Asymmetric Bis(alkoxycarbonylation) Reaction of Terminal Olefins Catalyzed by Palladium in the Presence of Copper(I) Triflate and a Chiral Bioxazoline Ligand

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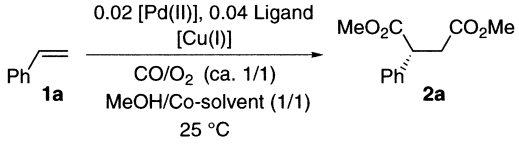
A palladium-catalyzed asymmetric bis(alkoxycarbonylation) reaction of terminal olefins in the presence of copper(I) triflate was achieved by using a chiral bioxazoline ligand, (4*S*,4′*S*)-4,4′-dibenzyl-4,4′,5,5′-tetrahydro-2,2′-bioxazole, under normal pressure of carbon monoxide and oxygen at 25 °C to give the corresponding optically active mono-substituted succinates with enantioselectivity up to 66% ee.

An asymmetric carbonylation reaction of olefins catalyzed by transition metals provides one of the most efficient methods to produce optically active carbonyl compounds, which are very important synthons for biologically active compounds. There have been intensive researches on the asymmetric monocarbonylation of prochiral olefins, that is, hydroformylation,[1] hydrocarboxylation,[2] hydro(alkoxycabonylation),[3] and carbonyl-copolymerization.[4] To the contrary, a limited number of the asymmetric biscarbonylation was reported. The palladium-catalyzed carbonylation reaction of styrene using atropisomeric diphosphanes gave the optically active dimethyl phenysuccinate along with oligomers containing two terminal methoxycarbonyl groups.[5a] Bis(alkoxycabonylation) of styrene in the presence of Chiraphos sulfide was also reported to proceed with low enantioselectivity.[5b] Thus, the asymmetric biscarbonylation of olefins is still regarded as one of the challenging problems in asymmetric carbonylation.

We have already reported on selective mono- and bis(alkoxycarbonylation) reactions catalyzed by palladium in the presence of copper(II) or copper(I) chloride to prepare esters and γ-butyrolactones from terminal olefins and homoallylic alcohols, respectively.[6,7] Furthermore, the asymmetric intra- and intermolecular bis(alkoxycarbonylation) of homoallylic alcohols catalyzed by palladium(II) and copper(I) salts was developed to afford the corresponding optically active γ-butyrolactones.[8] Herein, we wish to report on the bis(alkoxycarbonylation) reaction of terminal olefins catalyzed by palladium(II) and copper(I) salts under normal pressure of carbon monoxide and oxygen atmosphere to afford the corresponding optically active mono-substituted succinates.

First, a bis(alkoxycarbonylation) of styrene (**1a**) was examined on a combination of the palladium(II) and copper(I) salts in the presence of (4*S*,4′*S*)-4,4′-dibenzyl-4,4′,5,5′-tetrahydro-2,2′-bioxazole (**3A**) under a carbon monoxide and oxygen (ca. 1/1, v/v, 1 atm) atmosphere in MeOH at 25 °C (Eq. 1). A reaction using a 0.02 molar amount of $PdCl_2$ and 1.5 molar amounts of CuCl gave dimethyl phenylsuccinate (**2a**) in 42% yield. The optical yield of the obtained diester **2a** was determined to be 16% ee by a HPLC analysis (Entry 1 in Table 1). When allylpalladium chloride dimer was used instead of $PdCl_2$, the stereoselectivity was scarcely changed (Entry 2). To our disappointment, the carbonylation reaction utilizing $CuOTf(C_6H_6)_{0.5}$ instead of CuCl on combination with allylpalladium chloride dimer, by which the best result was realized in the asymmetric bis(alkoxycarbonylation) reaction of homoallylic alcohols,[8] did not proceed (Entry 3). It was found that the combination of $PdCl_2$ and a 0.5 molar amount of $CuOTf(C_6H_6)_{0.5}$ afforded **2a** with enhanced enantioselectivity of 64% ee (Entry 4). Using a 1.0 molar amount of $CuOTf(C_6H_6)_{0.5}$ decreased the chemical yield (Entry 5). In the present bis(alkoxycarbonylation), a small amount of methyl cinnamate was produced accompanied by **2a**; for example, 10% yield in the case of Entry 4.



(1)

Next, several other bioxazolines, **3B-D** and *ent*-**3E**, were used as chiral ligands for the bis(alkoxycarbonylation) reaction (Fig. 1). Although the carbonylation reactions proceeded,

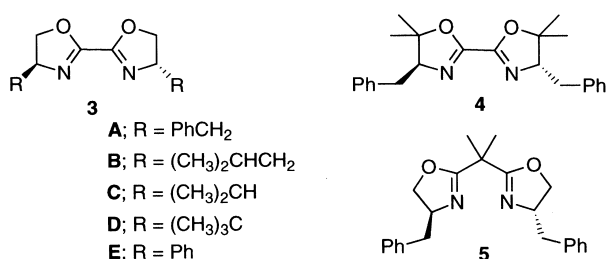


Fig. 1.

Table 1. Asymmetric Bis(alkoxycarbonylation) Reaction of Styrene (**1a**) under Various Conditions

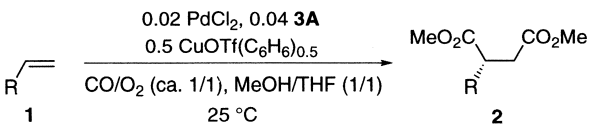
Entry	[Pd(II)]	[Cu(I)]	(Molar amounts)	Ligand	Co-solvent	Time/d	Yield of **2a**/%	ee/%[a]
1	$PdCl_2$	CuCl	1.5	**3A**	—	11	42	16
2	$(C_3H_5PdCl)_2$[b]	CuCl	1.5	**3A**	—	19	47	17
3	$(C_3H_5PdCl)_2$[b]	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	—	7	—	—
4	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	—	5	53	64
5	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	1.0	**3A**	—	7	41	64
6	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3B**	—	15	47	27
7	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3C**	—	3	27	48
8	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3D**	—	14	36	12
9	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	*ent*-**3E**[c]	—	7	35	42[d]
10	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**4**	—	4	51	41
11	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**5**	—	12	34	4
12	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	Et_2O	6	34	60
13	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	THF	6	73	66
14	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	DME	5	62	44
15	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	dioxane	5	67	60
16	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	CH_2Cl_2	5	64	40
17	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	$CHCl_3$	5	36	6
18	$PdCl_2$	$CuOTf(C_6H_6)_{0.5}$	0.5	**3A**	C_6H_6	5	57	20

a) Enantiomeric excess was determined by an HPLC analysis (Daicel Chiralcel OD-H). b) 0.01 molar amount of $(C_3H_5PdCl)_2$ was used. c) Enantiomer of **3E** was used ass a chiral ligand. d) (*S*)-Enantiomer was mainly obtained.

enantioselectivities were lower than that in the case of the benzyl substituted ligand **3A** (Entries 4, 6–9). The 5,5,5′,5′-tetramethyl substituted bioxazoline **4** appeared to be less selective than **3A** (Entry 10). By using a benzyl substituted bis(oxazoline) **5**, little enantioselectivity was realized (Entry 11).

Further, the effect of a co-solvent in MeOH was examined (Entries 4, 12–18). Although the optical yields were not significantly influenced by the co-solvent, except for $CHCl_3$ and benzene (Entries 17 and 18), the chemical yield was rather improved by using THF among the co-solvents examined (Entry 13).

Next, the bis(alkoxycarbonylation) reaction of several terminal olefins **1** was carried out by using a 0.02 molar amount of $PdCl_2$ and a 0.5 molar amount of $CuOTf(C_6H_6)_{0.5}$ in the presence of a 0.04 molar amount of bioxazoline **3A** under a carbon monoxide and oxygen (ca. 1/1, v/v, 1 atm) atmosphere in MeOH/THF (1/1, v/v) at 25 °C (Eq. 2). The results are summarized in Table 2. In the reaction of aromatic olefins **1b**, **c**, similar results to **1a** were obtained (Entries 1–3). Not only the aromatic olefins **1a–c**, but aliphatic terminal olefins **1d**, **e** could be the substrates of the bis(alkoxycarbonylation) (Entries 4 and 5).



(2)

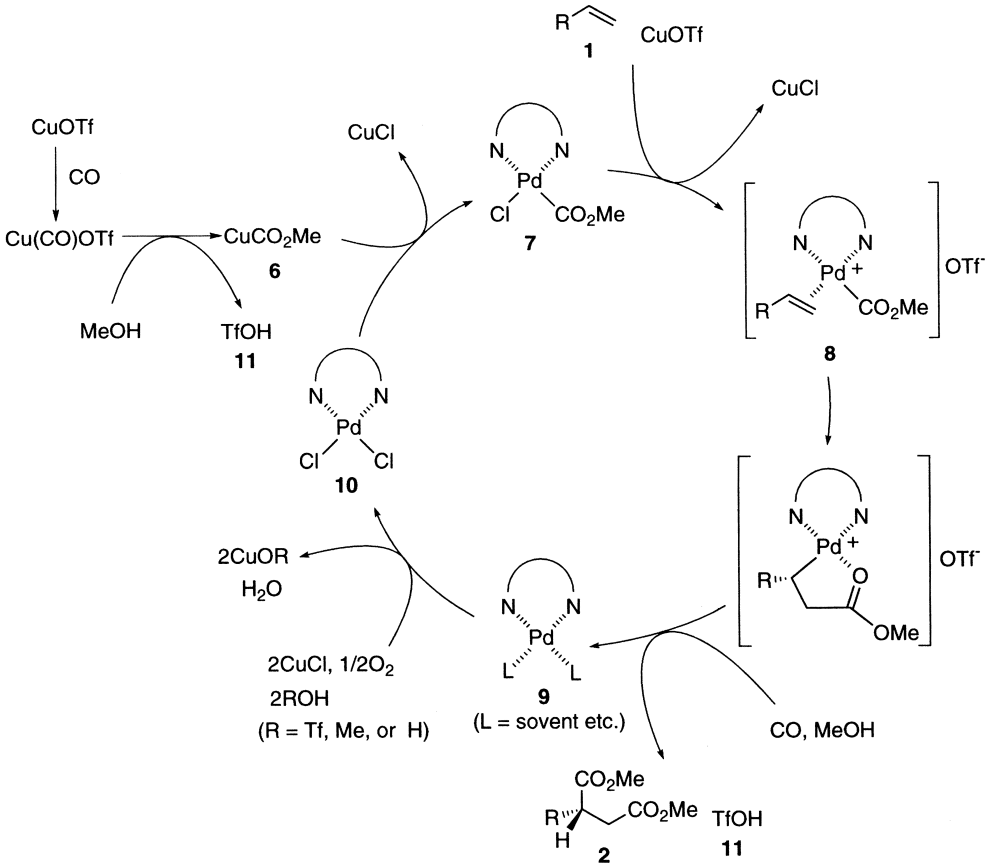
The absolute configurations of succinates **2a** and **2d** were determined to be *R* and *S*, respectively, by a comparison with the reported specific rotations,[9,10] which suggests that both carbonylations predominantly proceeded from a *re*-face of **1a** and **1d**. The absolute configurations of products **2b**, **2c** and **2e** were tentatively determined to be *R*, *R*, and *S*, respectively, based on the above fact.

Although the precise mechanism of the present reaction is still an open question, one possible reaction pathway is shown in Scheme 1. In the present carbonylation, copper might work not only as an oxidant, but also as a co-catalyst to generate active species.[11] That is, copper(I) triflate reacts with CO and MeOH successively to give the $CuCO_2Me$ species **6**,[12] and the methoxycarbonyl group was transferred to palladium chloride complex **10** with the chiral ligand **3** to generate complex **7**. Further, copper(I) triflate also reacts with **7** to afford a cationic palladium intermediate **8**, in which olefin can, strongly coordinate to the palladium metal. An attack of palladium upon internal carbon of the olefin (T_1 and T_2 in Fig. 2) might be more favorable than that on terminal carbon (T_3 and T_4 in Fig. 2) to avoid a direct repulsion between a substituent R in olefin and the methoxycarbonyl group. This was supported by the formation of methyl cinnamate as a side product in a reaction with styrene **2a** (R = Ph). Further, a steric hindrance between R and the substituent at C-4 of the bioxazoline ligand would disfavor the transition state T_1; thus, the transition state T_2 was most favored to produce an optically active mono-substituted succinate **2** along with palladium(0) complex **9**. Based on the

Table 2. Asymmetric Bis(alkoxycarbonylation) Reaction of Terminal Olefins **1**

Entry	**1**	R	Time/d	Yield of **2**/%	ee/%
1	**a**	Ph	6	73	66[a]
2	**b**	2-Np	11	43	64[a]
3	**c**	4-(*t*Bu)C_6H_4	8	74	60[a]
4	**d**	$PhCH_2$	16	35	59[a]
5	**e**	PhCH2CH_2	11	53	46[b]

a) Enantiometric excess was determined by an HPLC analysis (Daicel Chiralcel OD-H).
b) Enantiometric excess was determined by an HPLC analysis (Daicel Chiralcel OB-H).



Scheme 1.

fact that alkoxycarbonylation reaction of methyl cinnamate did not proceed under similar conditions, the pathway via α,β-unsaturated ester as an intermediate could be excluded. The palladium(II) catalyst **10** is regenerated by the oxidation of **9** by oxygen in the presence of copper(I) salt. During this oxidation step, copper(I) triflate might be partially produced again and recycled. By using a large amount of copper(I) triflate, liberated trifluoromethanesulfonic acid (**11**) might decompose the reactive palladium intermediate to decrease the chemical yield (Table 1, Entry 5). In the case of palladium complex with bis(oxazoline) ligand **5**, the 6-membered ring moiety consisting of palladium atom and bis(oxazoline) ligand **5** might adopt a distorted non-planar conformation in a transition state corresponding to **8**, in which the bis(oxazoline) ligand moiety is no longer C_2 symmetric.[13] Therefore, the carbonylation reaction using ligand **5** could proceed with little enantioselectivity.

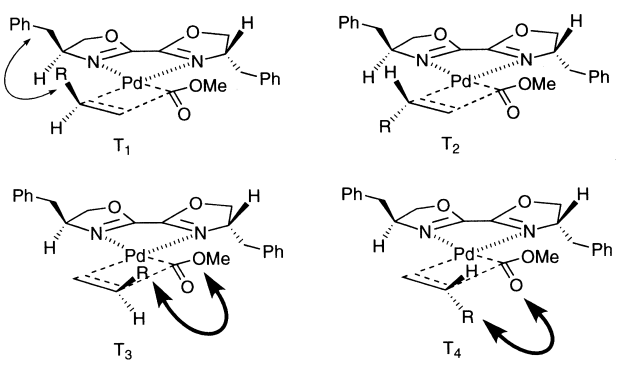


Fig. 2.

In summary, palladium-catalyzed asymmetric bis(alkoxycarbonylation) of terminal olefins was achieved utilizing the chiral bioxazoline ligand. This method provides a new entry for preparing optically active mono-substituted succinates.

Experimental

The melting point was determined with a micro melting apparatus (Yanagimoto-Seisakusho) and was uncorrected. The ^{1}H NMR spectra were recorded on a JEOL JNM-GX 400 or a JEOL Lambda 400 spectrometer with tetramethylsilane as an internal standard. The IR spectra were measured with a JASCO FT/IR-230 spectrometer. The MS spectra were measured with a Hitachi M-80, or a JMS-SX102A mass spectrometer. The specific optical rotations were recorded on a JASCO DIP-370 spectrometer. THF and Et_2O were freshly distilled from sodium diphenylketyl. All other solvents were distilled and stored over drying agents. Column chromatography and thin-layer chromatography (TLC) were performed on Wakogel C-300 and Merck's silica gel 60 PF_{254} (Art. 7749), respectively.

Chiral ligands **3**, **4** and **5** were prepared by the methods previously reported.[8,14]

The Representative Procedure of Asymmetric Bis(alkoxycarbonylation) for Styrene (1a): To a mixture of $PdCl_2$ (1.77 mg, 0.01 mmol), (4*S*,4′*S*)-4,4′-dibenzyl-4,4′,5,5′-tetrahydro-2,2′-bioxazole (**3A**) (6.44 mg, 0.02 mmol), and $CuOTf(C_6H_6)_{0.5}$ (63 mg, 0.25 mmol), a MeOH (2 mL) solution

of styrene (**1a**) (52 mg, 0.50 mmol) was added under an argon atmosphere, followed by the addition of THF (2 mL). The argon atmosphere was replaced with CO/O_2 (ca. 1/1, v/v) and the reaction mixture was stirred for 6 d at 25 °C. Sat. aqueous $NaHCO_3$ was added and the insoluble substance was filtered off through Celite. After the filtrate was extracted with ethyl acetate several times, the combined extracts were washed with water and brine, dried over Na_2SO_4, and condensed in vacuo. The residue was purified by TLC (SiO_2, hexane/ethyl acetate = 8/1, v/v) to give dimethyl (*R*)-phenylsuccinate (**2a**) (81 mg, 73%, 66% ee).

Dimethyl (*R*)-Phenylsuccinate (2a): Mp 54–55 °C (from hexane), (Ref. 15, 58–59 °C); $[\alpha]_D^{25}$ −95° (*c* 0.8, $CHCl_3$; 66% ee), (Ref. 9 (*S*)-isomer: $[\alpha]_D^{24}$ +50.7° (*c* 0.95, $CHCl_3$; 38% ee)); MS *m/z* (rel intensity) 222 (M^+, 1.26), 191 (17.10), 190 (68.59), 162 (88.14), 121 (100.00), 103 (39.33), 91 (17.15), 77 (25.95); IR (KBr) 3030, 2958, 1730, 1600, 1493, 1437, 1310, 1196, 1154, 997, 870, 728, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.67 (dd, J = 5.50, 17.09 Hz, 1H), 3.21 (dd, J = 10.07, 17.09 Hz, 1H), 3.67 (s, 3H), 3.68 (s, 3H), 4.09 (dd, J = 5.50, 10.07 Hz, 1H), 7.26–7.35 (m, 5H).

In a similar manner, other succinates **2b–e** were prepared from the corresponding olefins **1b–e**.

Dimethyl (*R*)-(2-Naphthyl)succinate (2b): An oil; $[\alpha]_D^{25}$ −95° (*c* 0.6, $CHCl_3$; 64% ee); MS *m/z* (rel intensity) 272 (M^+, 20.55), 240 (27.81), 212 (100.00), 182 (0.86), 171 (47.75), 153 (30.19), 128 (7.23); IR (neat) 3056, 2952, 1738, 1600, 1508, 1437, 1336, 1268, 1164, 1008, 861, 819, 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.77 (dd, J = 5.49, 17.09 Hz, 1H), 3.31 (dd, J = 10.07, 17.09 Hz, 1H), 3.68 (s, 3H), 3.69 (s, 3H), 4.27 (dd, J = 5.49, 10.07 Hz, 1H), 7.40 (dd, J = 1.83, 8.54 Hz, 1H), 7.45–7.51 (m, 2H), 7.74 (d, J = 1.83 Hz, 1H), 7.80–7.82 (m, 3H).

Dimethyl (*R*)-[4-(1,1-Dimethylethyl)phenyl]succinate (2c): An oil; $[\alpha]_D^{25}$ −64° (*c* 1.1, $CHCl_3$; 60% ee); MS *m/z* (rel intensity) 278 (M^+, 8.97), 263 (6.80), 246 (100.00), 231 (29.05), 218 (83.19), 203 (99.92), 177 (81.13), 145 (36.40), 117 (19.10), 91 (10.27); IR (neat) 2956, 1739, 1510, 1437, 1364, 1253, 1196, 1162, 1007, 849, 831 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (s, 9H), 2.65 (dd, J = 5.19, 17.09 Hz, 1H), 3.20 (dd, J = 10.38, 17.09 Hz, 1H), 3.68 (s, 6H), 4.07 (dd, J = 5.19, 10.38 Hz, 1H), 7.19 (d, J = 8.24 Hz, 2H), 7.34 (d, J = 8.24 Hz, 2H).

Dimethyl (*S*)-Benzylsuccinate (2d): An oil; $[\alpha]_D^{25}$ −18° (*c* 0.1, $CHCl_3$; 59% ee), (Ref. 10 (*S*)-isomer: $[\alpha]_D$ −27.3° (*c* 4.5, $CHCl_3$; > 98% ee)); MS *m/z* (rel intensity) 236 (M^+, 18.24), 204 (19.92), 176 (78.70), 163 (40.52), 145 (28.42), 131 (52.68), 117 (100.00), 91 (91.33); IR (neat) 3029, 2952, 1736, 1604, 1497, 1438, 1362, 1165, 1032, 1006, 746, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (dd, J = 4.89, 16.79 Hz, 1H), 2.68 (dd, J = 9.16, 16.79 Hz, 1H), 2.76 (dd, J = 8.22, 13.41 Hz, 1H), 3.05 (dd, J = 6.41, 13.41 Hz, 1H), 3.10–3.17 (m, 1H), 3.64 (s, 3H), 3.67 (s, 3H), 7.15 (d, J = 7.32 Hz, 2H), 7.20–7.32 (m, 3H).

Dimethyl (*S*)-(2-Phenylethyl)succinate (2e): An oil; $[\alpha]_D^{25}$ −10° (*c* 0.9, $CHCl_3$; 46% ee); MS *m/z* (rel intensity) 251 (M^++1, 5.36), 250 (M^+, 8.96), 187 (57.43), 146 (100.00), 144 (11.01), 117 (11.51), 114 (77.49), 104 (31.50), 91 (24.76); IR (neat) 3027, 2952, 1737, 1604, 1496, 1437, 1364, 1262, 751, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80–1.87 (m, 1H), 1.95–2.04 (m, 1H), 2.48 (dd, J = 5.18, 16.48 Hz, 1H), 2.61–2.67 (m, 2H), 2.76 (dd, J = 9.15, 16.48 Hz, 1H), 2.88 (m, 1H), 3.67 (s, 3H), 3.71 (s, 3H), 7.16–7.21 (m, 3H), 7.26-7.30 (m, 2H).

References

1 K. Nozaki, F. Shibahara, and T. Hiyama, *Chem. Lett.*, **2000**, 694; K. Nozaki, N. Sakai, T. Nanno, T. Higashijima, S. Mano, T. Horiuchi, and H. Takaya, *J. Am. Chem. Soc.*, **119**, 4413 (1997); F. Agbossou, J.-F. Carpentier, and A. Mortreux, *Chem. Rev.*, **95**, 2485 (1995); S. Gladiali, J. C. Bayón, and C. Claver, *Tetrahedron: Asymmetry*, **6**, 1453 (1995), and references cited therein.

2 H. Alper and N. Hamel, *J. Am. Chem. Soc.*, **112**, 2803 (1990).

3 P. Cao and X. Zhang, *J. Am. Chem. Soc.*, **121**, 7708 (1999); W.-Y. Yu, C. Bensimon, and H. Alper, *Chem. Eur. J.*, **3**, 417 (1997); H. Alper and N. Hamel, *J. Chem. Soc., Chem. Commun.*, **1990**, 135.

4 K. Nozaki, N. Sato, Y. Tonomura, M. Yasutomi, H. Takaya, T. Hiyama, T. Matsubara, and N. Koga, *J. Am. Chem. Soc.*, **119**, 12779 (1997); Z. Jiang and A. Sen, *J. Am. Chem. Soc.*, **117**, 4455 (1995); M. Brookhart, M. I. Wagner, G. G. A. Balavoine, and H. A. Haddou, *J. Am. Chem. Soc.*, **116**, 3641 (1994), and references cited therein.

5 a) S. C. A. Nefkens, M. Sperrle, and G. Consiglio, *Angew. Chem., Int. Ed. Engl.*, **32**, 1719 (1993). b) M. Hayashi, H. Takezaki, Y. Hashimoto, K. Takaoki, and K. Saigo, *Tetrahedron Lett.*, **39**, 7529 (1998).

6 K. Inomata, S. Toda, and H. Kinoshita, *Chem. Lett.*, **1990**, 1567; S. Toda, M. Miyamoto, H. Kinoshita, and K. Inomata, *Bull. Chem. Soc. Jpn.*, **64**, 3600 (1991).

7 Related intra- and intermolecular bis(alkoxycarbonylation): Y. Tamaru, M. Hojo, and Z. Yoshida, *J. Org. Chem.*, **56**, 1099 (1991).

8 Y. Ukaji, M. Miyamoto, M. Mikuni, S. Takeuchi, and K. Inomata, *Bull. Chem. Soc. Jpn.*, **69**, 735 (1996).

9 **2a**: J. Lehmann and G. C. Lloyd-Jones, *Tetrahedron*, **51**, 8863 (1995).

10 **2d**: E. Guibé-Jampel, G. Rousseau, and J. Salaün, *J. Chem. Soc., Chem. Commun.*, **1987**, 1080.

11 In the O_2 oxidation reaction of olefins catalyzed by palladium–copper systems, it has been proposed that copper works not as an oxidant of palladium but as co-catalyst cooperated with palladium to generate active species: T. Hosokawa and S.-I. Murahashi, *Acc. Chem. Res.*, **23**, 49 (1990).

12 Copper(I) compounds is well-known to absorb carbon monoxide to generate carbonyl complexes. Furthermore, carbonylation reactions of alcohols, amines, and water have been known to be catalyzed by Group 11 metals, in which alkoxycarbonyl-, carbamoyl-, and carboxyl-metal species are supposed as intermediates, respectively.[16] Thus, the $CuCO_2Me$ species might be a possible intermediate in the present reaction.

13 The distortion from planarity in the (1,3-diphenylallyl)palladium complex with the ligand *ent*-**5** was reported: M. Zehnder, M. Neuburger, P. von Matt, and A. Pfaltz, *Acta Crystallogr., Sect. C*, **C51**, 1109 (1995).

14 D. Müller, G. Umbricht, B. Weber, and A. Pfaltz, *Helv. Chim. Acta*, **74**, 232 (1991); U. Leutenegger, G. Umbricht, C. Fahrni, P. Matt, and A. Pfaltz, *Tetrahedron*, **48**, 2143 (1992); A. Pfaltz, *Acc. Chem. Res.*, **26**, 339 (1993).

15 D. E. James and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 1810 (1976).

16 M. I. Bruce, *J. Organometal. Chem.*, **44**, 209 (1972).