hydride sources such as BEt_3, $AlEt_3$, and $PhMe_2SiH$ did not provide better results (Table 1, entries 12–14). The addition of a base such as Cs_2CO_3, which Rovis and co-workers reported to be key to the nickel-catalyzed hydrocarboxylation of styrene derivatives,[5] did not enhance the yield.

Table 1. Rh-catalyzed hydrocarboxylation of styrene.



1a 2a

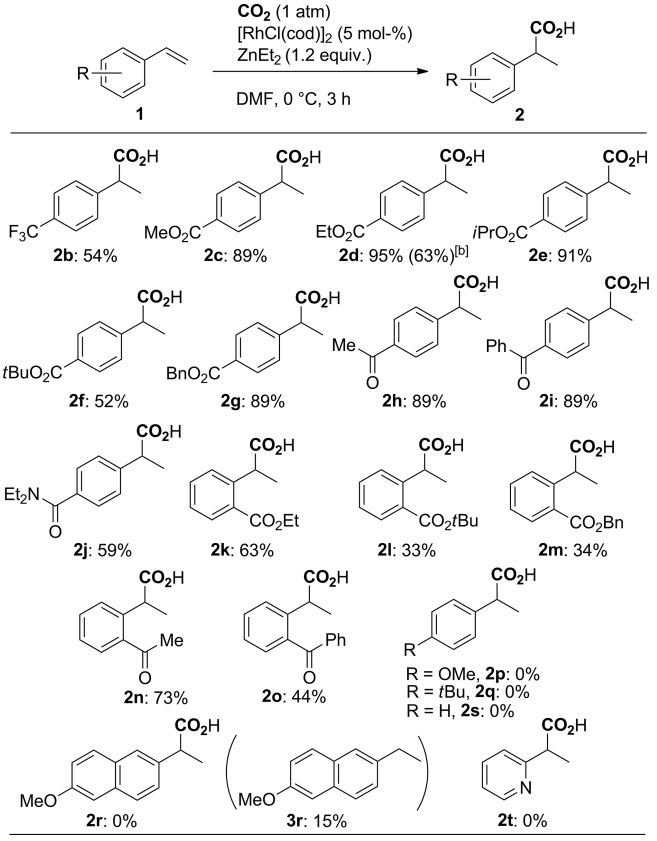
Entry	Hydride source (equiv.)	Solvent[a]	Conditions	Yield [%][c]
1	$ZnEt_2$ (2.5)	Et_2O	r.t., 12 h	0
2	$ZnEt_2$ (2.5)	CH_2Cl_2	r.t., 12 h	0
3	$ZnEt_2$ (2.5)	toluene	r.t., 12 h	0
4	$ZnEt_2$ (2.5)	acetone	r.t., 12 h	0
5	$ZnEt_2$ (2.5)	CH_3CN	r.t., 12 h	0
6	$ZnEt_2$ (2.5)	NMP	r.t., 12 h	0
7	$ZnEt_2$ (2.5)	DMSO	r.t., 12 h	trace
8	$ZnEt_2$ (2.5)	THF	r.t., 12 h	4
9	$ZnEt_2$ (2.5)	DMA	r.t., 12 h	12
10	$ZnEt_2$ (2.5)	DMF	r.t., 12 h	18
11	$ZnEt_2$ (1.2)	DMF[b]	0 °C, 3 h	33
12	BEt_3 (1.2)	DMF[b]	0 °C, 3 h	0
13	$AlEt_3$ (1.2)	DMF[b]	0 °C, 3 h	0
14	$HSiMe_2Ph$ (1.2)	DMF[b]	0 °C, 3 h	0

[a] 0.1 M concentration. NMP = 1-methylpyrrolidin-2-one. [b] 0.2 M concentration. [c] Yield of isolated product.

With the optimized reaction conditions (Table 1, entry 11), the scope of the styrene derivatives was investigated (Table 2). Relative to that obtained with *o*-CF_3-substituted styrene **1a**, the same electron-withdrawing CF_3 substituent in the *para* position with less steric hindrance led to a higher yield of **2b** (54 %). Moreover, similar electron-withdrawing ester and ketone substituents in the *para* position enhanced the reactivity to give products **2c**–**e** and **2g**–**i** in high yields, except for **2f** with a sterically more demanding *tert*-butyl group. A styrene derivative with an amide substituent also underwent the reaction, whereas the yield of **2j** was moderate. Similar to **2a**, electron-withdrawing ester and ketone substituents in the *ortho* position led to a decrease in the yields of **2k**–**o**. Unfortunately, electron-donating substituents such as methoxy and *tert*-butyl groups significantly retarded the carboxylation reaction (see substrates **1p**–**r**). Electron-neutral styrene **1s** and heteroaromatic 2-vinylpyridine **1t** also gave no products.

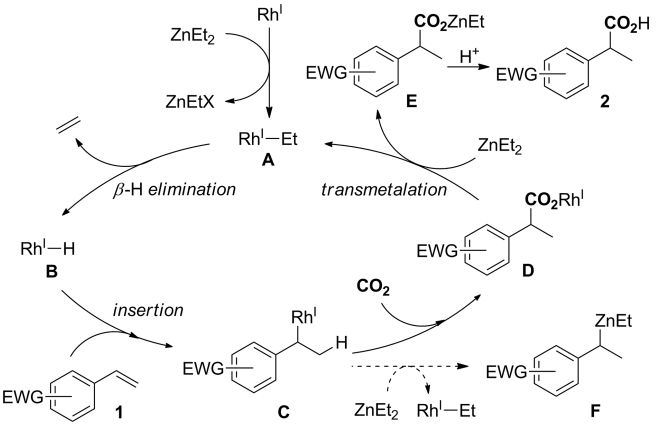
A plausible reaction mechanism is visualized in Scheme 2; we suggest intervention of the Rh^I–H species in this catalytic process. Transmetalation of the ethyl group between $[RhCl(cod)]_2$ and diethylzinc produces Rh^I–Et species **A**, which undergoes β-hydride elimination to generate active Rh^I–H species **B**. Insertion of the styrene derivative into Rh^I–H species **B** leads to σ-benzyl rhodium complex **C**,[11] which has high enough nucleophilicity for carbon dioxide to give carboxylated rhodium complex **D**. Finally, transmetalation between **D** and diethylzinc gives carboxylated zinc complex **E**, and Rh^I–Et species **A** is reformed at the same time. During the course of the

Table 2. Screening of styrene derivatives.[a]



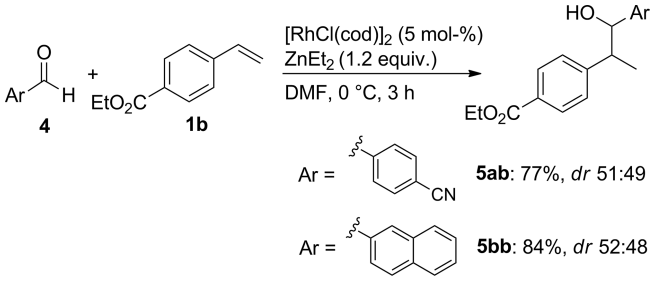
[a] Yields of isolated products are given. [b] $ZnEt_2$ (0.7 equiv.) was used.

investigation of **1r** as shown in Table 2, we confirmed that reduction product **3r** was obtained in up to 15 % yield. This result implies that benzylic zinc complex **F** would be generated by transmetalation between rhodium complex **C** and diethylzinc, whereas transmetalation back can be involved between **F** and a rhodium species. On the other hand, Rovis and co-workers already reported that combination of a naphthylmethylzinc reagent and carbon dioxide (1 atm) cannot undergo the carboxylation in THF at 23 °C.[5,12]



Scheme 2. Plausible reaction mechanism.

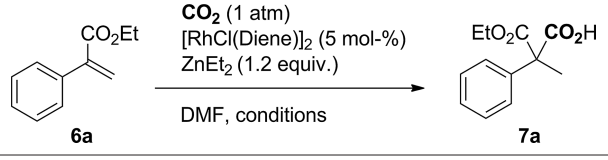
To support the generation of rhodium complex **C** in the catalytic cycle, aldehydes were examined rather than less-reactive carbon dioxide (Scheme 3).[13] As expected, reductive aldol-type products **5ab** and **5bb** were obtained in good yields under the reaction conditions with aldehydes **4** instead of carbon dioxide, despite low diastereoselectivities.



Scheme 3. Rh-catalyzed reductive aldol reaction.

Next, α,β-unsaturated carbonyl compounds were employed as a better hydride acceptor rather than the styrene derivatives (Table 3). The rhodium-catalyzed hydrocarboxylation of unsaturated ester **6a** gave a quantitative yield of desired product **7a** in DMF at 0 °C (Table 3, entries 1 and 2). The use of a substoichiometric amount of diethylzinc (0.7 equiv.) decreased the yield of **7a** to 66 % (Table 3, entry 1). The rhodium catalyst was also confirmed to be essential for the catalytic reaction (Table 3, entry 2). In addition, we examined other ligands such as norbornadiene (nbd) and ethylene; however, they only provided low to moderate yields of **7a** (Table 3, entries 3 and 4). The reaction did not proceed at –40 °C, but at –20 °C lower yields of **7a** were afforded (Table 3, entries 5–7). The optimized reaction temperature was thus set at 0 °C to give a quantitative yield of **7a**.

Table 3. Rh-catalyzed hydrocarboxylation of α,β-unsaturated carbonyl compound.

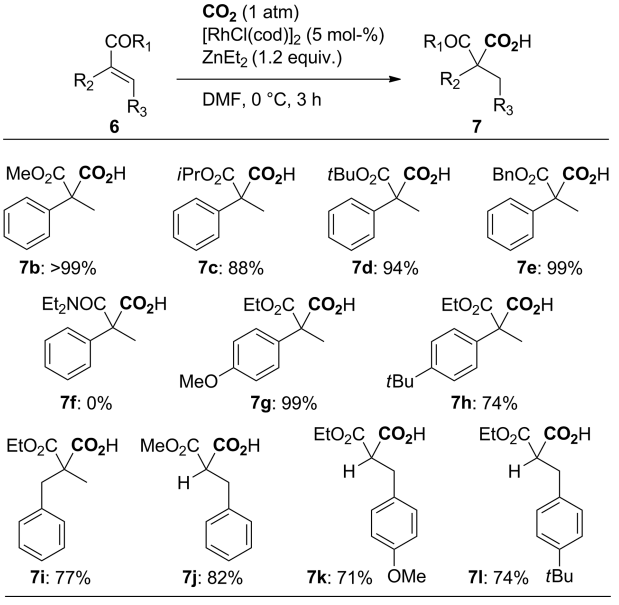


Entry	Diene	Conditions	Yield [%][a]
1	cod	0 °C, 3 h	>99 (66)[b]
2	cod	0 °C, 30 min	>99 (0)[c]
3	nbd	0 °C, 30 min	51
4	2 $H_2C=CH_2$	0 °C, 30 min	27
5	cod	–40 °C, 30 min	0
6	cod	–20 °C, 30 min	50
7	cod	–20 °C, 3 h	53

[a] Yield of isolated product. [b] $ZnEt_2$ (0.7 equiv.) was used. [c] Reaction was performed without $[RhCl(cod)]_2$.

The substrate scope of α,β-unsaturated carbonyls **6** was then screened (Table 4). α,β-Unsaturated esters bearing Me, *i*Pr, *t*Bu, and benzyl (Bn) substituents provided high yields, independent of steric hindrance (see products **7b**–**e**). However, α,β-unsaturated amides did not undergo the reaction. In sharp contrast to the styrene system, even with electron-donating substituents in the aromatic rings, the hydrocarboxylated products were obtained in good to high yields (see products **7g**–**h**). A benzyl substituent instead of a phenyl one was also employed to give product **7i** in 77 % yield. Even β-substituted esters provided good yields, irrespective of the electron-donating substituents in the aromatic rings (see products **7j**–**l**).

Table 4. Screening of α,β-unsaturated carbonyl compounds.[a]

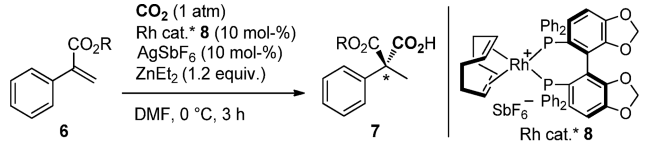


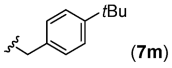
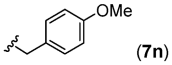
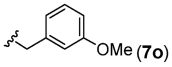
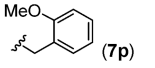
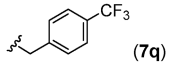
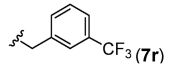
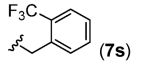
[a] Yield of isolated product.

The asymmetric catalysis of the present hydrocarboxylation of α,β-unsaturated esters with carbon dioxide was the final challenge in this project (Table 5). Various chiral phosphine and diene ligands were investigated, and cationic rhodium catalysts bearing bidentate triarylphosphine ligands such as 4,4′-bi-1,3-benzodioxole-5,5′-diylbis(diphenylphosphine) (SEGPHOS) were found to be efficient for this catalytic asymmetric system.[14] Moreover, the combination of (*S*)-SEGPHOS–Rh complex **8** and a catalytic amount of $AgSbF_6$ provided better and reproducible results (41 %, 50 % *ee*), than without $AgSbF_6$ (25 %, 42 % *ee*) (Table 5, entry 1 vs. 2). The effect of $AgSbF_6$ is currently under investigation. In view of the electronic effects of benzyl substituents, the electron-withdrawing CF_3 substituent provided higher yields than the electron-donating MeO substituent (Table 5, entries 8–10 vs. 11–13). Interestingly, the electron-donating MeO substituent constantly gave 60 % *ee*, irrespective of the position of the substituent (Table 5, entries 8–10). In sharp contrast, the electron-withdrawing CF_3 substituent afforded higher enantioselectivities, particularly at a position closer to the reaction center, namely, the *ortho* position (Table 5, entries 11–13).

On the basis of the absolute configuration of product **7b**,[14] a plausible model for the asymmetric induction can be proposed (Figure 1).[15,16] The corresponding (*Z*)-Rh^I–enolate is generated by insertion into the Rh^I–H species of the α,β-unsaturated esters in an *s-trans* fashion.[15a] Attack of the enolate to carbon dioxide by the *Si* face is prevented by the equatorial phenyl group on the phosphorus atom. Consequently, attack from the *Re* face of the rhodium side would be favored to afford the corresponding product (*S*)-**7**.

Table 5. Rh-catalyzed asymmetric hydrocarboxylation.



Entry	R	Yield (%)[b]	*ee* (%)
1[a]	Bn (**7e**)	25	42
2	Bn (**7e**)	41	50
3	Me (**7b**)	59	60
4	Et (**7a**)	46	66
5	*i*Pr (**7c**)	29	64
6	*t*Bu (**7d**)	14	50
7	 (**7m**)	60 (79)[c]	66
8	 (**7n**)	41 (86)[c]	60
9	 (**7o**)	53 (93)[c]	60
10	 (**7p**)	37 (75)[c]	60
11	 (**7q**)	67 (76)[c]	46
12	 (**7r**)	69 (74)[c]	52
13	 (**7s**)	64 (86)[c]	60

[a] Reaction was performed without $AgSbF_6$. [b] Yield of isolated product. [c] $[RhCl(cod)]_2$ (5 mol-%) was used instead of Rh cat.* **8**/$AgSbF_6$.

Conclusions

The catalytic hydrocarboxylation of olefins, such as styrene derivatives and α,β-unsaturated carbonyl compounds, with carbon dioxide (1 atm) was demonstrated. Only the combination of $[RhCl(cod)]_2$ as a catalyst and diethylzinc as a hydride source allowed effective hydrocarboxylation to provide the corresponding α-aryl carboxylic acids in moderate to excellent yields. In this catalytic process, we suggested intervention of the Rh^I–H species, which could be generated from a Rh^I complex and diethylzinc. Additionally, we also performed the catalytic asymmetric hydrocarboxylation of α,β-unsaturated esters with carbon dioxide by employing a chiral cationic rhodium complex, despite moderate enantioselectivities. The development of novel catalytic asymmetric reactions with carbon dioxide is ongoing in our laboratory.

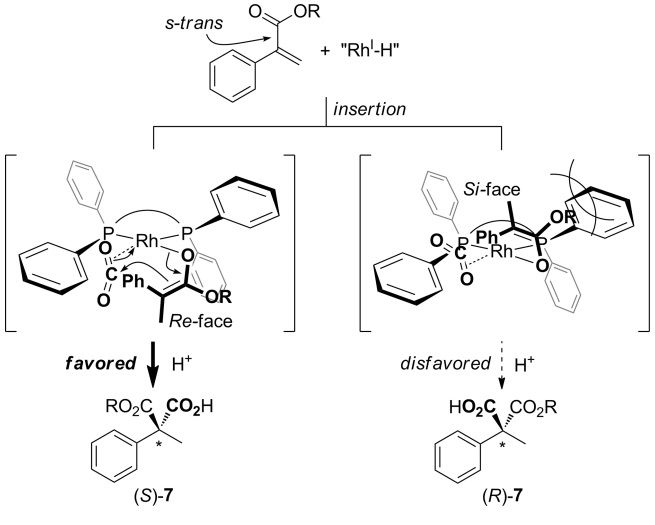


Figure 1. Plausible model for asymmetric induction.

Acknowledgments

This research was supported by the Japan Science and Technology Agency (JST) (ACT-C: Advanced Catalytic Transformation Program for Carbon utilization). The authors thank Takasago International Co. for a gift of (*S*)-SEGPHOS.

Keywords: Asymmetric catalysis · Hydrocarboxylation · Rhodium · Hydrides · Carboxylic acids

[1] For recent reviews of carbon dioxide fixation, see: a) T. Sakakura, J.-C. Choi, H. Yasuda, *Chem. Rev.* **2007**, *107*, 2365; b) S. N. Riduan, Y. Zhang, *Dalton Trans.* **2010**, *39*, 3347; c) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Hermann, F. E. Kühn, *Angew. Chem. Int. Ed.* **2011**, *50*, 8510; *Angew. Chem.* **2011**, *123*, 8662; d) Y. Tsuji, T. Fujihara, *Chem. Commun.* **2012**, *48*, 9956; e) I. Omae, *Coord. Chem. Rev.* **2012**, *256*, 1384.

[2] For selected recent reports, see: a) T. Fujihara, K. Nogi, T. Xu, J. Terao, Y. Tsuji, *J. Am. Chem. Soc.* **2012**, *134*, 9106; b) T. León, A. Correa, R. Martin, *J. Am. Chem. Soc.* **2013**, *135*, 1221; c) K. Sasano, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2013**, *135*, 10954; d) T. G. Ostapowicz, M. Schmitz, M. Krystof, J. Klankermayer, W. Leitner, *Angew. Chem. Int. Ed.* **2013**, *52*, 12119; *Angew. Chem.* **2013**, *125*, 12341; e) A. Correa, T. León, R. Martin, *J. Am. Chem. Soc.* **2014**, *136*, 1062; f) T. Fujihara, Y. Horimoto, T. Mizoe, F. B. Sayyed, Y. Tani, J. Terao, S. Sakaki, Y. Tsuji, *Org. Lett.* **2014**, *16*, 4960; g) Y. Liu, J. Cornella, R. Martin, *J. Am. Chem. Soc.* **2014**, *136*, 11212; h) T. Moragas, J. Cornella, R. Martin, *J. Am. Chem. Soc.* **2014**, *136*, 17702; i) K. Nogi, T. Fujihara, J. Terao, Y. Tsuji, *Chem. Commun.* **2014**, *50*, 13052; j) Y. Tani, T. Fujihara, J. Terao, Y. Tsuji, *J. Am. Chem. Soc.* **2014**, *136*, 17706; k) X. Wang, Y. Liu, R. Martin, *J. Am. Chem. Soc.* **2015**, *137*, 6467; l) X. Wang, M. Nakajima, R. Martin, *J. Am. Chem. Soc.* **2015**, *137*, 8924.

[3] J. K. Buer, *Inflammopharmacology* **2014**, *22*, 263.

[4] a) B. D. Strooper, G. König, *Nature* **2001**, *414*, 159; b) S. Weggen, J. L. Eriksen, P. Das, S. A. Sagi, R. Wang, C. U. Pietrzik, K. A. Findlay, T. E. Smith, M. P. Murphy, T. Bulter, D. E. Kang, N. Marquez-Sterling, T. E. Golde, E. H. Koo, *Nature* **2001**, *414*, 212; c) T. Jonsson, J. K. Atwal, S. Steinberg, J. Snaedal, P. V. Jonsson, S. Bjornsson, H. Stefansson, P. Sulem, D. Gudbjartsson, J. Maloney, K. Hoyte, A. Gustafson, Y. Liu, Y. Lu, T. Bhangale, R. R. Graham, J. Huttenlocher, G. Bjornsdottir, O. A. Andreassen, E. G. Jönsson, A. Palotie, T. W. Behrens, O. T. Magnusson, A. Kong, U. Thorsteinsdottir, R. J. Watts, K. Stefansson, *Nature* **2012**, *488*, 96.

[5] C. M. Williams, J. B. Johnson, T. Rovis, *J. Am. Chem. Soc.* **2008**, *130*, 14936.

[6] The Ni-mediated stoichiometric fixation of carbon dioxide: a) G. Burkhart, H. Hoberg, *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 76; *Angew. Chem.* **1982**, *94*, 75; b) H. Hoberg, Y. Peres, C. Krüger, Y.-H. Tsay, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 771; *Angew. Chem.* **1987**, *99*, 799.

[7] M. D. Greenhalgh, S. P. Thomas, *J. Am. Chem. Soc.* **2012**, *134*, 11900.

[8] a) C. Hayashi, T. Hayashi, T. Yamada, *Bull. Chem. Soc. Jpn.* **2015**, *88*, 862; b) C. Hayashi, T. Hayashi, S. Kikuchi, T. Yamada, *Chem. Lett.* **2014**, *43*, 565.

[9] M. Takimoto, Y. Nakamura, K. Kimura, M. Mori, *J. Am. Chem. Soc.* **2004**, *126*, 5956.

[10] For examples of the Rh-catalyzed direct carboxylation of arenes with carbon dioxide, see: a) H. Mizuno, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2011**, *133*, 1251; b) T. Suga, H. Mizuno, J. Takaya, N. Iwasawa, *Chem. Commun.* **2014**, *50*, 14360.

[11] There is a possibility that a π-benzyl rhodium complex is generated, for a review, see: B. M. Trost, L. Czabaniuk, *Angew. Chem. Int. Ed.* **2014**, *53*, 2826; *Angew. Chem.* **2014**, *126*, 2868, and references cited therein.

[12] A variety of functionalized organozinc reagents can undergo the addition reaction to carbon dioxide in the presence of stoichiometric amounts of $MgCl_2$ at room temperature, see: a) S. Bernhardt, A. Metzger, P. Knochel, *Synthesis* **2010**, 3802; b) A. Metzger, S. Bernhardt, G. Manolikakes, P. Knochel, *Angew. Chem. Int. Ed.* **2010**, *49*, 4665; *Angew. Chem.* **2010**, *122*, 4769.

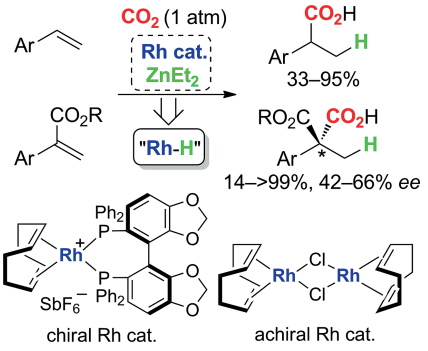
[13] a) S. J. Taylor, J. P. Morken, *J. Am. Chem. Soc.* **1999**, *121*, 12202; b) S. J. Taylor, M. O. Duffey, J. P. Morken, *J. Am. Chem. Soc.* **2000**, *122*, 4528; c) A. E. Russell, N. O. Fuller, S. J. Taylor, P. Aurriset, J. P. Morken, *Org. Lett.* **2004**, *6*, 2309.

[14] See the Supporting Information.

[15] a) H. Nishiyama, T. Shiomi, Y. Tsuchiya, I. Matsuda, *J. Am. Chem. Soc.* **2005**, *127*, 6972; b) Y. Motoyama, Y. Koga, K. Kobayashi, K. Aoki, H. Nishiyama, *Chem. Eur. J.* **2002**, *8*, 2968.

[16] T. Hayashi, M. Takahashi, Y. Takaya, M. Ogasawara, *J. Am. Chem. Soc.* **2002**, *124*, 5052.

Received: March 18, 2016
Published Online: ■



The Rh-catalyzed hydrocarboxylation of styrene derivatives and α,β-unsaturated carbonyl compounds with CO_2 is shown. The use of $[RhCl(cod)]_2$ (cod = cyclooctadiene) as a catalyst and diethylzinc as a hydride source provides the corresponding α-aryl carboxylic acids in moderate to excellent yields. Additionally, this catalyst system can be used in the asymmetric version of this reaction.

DOI: 10.1002/ejoc.201600338