Cis-Selective Asymmetric Cyclopropanation of Olefins Catalyzed by Five-Coordinate [RuCl(PNNP)]$^+$ Complexes

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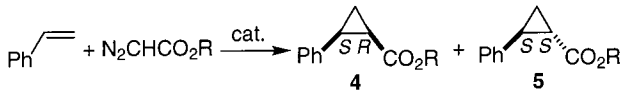
The five-coordinate complex [RuCl(**1a**)]PF_6 (**3a**; **1a** = (*S*)-*N*,*N*′-bis[2-(diphenylphosphino)-benzylidene]-2,2′-diamino-6,6′-dimethylbiphenylene) catalyzes the cyclopropanation of styrene by decomposition of diazoesters. The cis cyclopropane derivative is formed with moderate selectivity (cis:trans ratio is 48:52), but high enantioselectivity (90−96% ee). The related species [RuCl(**1b**)]PF_6 (**3b**; **1b** = *N*,*N*′-bis[2-(diphenylphosphino)benzylidene]-(1*S*,2*S*)-diaminocyclohexane) gives the cis product with selectivity up to 95% and enantioselectivity up to >99% ee. High cis selectivity is obtained also with 2,5-dimethyl-2,4-hexadiene as substrate. Complex **3a** yields ethyl chrysanthemate with 94% cis selectivity and enantioselectivity up to 80% ee. The putative carbene intermediate *trans*-[RuCl(C(H)COOEt)(**1b**)]$^+$ (**11b**) was prepared and characterized spectroscopically in solution. Its reaction with styrene gives the cyclopropane derivative with 98:2 cis:trans selectivity. The steric constraints in the transition states involving **11b** and styrene were estimated by means of molecular modeling calculations. The relative total energies of the four diastereomeric aggregates follow the experimental enantio- and diastereoselectivity trends. The model proposed also predicts the correct absolute configuration of both cis and trans cyclopropane products.

Introduction

The most striking progress in the asymmetric cyclopropanation of olefins is the development of catalysts affording trans cyclopropane derivatives with high enantio- and diastereoselectivity.[1] With styrene, semicorrin and bis(oxazoline) copper catalysts have been developed that afford both the trans product and the cis one with high enantioselectivity, but always favor the trans isomer (Scheme 1).[2−7] More recently, ruthenium complexes containing tridentate nitrogen donors (pybox)[8] and cobalt(III) salen systems[9] have further improved the trans diastereoselectivity.

In contrast, after Kodadek's pioneering work with rhodium chiral porphyrins,[10] catalytic systems for the efficient diastereo- and enantioselective formation of cis cyclopropane derivatives have been developing slowly. Doyle has shown that also dirhodium(II) carboxamidates can give higher enantioselectivities for the cis cyclopropane than for the trans isomer. However, the trans isomer is generally the major product.[11] A breakthrough has been recently achieved by Katsuki, whose ruthenium nitrosyl complexes [RuCl(salen)(NO)] give highly enantio- and cis-selective cyclopropanation of styrenes upon irradiation with visible light.[12]

Scheme 1



4 **5**

We recently reported the synthesis of some five-coordinate species [RuCl(PNNP)]$^+$, where PNNP are tetradentate ligands with a P_2N_2 donor set.[13] These complexes catalyze the asymmetric epoxidation of olefins by hydrogen peroxide. We find now that [RuCl(PNNP)]$^+$ (PNNP is **1a** or the already reported **1b**,[13b] Chart 1) catalyze the cyclopropanation of styrene with diazoesters giving the cis isomer **4** with high diastereo- and enantioselectivity.

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(10) See, for instance: (a) Maxwell, J. L.; O'Malley, S.; Brown, K. C.; Kodadek, T. *Organometallics* **1992**, *11*, 645. (b) O'Malley, S.; Kodadek, T. *Organometallics* **1992**, *11*, 2299.

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(12) (a) Uchida, T.; Irie, R.; Katsuki, T. *Synlett* **1999**, 1793. (b) Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron* **2000**, *56*, 3501. (c) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 3647.

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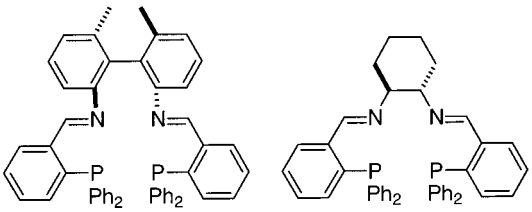
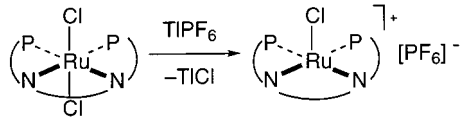
Chart 1



Scheme 2



Results and Discussion

[RuCl(PNNP)]$^+$ Complexes. The new ligand (*S*)-*N*,*N*′-bis[2-(diphenylphosphino)benzylidene]-2,2′-diamino-6,6′-dimethylbiphenylene (**1a**) was prepared by condensation of P(*o*-C(H)O-C_6H_4)Ph_2 (2 equiv) with enantiomerically pure (*S*)-2,2′-diamino-6,6′-dimethylbiphenylene by the procedure previously reported for *N*,*N*′-bis[2-(diphenylphosphino)benzylidene]-(1*S*,2*S*)-diaminocyclohexane (**1b**).[13b] As for other PNNP ligands, the yield is nearly quantitative (95%). The ^{31}P NMR spectrum of **1a** shows a singlet at δ −13.6 for the two equivalent phosphorus atoms. The two imino protons give a doublet at δ 8.9 ($J_{P,H}$ = 5.5 Hz) in the ^{1}H NMR spectrum. The IR spectrum (KBr) shows one band at 1624 cm^{-1} for the C═N stretching vibration. The CH_2Cl_2, $CHCl_3$, or toluene solutions of **1a** and **1b** are stable toward oxidation and hydrolysis when exposed to the atmosphere for days.

The reaction of **1a** with [$RuCl_2(PPh_3)_3$] in boiling toluene, benzene, or $CDCl_3$ gives the red six-coordinate complex *trans*-[$RuCl_2$(**1a**-κ^4*P*,*N*,*N*,*P*)] (**2a**) as the only isomer, as supported by the singlet at δ 46.5 in the ^{31}P NMR spectrum. Complex [$RuCl_2$(**1b**)] (**2b**) was prepared by reaction of **1b** with [$RuCl_2(PPh_3)_3$] in CH_2Cl_2 at room temperature. Under these conditions **2b** is formed as a mixture of trans and cis-β isomers in a 3:1 ratio, as reported previously.[13b]

The six-coordinate complex [$RuCl_2$(**1a**)] (**2a**) reacts with Tl[PF_6] in CH_2Cl_2 to give the brown five-coordinate species [RuCl(**1a**)]PF_6 (**3a**) (Scheme 2). The latter complex is isolated by addition of hexane or pentane to the reaction solution after filtering off the thallium chloride. The formulation of **3a** is supported by MS (FAB$^+$) and by the appearance of two doublets in the ^{31}P NMR spectrum at δ 80.8 and 42.9 (J = 27.6 Hz), in the range expected for five-coordinate [$RuXN_2P_2$]$^+$ complexes (X = halide).[13b,14] It should be noted that both *trans*-**2a** and *trans*-**2b** react with Tl[PF_6] in CH_2Cl_2 at room temperature, whereas the related species *trans*-[$RuCl_2$(PNNP)] (PNNP = *N*,*N*′-bis[2-(diphenylphosphino)*benzyl*]-(1*S*,2*S*)-di*amino*cyclohexane, **1c**; (*S*)-*N*,*N*′-bis[2-(diphenylphosphino)benzylidene]-2,2′-diamino-1,1′-bi*naphthylene*, **1d**) are completely unreactive under the same conditions.[13b] In view of the similarity between ligands **1a** and **1d**, and **1b** and **1c**, these reactivity differences are surprising. Indeed, the bis(imino) complex [$RuCl_2$(**1b**)] and the bis(amino) derivative [$RuCl_2$(**1c**)] have very similar metrical parameters, despite the different donor properties of the PNNP ligands.[15]

We have already reported the preparation of [RuCl(**1b**)]PF_6 (**3b**) from **2b** and its high reactivity toward most oxygen donors and, in particular, water.[13b] In contrast, the biphenyl-bridged [RuCl(**1a**)]PF_6 (**3a**) is nearly unreactive toward water or other oxygen donors, such as THF. This is analogous to what was previously observed for the five-coordinate derivative with the binaphthyl-bridged ligand **1d**. The reduced oxophilicity in the biphenyl and binaphthyl derivatives is apparently due to a combination of steric and electronic factors.

Asymmetric Cyclopropanation. The five-coordinate complexes **3a** and **3b** were used as catalyst precursors for the asymmetric cyclopropanation of styrene and 2,5-dimethylhexa-2,4-diene with different diazo esters (Scheme 1). The precatalysts **3a** and **3b** were prepared in situ from the corresponding dichloro derivatives **2a** and **2b** by chloride abstraction. The complexes **2a** or **2b** were treated with Tl[PF_6] (1 equiv) in CH_2Cl_2 overnight, after which TlCl was filtered off over Celite, and the resulting red-brown solution was added to the olefin (and decane, as internal standard for GC analysis). Complex **3a**, containing the biphenyl-bridged ligand **1a**, gives quantitative precipitation of TlCl, whereas TlCl tends to precipitate slowly from the solutions of [RuCl(**1b**)]PF_6 (**3b**). In general, the chloride abstraction is necessary for catalytic activity, as the dichloro complexes **2a** and **2b** are catalytically unreactive.[16]

The cyclopropanation reactions were carried out adding slowly a CH_2Cl_2 solution (1 mL) of N_2C(H)COOR (R = Et or Bu^t) to a solution containing styrene (1 equiv) and the catalyst in CH_2Cl_2 (1 mL) at room temperature over 6 h. The reaction solutions were protected from light. Precatalyst **3a** (5 mol %) gave the cis and trans cyclopropane derivatives in 40:60 ratio (Table 1, run 1) with a total yield of 84%. The catalytic system shows a similar performance when a substrate-to-catalyst ratio of 100:1 is used (run 2).

The analysis of the stereochemical course of the reaction catalyzed by **3a** is intriguing. Indeed, the enantiomeric excess of the cis derivative **4** is generally higher than 90%, whereas the trans product **5** is formed with enantioselectivities not exceeding 55%. Apart from some exceptions,[10−12] this observation is contrary to what is observed with most catalytic systems.[1−9] This prompted us to test the already known five-coordinate complex [RuCl(**1b**)]PF_6 (**3b**). The reaction catalyzed by **3b** (5 mol %) afforded the cis product **4** with good diastereo- and enantioselectivity (91:9 cis:trans ratio, 87% ee, run 5). As observed with **3a**, the residual trans isomer is formed with low enantioselectivity. Higher ee

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(16) No reaction is observed at room temperature in the presence of **2b**. A slight catalytic activity can be observed with the dichloro derivative **2b** in dichloroethane at reflux (43% conversion, 3% yield, 86:14 cis-to-trans ratio), but **1** and **2** are formed with low enantioselectivity (4 and 2% ee, respectively), suggesting that the largest contribution to the reaction is due to the uncatalyzed (thermic) reaction.

Table 1. Cyclopropanation of Styrene Catalyzed by 3a,b[a]

run	cat.	R	conv. (%)	yield (%)	cis:trans	ee (%) cis	ee (%) trans
1	**3a**	Et	99	84	40:60	90	55
2[b]	**3a**	Et	80	67	48:52	93	40
3[c]	**3a**	Et	80	53	38:62	91	54
4	**3a**	Bu^t	89	67	3:97	96	38
5	**3b**	Et	70	41	91:9	87	24
6[d]	**3b**	Et	60	31	93:7	92	3
7[e]	**3b**	Et	36	12	95:5	92	2
8[f]	**3b**	Et	31	8	84:16	82	8
9[c]	**3b**	Et	42	5	57:43	61	5
10[d]	**3b**	Bu^t	20	13	83:17	>99	0

[a] Reaction conditions: $N_2C(H)COOEt$ (51 μL, 0.42 mol) in CH_2Cl_2 (1 mL) was added over 6 h to a CH_2Cl_2 solution (1 mL) of the olefin (0.42 mol) and **3** (21 μmol, 5 mol %), 20 h total reaction time. [b] 1 mol % catalyst was used. [c] In THF as solvent. [d] The diazoester was dried before the reaction, but not distilled. [e] At 0 °C. [f] Diazoester added in one portion.

values of **4** (up to 92%) are achieved by using diazoesters that have been dried over molecular sieves, but not distilled (run 6). The improvement of the enantioselectivity, however, is at cost of the reaction yield. Running the reaction catalyzed by **3b** at 0 °C gives 95% diastereoselectivity and 92% ee for **4** (run 7).

The chemical yields of the catalytic reactions are, at best, only moderate. This is possibly because of catalyst deactivation. Indeed, longer reaction times do not improve the cyclopropane yield. However, it should be noted that no excess reagent is used, whereas most published systems use a 4-fold excess of the olefin. In fact, yield and selectivity did not improve when an excess either of olefin (2 equiv) or of diazoacetate (10 equiv) was used. The critical factor was instead the slow and continuous addition of the diazoacetate over several hours. Under these conditions, the formation of maleate and fumarate is kept to a minimum. Addition of the diazoester in one portion gives lower diastereo- and enantioselectivity (run 8).

We also investigated the effect of changing the ester substituent and reaction solvent. With both catalysts **3a** and **3b**, increasing the steric bulk of the ester chain favors the formation of the trans isomer. In the case of **3a**, this leads to the formation of nearly pure *trans*-**4**, but with low enantioselectivity (38% ee, run 4). In the case of catalyst **3b**, $N_2C(H)COOBu^t$ gives enantiopure cis isomer **4**, but with slightly decreased diastereoselectivity (83%, run 10). The formation of the trans isomer **5** is also favored with THF as solvent (see below).

Further, we assessed the formation of maleate (**6**) and fumarate (**7**) by monitoring selected reaction solutions (under standard reaction conditions) by means of ^{1}H NMR spectroscopy.[17] Maleate and fumarate are first detected after 4 h reaction time. After 20 h reaction time, maleate and fumarate are present in a 3:1 ratio and their total yield does not exceed 10% (based on starting diazoester). At this time, unreacted ethyl diazoacetate is present in the reaction solution. To check whether the formation of **6** and **7** is catalyzed by the five-coordinate complexes **3**, a control reaction was run with ethyl diazoacetate and **3a** or **3b** under standard conditions but without added olefin. Complex **3a** gave diethyl maleate with 45% yield and 95% selectivity after 20 h, whereas **3b** is less reactive (25% yield after 72 h, 90% selectivity). As complexes **3** catalyze the homocoupling of diazoacetate with much higher cis selectivity than in the homocoupling side reaction during cyclopropanation, we speculate that the formation of **6** and **7** in the latter reaction is not catalyzed by **3**.[18] The stereoselective formation of maleate is noteworthy, and few systems have been reported to effectively perform this transformation.[19]

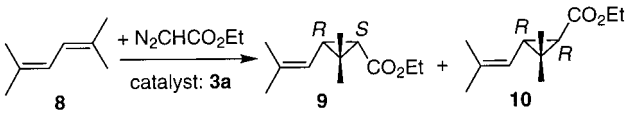
(17) GC analysis of the coupling products is inadequate, as ethyl diazoacetate dimerizes to fumarate and maleate during the chromatographic analysis.

Table 2. Cyclopropanation of 2,5-Dimethyl-2,4-hexadiene (8) Catalyzed by 3a,b[a]

run	cat.	mol %	conv. (%)	yield (%)	cis:trans	ee cis (%)
1[b]	**3a**	1	27	9	92:8	80
2[c]	**3a**	1	49	18	92:8	75
3	**3a**	5	55	18	94:6	75
4[b]	**3b**	5	9	0		

[a] Reaction conditions: see Table 1, footnote *a*. The ee of the trans isomer was not determined. [b] No purification. [c] The diazoester was dried before the reaction, but not distilled.

Scheme 3



The optimization of the reaction solvent was limited by the high oxophilicity of complex **3b**, as only chlorinated solvents can be used. Indeed, O or N donors block the active site of the catalyst effectively and form relatively stable adducts.[13b] Accordingly, **3b** is an ineffective catalyst in THF and gives low yield and enantioselectivity (run 9). In contrast, **3a** does not form adducts with THF, which can then be used as solvent. However, the selectivity with both catalysts shifts toward the formation of the trans cyclopropanation product in THF (runs 3, 9). Aromatic solvents (benzene or toluene) are ineffective owing to the low solubility of the cationic species **3**.

To assess the scope of the $[RuCl(PNNP)]^+$ catalysts, we investigated the cyclopropanation of 2,5-dimethyl-2,4-hexadiene (**8**), a trisubstituted olefin, with $N_2C(H)$-COOEt to give ethyl chrysanthemate (Scheme 3). Complex **3a** is moderately active with the sterically hindered diolefin **8**, whereas **3b** does not give any cyclopropanation product (Table 2). Modest yields of **9** and **10** are obtained only with dried and distilled ethyl diazoacetate (runs 2, 3). Increasing the catalyst-to-substrate ratio from 1 to 5% does not improve the yield. In all cases, excellent cis selectivity is obtained (>90%). The cis isomer **9** is formed with fair enantioselectivity (75−80% ee). To the best of our knowledge, this is the best cis selectivity ever obtained in the cyclopropanation of **8**, as the reported catalysts give prevalently the trans isomer.[20] Thus, **3a** gives access to the cis cyclopropa-

(18) Decomposition products of **3**, or the uncatalyzed thermal decomposition of the diazoester, can be responsible for the formation of **6** and **7** during cyclopropanation.

(19) (a) Baratta, W.; Del Zotto, A.; Rigo, P. *Chem. Commun.* **2997**, 2163. (b) Del Zotto, A.; Baratta, W.; Verardo, G.; Rigo, P. *Eur. J. Org. Chem.* **2000**, 2795.

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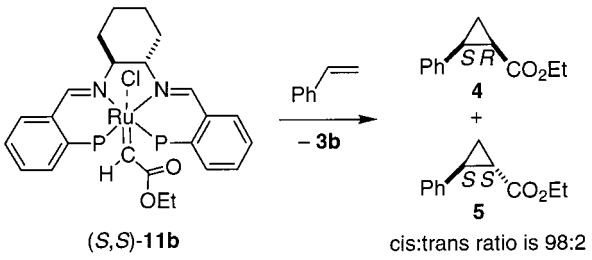
Scheme 4



nation product of a conjugated diolefin even in the absence of halogen substituents in the vinylic positions.

Some general comments are appropriate at this stage. The first observation is that the cyclopropanation of styrene gives the cis derivative **4** with as good a selectivity and enantioselectivity as the best ever obtained and are comparable with those of the [RuCl(salen)(NO)] system.[12a,b] The $[RuCl(PNNP)]^+$ and [RuCl(salen)(NO)] systems are similar, but the five-coordinate system is intrinsically reactive in view of its 16-electron configuration and does not need to be photoactivated. An intriguing feature of the cyclopropanation of styrene is that catalysts **3** give the cis and trans isomers **4** and **5** with reversed configuration at the cyclopropane C(1) atom, whereas the configuration at C(2) is the same in both. Katsuki observed the same stereochemical course in the reaction catalyzed by [RuCl(salen)(NO)].[12a,b] However, this is contrary to what is typically observed in the cyclopropanation of styrene catalyzed by Cu-based,[2−7] rhodium(II) carboxamidato,[21] and ruthenium pybox[8] complexes. With these systems, the configuration at C(1) is the same in the major cis and trans isomers. This peculiarity prompted us to investigate the mechanism of stereocontrol. With this aim in mind, we investigated the nature of the carbene intermediate first.

[RuCl(C(H)COOEt)(1b)]PF_6. Treatment of complex **3a** with ethyl diazoacetate (1 equiv, CD_2Cl_2, room temperature) gave only the starting five-coordinate complex and a mixture of fumarate and maleate. In contrast, complex **3b** reacts with ethyl diazoacetate under the above conditions to give the carbene derivative *trans*-[RuCl(C(H)COOR)((*S*,*S*)-**1b**)] (**11b**) (Scheme 4). As **11b** is stable for 1−2 h at room temperature or for ca. 12 h at −80 °C, it was characterized in solution by ^1H, ^{31}P, and ^{13}C NMR spectroscopy.

The ^1H NMR spectrum of **11b** features the signal of the carbene hydrogen atom Ru=C*H* as a doublet of doublets (δ 16.94, $J_{P,H}$ = 7.3 and 13.1 Hz). The resonance of the carbene ^{13}C atom appears as a double of doublets at δ 324 in the ^{13}C NMR spectrum. The $J_{P,C}$ coupling constants (25.3 and 31.7 Hz) indicate a cis arrangement of the carbene ligand with respect to both P atoms. The NMR data of the $RuP_2(=C(H)CO_2Et)$ fragment in **11b** are similar to those of the related complexes $[RuCl_2(=C(H)CO_2R)P_2]$[22] and rule out a trans arrangement of the carbene and one phosphine ligand. Furthermore, **11b** was formed as a single isomer in

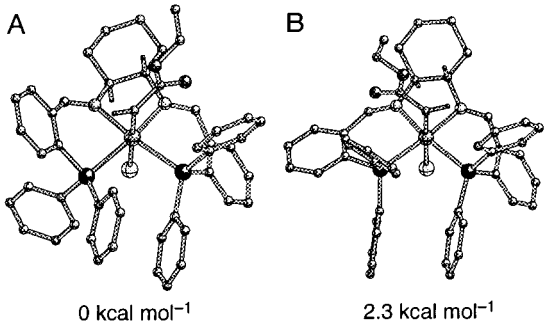


Figure 1. Minimized conformations of the carbene complex [RuCl(C(H)COOEt)((*S*,*S*)-**1b**)] (**11b**) (with relative energies).

several experiments carried out at room temperature.[23] We conclude that the carbene complex **11b** is the thermodynamic product featuring a C−Ru−Cl arrangement as depicted in Scheme 4. In fact, the mutual trans arrangement of the carbene ligand (a π-acceptor) and chloride (a π-donor) is favored in view of the resulting push−pull interaction.[24]

Complex **11b** reacts instantaneously with styrene (1 equiv) at room temperature to give the cyclopropane derivatives **4** and **5** (Scheme 4). The reaction is essentially quantitative and yields **4** and **5** in 98:2 ratio, as determined by GC analysis.

Molecular Modeling. On the basis of the reaction of the intermediate carbene complex **11b** with styrene, we modeled the putative "transition states" of the carbene-transfer step using the Cerius2 program.[25] In the first step, the two conformations of the ester chain of the carbene ligand were optimized using a Ru−C(carbene) bond order of 2. This gave optimized bond lengths of 2.015 Å (**A**) and 2.092 Å (**B**) for the two possible ester chain configurations when the ester group is ethyl (Figure 1).[26] The conformation **A** leads to the (1*R*) cyclopropane derivatives (Figure 2) and is 2.3 kcal mol^{-1} more stable than **B**, which gives the (1*S*) isomers. However, it is the energy of the "transition states" (TS) **4*** and **5*** between **11b** and the incoming styrene molecule that dictates the overall stereochemical outcome of the reaction, rather than the orientation of the ester chain alone (see below).[27]

In both conformers **A** and **B**, only one trajectory is available for the approach of the olefin. This occurs along a Ru−N vector, as attack along the Ru−P vectors is blocked by the bulky PPh_2 groups, and the ester group blocks the remaining Ru−N trajectory. Figure 2 shows how the choice of the enantioface of the olefin determines the configuration at C(2) of the cyclopropane

(21) Doyle, M. P.; Winchester, W. R.; Hoorn, J. A. A.; Lynch, V.; Simonsen, S. H.; Gosh, R. *J. Am. Chem. Soc.* **1993**, *115*, 9968.

(22) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem.* **1995**, *107*, 2179.

(23) In contrast, the reaction of **3b** with ethyl diazoacetate at −50 °C gives two different carbene complexes **11b′** and **11b″**. In both complexes the carbene ligand is cis to both phosphines, as indicated by the P,C(carbene) coupling constants (see Experimental Part). Thus, we assume that these species are the two cis-β isomers featuring a trans C−Ru−N arrangement.

(24) Caulton, K. G. *New J. Chem.* **1994**, *18*, 25.

(25) Cerius2 uses the Universal Force Field (UFF): Rappé, A. K.; Casewit, C. J.; Colwell, K. S.; Goddard, W. A., III; Skiff, W. M. *J. Am. Chem. Soc.* **1992**, *114*, 10024. Rappé, A. K.; Colwell, K. S.; Casewit, C. J. *Inorg. Chem.* **1993**, *32*, 3438.

(26) These values are in reasonable agreement with the experimental value of 1.861(3) Å found in $[RuCl_2(=CH\text{-}o\text{-}OMeC_6H_4)(PPh_3)]_2$: Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791.

(27) In a MM study of the rhodium(II) carbamidato system, Doyle has reported similar considerations.[21]

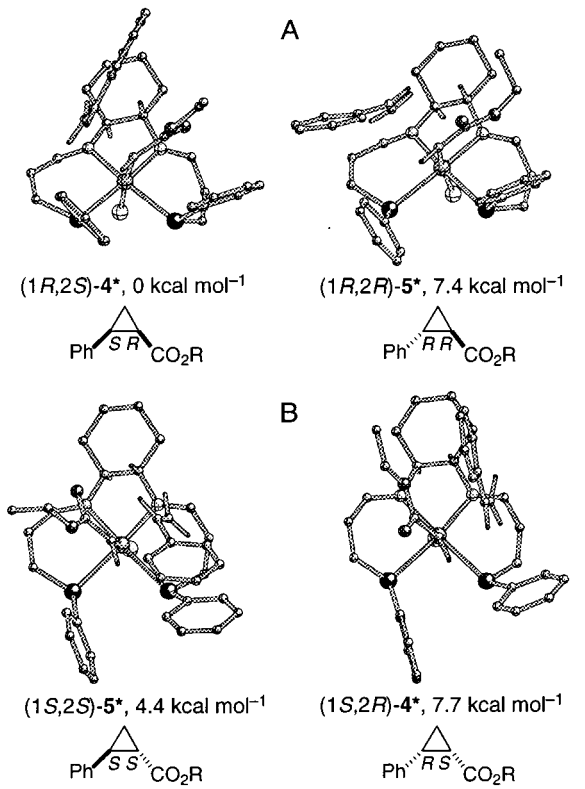


Figure 2. Minimized "transition states" between the carbene complex [RuCl(C(H)COOEt)((*S*,*S*)-**1b**)] (**11b**) and styrene (with relative energies), and absolute configurations of the cyclopropanation product. Only relevant parts of the complex are shown.

product. The configuration at C(1) results from the orientation of the ester chain relative to the direction of attack.

Next, we minimized the conformational energies of the four diastereomeric "transition states" **4*** and **5***. The C(carbene)−C(2) and C(carbene)−C(1) distances were kept fixed at 2.4 and 2.6 Å, respectively. The double bond of the olefin was kept parallel to the Ru−C vector and approximately perpendicular to the N−Ru one (Figure 2). This mode of approach is generally assumed[1] in the interpretation of the stereochemical outcome of cyclopropanation reactions.[28] The relative energy values summarized in Figure 1 show that the energetically favored TS leads to (1*R*,2*S*)-**4**. This can be explained by the observation that the vinyl H atoms of the olefin and the H atom on the nearest sp^3 carbon (on the C_6H_{10} ring) are oriented anti. A contact between the phenyl group of styrene and that of the PPh_2 group disfavors the attack of the olefin with the opposite enantioface, which leads to the minor cis isomer (1*R*,2*R*)-**5**.

The preferred TS that leads to a trans isomer is (1*S*,2*S*)-**5***, whose energy is 4.4 kcal mol^{-1} higher than that of (1*R*,2*S*)-**4***. It derives from the attack onto the carbene complex **11b** having the opposite conformation of the ester chain, that is, **B**. This explains the inversion of configuration at C(1) on going from (1*R*,2*S*)-**4** to (1*S*,2*S*)-**5**. The configuration at C(2) is the same as in (1*R*,2*S*)-**4**, as the olefin approaches with the same enantioface. In general, the (*S*)-configuration at C(1) is disfavored, as (1*S*,2*S*)-**5** and (1*S*,2*R*)-**4** derive from the attack along the sterically hindered trajectory passing between a phenyl group of the ligand and the axial H atom on the tertiary carbon of the cyclohexanediyl ring.

Table 3. Relative Energies of "Transition States" Formed by [RuCl(C(H)COOR)(1b)]$^+$ (11b) and Styrene (kcal mol^{-1})[a]

R	(1*R*,2*S*)	(1*S*,2*S*)	(1*R*,2*R*)	(1*S*,2*R*)
Et	0	4.4	7.4	7.7
Bu^t [b]	11.2	12.6	14.0	19.5
Bu^t [c]	0	1.3	2.8	8.3

[a] Configurations refer to the cyclopropane product. [b] Values relative to (1*R*,2*S*)-**4***, R = Et. [c] Values relative to (1*R*,2*S*)-**4***, R = Bu^t.

The energy gap of 7.7 kcal mol^{-1} between the TS's of the cis isomers, (1*R*,2*S*)-**4*** and (1*S*,2*R*)-**4***, is larger than that of 3.0 kcal mol^{-1} between the TS's of the trans ones, (1*S*,2*S*)-**5*** and (1*R*,2*R*)-**5*** (Table 3). This is in qualitative agreement with the much higher enantioselectivity observed for the cis isomer **4** than for **5**. The calculated energy ordering also reflects the experimental cis selectivity. Furthermore, it also yields the experimentally observed absolute configurations both for **4** and for **5**. The model is also in agreement with the decreasing cis selectivity on going from the ethyl to the *tert*-butyl ester (Table 1, runs 4, 10), as the energy gap between (1*R*,2*S*)-**4*** and (1*S*,2*S*)-**5*** decreases from 4.4 to 1.3 kcal mol^{-1} in this series. Finally, the calculations account also for the increasing enantioselectivity of **4** with increasing steric bulk of the ester chain. Indeed, the energy difference between the enantiomers of **4** increases from 7.7 to 8.3 kcal mol^{-1} on going from Et to Bu^t.

As a final observation, ligand **1b** has the same conformation in all structures and directs the approach of the olefin by means both of the phenyl substituent and of the cyclohexanediyl ring.

Concluding Remarks

The steric features of the PNNP ligand **1b** account for the remarkable enantio- and cis selectivity observed, which are not far from the highest ever observed.[1,12a,b] As compared with recent applications of phosphorus-containing ligands in asymmetric cyclopropanation,[29] complex **3b** and Katsuki's catalyst [RuCl(salen)(NO)] (**12**) show exceptionally high cis selectivity in the asymmetric cyclopropanation of terminal olefins. At difference with the Ru- and Co-salen systems mentioned above,[12] **3a**,**b** do not require chiral or bulky ester groups or any additive to improve the selectivity. The molecular modeling studies cast some light on the nature of the cis selectivity in the case of ligand **1b**. As shown in

(28) The only exception to this general assumption we are aware of has been suggested by Kodadek to explain the cis selectivity observed with rhodium porphyrins. According to his model, the olefin attacks the carbene with the C=C double bond perpendicular to the M−C vector and parallel to the plane of the porphyrin. However, the olefin rotates before reaching the transition state, and the side-on approach also leads to an end-on transition state in which both double bonds are parallel.[10]

(29) (a) Song, J. H.; Cho, D. J.; Jeon, S. J.; Kim, Y. H.; Kim, T. J.; Jeong, H. H. *Inorg. Chem.* **1999**, *38*, 893. (b) Brunel, J. M.; Legrand, O.; Reymond, S.; Buono, G. *J. Am. Chem. Soc.* **1999**, *121*, 5807. (c) Lee, H. M.; Bianchini, C.; Jia, G.; Barbaro, P. *Organometallics* **1999**, *18*, 1961. (d) Stoop, R. M.; Bauer, C.; Setz, P.; Wörle, M.; Wong, T. Y. H.; Mezzetti, A. *Organometallics* **1999**, *18*, 5691. (e) Bianchini, C.; Lee, H. M. *Organometallics* **2000**, *19*, 1833. (f) Braunstein, P.; Naud, F.; Pfaltz, A.; Rettig, S. J. *Organometallics* **2000**, *19*, 2676.

Chart 2

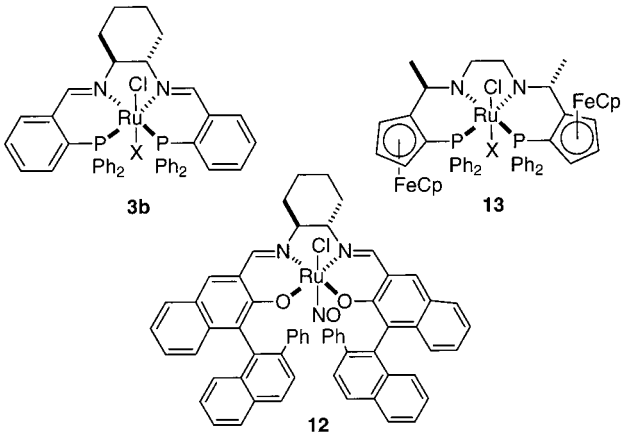


Chart 2, **3b** and **12** possess similar steric features concerning the possible approach trajectories of the incoming olefin. In both complexes, bulky groups (either PPh_2 or 1-phenyl-naphthyl) block the approach along the Ru−P or Ru−O vector, and the cyclohexyl moiety directs the approach along one Ru−N direction. The presence of the latter stereogenic element is apparently pivotal for high cis selectivity. Indeed, the apparently related complex **13**, in which the cyclohexenediyl moiety is missing, prevalently forms the trans cyclopropane derivative with selectivity in the range 66−98%.[29a]

Experimental Part

General Comments. Reactions with air- or moisture-sensitive materials were carried out under an argon atmosphere using Schlenk techniques. Styrene, (1*S*,2*S*)-(+)-1,2-diaminocyclohexane, 2,5-dimethyl-2,4-hexadiene, and ethyl chrysanthemate (30:70 mixture of cis and trans) were obtained from Fluka AG. 2-(Diphenylphosphino)benzaldehyde was purchased from Aldrich, Tl[PF_6] from Strem Chemicals, and ethyl *trans*-2-phenylcyclopropane from Lancaster. Enantiomerically pure (*S*)-2,2′-diamino-6,6′-dimethylbiphenylene was obtained from Solvias AG (Basel). Ligand **1b** and complexes **2b** and **3b** were prepared as previously reported.[13b] ^1H and ^{31}P NMR spectra were recorded on Bruker DPX spectrometers. ^1H and ^{13}C positive chemical shifts in ppm are downfield from tetramethylsilane. ^{31}P NMR spectra were referenced to external 85% H_3PO_4. Mass spectra were measured by the MS service of the Laboratorium für Organische Chemie (ETH Zürich). A 3-NOBA (3-nitrobenzyl alcohol) matrix and a Xe atom beam with a translational energy of 8 keV were used for FAB^+ MS. Optical rotations were measured using a Perkin-Elmer 341 polarimeter with a 1 dm cell. Elemental analyses were carried out by the Laboratory of Microelemental Analysis (ETH Zürich). Molecular modeling calculations were performed on a Silicon Graphics O_2 platform with the Cerius2 program (MSI) using standard UFF settings.

(*S*)-*N*,*N*′-Bis[2-(diphenylphosphino)benzylidene]-2,2′-diamino-6,6′-dimethylbiphenylene, (*S*)-1a. (*S*)(−)-2,2′-Diamino-(*S*)-6,6′-dimethylbiphenylene (292 mg, 1.38 mmol) and 2-diphenylphosphinobenzaldehyde (800 mg, 2.76 mmol) were refluxed in toluene (15 mL) in a Dean-Stark apparatus for 14 h. Evaporation of the solvent in a vacuum and recrystallization of the resulting yellow oil from toluene/MeOH (4:1) gave a yellow solid. Yield: 998 mg (96%). Mp: 69 °C. $[\alpha]_D^{20}$: −224.9 ± 2 (c = 1, $CHCl_3$). ^1H NMR: δ 8.9 (d, 2H, N=C*H*, $J_{P,H}$ = 5.5 Hz), 7.7−6.75 (m, 32H, arom.), 6.3 (d, 2H, arom.), 1.9 (s, 6H, 2CH_3). ^{31}P NMR: δ −13.6 (s, 2P). IR (KBr, cm^{-1}): 1624 (s, ν_{CN}). MS (FAB^+) (*m*/*z*): 757 ([M + H]$^+$, 61), 756 (M^+, 24), 468 ([M + H − N=CPPh_2]$^+$, 100).

[$RuCl_2$(1a)], 2a. [$RuCl_2(PPh_3)_3$] (635 mg, 0.66 mmol) and **1a** (500 mg, 0.66 mmol) were refluxed in toluene (20 mL) overnight. Partial evaporation of the solvent gave a bordeaux-red solid that was recrystallized from CH_2Cl_2/pentane. Yield: 536 mg (90%). ^1H NMR (250 MHz, $CDCl_3$): 8.6 (d, 1H, N=C*H*, J = 6.2), 7.6−6.7 (m, 34H, arom), 6.0 (d, 1H, J = 6.2 Hz, N=C*H*), 1.9 (s, 6H, 2 CH_3). ^{31}P NMR (101 MHz, $CDCl_3$): 46.5 (s, 2P). MS (FAB^+) (*m*/*z*): 930 ([M + 2 H]$^+$, 100), 928 (M^+, 50), 893 [(M − Cl]$^+$, 22). Anal. Calcd for $C_{52}H_{42}Cl_2N_2P_2Ru\cdot 0.5CH_2Cl_2$: C, 64.92; H, 4.46; N: 2.88. Found: C, 65.10; H, 4.94; N, 2.58.

[RuCl(1a)]PF_6, 3a. Complex **2a** (185 mg, 0.199 mmol) and Tl[PF_6] (10 mg, 0.20 mmol) were stirred in CH_2Cl_2 (15 mL) for 14 h. The precipitated TlCl was filtered off over Celite. Addition of pentane to the resulting clear solution and partial evaporation of the solvent gave a brown solid that was recrystallized from CH_2Cl_2/pentane. The complex tenaciously retains variable amounts of crystallization solvents, resulting in erratic elemental analyses. Yield: 124 mg (60%). ^1H NMR (300 MHz, $CDCl_3$): δ 8.90 (d, 1 H, $J_{H,H'}$ = 9.6 Hz, N=C*H*), 7.9−6.3 (m, 34H, arom), 4.40 (d, 1 H, $J_{H,H'}$ = 7.8 Hz, N=C*H*). ^{31}P NMR: 80.8 (d, 2P, $J_{P,P'}$ = 27.6 Hz), 42.9 (d, 2P, $J_{P,P}$ = 27.6 Hz). MS (FAB^+) (*m*/*z*): 893 (M^+, 100), 858, ([M − Cl]$^+$, 6).

Typical Catalytic Run. Complex **3a** (20 mg, 21 μmol, 5 mol %) and Tl[PF_6] (7.3 mg, 21 μmol) were dissolved in CH_2Cl_2 (1 mL) and stirred overnight, and then TlCl was filtered off and the resulting red-brown solution was added to the olefin (0.42 mmol) and decane (50 mg, as internal standard). A solution of the diazoester (0.42 mmol) in CH_2Cl_2 (1 mL) was added with a syringe pump over 6 h. The solution, which was protected from light throughout the reaction, was stirred for an additional 14 h at room temperature and then analyzed by GC. The reactions with a substrate-to-catalyst ratio of 100:1 (1 mol % catalyst) were performed using more olefin (2.1 mmol) and diazoester (2.1 mmol). Yields were obtained by GC. In selected instances, we isolated the cyclopropanation product by column chromatography. The isolated yields are within ±10% of those obtained by GC.

A control reaction without the catalyst indicated that the cyclopropane derivatives **4** and **5** were formed only in traces under the conditions used. The yields of the uncatalyzed reaction were 0.03% and 0.13% for the cis and trans products, respectively.

Analytic Details (GC, ee, Absolute Configuration). Ethyl 2-Phenyl-cylopropanecarboxylate. Achiral GC analysis: Macherey-Nagel SE 54, 30 m, He carrier (92 kPa). Temperature program: 50 °C isotherm for 5 min, then to 200 °C at 5 °C min^{-1}. R_t (min): styrene, 10.2; decane, 14.25; ethyl *cis*-2-phenylcyclopropanecarboxylate, 28.2; ethyl *trans*-2-phenylcyclopropanecarboxylate, 29.7. Chiral GC analysis: Supelco Beta Dex 120, 1.4 mL He min^{-1}; temperature program: 110 °C for 10 min, 5 °C min^{-1} to 150 °C, isotherm for 20 min. R_t (min): *cis*-(1*R*,2*S*), 26.0; *cis*-(1*S*,2*R*), 26.38; *trans*-(1*R*,2*R*), 28.09; *trans*-(1*S*,2*S*), 28.34. The GC peaks were attributed by comparison with an authentic sample with a known *E*/*Z* ratio (99:1, Lancaster). The absolute configurations are (1*R*,2*S*) for **4** and (1*S*,2*S*) for **5** (by the sign of the optical rotation of the isolated products).[30]

***tert*-Butyl 2-Phenylcyclopropanecarboxylate.** Achiral GC analysis: Macherey-Nagel SE 54, 30 m, He carrier (92 kPa). Temperature program: 50 °C isotherm for 5 min, then to 200 °C at 5 °C min^{-1}. R_t (min): styrene, 10.0; decane, 14.10; *tert*-butyl *cis*-2-phenylcyclopropanecarboxylate, 29.95; *tert*-butyl *trans*-2-phenylcyclopropanecarboxylate, 31.29. Chiral GC analysis: Supelco Beta Dex 120, 1.4 mL He min^{-1}; temperature program: 110 °C for 10 min, 5 °C min^{-1} to 150 °C, isotherm for 20 min. R_t (min): *cis*-(1*R*,2*S*), 27.68; *cis*-(1*S*,2*R*), 28.06; *trans*-(1*R*,2*R*), 31.08; *trans*-(1*S*,2*S*), 31.26. Product isolated from a catalysis run was used for GC calibration. The

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absolute configuration of **5** is (1*S*,2*S*), as indicated by the positive sign of the optical rotation of the isolated product.[31] The absolute configuration of **4** is assumed to be (1*R*,2*S*) on the basis of GC retention times and by analogy with the ethyl derivative.

Ethyl Chrysanthemate. Achiral GC analysis: Macherey Nagel SE 54, 30 m, He carrier (92 kPa). Temperature program: 50 °C isotherm for 5 min, then 3 °C min^{-1} to 150 °C, 10 °C min^{-1} to 200 °C. R_t (min): **8**, 9.95; decane, 16.75; ethyl *cis*-chrysanthemate, 30.7; ethyl *trans*-chrysanthemate, 31.1. The GC peaks were attributed by comparison with a commercially available authentic sample with a known *E*/*Z* ratio (70:30, as determined by ^{1}H NMR spectroscopy). The enantiomeric excess of **9** was determined by trans-esterification with (−)-menthol according to the following procedure. The crude reaction solution was eluted over alumina with hexane/ethyl acetate (9:1). Evaporation of the solvents gave a colorless oil. A portion (20 mg) of this oil was dissolved in a toluene solution (0.7 mL, 0.25 M) of pyridine (0.175 mmol). $SOCl_2$ (0.7 mL of a 0.7 M toluene solution, 0.5 mmol) and (−)-menthol (0.7 mL of a 1.4 M toluene solution, 0.98 mmol) were added thereto. The mixture was refluxed for 1 h and then diluted with Et_2O and extracted three times with 0.1 M phosphate buffer (Na_3PO_4, pH = 3), followed by saturated $NaHCO_3$. The crude product was concentrated and analyzed by GC. GC analysis: Macherey-Nagel SE 54, 30 m, He carrier (92 kPa). Temperature program: 50 °C to 200 °C at 1 °C min^{-1}. R_t (min): 142.8 (1*S*,3*R*), 144.6 (1*R*,3*S*). For run 1 of Table 2, the enantiomeric excess of **9** was independently determined by integration of the ^{1}H NMR spectrum of the mixture of **9** and **10** in the presence of the chiral shift reagent tris[3-(propylhydroxymethylene)-*d*-camphorato]europium(III). Integration of the cyclopropane methyl signal at δ 1.68 gave the same value (80% ee). As isolated **9** has negative α, its absolute configuration is (1*S*,3*R*) by correlation with the optical rotation of the acid.[32]

Observation of [RuCl(C(H)COOEt)((*S*,*S*)-1b)]PF_6, 11b. Complex **2b** (40 mg, 48 μmol) and Tl[PF_6] (17 mg, 48 μmol) were stirred at room temperature overnight in 3 mL of CH_2Cl_2. TlCl was filtered over Celite, CH_2Cl_2 was removed under vacuum, and CD_2Cl_2 and ethyl diazoacetate (5 μL, 48 μmol) were added. ^{1}H NMR (250 MHz, CD_2Cl_2): 16.9 (d×d, 1 H, $J_{P,H}$ = 7.3 Hz, $J_{P',H}$ = 13.1 Hz). ^{31}P NMR (101 MHz, CD_2Cl_2): 37.6 (d, 1P, $J_{P,P'}$ = 29.8 Hz), 28.1 (d, 1P, $J_{P,P'}$ = 29.8 Hz), −144.4 (septet, 1 P, $J_{P,F}$ = 714 Hz, PF_6). ^{13}C NMR (75 MHz, CD_2Cl_2, −80 °C): δ 324.1 (d×d, 1 C, $J_{P,C}$ = 25.3, $J_{P',C}$ = 31.7 Hz).

Performing the same reaction at −50 °C gave a mixture of two different carbene complexes, **11b′** (43%) and **11b″** (37%), along with **11b** (20%). **11b′**: ^{1}H NMR (250 MHz, CD_2Cl_2): 15.5 (d×d, 1 H, $J_{P,H}$ = 12.5 Hz, $J_{P',H}$ = 5.2 Hz). ^{31}P NMR (202 MHz, CD_2Cl_2, −50 °C): 44.1 (br, 1P) (data from a P,H correlation experiment, no cross-peak for the second P atom due to small $J_{P,H}$). **11b″**: ^{1}H NMR (250 MHz, CD_2Cl_2): 15.0 (d×d, 1 H, $J_{P,H}$ = 10.0 Hz, $J_{P',H}$ = 4.8 Hz). ^{31}P NMR (202 MHz, CD_2Cl_2, −50 °C): 45.2 (br, 1P) (see **11b′** for signal of second P atom).

Molecular Modeling. Molecular modeling calculations were performed on a Silicon Graphics O_2 platform with the Cerius2 program (MSI) (standard UFF settings). The two conformations of the ester chain in the carbene intermediate [RuCl(C(H)COOEt)(**3b**)] were minimized first. The conformation **A** is more stable by 2.3 kcal mol^{-1} than **B**. With *tert*-butyl as the ester group, the energy difference between **A** and **B** increases to 4.0 kcal mol^{-1}. Then, the transition states were simulated by positioning the styrene molecule with fixed C(carbene)−C(2) and C(carbene)−C(1) distances (2.4 and 2.6 Å, respectively). During minimization, the geometry of the Ru═C···C(1)═C(2) moiety was kept fixed with C(carbene)−C(2) and carbene−C(1) distances of 2.4 and 2.6 Å, respectively. The positions of ruthenium and of the P atom anti to the incoming olefin were also kept constant. The final energy values were calculated with the contribution of all atoms. Relative energy values are given in Table 3.

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OM010020P

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