Synthesis of an Axially Dissymmetric Biphenylcarboxylate Ligand, BDME, and Asymmetric Cyclopropanation of Olefins with Diazoacetate Catalyzed by Its Dirhodium(II) Complex[1]

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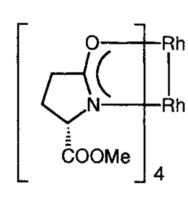
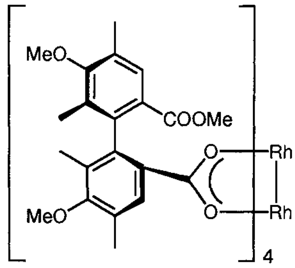
Abstract: An axially dissymmetric biphenylcarboxylate ligand, BDME (**4**), has been newly designed and prepared. The dirhodium(II) complex (**1**) of (**4**) proved to be an excellent catalyst in asymmetric cyclopropanation of styrene with *d*-menthyl diazoacetate affording *d*-menthyl *cis*- 2- phenyl-cyclopropane-1-carboxylate of 99% de.

Rhodium(II) carboxylates are widely acknowledged to be the most effective catalysts for metal carbene transformations of diazo compounds.[2] Comparison of enantiocontrol in metal-carbene reactions catalyzed by representatives of dirhodium(II) catalysts defines the structural features of chiral ligands that control their selectivity. Finally, comparative reactivity and selectivity data suggest the stereoelectronic and steric factors that contribute to the effectiveness of dirhodium(II) catalysts for highly enantioselective transformations. We have already demonstrated the steric and electronic effects of substrates and chiral rhodium catalysts in asymmetric cyclopropanation.[3] It was found that electron-rich catalysts were efficient for asymmetric cyclopropanation.



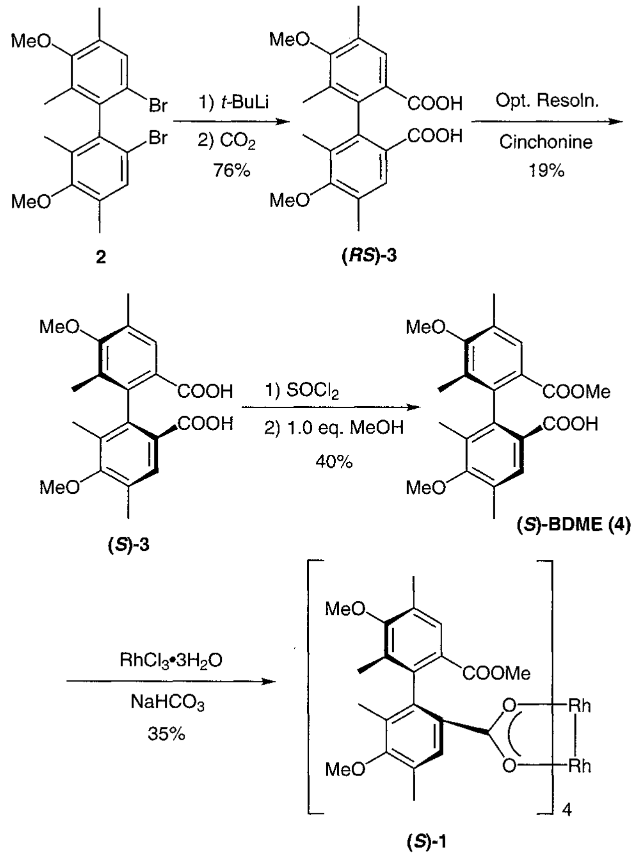
$Rh_2[(S)\text{-MEPY}]_4$



$Rh_2[(S)\text{-BDME}]_4$ (**1**)

6'-Methoxycarbonyl-3,3'-dimethoxy-2,2',4,4'-tetramethyl-1,1'-biphenyl-6-carboxylate (BDME) (**4**) has a biphenyl moiety and its asymmetric source is derived from the carbon (1)-carbon (1') axiality. The steric and electronic characteristics based on its skeleton are remarkably different from those of other chiral ligands. We anticipated that it was necessary to possess an axially dissymmetric biaryl skeleton for the ligand to be successfully applied for dirhodium(II)-catalyzed asymmetric cyclopropanation. Asymmetric cyclopropanations of several olefins with diazoacetates catalyzed by dirhodium(II) chiral carboxylate complexes have been reported by many groups[2] and these complexes are efficient catalysts for diastereoselective cyclopropanation, but low enantioselectivities were obtained. In this communication, we describe the preparation of dirhodium(II) tetrakis[6'-methoxycarbonyl-3,3'-dimethoxy-2,2',4,4'-tetramethyl-1,1'-biphenyl-6-carboxylate]; $Rh_2[(S)\text{-BDME}]_4$ (**1**) and the asymmetric cyclopropanation of olefins with diazoacetate catalyzed by the dirhodium(II) complex of optically pure (**1**).

Optically pure BDME was synthesized by the procedure shown in Scheme 1. After dilithiation of racemic dibromide **2**[4] in tetrahydrofuran at -70°C, carboxylation with dry ice furnished dicarboxylic acid (**3**). Optical resolution of the racemic **3** was achieved by using cinchonine as resolving agent. The optical purity of resolved **3** was determined to be 100% ee by HPLC analysis (Waters; Opti-Pac TP). The absolute configuration of optically pure **3** was determined to be *S* by comparison of its CD spectra with that of (*R*)-(-)-BIPHEMP[5] whose absolute configuration was previously determined by X-ray crystallography.



Scheme 1

BDME (**4**) was obtained by treatment with thionyl chloride followed by esterification of 1.0 equivalent MeOH.[6] The dirhodium(II)-BDME[7] complex was prepared by treating rhodium trichloride with **4** in EtOH and H_2O.[8] The structure of the complex was determined by ^{1}H-NMR and elemental analysis. Doyle reported a chiral carboxyamide ligand, the dirhodium(II) complex $Rh_2[(S)\text{-MEPY}]_4$,[9] which was revealed to be an efficient catalyst in the asymmetric cyclopropanation of several olefins with diazoacetates. Therefore we carried out the asymmetric cyclopropanation of olefins with diazoacetates catalyzed by $Rh_2[(S)\text{-BDME}]_4$ (**1**) and $Rh_2[(S)\text{-MEPY}]_4$ for comparison of the catalytic activity and enantioselectivity.

The typical experimental procedure was exemplified by the reaction of styrene and *t*-butyl diazoacetate using complex (**1**) as catalyst: A solution of *t*-butyl diazoacetate (0.6 mmol) in CH_2Cl_2 (1.6 ml) was added dropwise to a stirred mixture of styrene (0.6 ml, 5.8 mmol) and $Rh_2[(S)\text{-BDME}]_4$ (0.6×10^{-3} mmol) in dry CH_2Cl_2 (5 ml) under an argon atmosphere. The reaction mixture was stirred for 16 h, and then *cis*-decalin (4.2 mg) was added as an internal standard for GC analysis to determine the yield. The *cis/trans* isomer ratio was determined by capillary GC. The mixture was evaporated and the residue was purified by preparative TLC (silica gel, hexane:ether=10:1) to give *t*-butyl *trans*- and *cis*-2-phenyl cyclopropane-1-carboxylates. The extent of asymmetric induction and the absolute configuration were determined by the procedure reported in reference 10. Table 1 summarizes the result of asymmetric cyclopropanation of olefins with diazoacetates.

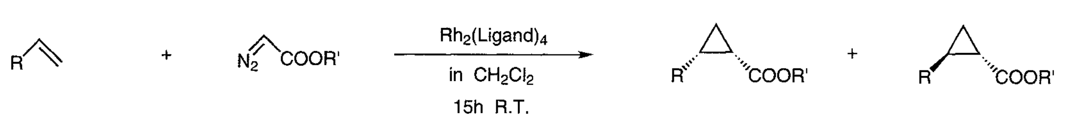


Table 1. Asymmetric Cyclopropanation of Olefins with Diazoacetates Catalyzed by $Rh_2[(S)\text{-BDME}]_4$ (**1**)

Entry	Ligand	[Catalyst]	R	R'	Yield[a]	*cis* / *trans*[b]	E.e. (*cis*)[c]	E.e. (*trans*)[c]	Config. (*cis*)[d]	Config. (*trans*)[d]
1	(*S*)-BDME	0.1 mol%	Ph	Et	98	69:31	53	57	1*S*,2*R*	1*S*,2*S*
2	(*S*)-MEPY	0.1 mol%	Ph	Et	trace					
3	(*S*)-MEPY	1.0 mol%	Ph	Et	32	41:59	37	54	1*S*,2*R*	1*S*,2*S*
4	(*S*)-BDME	0.1 mol%	Ph	*t*-Bu	80	69:31	62	57	1*S*,2*R*	1*S*,2*S*
5	(*S*)-MEPY	1.0 mol%	Ph	*t*-Bu	22	50:50	82	48	1*S*,2*R*	1*S*,2*S*
6	(*S*)-BDME	0.1 mol%	Naphthalen-2-yl	*t*-Bu	59	52:48	87	35	—	—
7	(*S*)-MEPY	1.0 mol%	Naphthalen-2-yl	*t*-Bu	8	48:52	81	84	—	—
8	(*S*)-BDME	0.1 mol%	Ph	*d*-Mentyl	100	63:37	99	45	1*S*,2*R*	1*S*,2*S*
9	(*S*)-MEPY	1.0 mol%	Ph	*d*-Mentyl	64	43:57	91	24	1*S*,2*R*	1*S*,2*S*

a) Yields were obtained by GC analysis using internal standard *cis*-decalin; b) by capillary GC; c) by GC, using Chirasil DEX-CB; d) see ref. 10 for the determination of absolute configuration of the products

Although the reaction catalyzed with $Rh_2[(S)\text{-BDME}]_4$ went to completion in the presence of 0.1 mol% of catalyst, it barely proceeded with $Rh_2[(S)\text{-MEPY}]_4$ (entry **1-3**). Another point to be mentioned is that $Rh_2[(S)\text{-BDME}]_4$ showed high *cis*-selectivity, differing from $Rh_2[(S)\text{-MEPY}]_4$ catalyzed cyclopropanation which showed opposite *trans*-selectivity. In addition, the *cis*-cyclopropanecarboxylate with up to 99% de could be obtained, when the *d*-menthyl group as chiral auxiliary was introduced.

Although the details of these reactions have still not been revealed, we are working under the assumption that metalla-cyclobutane intermediates are involved. Further investigations along this line are in progress, and application to asymmetric cyclopropanation catalyzed by this dirhodium(II) complex will be reported in the near future.

References and Notes

(1) Asymmetric Reactions Catalyzed by Chiral Metal Complexes. LXXVII.

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(6) (*S*)-BDME: ^1H-NMR ($CDCl_3$) δ: 7.63 (d, 2H, J=2.70 Hz), 3.73 (s, 6H), 3.67 (s, 3H), 2.36 (s, 6H), 1.80 (s, 6H); MS: m/z=372 (M^+); $[\alpha]_D^{25}$ -4.70 (*c* 1.27 $CHCl_3$).

(7) $Rh_2[(S)\text{-BDME}]_4$: ^1H-NMR ($CDCl_3$) δ: 7.72 (d, 2H, J=3.63 Hz), 3.74 (s, 6H), 3.61 (s, 3H), 2.25 (s, 6H), 1.62 (s, 6H); elemental analysis: C=59.57%; H=5.39% (calc. for $C_{84}H_{92}O_{24}Rh_2$; C=59.65%; H=5.48%).

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