New Chiral Ruthenium Bis(oxazolinyl)pyridine Catalyst. Efficient Asymmetric Cyclopropanation of Olefins with Diazoacetates

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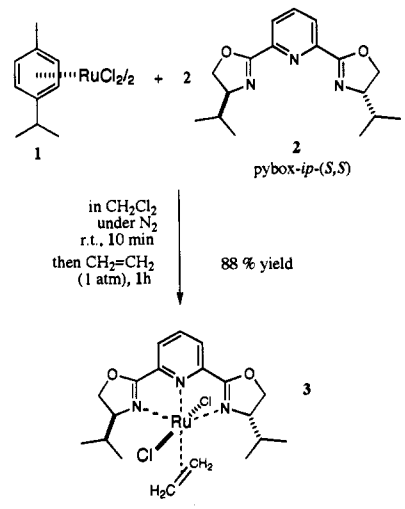
Cyclopropanation of olefins with diazoacetates has been one of the highlights of metal-catalyzed asymmetric synthesis in terms of both academic curiosities and industrial interests since Nozaki and co-workers initiated it about 30 years ago.[1] Its efficiency has recently been refined by chiral copper[2] and rhodium[3] catalysts with new auxiliaries. We report herein an asymmetric cyclopropanation of olefins and diazoacetates with a powerful new chiral ruthenium catalyst in combination with bis(oxazolinyl)pyridine (pybox), which was developed by us as a chiral ligand for the rhodium-catalyzed hydrosilylation.[4] The catalytic activities of several ruthenium complexes for cyclopropanation with diazoacetates were reported in the early 1980s and proved to be nearly comparable to or less than those of copper and rhodium catalysts.[5]

Scheme 1



We adopted $[Ru^{II}Cl_2(p\text{-cymene})]_2$ (**1**)[6] as a readily available and stable precursor. Addition of a chiral ligand pybox-ip-(*S,S*) (**2**)[4] to a solution of **1** in dichloromethane gave a dark red solution, which was stirred for 1 h at room temperature under ethylene atmosphere (1 atm) to give *trans*-Cl_2Ru(pybox-ip)($CH_2{=}CH_2$) (**3**) in 88% as a single product (Scheme 1).[7] The C_2-symmetrical structure of **3** was confirmed on the basis of its ^1H and ^{13}C NMR spectra. Similar *trans*-Cl_2Ru(pybox-ip)X complexes [X = CO and *t*-BuNC] were obtained by reaction with carbon monoxide (1 atm) and *tert*-butylisonitrile (1.2 equiv).[8] We thought that the dark red solution might contain an unsaturated coordination species Ru(pybox-ip)Cl_2 or Ru(pybox-ip)Cl_2(solv). We found that the dark red solution and the ethylene complex **3** could dimerize ethyl diazoacetate to produce a mixture of the corresponding maleate and the fumarate in high yields.[9] In this respect, Collman[9a] and Woo[9b] successfully isolated ruthenium– and osmium–carbene complexes of porphyrin derivatives by reaction with diazoacetates, respectively. However, we could not detect the corresponding ruthenium–carbene complex by ^1H NMR study.

Fortunately, we found that the dark red solution from **1** and **2** (2–4 equiv) as an *in situ* catalyst (Ru, 2 mol % to diazoacetate, *ton* = 50) (runs 1–5, Table 1) and also the Ru(pybox-ip)(ethylene) complex **3** (1–2 mol %) (runs 6–12) can catalyze the cyclopropanation of diazoacetates (3.0 mmol) and styrene (15 mmol) to give the corresponding 2-phenylcyclopropanecarboxylates, the *trans*-isomer **4**, and the *cis*-isomer **5**, in extremely high *trans–cis* selectivity (90:10–98:2) and high enantioselectivity up to 96–97% ee (1).[10] The *trans–cis* ratio (**4**/**5**) increased with the increase of bulkiness of the ester group (Me < Et < *t*-Bu ≅ Ment; Ment

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(7) **3** (88%, 0.29 mmol) with **1** (0.16 mmol) and **2** (0.33 mmol): dark red solids; mp 103–104 °C dec; ^1H NMR (270 MHz, $CDCl_3$, TMS) δ 0.78 (d, J = 6.8 Hz, 6 H), 1.01 (d, J = 7.3 Hz, 6 H), 2.47 (m, 2 H), 4.43 (m, 2 H, NC*H*), 4.82 (m, 2 H, *H* of OC*H*), 4.89 (m, 2 H, *H* of OC*H*), 4.94 (m, 2 H, ethylene), 5.26 (m, 2 H, ethylene), 7.89 (broad, 3 H); ^{13}C NMR (67.8 MHz, $CDCl_3$, TMS) δ 14.30 (q), 19.08 (q), 29.46 (d), 70.46 (d), 71.00 (t, O*C*-H_2), 71.68 (t, ethylene), 123.2 (d), 133.4 (d), 145.9 (s), 163.6 (s); EA CHN.

(8) *trans*-Cl_2Ru(pybox-ip)(CO), 92% yield. *trans*-Cl_2Ru(pybox-ip)(CN*t*-Bu), 81% yield. These complexes are air-stable and have no catalytic activity of dimerization and cyclopropanation below 40 °C.

(9) High ratios of the maleate and the fumarate were observed: total yield, ratio (N_2CHCO_2R): for R = Et, 83%, 73:27; for R = *i*-Pr, 93%, 78:22; for R = *t*-Bu, 83%, 92:8. Similar *cis*-selectivity with Ru- and Os-porphyrins, see: (a) Collman, J. P.; Rose, E.; Venburg, G. D. *J. Chem. Soc., Chem. Commun.* **1993**, 934–935. (b) Smith, D. A.; Reynolds, D. N.; Woo, L. K. *J. Am. Chem. Soc.* **1993**, *115*, 2511–2513. (c) Woo, L. K.; Smith, D. A. *Organometallics* **1992**, *11*, 2344–2346.

(10) The cyclopropanation of styrene and ethyl diazoacetate with Cu(I)-OTf$(C_6H_6)_{0.5}$ or $Rh(II)_2(OAc)_4$ in the presence of pybox-ip (4 equiv) gave moderate yields of **4** and **5** (ca. 7:3) but low enantioselectivity (<10% ees).

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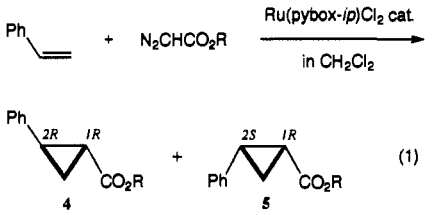
Table 1. Asymmetric Cyclopropanation of Styrene and Diazoacetates with Ru(pybox-ip) Catalysts[a]

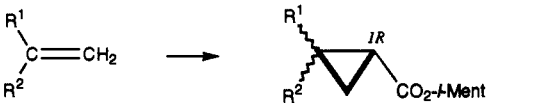
			product 4 (*trans*) and 5 (*cis*)			
					% ee	
run	catalyst	N_2CHCO_2R, R	yield (%)	ratio 4:5	4	5
1	**1** + **2**	Et[b]	69	92:8	88	78
2	**1** + **2**	Et[c]	66	92:8	89	75
3	**1** + **2**	*t*-Bu[c]	81	97:3	94	85
4	**1** + **2**	*d*-Ment[c]	85	95:5	86	95
5	**1** + **2**	*l*-Ment[c]	87	95:5	95	76
6	**3**	Me	74	90:10	88	70
7	**3**	Et	73	91:9	89	79
8	**3**	*t*-Bu	65	97:3	94	87
9	**3**	*d*-Ment	82	97:3	87	97
10	**3**	*l*-Ment	83	97:3	96	80
11	**3** + **2**	*l*-Ment[d]	84	98:2	96	84
12	**3**	*l*-Ment[e]	82	97:3	96	80

[a] Styrene (15 mmol), diazoacetate (3.0 mmol, ca. 1 N in CH_2Cl_2), catalyst **1** + **2**, $[RuCl_2(p\text{-cymene})]_2$ (**1**) (0.03 mmol) and pybox-ip (**2**) (2 or 4 equiv to Ru), catalyst **3**, *trans*-$RuCl_2$(pybox-ip)(C_2H_4) (0.06 mmol), CH_2Cl_2 (2 mL), 20–25 °C, ca. 8 h for addition of diazoacetate then stirring for 4–12 h. Isolated yields. The ratios are determined by ^{1}H NMR. The % ees are determined by chiral capillary GLPC (column, Astec B-DA, 30 m) with the corresponding methyl ester. Absolute configuration: (1*R*,2*R*) for **4**, (1*R*,2*S*) for **5**. [b] **2** (2 equiv to Ru). [c] **2** (4 equiv to Ru). [d] **2** (3 equiv to **3**). [e] **3** (0.03 mmol, *ton* = 100).

= menthyl) of diazoacetates.[11] It is noteworthy that the complex catalyst **3** gave high selectivities by itself with no complementary addition of pybox-ip, in comparison to the *in situ* system employed with an excess of pybox-ip. An extra addition of **2** (3 equiv) to **3** caused no significant improvement except a slight increase of the % ee of **5** (run 11). Moreover, the catalytic efficiency of **3** did not decrease even when 1 mol % of **3** (*ton* = 100) was used (run 12).[12]



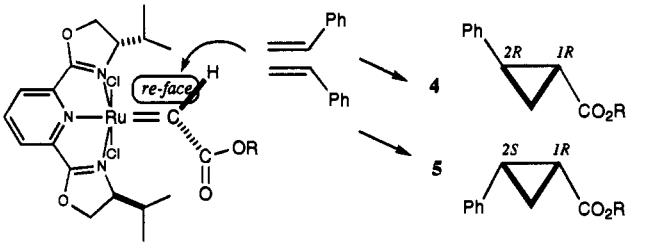
Other olefins such as 1-heptene (**6**), 1,1-diphenylethylene (**7**), and 4-methyl-1,3-pentadiene (**8**) were subjected to cyclopropanation with **3** and *l*-menthyl diazoacetate under the same condition as employed in run 10 of Table 1. We also obtained the corresponding *trans*- and *cis*-cyclopropane derivatives **9**–**11** in high % ees up to 99% (see Figure 1). However β-methylstyrene



olefin	product	R^1	R^2	yield (%)	ratio (*t*:*c*)	% ee *trans*	*cis*
6 →	**9**	n-C_5H_{11}	H	40	94:6	99	95
7 →	**10**	Ph	Ph	55	-	65	
8 →	**11**	Me_2C=CH-	H	86	79:21	98	79

Figure 1. Cyclopropanation of **6**, **7**, and **8** with **3** and *l*-menthyl diazoate under the conditions used for run 10 of Table 1.

Scheme 2



and 2,5-dimethyl-2,4-hexadiene could not be cyclopropanated in the same conditions.

The stereochemistry in the cyclopropane products resulting from use of PhHC=CHD can suggest whether the intermediary Ru–carbene species may transfer the carbene moiety to an olefin concertedly or via cationic process. We could not detect any loss of the stereochemistry in **4** and **5** with methyl diazoacetate.[13] The critical step of the prochiral face selection by styrene on the hypothetical ruthenium–carbene species is illustrated in Scheme 2. We assume that *trans*-Cl_2Ru(pybox-ip), having one vacant metal coordination site, may be a common active catalyst for the *in situ* system and the complex catalyst **3** in their catalytic cycles.

Thus we disclose a catalytic asymmetric cyclopropanation of olefins with diazoacetates by the new chiral ruthenium–pybox system. Further studies on the scope and limitations of its synthetic application and metal coordination chemistry are now under way.

Acknowledgment. H.N. acknowledges the Asahi Glass Foundation, and K.I. is grateful to the Ministry of Education, Science, and Culture of the Japanese government (Grant-in-Aid for Priority Areas 05236217) for financial support.

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(12) Other bulky substituents on pybox in place of the iso propyl group were examined. However *tert*-butyl- and phenylpybox[4b] gave poorer results in yields and % ees, in contrast to the *tert*-butyl substituents of the bidentate semicorrin[2a–c] and bisoxazolines.[2d–g]

(13) Products **4** and **5** (R = Me), 47% yield, 88:12, 89% ee and 74% ee. ^{1}H NMR: for the starting styrene, δ 5.23 (0.69 H, *trans*-H_β to Ph) and 5.74 (0.31 H, *cis*-H_β to Ph); for **4**, $H_{C(3)}$, δ 1.32 (0.31 ± 0.02 H) and 1.60 (0.69 ± 0.02 H); for **5**, $H_{C(3)}$, δ 1.45 (0.69 ± 0.02 H) and 1.71 (0.31 ± 0.02 H). For the mechanisms, see: (a) Brown, K. C.; Kodadek, T. *J. Am. Chem. Soc.* **1992**, *114*, 8336–8338. (b) Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53–61. (c) Brookhart, M.; Kegley, S. E.; Husk, G. R. *Organometallics* **1984**, *3*, 650–653. See also ref 1b,f and references cited therein.