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# Chiral Semicorrins and Related Nitrogen Heterocycles as Ligands in Asymmetric Catalysis

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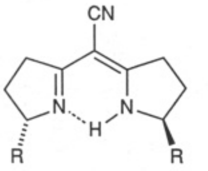
Over the past two decades, asymmetric catalysis has evolved into a very dynamic, rapidly growing area of research, attracting an increasing number of chemists from various disciplines. As a result, powerful synthetic catalysts have become available which exhibit levels of enantioselectivity previously considered beyond reach for nonenzymatic processes.[1] Most of these catalysts are metal complexes containing a chiral organic ligand which controls a metal-mediated process in such a way that one of two enantiomeric products is formed with high preference over the other. However, despite impressive achievements as, e.g., in the reduction of C═C and C═O double bonds[1,2] or in the epoxidation of olefins,[3] the number of efficient, truly useful enantioselective catalysts is still limited. Thus, the main efforts of future research will continue to focus on the improvement of existing methods and on the search for new catalysts. In addition, it will become increasingly important to develop more rational guidelines for the design of new ligands and catalysts, based on mechanistic considerations rather than intuition or purely empirical rules.



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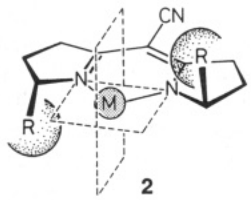

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Inspired by the structures of corrinoid and porphinoid metal complexes, which in nature play a fundamental role as biocatalysts, we have developed a route to chiral $C_2$-symmetric semicorrins **1**, a class of bidentate nitrogen ligands specifically designed for enantioselective catalysis.[4] This Account reviews the synthesis and application of chiral semicorrins and structurally related nitrogen heterocycles and illustrates the potential of these ligands for the stereocontrol of metal-catalyzed reactions.

## Chiral $C_2$-Symmetric Semicorrins

Semicorrins have been previously prepared as intermediates in the synthesis of corrinoid and hydroporphinoid compounds.[5,6] The classic route by imino ester–enamine condensation, devised by Eschenmoser,[5] is ideally suited for preparing chiral $C_2$-symmetric semicorrins **1**. Starting from L-pyroglutamic acid [(−)-**3**] or from the D-enantiomer, which are both commercially available at moderate prices, the crystalline, enantiomerically pure diesters (−)-**1a** and (+)-**1a** are readily synthesized in multigram quantities with an overall yield of 30–40% (Scheme I).[7,8] The diesters can be converted to a variety of differently substituted semicorrins such as **1b** or **1c** by selective transformation of the ester groups.[7–9] Alternatively, the substituents at the stereogenic centers may be altered at the first stage of the synthesis by modifying the carboxyl group of pyroglutamic acid.[4a,9] This allows the ligand structure to be adjusted to the specific requirements of a particular application and provides a means for optimizing the selectivity of a catalyst in a systematic manner.

The semicorrins **1** possess a number of structural features that make them attractive ligands for the stereocontrol of metal-catalyzed reactions. First, the geometry of the vinylogous amidine system is ideal for coordinating a metal ion. Accordingly, semicorrins form stable chelate complexes with a variety of metal ions such as Co(II), Rh(I), Ni(II), Pd(II), or Cu(II).[7,10,11] Depending on the metal ion, the ligand structure, and the reaction conditions, either mono- or bis(semicorrinato) complexes are obtained.

Andreas Pfaltz was born in Basel, Switzerland, in 1948. He studied at the ETH in Zürich, where he completed his Ph.D. thesis in 1978 under the guidance of Albert Eschenmoser. After a postdoctoral stay at Columbia University with Gilbert Stork, he returned to the ETH. There he began his independent research and was appointed Privatdozent in 1987. In 1990 he joined the faculty at the University of Basel as professor of organic chemistry. His research interests are in the areas of synthetic organic and organometallic chemistry, with special emphasis on asymmetric catalysis. He is also involved in collaborative research with colleagues at the ETH and at the University of Marburg, concerning the structure and function of coenzyme F430, a porphinoid nickel complex which catalyzes methane formation in methanogenic bacteria.

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(9) Leutenegger, U. Dissertation; ETH-Zürich, No. 9091, 1990.

(10) Johnson, A. P.; Wehrli, P.; Fletcher, R.; Eschenmoser, A. *Angew. Chem.* **1968**, *80*, 622; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 623.

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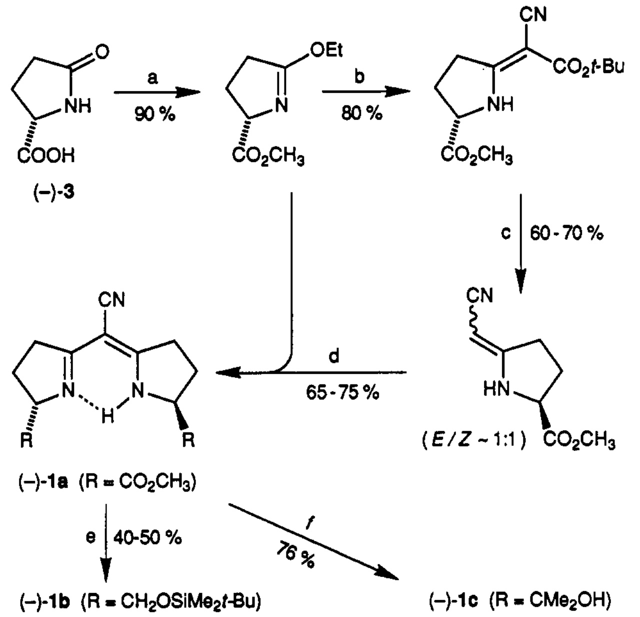
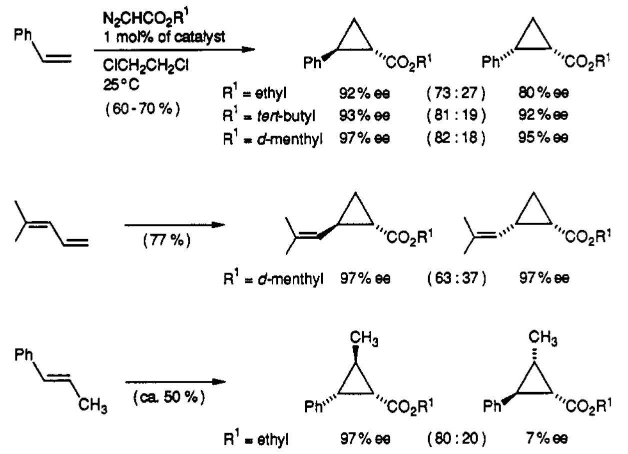
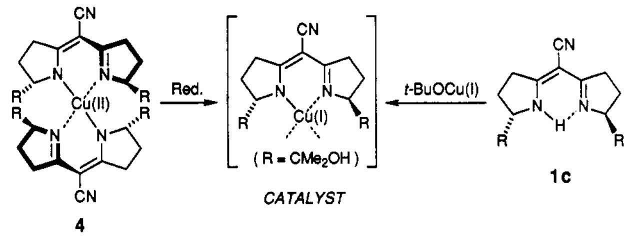
**Scheme I**[a]



[a] Reagents: (a) MeOH, $H^+$, reflux; $Et_3O^+BF_4^-$, $CH_2Cl_2$, reflux; (b) $NCCH_2CO_2$-*t*-Bu, 100 °C; (c) $CF_3CO_2H$, 23 °C; (d) $CF_3CO_2H$, $ClCH_2CH_2Cl$, 65 °C; (e) $LiBH_4$, THF, 23 °C, or $NaBH_4$, THF/$H_2O$ (4:1), reflux; $Me_2$-*t*-BuSiCl, imidazole, DMF, 40 °C; (f) MeMgBr, $Et_2O$, 0–23 °C.

**Scheme II**





The planar π-system and the two five-membered rings confine the conformational flexibility of the ligand framework. This simplifies the problem of predicting or analyzing the three-dimensional structure of semicorrin metal complexes. Moreover, the conformational rigidity of the ligand system and its $C_2$-symmetry should have a favorable effect on the stereoselectivity of a metal-catalyzed process, as they restrict the number of possible catalyst–substrate arrangements and the number of competing diastereomeric transition states.[12] The two substituents at the stereogenic centers are located in close proximity to the coordination site. As shown in formula **2**, they shield the metal ion from two opposite directions and, therefore, are expected to have a distinct, direct effect on a reaction taking place in the coordination sphere. All these properties facilitate an analysis of the possible interactions between catalyst and substrate which determine the stereoselectivity of a metal-catalyzed process and should make it easier to approach the problem of developing an enantioselective catalyst in a straightforward, rational manner.

## Enantioselective Cyclopropanation

The first successful application of semicorrin metal complexes that we investigated was the copper-catalyzed enantioselective cyclopropanation of olefins with diazo compounds. This reaction has its origin in the pioneering work of Nozaki and co-workers with chiral Cu–salicylaldimine complexes as catalysts.[13,14] Systematic variation of the chiral ligand by Aratani et al.[15] eventually led to highly efficient catalysts which allow the preparation of chrysanthemic acid and related compounds in high enantiomeric purity. The Aratani catalyst is also used on an industrial scale for the cyclopropanation of 2-methyl-1-propene with ethyl diazoacetate. Recently, another promising catalyst, a dinuclear rhodium(II) complex with methyl pyroglutamate as chiral ligand, has been described by Doyle et al.[14,16]

The potential of semicorrin copper catalysts is illustrated by the reaction of styrene with diazoacetates (Scheme II).[7a,17] The highest selectivities were obtained with the bulky ligand **1c**. The stable crystalline bis(semicorrinato)copper(II) complex **4** serves as a convenient catalyst precursor. The actual catalyst, which is presumed to be a mono(semicorrinato)copper(I) complex, is formed in situ either by heating in the presence of the diazo compound or by reduction with phenylhydrazine at room temperature.[17] Alternatively, the catalyst may be generated from the free ligand **1c** and Cu(I)–*tert*-butoxide. Reactions were usually carried out at room temperature in the presence of 1 mol % of catalyst. Depending on the structure of the diazo compound, the enantiomeric purity of the trans products ranged between 92 and 97% ee. Other monosubstituted and some 1,2-disubstituted olefins were also converted to cyclopropanecarboxylates with high enantiomeric excesses[17,18] (for a tentative mechanistic model rationalizing the observed stereoselectivities, see ref 17). The relatively poor trans–cis selectivity in the cyclopropanation of terminal olefins is a general problem, which is also observed with other catalysts.[14] The trans/cis ratio is essentially independent of the catalyst

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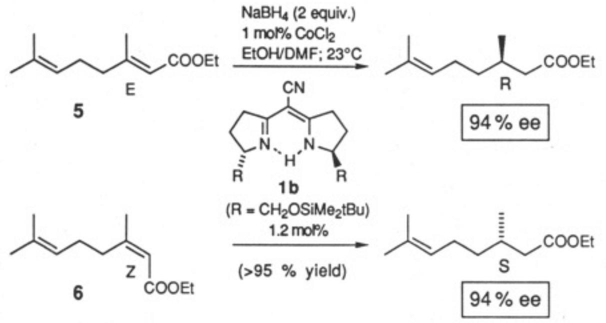
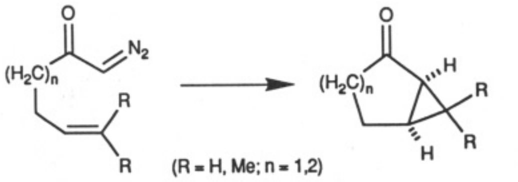
**Scheme III**



structure, but increases if ethyl diazoacetate is replaced by sterically more demanding diazo esters.[19] (Semicorrinato)copper catalysts have also been employed for intramolecular cyclopropanation reactions (eq 1; 75–92 % ee) and for the cyclopropanation of 1,2-trans-disubstituted olefins with diazomethane (70–80% ee).[4a,11,18]



(1)

## Enantioselective Conjugate Reduction of $\alpha,\beta$-Unsaturated Carboxylic Esters and Amides

Cobalt semicorrin complexes were found to catalyze the reduction of electrophilic C=C double bonds using sodium borohydride as reducing agent.[20] In the presence of 0.1–1 mol % of catalyst, formed in situ from $CoCl_2$ and ligand **1b**, $\alpha,\beta$-unsaturated carboxylic esters were cleanly reduced to the corresponding saturated esters in essentially quantitative yield and with high enantiomeric excess. A representative example is shown in Scheme III: ethyl geranate **5** and the (*Z*)-isomer **6** are both converted to ethyl citronellate with 94% ee.[20a] Depending on the double bond geometry, either the (*R*)- or (*S*)-enantiomer is obtained. The isolated double bond is inert under these conditions.

Excellent results have also been obtained with carboxamides such as **7**, **8**, or **9** and analogous primary and secondary amides (Scheme IV).[20b] Even at substrate/catalyst ratios as high as 10 000:1, the enantiomeric excess of **10** stayed above 95%, although the reaction became impracticably slow (90% conversion after 14 days). Tertiary amides, on the other hand, react rather sluggishly and with distinctly lower enantioselectivity. The diene–carboxamide **13** is reduced with high regio- and enantioselectivity; **14** is formed with a preference of ≥95:5 over the corresponding $\alpha,\beta$-unsaturated amide. Unfortunately, the method could not be extended to $\alpha,\beta$-unsaturated ketones because the uncatalyzed (nonselective) reaction with sodium borohydride proceeds at a rate similar to that of the (semicorrinato)cobalt-catalyzed process.

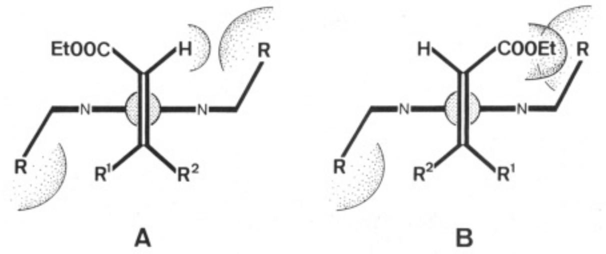
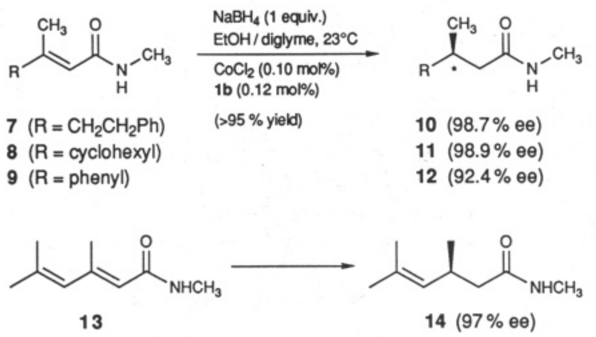


**Figure 1.** Schematic representation of possible transition states in the cobalt-catalyzed conjugate reduction (the cobalt-bound hydride has been omitted for clarity).

**Scheme IV**



Deuteration experiments, using either $NaBD_4$ in EtOH/DMF or $NaBH_4$ in EtOD/DMF, revealed that the $\beta$-H atom in the product stems from borohydride, whereas the H atom introduced into the $\alpha$-position comes from ethanol.[21] Formation of the $\alpha$-(C–H) bond was found to be nonstereoselective. Accordingly, the reduction of analogous substrates with an $\alpha$- instead of a $\beta$-alkyl substituent leads to racemic products.[20b,21]

A tentative rationale for the stereoselectivity of semicorrin cobalt catalysts is proposed in Figure 1.[4] We assume that a (semicorrinato)Co(I) complex is generated under the reaction conditions, which initiates the catalytic cycle by forming a $\pi$-complex with the electrophilic C=C bond of the substrate. Hydride transfer from $NaBH_4$ to the metal center of the catalyst–substrate complex, followed by an intramolecular hydride shift from cobalt to the $\beta$-C atom of the substrate, then leads to a cobalt enolate, which is protonated by the solvent. An alternative mechanism, involving conjugate addition of a Co(I) complex to the substrate, hydride transfer from $NaBH_4$ to the resulting Co(III)–alkyl intermediate, and subsequent formation of the $\beta$-(C–H) bond by reductive elimination, may also be formulated. Both pathways imply that the $\beta$-H atom is introduced at the same side of the C=C bond which is bound to the catalyst. If we assume that the transition states of the enantioselectivity-determining step resemble the hypothetical $\pi$-complexes schematically drawn in Figure 1, the stereoselectivity of the reaction may be rationalized in the following way: of the two transition structures A and B leading to opposite enantiomers, B is expected to be higher in energy because of the steric repulsion between the ester (or amide) group of the substrate and the semicorrin ligand. Therefore, the reaction should prefer a pathway via A, in accordance with the experimental findings.

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[19] Recently, high trans selectivities have been reported for cyclopropanation reactions using diazoacetic acid esters derived from 2,6-di-*tert*-butyl-4-methylphenol (BHT; see Table I and ref 31a) or dicyclohexylmethanol (ref 30b).

[20] (a) Leutenegger, U.; Madin, A.; Pfaltz, A. *Angew. Chem.* **1989**, *101*, 61; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 60. (b) von Matt, P.; Pfaltz, A. *Tetrahedron: Asymmetry* **1991**, *2*, 691.

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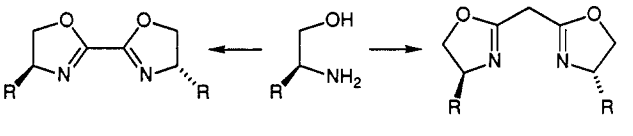
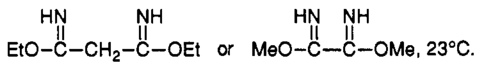
**Scheme V**



Method A: 1. $MeO_2C$-$CH_2$-$CO_2Me$ or $MeO_2C$-$CO_2Me$, 80-100°C; 2. $SOCl_2$, 50-80°C; 3. NaOH, EtOH, THF, 70-80°C.

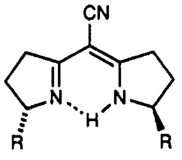
Method B:



$EtO{-}\overset{\overset{\displaystyle HN}{\|}}{C}{-}CH_2{-}\overset{\overset{\displaystyle NH}{\|}}{C}{-}OEt$ or $MeO{-}\overset{\overset{\displaystyle HN}{\|}}{C}{-}\overset{\overset{\displaystyle NH}{\|}}{C}{-}OMe$, 23°C.

## Semicorrin Analogues: 5-Azasemicorrins and Bis(oxazolines)

Because of the electron-rich vinylogous amidine system and the negative charge, semicorrins are expected to act as σ- and π-electron donors which distinctly reduce the electrophilicity of a coordinated metal ion. However, for certain applications it would be desirable to employ structurally analogous neutral ligands which are weaker electron donors, or even π-acceptors. Possible candidates for neutral ligands of this type are the 5-azasemicorrins **17**, the bioxazolines **18**, and the methylenebis(oxazolines) **19**.



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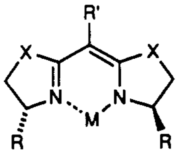
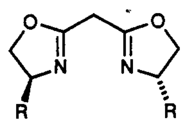
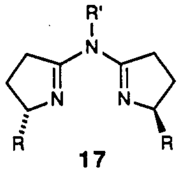


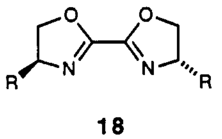
**16**



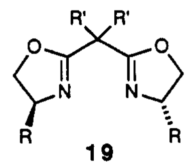
**15**



**17**



**18**

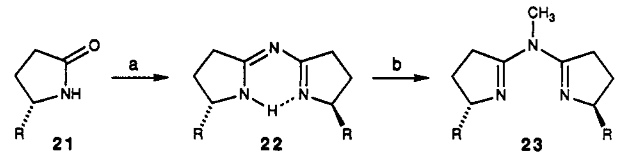


**19**

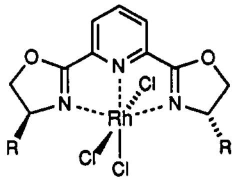
Methylenebis(oxazolines) **15**, derived from malonate, are close structural analogues of the semicorrins **1**. Removal of a proton at the methylene bridge leads to anionic ligands which, as shown in formula **16**, provide essentially the same steric environment for a coordinated metal ion as their semicorrin counterparts and, therefore, we thought, could be useful substitutes for semicorrins.

Chiral oxazolines of this type are attractive ligands because they are easily accessible from amino alcohols (Scheme V;[22] see also ref 23). A wide variety of enantiomerically pure amino alcohols are commercially available while others are readily prepared by reduction of α-amino acids. Although oxazolines have frequently served as versatile chiral auxiliaries in asymmetric synthesis,[24] their potential as ligands for enantioselective catalysts has not been recognized until quite recently. Just after we had started to investigate $C_2$-symmetric bis(oxazolines), first reports appeared in the literature, describing the application of chiral oxazolines for the stereocontrol of metal-catalyzed reactions. Bidentate oxazoline ligands derived from pyridine-2-carboxylate were used for the Rh-catalyzed hydrosilylation of ketones and for the Cu-catalyzed monophenylation of *meso*-diols with $Ph_3Bi(OAc)_2$.[25] Nishyiama et al. developed an interesting new class of $C_2$-symmetric tridentate bis(oxazoline) ligands.[26] The corresponding Rh(III) complexes **20**, after treatment with $AgBF_4$, proved to be efficient enantioselective catalysts for the hydrolsilylation of ketones. A series of related oxazoline metal complexes has been described by Bolm and coworkers.[27]

**Scheme VI**[a]



[a] Reagents: (a) See text. (b) MeI, 23 °C; $NaHCO_3$, $CH_2Cl_2$, $H_2O$.



(Nishiyama *et al.*)[26]

**20**

5-Azasemicorrins **23** are readily prepared by N-methylation of an appropriate precursor **22** which can be synthesized from a butyrolactam **21** either by a four-step sequence via the corresponding amidine or in one step with bis(trimethylsilyl)amine and *p*-toluenesulfonic acid, using a procedure developed by Vorbrüggen[29] for the conversion of amides to amidines (Scheme VI).[28]

The obvious first test of methylenebis(oxazolines) **15** was the copper-catalyzed cyclopropanation of styrene with diazoacetates. Among the various derivatives that we had prepared (**15**; R = benzyl, *sec*-alkyl, phenyl, *tert*-butyl), the bulky *tert*-butyl-substituted derivative proved to be the most effective ligand, giving similarly high enantiomeric excesses as the semicorrin **1c** (R = $CMe_2OH$). When this work was essentially completed, Masamune and co-workers reported the results of an independent parallel study.[30] They had prepared the very same methylenebis(oxazoline) derivatives **15** and applied them to the copper-catalyzed cyclopropanation of olefins. Consistent with our studies, by far the best selectivities were obtained with the copper complex **25** of the di-*tert*-butyl-substituted ligand (Table I). In addition to styrene, a series of terminal and disubsti-

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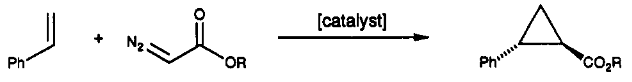
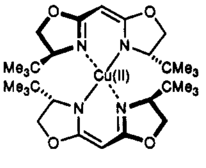
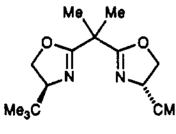
**Table I. Enantioselective Cyclopropanation of Styrene**



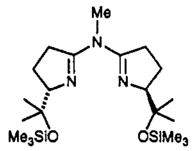
| | | | |
|---|---|---|---|
| **25**/PhNHNH$_2$[22,30a] | R = ethyl | trans/cis = 75:25 | 90% ee (*R*, *R*) |
| | *tert*-butyl | 80:20 | 94% ee (*R*, *R*) |
| | *l*-menthyl | 86:14 | 98% ee (*R*, *R*) |
| **26**/Cu(I)OTf[31] | R = ethyl | trans/cis = 73:27 | 99% ee (*R*, *R*) |
| | *tert*-butyl | 81:19 | 96% ee (*R*, *R*) |
| | BHT | 94: 6 | 99% ee (*R*,*R*) |
| **27**/Cu(I)OTf[28] | R = ethyl | trans/cis = 75:25 | 94% ee (*S*, *S*) |
| | *tert*-butyl | 86:14 | 96% ee (*S*, *S*) |
| | *d*-menthyl | 84:16 | 98% ee (*S*, *S*) |



**25**



**26**



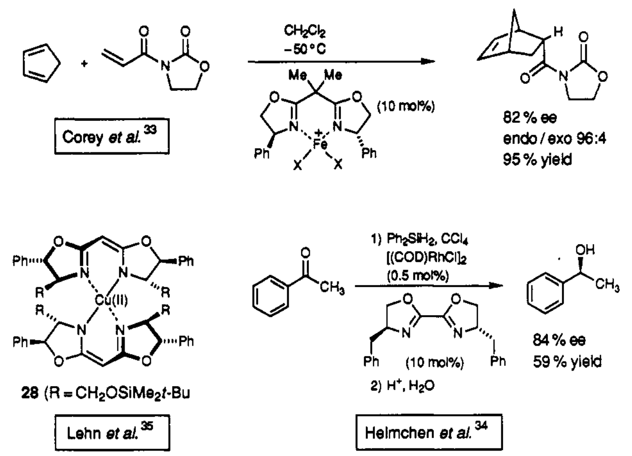
**27**

tuted trans olefins were converted to cyclopropanes with high enantiomeric excesses.[30a] More recently, Lowenthal and Masamune showed that the method works well also for certain trisubstituted and unsymmetrical disubstituted cis olefins if the di-*tert*-butyl-substituted ligand **15** is replaced by structurally modified bis(oxazolines).[30b]

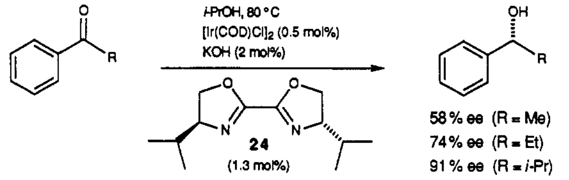
A related but even more selective, highly efficient catalyst, prepared from the neutral bis(oxazoline) ligand **26** and copper(I) triflate, was described by Evans et al. (Table I).[31] Terminal olefins such as styrene and 2-methylpropene were converted to cyclopropanecarboxylates with up to 99% ee, using substrate/catalyst ratios as high as 1000:1. The same catalyst was used for an analogous enantioselective aziridine formation. In view of these results, we briefly investigated analogous catalysts derived from neutral 5-azasemicorrins and copper(I) triflate. The best results were obtained with sterically demanding ligands such as **27**. Taking the enantiomeric purity of the trans product obtained from ethyl diazoacetate and styrene as a measure, the selectivities of the azasemicorrin catalysts ranged between those of the Evans catalyst and the semicorrin- and bis(oxazoline)–Cu complexes **4** and **25**.

The potential of $C_2$-symmetric bis(oxazolines) has also been recognized by other groups (Scheme VII).[32] Corey et al. reported an example of an enantioselective Diels–Alder reaction catalyzed by an Fe(III)–bis(oxazoline) complex.[33] Helmchen and co-workers prepared a series of differently substituted bioxazolines and analogous bithiazolines which they employed in the rhodium-catalyzed enantioselective hydrosilylation of acetophenone.[34] The Lehn group described the synthesis and X-ray analysis of the crystalline Cu(II)–bis(oxazoline) complex **28**.[35] The crystal structures of **28** and the analogous bis(semicorrinato) complex **4**[7b] demonstrate the close structural resemblance of semicorrin and methylenebis(oxazoline) ligands. The preparation of Rh(I), Ru(II), Cu(I), and Pd(II) complexes of bioxazolines **18** was reported by Onishi and Isagawa.[36]

**Scheme VII**



Although screening of various Rh–, Ru–, and Ir–bis(oxazoline) complexes did not reveal any apparent reactivity toward molecular hydrogen, we found that (bioxazoline)iridium(I) complexes, prepared in situ from $[Ir(COD)Cl]_2$, catalyze the reduction of ketones using 2-propanol as hydride donor. Enantioselective hydrogen-transfer reactions of this type have been extensively studied by Mestroni and co-workers.[37] The best selectivity was observed in the reduction of isopropyl phenyl ketone using ligand **24** (eq 2; 91% ee at 70% conversion, 88% ee at 93% conversion).[22] These results compare favorably to the selectivities reported for other iridium catalysts.[37] Dialkyl ketones proved to be unreactive under these conditions. Iridium complexes with the neutral bis(oxazoline) ligand **19** (R = *i*-Pr, R′ = Me) or with anionic semicorrin or bis(oxazoline) ligands did not exhibit any significant catalytic activity.



(2)

Another area of application for neutral azasemicorrin and bis(oxazoline) ligands, which we are currently exploring, are Pd-catalyzed nucleophilic allylic substitutions.[38] The search for efficient enantioselective catalysts for this versatile, widely used class of reactions

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[32] For a short review, see: Bolm, C. *Angew. Chem.* **1991**, *103*, 556; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 542.

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[34] Helmchen, G.; Krotz, A.; Ganz, K. T.; Hansen, D. *Synlett* **1991**, 257.

[35] Hall, J.; Lehn, J.-M.; DeCian, A.; Fischer, J. *Helv. Chim. Acta* **1991**, *74*, 1.

[36] Onishi, M.; Isagawa, K. *Inorg. Chim. Acta* **1991**, *179*, 155.

[37] Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051.

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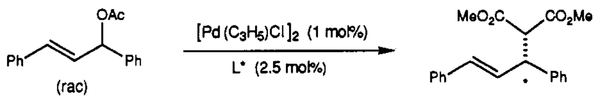
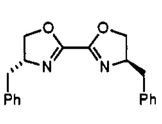
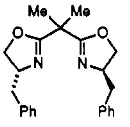
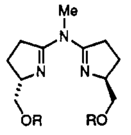
**Table II. Enantioselective Allylic Alkylation**

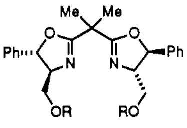


| Ligand | Conditions | % Yield | % ee |
|---|---|---|---|
| 29 | $NaCH(CO_2Me)_2$, THF, 50°C | 86 | 77 (*R*) |
| 30 | " | 85 | 76 (*R*) |
| 30 | $CH_2(CO_2Me)_2$, BSA, KOAc, $CH_2Cl_2$, 23°C | 97 | 88 (*R*) |
| 23a | " | 99 | 95 (*R*) |
| 31 | " | 97 | 97 (*S*) |


**29**


**30**


**23a** (R = $SiMe_2t$-Bu)

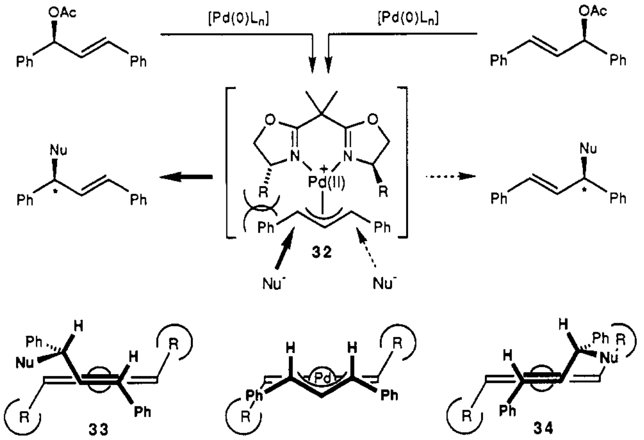

**31**

is an important goal of current research in this field.[39] During the last years, a number of chiral phosphine complexes have been reported that catalyze the conversion of achiral or racemic allylic substrates to optically active substitution products. Chiral nitrogen ligands, on the other hand, have received much less attention.[39g]

Palladium complexes with neutral bis(oxazoline) and azasemicorrin ligands were found to be efficient catalysts for the reaction of allylic acetates such as 1,3-diphenyl-2-propenyl acetate with dimethyl malonate (Table II).[22,28] The most effective ligands that we have found so far are the azasemicorrin **23a**[28] and the methylenebis(oxazoline) **31**.[41] The best results were obtained in apolar solvents using a mixture of dimethyl malonate and *N*,*O*-bis(trimethylsilyl)acetamide (BSA), according to a procedure described by Trost.[40] The catalytic process was initiated by addition of a catalytic amount of potassium acetate. Under these conditions, in the presence of 1–2 mol % of catalyst, the reaction proceeded smoothly at 0–23 °C to give the desired product in high enantiomeric purity and essentially quantitative yield.[42]

How can we explain the remarkable enantioselectivities induced by these ligands? According to the generally accepted mechanism of Pd-catalyzed allylic alkylation,[38,39b,h] the reaction is assumed to proceed by the pathway shown in Scheme VIII. Because the two substituents at the allylic termini are identical, the same (allyl)palladium(II) intermediate **32** is formed starting from the two enantiomers of the racemic substrate. The enantioselectivity of the overall reaction is determined by the regioselectivity of the subsequent step involving nucleophilic cleavage of one of the Pd–C bonds, a type of process which has been shown to take place with inversion of configuration.[39b,g,h] Under the influence of the chiral ligand, the nucleophile attacks preferentially one of the two allylic termini. So the question is, what factors determine the regioselectivity of this step.

## Scheme VIII



Some clues are provided by the crystal structures of two (allyl)palladium complexes with the bis(oxazoline) **30** (Figure 2).[43] The complex with the unsubstituted allyl ligand shows the expected square-planar coordination geometry of Pd(II) and an almost planar conformation of the methylenebis(oxazoline) ligand framework. The structure of the corresponding (1,3-diphenylallyl)palladium complex **32**, which is the actual intermediate in the catalytic reaction shown in Scheme VIII, is strikingly different. As a consequence of the steric repulsion between the allylic phenyl group and the adjacent benzyl substituent at the oxazoline ring, the bis(oxazoline) ligand adopts a strongly distorted, nonplanar conformation. The repulsive interaction between the chiral ligand and one of the allylic termini is also reflected in the bond lengths and bond angles of the $[PdC_2N_2]$ core (see Figure 2). From the absolute configuration of the product we know that the nucleophile preferentially attacks the longer, more strained Pd–C bond (see Scheme VIII), suggesting that the release of steric strain, associated with the cleavage of this bond, may be one of the factors responsible for enantioselection. This concept of regioselectivity control by steric activation of one of the Pd–C bonds differs from previously developed concepts which are based on direct interactions between the chiral ligand and the nucleophile.[39a,c,44] Another possible factor contributing to the observed selectivity may be related to the thermodynamic stability of the resulting Pd(0)–olefin complexes which are postulated as primary products.[39h] Assuming a square-planar coordination geometry,[45] the Pd(0) complex **33** of the major product enantiomer is expected to be more stable than **34**, on the basis of steric considerations. Analogous steric interactions

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(39) (a) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143. (b) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033. Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046. (c) Hayashi, T.; Yamamoto, A.; Hagihara, T.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 191. Hayashi, T. *Pure Appl. Chem.* **1988**, *60*, 7. (d) Okada, Y.; Minami, T.; Umezu, Y.; Nishikawa, S.; Mori, R.; Nakayama, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 667. (e) Yamaguchi, M.; Shima, T.; Yamagishi, T.; Hida, M. *Tetrahedron: Asymmetry* **1991**, *2*, 663. (f) Trost, B. M.; Van Vranken, D. L. *Angew. Chem.* **1992**, *104*, 194; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 228. Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327. (g) Togni, A. *Tetrahedron: Asymmetry* **1991**, *2*, 683. (h) Review: Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257.

(40) Trost, B. M.; Brickner, S. J. *J. Am. Chem. Soc.* **1983**, *105*, 568. See also refs 38b and 39a.

(41) Koch, G.; Pfaltz, A. Unpublished results.

(42) Even higher selectivities have recently been obtained with 2-(2′-phosphinoaryl)-2-oxazolines as chiral ligands. Von Matt, P.; Pfaltz, A. *Angew. Chem.*, in press.

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(44) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857.

(45) See, e.g., Mingos, D. M. P. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 3, Section 19.4.3.

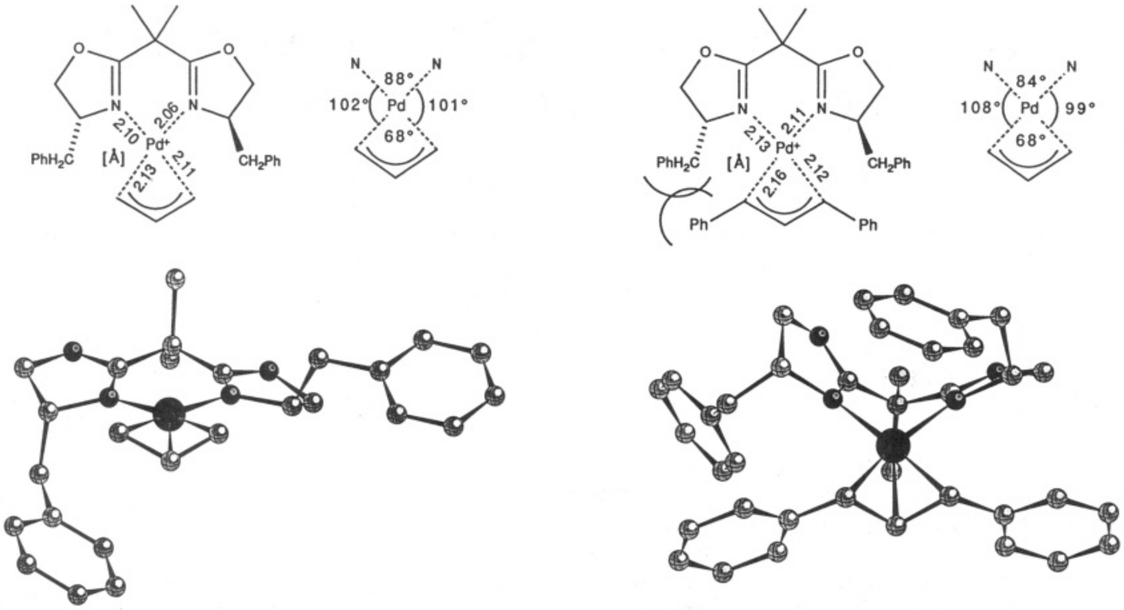

**Figure 2.** Crystal structures of [(allyl)Pd$^{II}$(**30**)]$^+$ $PF_6^-$ and [(1,3-diphenylallyl)Pd$^{II}$(**30**)]$^+$ $PF_6^-$ (the $PF_6^-$ ions are not shown).[43]

between the chiral ligand and the coordinated substrate should also be present in the corresponding transition states.

## Conclusion

The straightforward concept of a conformationally rigid ligand scaffold with two lateral stereogenic centers, arranged in a $C_2$-symmetric fashion in close proximity to the coordination sphere, has led to effective ligands for the stereocontrol of metal-catalyzed reactions. The remarkable enantioselectivities induced by semicorrins and structurally related 5-azasemicorrins and bis(oxazolines) point to a considerable potential of these ligands in asymmetric catalysis. Starting from commercially available amino alcohols or amino acids, a wide variety of such ligands can be prepared in enantiomerically pure form. By proper selection of the ligand structure, the steric influence, the coordination geometry, and the electronic properties of the ligand can be adjusted to the specific requirements of a particular application. The ready access to these ligands and the ease of modifying their structures offer excellent opportunities for the development of tailor-made enantioselective catalysts for many other classes of reactions.

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