Styrene Cyclopropanation and Ethyl Diazoacetate Dimerization Catalyzed by Ruthenium Complexes Containing Chiral Tridentate Phosphine Ligands

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Various five-coordinate ruthenium(II) complexes of the general formula $RuCl_2L$, where L is a chiral triphosphine ligand, have been tested as catalyst precursors for the cyclopropanation of styrene using ethyl diazoacetate (EDA) as the carbene source. Some of the complexes investigated have been found to catalyze the cyclopropanation reaction, but the conversions to cyclopropanes and the diastereoselectivities were generally poor. With all the catalyst precursors investigated, the dimerization of ethyl diazoacetate to diethyl maleate or diethyl fumarate largely prevailed over cyclopropanation. The best performance was obtained with the complex $RuCl_2$(ttp*) (**2**; ttp* = (*S*,*S*)-$PhP(CH_2CHMeCH_2PPh_2)_2$) which gave ca. 21% of cyclopropanes, 42% of olefins, and 1% of metathesis products. The highest enantiomeric excess was 35% for the (*Z*)-2-phenylcyclopropanecarboxylate. In the presence of silver triflate, **2** gave rise to a much more active and selective catalyst system, as the yield in cyclopropanation products increased up to 84%. Neither the regioselectivity nor the diastereoselectivity was appreciably improved, however. The carbene complexes $RuCl_2$(ttp*)(=$CHCO_2Et$) and $RuCl_2$(ttp)(=$CHCO_2Et$), where ttp is the achiral ligand $PhP(CH_2CH_2CH_2PPh_2)_2$, were isolated and characterized by multinuclear NMR spectroscopy. These carbene complexes were found to react with an excess of ethyl diazoacetate to give exclusively diethyl maleate and diethyl fumarate in a 95:5 ratio. The selective formation of cyclopropanation products was conversely observed upon reaction with styrene in the presence of silver triflate. In the absence of a chloride scavenger, cyclopropanes were still formed together with an appreciable amount of the metathesis product PhHC=$CHCO_2Et$.

Introduction

Asymmetric cyclopropanation reactions are attracting considerable attention due to the increasing demand for optically pure cyclopropanes.[1] Several methods have been developed for the asymmetric synthesis of cyclopropanes. One of the most efficient procedures involves the metal-catalyzed decomposition of diazoacetate derivatives in the presence of alkenes.[2] Among transition-metal catalysts, those containing copper, rhodium, and palladium have largely proved to be the most efficient in terms of both activity and chemo- or stereoselectivity.[2] Recently, however, some ruthenium-based catalysts have been developed for asymmetric cyclopropanation reactions.[3,4] In general, ruthenium catalysts exhibit excellent activity but may be less chemoselective than rhodium catalysts due to the formation of less electrophilic carbenoid species. The much lower cost of ruthenium as compared to rhodium and the remarkable tolerance of ruthenium catalysts to various organic functionalities, however, motivate the current interest in the design of ruthenium-based catalysts for the asymmetric cyclopropanation of alkenes, particularly when diazo compounds are utilized to produce the carbene moiety.

Excellent catalytic activity and stereoselectivity for cyclopropanation reactions have been observed for ruthenium complexes with either chiral tridentate bis-

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(1) (a) Reissig, H. U. *Top. Curr. Chem.* **1988**, *144*, 73. (b) Wong, H. N. C.; Hon, M. Y.; Tse, C. W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165.

(2) (a) Singh, V. K.; DattaGupta, A.; Sekar, G. *Synthesis* **1997**, 137. (b) Aratani, T. *Pure Appl. Chem.* **1985**, *57*, 1839. (c) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (d) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411. (e) Doyle, M. P. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 3, pp 63−99. (f) Davies, H. L. M. *Aldrichim. Acta* **1997**, *30*, 107. (g) Zhou, S. M.; Deng, M. Z.; Xia, L. J.; Tang, M. H. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2845.

(3) (a) Doyle, M. P.; Peterson, C. S.; Zhou, Q. L.; Nishiyama, H. *J. Chem. Soc., Chem. Commun.* **1997**, 211. (b) Park, S. B.; Sakata, N.; Nishiyama, H. *Chem. Eur. J.* **1996**, *2*, 303. (c) Nishiyama, H.; Aoki, K.; Itoh, H.; Iwamura, T.; Sakata, N.; Kurihara, O.; Motoyama, Y. *Chem. Lett.* **1996**, 1071. (d) Park, S. B.; Murata, K.; Matsumoto, H.; Nishiyama, H. *Tetrahedron: Asymmetry* **1995**, *6*, 2487. (e) Nishiyama, H.; Park S. B.; Itoh, K. *Chem. Lett.* **1995**, 599. (f) Nishiyama, H.; Itoh, Y.; Sugawara, Y.; Matsumoto, H.; Aoki, K.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1247. (g) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S. B.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223. (h) Park, S. B.; Nishiyama, H.; Itoh, Y.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1994**, 1315.

(4) (a) Galardon, E.; Le Maux, P.; Toupet, L.; Simonneaux, G. *Organometallics* **1998**, *17*, 565. (b) Galardon, E.; Le Maux, P.; Simonneaux, G. *J. Chem. Soc., Chem. Commun.* **1997**, 927. (c) Lo, W. C.; Che, C. M.; Cheng, K. F.; Mak, T. C. W. *J. Chem. Soc., Chem. Commun.* **1997**, 1205. (d) Frauenkron, M.; Berkessel, A. *Tetrahedon Lett.* **1997**, *38*, 7175.

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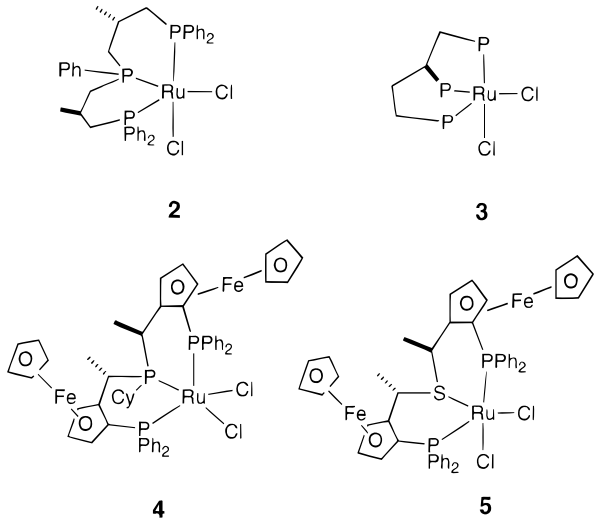
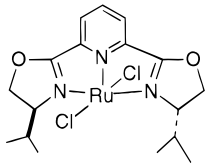
Chart 1



(oxazolinyl)pyridine ligands[3] or chiral porphyrin ligands.[4] In the reactions assisted by $RuCl_2$(pybox)(CH_2=CH_2) (pybox = bis(oxazolinyl)pyridine),[3d,f] the active catalyst is believed to be the five-coordinate species $RuCl_2$(pybox) (**1**).



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The high efficiency of the $RuCl_2$(pybox) system in inducing asymmetry and the fact that the tris(phosphine) dichloride complex $RuCl_2(PPh_3)_3$ is an effective cyclopropanation catalyst under mild reaction conditions[5] prompted us to investigate the catalytic activity of various dichlororuthenium complexes containing chiral tridentate phosphine ligands.

Herein, we report a study in which the Ru(II) chiral complexes illustrated in Chart 1 have been employed to mediate the carbene transfer from ethyl diazoacetate to styrene. Although the results are not as good as we expected, we are confident that the information obtained may contribute to expand the knowledge of the factors that govern the chemo- and diastereoselectivity of these industrially relevant reactions.

Experimental Section

General Information. All manipulations were carried out under a dinitrogen atmosphere using standard Schlenk techniques. Solvents were distilled under dinitrogen over sodium−benzophenone (hexane, diethyl ether, THF), or calcium hydride (dichloromethane). The starting materials $RuCl_2(DMSO)_4$,[6] $RuCl_2$(ttp) (ttp = $PhP(CH_2CH_2CH_2PPh_2)_2$),[7] $RuCl_2$(ttp*) (ttp* = (*S*,*S*)-$PhP(CH_2CHMeCH_2PPh_2)_2$),[8] $RuCl_2$[(*R*)-(*S*)-Pigiphos] (Pigiphos = bis{(*S*)-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]-ethyl}cyclohexylphosphine) and $RuCl_2$[(*R*)-(*S*)-S-Pigiphos] (S-Pigiphos = bis{(*S*)-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]-ethyl} sulfide)[9] were prepared according to literature methods. All the other reagents were used as purchased from Aldrich or Strem Chemical Co. Microanalyses were performed by either MHW Laboratories (Phoenix, AZ) or the ISSECC-CNR. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. ^{1}H, ^{31}P, and ^{13}C NMR spectra were collected on JEOL EX-400 or Bruker ARX-300 and ARX-200 spectrometers. ^{1}H and ^{13}C NMR chemical shifts are relative to TMS; ^{31}P NMR chemical shifts are relative to 85% H_3PO_4. GC analyses were performed on a Shimadzu GC-14 A gas chromatograph equipped with a flame ionization detector and a 30 m (0.25 mm i.d., 0.25 μm FT) SPB-1 Supelco fused silica capillary column. Calibration curves were constructed using the GC internal standard biphenyl and known amounts of diethyl fumarate, diethyl maleate, ethyl *trans*-2-phenylcyclopropanecarboxylate, and ethyl *cis*-2-phenylcyclopropanecarboxylate. Yields of catalytic runs were determined from the calibration curves using the same GC standard. GC/MS analyses were performed on a Shimadzu QP 2000 apparatus equipped with a column identical with that used for GC analyses. Chiral capillary GC analyses were performed on a Shimadzu GC-17A gas chromatograph equipped with a flame ionization detector and a Chiraldex G-TA capillary column (40 m × 0.25 mm i.d.).

(*S*)-$MsOCH_2CH(OMs)CH_2CH_2OMs$. To a 50 mL dichloromethane solution of 2.00 g (19.3 mmol) of (*S*)-(−)-1,2,4-butanetriol was added dropwise a solution of mesyl chloride (59 mmol) in dichloromethane (5 mL). During the addition, the reaction mixture was kept at −20 °C. After the solution was stirred at room temperature for 0.5 h, water was added (50 mL). The dichloromethane layer was separated and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and 50 mL of methanol was added to give a white solid. Yield: 5.12 g, 78%. Anal. Calcd for $C_7H_{16}O_9S_3$: C, 24.70; H, 4.74. Found: C, 24.88; H, 4.60. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 2.21 (q, 2 H, J(HH) = 5.9 Hz, CH_2CH_2O), 3.08 (s, 3 H, OMs), 3.11 (s, 3 H, OMs), 3.16 (s, 3 H, OMs), 4.31−4.53 (m, 4 H, CH_2CH_2O, CH_2O), 5.09 (m, 1 H, CHO). ^{13}C{^{1}H} NMR (75.48 MHz, $CDCl_3$): δ 30.9 (s, CH_2CH_2O), 37.5 (s, *C*OMs), 37.8 (s, *C*OMs), 38.7 (s, *C*OMs), 64.6 (s, OMs), 69.3 (s, OMs), 74.6 (s, OMs).

(*R*)-$Ph_2PCH_2CH(PPh_2)CH_2CH_2PPh_2$ (etp*, 6). (*S*)-$MsOCH_2CH(OMs)CH_2CH_2OMs$ (2.7 g, 7.93 mmol), dissolved in 75 mL of THF, was added dropwise to a solution of 50 mL of 0.5 M potassium diphenylphosphide (25 mmol) in THF. After the mixture was stirred at room temperature for 4 h, the solvent was removed under vacuum. The oily residue was dissolved in 100 mL of benzene and then washed twice with water (100 mL). The benzene layer was separated. The solvent was removed to give a yellow oil. The crude product was purified by column chromatography using silica gel as the stationary phase and 5% ethyl acetate/hexane as eluent. The ligand etp* was obtained as an off-white solid after the solvent was removed under vacuum. Yield: 1.69 g, 35%. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.94−2.04 (m, 3 H, CH, CH_2), 2.59−2.64 (m, 4 H, CH_2), 7.22−7.39 (m, 30 H, aromatic protons). ^{31}P{^{1}H} NMR (121.49 MHz, $CDCl_3$): δ −21.8 (d, J(PP) = 18.5 Hz), −16.6 (s), −5.9 (d, J(PP) = 18.5 Hz). ^{13}C{^{1}H} NMR (75.48 MHz, $CDCl_3$): δ 25.4 (t, J(PC) = 11.8 Hz), 27.0 (ddd, J(PC) = 18.8, 14.3, 10.0 Hz), 30.0 (dd, J(PC) = 17.0, 12.7 Hz), 33.6 (q, J(PC) = 13.3 Hz, aliphatic carbon atoms); 128.0−139.2 (m, aromatic carbons).

$RuCl_2$(etp*) (3). A mixture of 0.21 g of etp* (0.34 mmol) and 0.12 g of $RuCl_2(DMSO)_4$ (0.25 mmol) in 10 mL of dichloromethane was stirred at room temperature for 2 days. The reaction mixture was then passed through a silica gel column and was eluted with acetone to remove some brown species.

(5) Demonceau, A.; Lemoine, C. A.; Noels, A. F.; Chizhevsky, I. T.; Sorokin, P. V. *Tetrahedron Lett.* **1995**, *36*, 8419.
(6) Evans, I. P.; Spencer, A.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1973**, 204.
(7) Albinati, A.; Jiang, Q.; Rugger, H.; Venanzi, L. M. *Inorg. Chem.* **1993**, *32*, 4940.
(8) Jia, G.; Lee, H. M.; Williams, I. D. *Organometallics* **1996**, *15*, 4235.
(9) Barbaro, P.; Bianchini, C.; Togni, A. *Organometallics* **1997**, *16*, 3004.

The product portion (yellow band) was eluted with MeOH. The solvent was removed under vacuum, and 20 mL of diethyl ether was added to give a yellow solid. The solid was washed with diethyl ether and dried under vacuum overnight. Yield: 0.12 g, 62%. Anal. Calcd for $C_{40}H_{37}Cl_2P_3Ru$: C, 61.39; H, 4.77. Found: C, 61.12; H, 4.96. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.66 (t, J(HH) = 13.3 Hz, 1 H, CH_2), 2.19−2.76 (m, 3 H, CH_2), 3.12−3.63 (m, 2 H, CH_2), 4.39 (br d, J(PH) = 41.4 Hz, 1 H, CHP), 6.60−7.95 (m, 30 H, aromatic protons). ^{31}P{^{1}H} NMR (121.51 MHz, $CDCl_3$): δ 12.8 (dd, J(PP) = 50.3, 38.3 Hz), 68.7 (dd, J(PP) = 50.5, 13.7 Hz), 78.0 (dd, J(PP) = 38.3, 13.7 Hz).

$RuCl_2$(ttp*)(=$CHCO_2Et$) (7). A mixture of 0.20 g of $RuCl_2$(ttp*) (0.26 mmol) and 0.28 mL of ethyl diazoacetate (2.66 mmol) in 10 mL of dichloromethane was stirred at room temperature for 3.5 h. The solvent was reduced to 1 mL under vacuum, and 40 mL of diethyl ether was added to give a yellow solid. The solid was filtered off, washed with diethyl ether, and dried under vacuum overnight. Yield: 0.19 g, 86%. Anal. Calcd for $C_{42}H_{47}Cl_2P_3O_2Ru$: C, 59.44; H, 5.58. Found: C, 59.75; H, 5.64. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 0.67 (t, J(HH) = 19.7 Hz, 3 H, $CO_2CH_2CH_3$), 0.85−3.48 (m, 10 H, $2CH_2CHCH_2$), 0.92 (d, J(HH) = 6.4 Hz, 3 H, CH_3), 1.46 (d, J(HH) = 6.7 Hz, 3 H, CH_3), 4.26 (q, J(HH) = 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 6.55−7.93 (m, 25 H, aromatic protons), 18.30 (br s, 1 H, =CH). ^{13}C{^{1}H} NMR (75.48 MHz, $CDCl_3$): δ 13.3 (s, CH_3), 26.2 (s, CH_3), 26.4 (t, J(PC) = 3.9 Hz, CH_3), 27.4 (m, $2CH_2CHCH_2$), 33.3 (dd, J(PC) = 36.1, 24.4 Hz, $2CH_2CHCH_2$), 38.3 (dd, J(PC) = 23.3 Hz, $2CH_2CHCH_2$), 39.5 (d, J(PC) = 30.9 Hz, $2CH_2CHCH_2$), 59.8 (s, CO_2CH_2), 126.6−138,0 (m, aromatic carbons), 173.6 (t, J(PC) = 4.9 Hz, C=O), 319.6 (q, J(PC) = 12.3 Hz, =CH). ^{31}P{^{1}H} NMR (121.49 MHz, $CDCl_3$, AMQ pattern): δ 4.7 (M, PPh_2), 10.7 (A, PPh_2), 24.7 (Q, PPh); J(PPh−PPh_2) = 36.1 Hz, J(PPh_2−PPh_2) = 289.1 Hz. These coupling constants were obtained by computer simulation of the experimental spectra using the program NMR″ (version 1.0, Calleo Scientific Software Publishers, 1989).

$RuCl_2$(ttp)(=$CHCO_2Et$) (9). A mixture of 0.40 g of $RuCl_2$(ttp) (**8**; 0.71 mmol) and 374 μL of ethyl diazoacetate (3.56 mmol) in 30 mL of dichloromethane was stirred at room temperature for 3.5 h. The solvent was removed completely under vacuum, and a mixture of 10 mL of diethyl ether and 30 mL of petroleum ether was added to give a greenish yellow solid. The solid was filtered off, washed with petroleum ether, and dried under vacuum overnight. Yield: 0.59 g, 95%. Anal. Calcd for $C_{44}H_{51}Cl_2P_3O_2Ru$: C, 60.27; H, 5.87. Found: C, 60.42; H, 5.90. ^{1}H NMR (200.14 MHz, CD_2Cl_2): δ 0.68 (t, J(HH) = 7.2 Hz, 3 H, $CO_2CH_2CH_3$), 1.87−3.43 (m, 12 H, aliphatic protons), 2.91 (q, J(HH) = 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 6.78 (td, J(HH) = 9.4, 1.2 Hz, 2 H), 6.99 (J(HH) = 7.7, 1.8 Hz, 2 H), 7.03−7.87 (m, 21 H, aromatic protons), 18.32 (q, J(PH) = 3.0 Hz, 1 H, =CH). ^{13}C{^{1}H} NMR (50.33 MHz, CD_2Cl_2): δ 19.5 (s, $2CH_2CH_2CH_2$), 26.3 (t, J(PC) = 14.1 Hz, $2PPh_2CH_2$), 28.6 (d, J(PC) = 32.3 Hz, $2PPhCH_2$), 60.3 (s, CO_2CH_2), 127.4−137.2 (m, aromatic carbons), 174.7 (q, J(PC) = 2.4 Hz, C=O), 322.3 (q, J(PC) = 12.1 Hz, =CH). ^{31}P{^{1}H} NMR (81.02 MHz, CD_2Cl_2): δ 3.3 (d, J(PPh−PPh_2) = 36.7 Hz, PPh_2), 16.3 (t, J(PPh−PPh_2) = 36.7 Hz, PPh).

Reaction of the Carbene Complex $RuCl_2$(ttp*)(=$CHCO_2Et$) (7) with Ethyl Diazoacetate. To a $CDCl_3$ solution (0.5 mL) of 10 mg of **7** (0.01 mmol) in an NMR tube was added 52.5 μL of ethyl diazoacetate (0.5 mmol). ^{1}H NMR spectra were immediately recorded, showing the formation of diethyl maleate and diethyl fumarate in a 95:5 ratio.

Reaction of the Carbene Complex $RuCl_2$(ttp)(=$CHCO_2Et$) (9) with Styrene. To a dichloroethane solution (2.0 mL) of 18 mg of **9** (0.02 mmol) was added 1.72 mL of styrene (15 mmol) without or with 10 mg of silver triflate (0.04 mmol). The mixture was stirred for 19 h. GC analyses using biphenyl as internal standard showed the formation of only cyclopropanes in the presence of silver triflate. In the absence of silver triflate, the formation of cyclopropanes was accompanied by that of the metathesis product PhHC=$CHCO_2Et$.

Table 1. Decomposition of Ethyl Diazoacetate in the Presence of Styrene by Chiral Ruthenium Complexes[a]

entry no.	catalyst	product				
		A (ee)	**B** (ee)	**C**	**D**	**E**
1	$RuCl_2$(ttp*)	12.8 (14)	8.6 (35)	5.2	36.7	1.1
2	$RuCl_2$(ttp*)[b]	3.2 (18)	0.3	0.4	84.0	
3	$RuCl_2$(etp*)	6.6 (1.2)	2.8 (5)	7.0	83.0	1.2
4	$RuCl_2$[(*R*)-(*S*)-Pigiphos]	*c*	*c*	*c*	31.0	
5	$RuCl_2$[(*S*)-(*R*)-S-Pigiphos]	*c*	*c*	*c*	48.0	
6	$RuCl_2$(ttp*)/AgOTf	49.2 (17)	34.8 (40)	1.3	14.7	
7	$RuCl_2$(ttp*)/[NEt_4]Cl	9.0 (13)	6.1 (32)	3.4	23.9	

[a] Reactions were carried out at room temperature unless otherwise stated. Yields and ee's are given in percent. The structures of the products are shown in eq 1. [b] Reactions carried out at −76 °C. [c] Not detectable by ^{1}H NMR. Trace amounts were found by the GC analysis.

Catalytic Cyclopropanation Reactions. A 100 mL dichloromethane solution containing ethyl diazoacetate (3.0 mmol) was added dropwise to a dichloromethane solution (10 mL) containing the catalyst precursor (either **2** or **3**, 0.06 mmol) and styrene (1.72 mL, 15 mmol) at room temperature over a period of 24 h.

Some reactions were carried out as above but in the presence of either silver triflate (0.02 or 0.04 mmol) or [NEt_4]Cl (0.10 mmol). Independent reactions with silver triflate alone did not show any cyclopropanation activity.

At the end of the reactions, the solvent was removed under vacuum and the organic products were extracted with *n*-pentane. The product composition was determined by either ^{1}H NMR spectroscopy or GC. In the first case, the *n*-pentane solution was concentrated under reduced pressure and the yields of the products were determined by ^{1}H NMR integration of the residual oil. When the yields of the products were determined by GC, biphenyl was used as internal standard. The optical yields of the cyclopropanation products were obtained by subjecting the residual oil to silica gel chromatography with hexanes−ether as eluents. The pure esters of the cyclopropanation products were then hydrolyzed to give the corresponding acids (1 mmol of ester, 3.6 mL of MeOH, 2.2 mL of 25% NaOH, 4 h at reflux temperature). The optical yields were obtained from the specific rotations of the cis ($[\alpha]_D$(cis) = +30°)[10] and trans acids ($[\alpha]_D$ = +381°).[11] The enantiomeric excesses (ee) were also determined by chiral capillary GC.

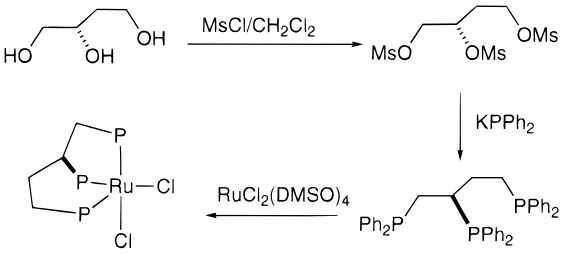
Catalytic reactions with complexes **4** and **5** were carried out similarly at room temperature. The amounts of catalysts and reagents were as follows: styrene, 5 mmol in 10 mL of dichloromethane; catalyst, 0.02 mmol; ethyl diazoacetate, 1 mmol in 100 mL of dichloromethane. The results of all reactions are collected in Table 1.

Results and Discussion

Synthesis and Characterization of the Chiral Ruthenium Complex $RuCl_2$(etp*). The catalyst precursors used in this study include the chiral complexes $RuCl_2$(ttp*) (**2**),[8] $RuCl_2$(etp*) (**3**), $RuCl_2$[(*R*)-(*S*)-Pigiphos] (**4**)[9] and $RuCl_2$[(*R*)-(*S*)-S-Pigiphos] (**5**).[9] The new complex **3** was obtained by treatment of $RuCl_2(DMSO)_4$ with the ligand (*R*)-$Ph_2PCH_2CH(PPh_2)CH_2CH_2PPh_2$ (etp*), which

(10) Aratani, A.; Nakanishi, Y.; Nozaki, H. *Tetrahedron* **1970**, *26*, 1675.
(11) Inouye, Y.; Sugita, T.; Walborsky, H. M. *Tetrahedron* **1964**, *20*, 1695.

Scheme 1

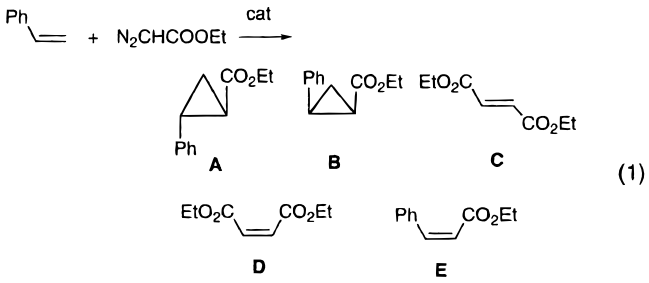


was synthesized according to the procedure shown in Scheme 1. This involves the treatment of commercially available (*S*)-$HOCH_2CH(OH)CH_2CH_2OH$ with MsCl in CH_2Cl_2 to give (*S*)-$MsOCH_2CH(OMs)CH_2CH_2OMs$, followed by reaction with $KPPh_2$. A slightly different synthetic protocol for etp* is reported in the literature.[12]

The ^{31}P NMR spectrum of **3** in $CDCl_3$ shows an AMQ pattern which is consistent with a facial (*fac*) bonding mode of the triphosphine ligand. Analogous coordination geometries were determined by X-ray diffraction analysis in the related *fac* complexes $RuCl_2[PhP(CH_2CH_2CH_2PR_2)_2]$ (R = Ph,[7] Cy[13]) and $RuCl_2[(R)$-(S)-Pigiphos].[9]

Catalytic Reactions. The catalytic activity of the ruthenium complexes **2**−**5** for the cyclopropanation of styrene with ethyl diazoacetate was investigated in routine experimental conditions.

The addition of ethyl diazoacetate (diluted in CH_2Cl_2) to a CH_2Cl_2 solution containing styrene and one of the catalyst precursors shown in Chart 1 led to the formation of either a mixture of cyclopropanation (**A**, **B**) and dimerization products (**C**, **D**) or exclusively dimerization products (eq 1). In some cases, a small but detectable amount of the metathesis product PhH-C=$CHCO_2Et$ (**E**) was also formed.



(1)

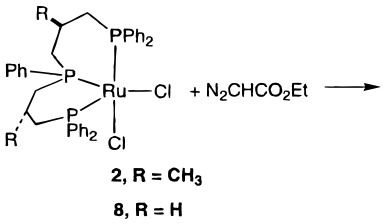
As shown in Table 1, only complexes **2** and **3** are capable of generating a cyclopropanation catalyst with moderate activity, however. In fact, the major product of all reactions is diethyl maleate (**D**), formed by dimerization of ethyl diazoacetate. Moreover, the low yield of cyclopropanes using **2** or **3** is also accompanied by modest *E*/*Z* ratios as well as low enantioselectivities. The major cyclopropanation products exhibit the 1*R*,2*R* and 1*R*,2*S* configurations for the *E* and *Z* stereoisomers, respectively. Decreasing the reaction temperature increases the *E*/*Z* cyclopropane ratio and also favors the formation of the cis alkene (entry 2).

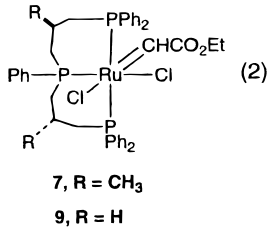
As is generally agreed for other metal-catalyzed cyclopropanation reactions applying EDA as the carbene source, the low cyclopropanation activity of our catalysts is most likely due to the kinetically competitive diazoacetate dimerization to give diethyl maleate and diethyl fumarate.[2,3] Indeed, all of the ruthenium complexes investigated are catalytically active for alkene production. For example, ethyl diazoacetate was rapidly consumed to give a mixture of the cis and trans alkenes in the presence of **2** and **3** (in situ NMR experiments). As was previously reported for similar reactions catalyzed by ruthenium and osmium complexes, the formation of the cis isomer diethyl maleate predominates over that of the trans isomer.[14−17] The selectivity for diethyl maleate using **4** or **5** is excellent indeed, as no trace of diethyl fumarate was detected by ^1H NMR spectroscopy.

The chemoselectivity of the reactions was remarkably improved by performing the decomposition of EDA in the presence of a chloride scavenger such as AgOTf. The yield in cyclopropanation products indeed increased up to 84% (run 6), but neither the regioselectivity nor the diastereoselectivity was appreciably improved. In contrast, the addition of a slight excess of $[NEt_4]Cl$ to the catalytic mixture decreased the catalytic activity without substantially affecting either the chemoselectivity or the diastereoselectivity (entry 7). The presence of free Cl^-, however, inhibited the formation of the metathesis product.

Mechanistic Studies. It is generally agreed that carbene species are key intermediates in transition-metal-catalyzed cyclopropanation reactions as well as alkene formation via dimerization of diazo reagents.[2] A few such carbene intermediates have been isolated, e.g. with osmium and ruthenium porphyrins[14,15,17] and with ruthenium bis(oxazolinyl)pyridine systems.[3e]

To prove the formation of a carbene complex in the catalytic reactions herein described, we have investigated the stoichiometric reaction of **2** with N_2CHCO_2Et. Our attempt was successful, as the carbene complex $RuCl_2(ttp^*)(=CHCO_2Et)$ (**7**) was cleanly isolated by treatment of **2** with ethyl diazoacetate (eq 2).



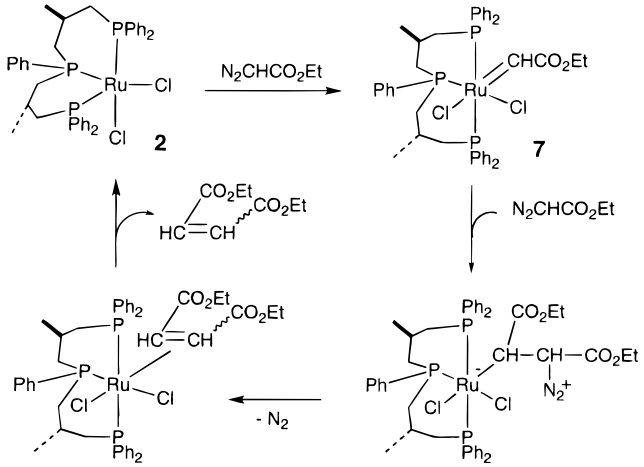


(2)

The presence of a carbene ligand in **7** is unambigu-

(12) Brunner, H.; Lautenschlager, H. J. *Synthesis* **1989**, 706.
(13) Jia, G.; Lee, I.; Meek, D. W.; Gallucci, J. C. *Inorg. Chim. Acta* **1990**, *177*, 81.
(14) Collman, J. P.; Rose, E.; Venburg, G. D. *J. Chem. Soc., Chem. Commun.* **1993**, 934.
(15) Woo, L. K.; Smith, D. A. *Organometallics* **1992**, *11*, 2344 and references therein.
(16) Nishiyama, H.; Park, S. B.; Haga, M.; Aoki, K.; Itoh, K. *Chem. Lett.* **1994**, 1111.
(17) (a) Smith, D. A.; Reynolds, D. N.; Woo, L. K. *J. Am. Chem. Soc.* **1993**, *115*, 2511 and references therein. (b) Djukic, J. P.; Smith, D. A.; Young, V. G., Jr.; Woo, L. K. *Organometallics* **1994**, *13*, 3020.

Scheme 2

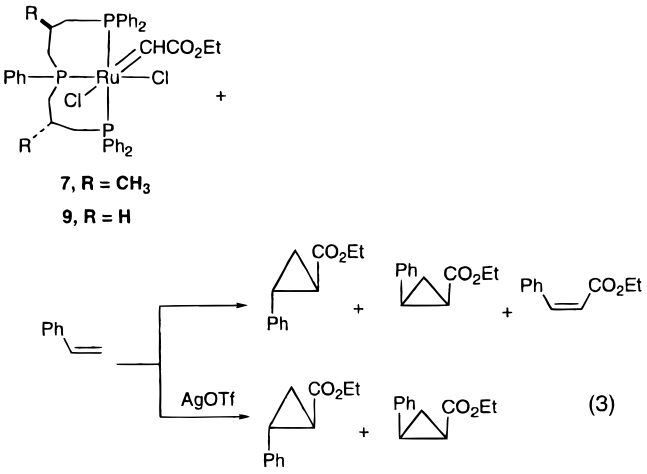


ously shown by the $^{13}C\{^1H\}$ and ^1H NMR spectra, which contain typical resonances at 319.6 and 18.30 ppm for the carbene carbon atom and its hydrogen atom, respectively.[3e] A change in the coordination mode of the triphosphine ttp* ligand from *fac* to *mer* is clearly demonstrated by the large coupling constant between the terminal PPh_2 groups (289.1 Hz).[18] This structural assignment is also consistent with the ^{13}C NMR spectrum, in which the quartet multiplicity of the signal due to the carbene carbon atom ($J(PC) = 12.3$ Hz) shows the carbene group to be located cis to the three phosphorus atoms of the ttp* ligand. An identical structure is displayed by the derivative $RuCl_2$(ttp)(=$CHCO_2Et$) (**9**), which was similarly isolated by reaction of $RuCl_2$-(ttp) (**8**) with the diazo compound in dichloromethane. This achiral complex was prepared in order to use a less expensive ligand in the mechanistic studies.

The direct involvement of a carbene species in the dimerization of ethyl diazoacetate has been confirmed by the independent reaction of isolated **7** with ethyl diazoacetate, which quickly produced diethyl maleate and diethyl fumarate in a ratio of 95:5. A mechanism for the formation of the alkene is proposed in Scheme 2 on the basis of previous reports on Ru-assisted EDA decompositions.[2e] Consistent with this mechanism, we have found that the coordinatively saturated complex $RuCl_2(PPh_3)[n\text{-}PrN(CH_2CH_2PPh_2)_2]$[19] failed to react with N_2CHCO_2Et to give a carbene complex and, consequently, was inactive for the dimerization of ethyl diazoacetate as well as the cyclopropanation of styrene.

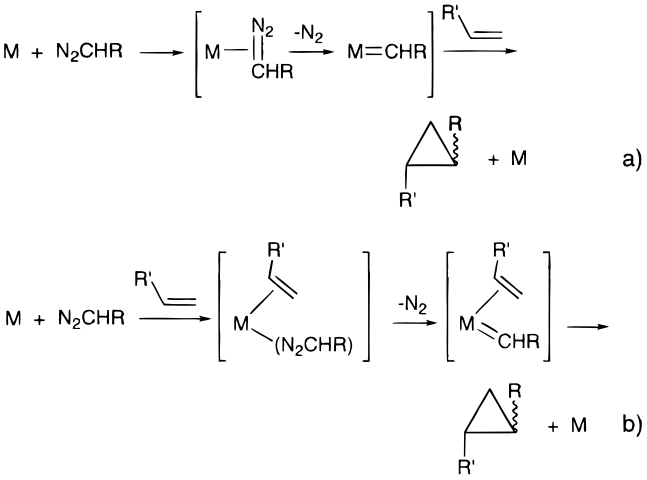
As further chemical evidence of the presence of a carbene ligand in **7** and **9**, cyclopropanation products were obtained by their treatment with an excess of styrene in dichloromethane at room temperature (eq 3). Consistent with the results of the catalytic reactions, also the metathesis product (*Z*)-PhHC=$CHCO_2Et$ was formed, although in trace amounts. In the presence of 2 equiv of silver triflate, the reactions gave exclusively 2-phenylcyclopropanecarboxylates with the same *E*/*Z* ratio of the catalytic runs.

The formation of cyclopropanes via metal-mediated carbene transfer from diazo compounds to alkenes has been proposed to involve two principal mechanisms, i.e.



the carbenoid path a and the coordination path b (Scheme 3).

Scheme 3



In general, rhodium and copper catalysts act according to path a, while palladium catalysts coordinate the alkene (path b). In many cases, however, both types of mechanisms contribute to the overall process.[20] The Ru(II) pybox complex **1** has been shown to display a carbenoid type of behavior, and the carbene transfer was suggested to be the rate-determining step.[3b] Like the pybox system, our Ru(II) precursors stabilized by the triphosphine ligands ttp* and ttp form six-coordinate carbene complexes upon reaction with EDA. An intermolecular carbenoid mechanism seems to be very unlikely, however, as cyclopropanation is invariably accompanied by alkene metathesis, which obviously requires the coordination of the alkene to occur.[21] On the other hand, a contribution of the carbenoid mechanism cannot be disregarded a priori, particularly as one considers that the carbene ligands in **7** and **9** seem to be more electrophilic ($\delta_{Ru=C}$ 319.6 and 322.3) than those in $RuCl_2$(pybox)(=$CHCO_2R$) ($\delta_{Ru=C}$ ca. 305).[3b]

In intermediates such as **7** and **9**, a vacant site for the alkene may be provided by either Cl^- decoordination or phosphine arm unfastening. This latter process has

(18) Garrou, P. E. *Chem. Rev.* **1981**, *81*, 229.
(19) Bianchini, C.; Peruzzini, M.; Romerosa, A.; Zanobini, F. *Organometallics* **1995**, *14*, 3152 and references therein.
(20) Anciaux, A. J.; Hubert, A.; Noels, A. F.; Petiniot, N.; Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695.
(21) *Principles and Applications of Organotransition Metal Chemistry*; Collman, J. P., Hegedus, L. S., Norton, J. R., Finke, R. G., Eds.; University Science Books: Mill Valley, CA, 1987; p 475.

several precedents for polyphosphine metal complexes in catalysis.[22] Consistent with the simultaneous coordination of alkene and carbene at the ruthenium center, we have found that the catalytic activity increases by performing the cyclopropanation reactions in the presence of a chloride scavenger, while it decreases in the presence of $[NEt_4]Cl$.

In the absence of a deeper investigation including a theoretical analysis, any interpretation of the different behaviors of the pybox and etp* catalyst precursors would be absolutely speculative. Both steric and electronic effects may indeed control the carbene transfer. For analogous reasons, we cannot account for the poor diastereoselectivity of the cyclopropanation reactions catalyzed by **2**. In fact, if the reaction requires either phosphine unfastening or ligand isomerization (from *fac* to *mer*) to occur, then it is obvious that the stereocontrol exerted by the chiral catalyst cannot be as efficient as it might be. Indeed, preliminary results in asymmetric hydrogenation of prochiral olefins with **2**, without being spectacular, are quite promising and suggest that ttp* will receive further attention in asymmetric catalysis.[22]

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OM9900667

(22) (a) Bianchini, C.; Meli, A.; Peruzzini, M.; Vizza, F.; Frediani, P.; Ramirez, J. A. *Organometallics* **1990**, *9*, 226 and references therein. (b) Bianchini, C.; Farnetti, E.; Graziani, M.; Nardin, G.; Vacca, A.; Zanobini, F. *J. Am. Chem. Soc.* **1990**, *112*, 9190. (c) Bianchini, C.; Meli, A.; Peruzzini, M.; Frediani, P.; Bohanna, C.; Esteruelas, M. A.; Oro, L. *Organometallics* **1992**, *11*, 138. (d) Kiss, G.; Horváth, I. T. *Inorg. Chem.* **1991**, *10*, 3798.

(23) Lee, H. M. Ph.D. Thesis, The Hong Kong University of Science and Technology, 1997; p 169.