21. C_2-Symmetric 4,4',5,5'-Tetrahydrobi(oxazoles) and 4,4',5,5'-Tetrahydro-2,2'-methylenebis[oxazoles] as Chiral Ligands for Enantioselective Catalysis

Preliminary Communication

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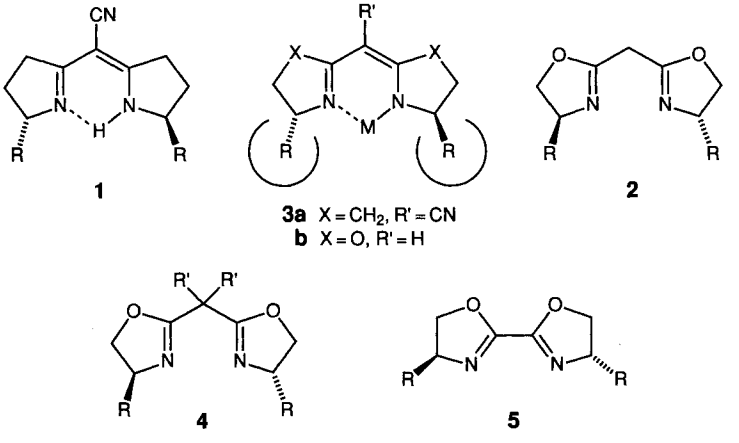
The synthesis of a series of enantiomerically pure, C_2-symmetric 4,4',5,5'-tetrahydro-2,2'-methylenebis[oxazoles] and 4,4',5,5'-tetrahydro-2,2'-bi(oxazoles) is reported. Copper complexes with anionic tetrahydromethylenebis[oxazole] ligands are efficient catalysts for the enantioselective cyclopropane formation from olefins and diazo compounds (up to 96% ee in the reaction of styrene with menthyl diazoacetate). Tetrahydrobi(oxazole)iridium(I) complexes were found to catalyze transfer hydrogenations of aryl alkyl ketones with i-PrOH (up to 91% ee). Tetrahydrobi(oxazole)palladium complexes can be used as enantioselective catalysts for allylic nucleophilic substitution (up to 77% ee in the reaction of PhCH=CHCH(OAc)Ph with $NaHC(COOMe)_2$).

Introduction. – In our previous papers in this series [1–3], we have reported on the synthesis and application of chiral semicorrins **1**, a class of bidentate ligands specifically designed for enantioselective control of metal-catalyzed reactions. Essential structural features of the semicorrins **1** are the conformationally rigid ligand framework and the C_2-symmetric arrangement of the stereogenic centers in close proximity to the coordination site. In a metal complex, the substituents at the stereogenic centers effectively shield the metal ion from two opposite directions and, therefore, should have a distinct effect on the stereochemical course of a reaction taking place in the coordination sphere. So far, we have found two promising areas of application for semicorrin ligands: [Cu(semicorrinato)]-catalyzed cyclopropane formation from olefins and diazo compounds (up to 97% ee [1][3]) and [Co(semicorrinato)]-catalyzed conjugate reduction of α,β-unsaturated carboxylic esters and amides (up to 99% ee [2][3]).

Symmetric 4,4',5,5'-tetrahydro-2,2'-methylenebis[oxazoles] **2** are structurally closely related to the semicorrins **1**. Removal of a proton at the methylene bridge leads to anionic ligands which provide essentially the same steric environment for a coordinated metal ion as the corresponding semicorrinates (*cf.* **3**). Chiral tetrahydrobis[oxazoles] of this type can be easily synthesized from amino alcohols and malonic acid. Starting from other dicarboxylic

[1]) Diploma thesis, ETH Zürich, summer semester 1990.

acids, a variety of related ligands such as **4** and **5** can be prepared[2]). The ligands **4**, containing two substituents at the methylene bridge which prevent deprotonation at that position, are neutral analogs of the potentially anionic ligands **2**. The tetrahydrobi(oxazoles) **5**, derived from oxalic acid, are of interest because of their π-acceptor properties and the different coordination geometry compared to ligands of type **1**, **2**, and **4** which all form six-membered chelate rings. Considering the easy access to these compounds [7] and the wide variety of readily available, enantiomerically pure amino alcohols which can serve as starting materials, we decided to prepare representative examples for each class of dihydrooxazole ligands **2**, **4**, and **5**, and to evaluate their potential for the stereochemical control of metal-catalyzed reactions. A recent publication by *Masamune* and coworkers [8], describing enantioselective cyclopropane formation from olefins catalyzed by tetrahydro-methylenebis[oxazole]-derived copper complexes of type **3b**, prompts us to report our results in preliminary form[3]).



Chiral Tetrahydrobi(oxazole) and Tetrahydro-methylenebis[oxazole] Ligands. – The syntheses of various tetrahydro-methylenebis[oxazole] derivatives are summarized in *Scheme 1*. The required enantiomerically pure amino alcohols **6a–e** and **9** were either commercially available or could be easily prepared from α-amino acids by reduction with $LiAlH_4$. Conversion to the corresponding diamides **7a–e**, followed by treatment with $SOCl_2$

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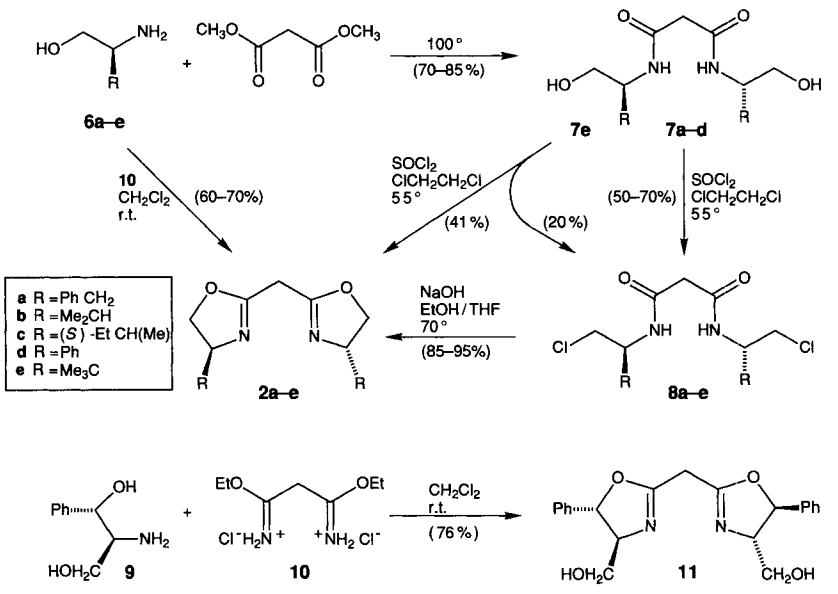
[2]) Although chiral dihydrooxazole derivatives of type **2** and **5** have been known for some time [4], they have not been used in asymmetric synthesis. For enantioselective metal catalysts based on chiral dihydrooxazoles derived from pyridine-2-carboxylate and C_2-symmetric tetrahydrobis[oxazoles] derived from pyridine-1,5-dicarboxylate, see [5]. The synthesis of tetrahydrobis[oxazole] ligands derived from benzene-1,2- and -1,3-dicarboxylate is described in [6].

Note added in proof: *Helmchen* and *Krotz* have recently studied the enantioselective hydrosilylation of acetophenone using Rh catalysts with ligands of type **2** and **5** (*G. Helmchen*, personal communication; see *A. Krotz*, Dissertation, University of Heidelberg, 1991).

[3]) While preparing this manuscript, we learned that *Evans* and coworkers have also synthesized various tetrahydrobi(oxazole) and tetrahydro-methylenebis[oxazole] ligands of type **2**, **4**, and **5**. With Cu^I complexes of neutral ligands **4** as catalysts, they obtained excellent enantioselectivities in the cyclopropane formation from olefins [9].

Scheme 1

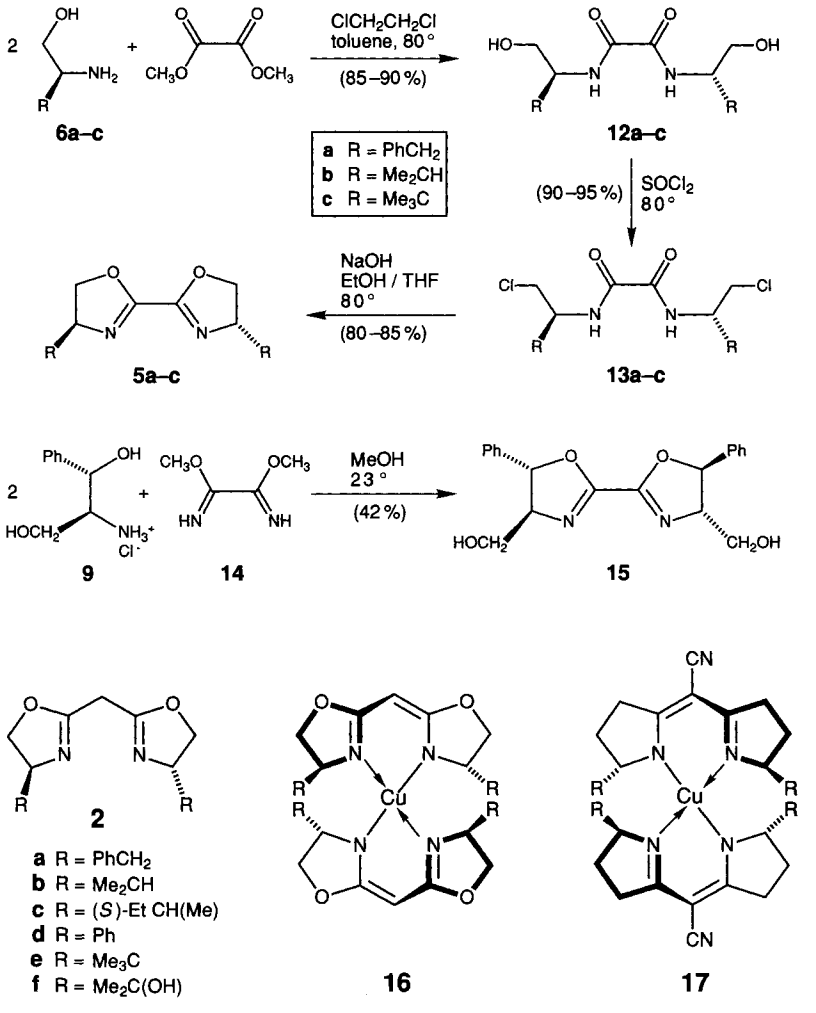


and base-induced cyclization afforded, *via* **8a–e**, enantiomerically pure tetrahydrobis[oxazoles] **2a–e** in 35–50% overall yield. The analogous sequence, starting from dimethylmalonyl dichloride and **6b**, led to the tetrahydrobis[oxazole] **4** (R = i-Pr, R' = Me). Alternatively, such ligands may be prepared in one step from the corresponding amino alcohols by condensation with the imidate **10** (*Scheme 1*, **6** + **10** → **2** and **9** + **10** → **11**) [10] or, as described by *Masamune* and coworkers [8], by treating *N*-(hydroxyalkyl)amides **7** with Me_2SnCl_2.

Starting from amino alcohols **6a–c** and dimethyl oxalate, enantiomerically pure tetrahydrobi(oxazoles) **5a–c** were obtained in excellent overall yields *via* **12a–c** and **13a–c** (*Scheme 2*) [4a]. Tetrahydrobi(oxazole) formation in one step *via* imidate/amino alcohol condensation is also possible in this case, as illustrated by the selective transformation of the dihydroxyamine **9** and **14** to **15** in 42% yield (non-optimized conditions). The diimidate **14** is readily prepared from cyanogen which is generated *in situ* from NaCN by oxidation with $CuSO_4$ and trapped by NaOMe [11].

Enantioselective Cyclopropane Formation with Tetrahydro-methylenebis[oxazole]copper Catalysts. – To compare the tetrahydro-methylenebis[oxazole] ligands **2** to the corresponding semicorrins **1**, we studied the Cu-catalyzed cyclopropane formation from styrene and menthyl diazoacetate **18**, a reaction which we had previously investigated using (semicorrinato)copper catalysts [1][3a]. The copper catalysts were generated *in situ* from the corresponding tetrahydrobis[oxazoles] **2** and Cu^{I}(*t*-BuO), or from the Cu^{II} complexes **16** by reduction with phenylhydrazine [1c]. The complexes **16** were readily formed from the ligands **2a–d** under the same conditions as the analogous bis(semicorrinato)copper

Scheme 2

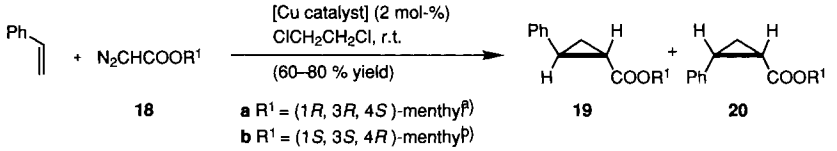


compounds **17** ($Cu(OAc)_2$, MeOH, room temperature) [1b]. The *t*-Bu-substituted tetrahydrobis[oxazole] **2e** proved to be less reactive. In this case, it was necessary to deprotonate the ligand with a strong base, such as BuLi in THF, before adding $CuBr_2$. In contrast to the complexes with less bulky ligands **2a–d**, complex **16** with ligand **2e** (R = *t*-Bu) had to be isolated and purified under non-aqueous conditions by filtration through neutral alumina with CH_2Cl_2 and subsequent recrystallization from cyclohexane or petroleum ether (*cf.* also the procedure in [8]).

Copper complexes of the tetrahydrobis[oxazole] ligands **2a–f** and **11** were all found to be efficient catalysts. In the presence of 1–2 mol-% of catalyst at room temperature, styrene

and diazoacetates **18** were converted to optically active 2-phenyl-1-carboxylates **19** and **20** in chemical yields of 60–80% (*Table 1*). By far the best enantioselectivity was obtained with the *t*-Bu-substituted ligand **2e**. In this case, the catalyst generated from the Cu^{II} complex **16** by reduction with phenylhydrazine proved to be superior to the Cu^{I} catalyst prepared with Cu^{I}(*t*-BuO), whereas with all other tetrahydrobis[oxazole] ligands, the Cu^{I}(*t*-BuO) method gave better results. *Entries i* and *k* allow a direct comparison between the semicorrin and the tetrahydro-methylenebis[oxazole] ligand systems **1** and **2**. In our previous studies [1][3a], ligand **1** (R = $Me_2C(OH)$) was found to be clearly the most selective of a series of differently substituted semicorrins, affording very high enantiomeric excesses with various terminal olefins. In the tetrahydrobis[oxazole] series, the analogous $Me_2C(OH)$-substituted ligand **2f**[4]) proved to be less effective.

Table 1. *Enantioselective Cyclopropane Formation from Styrene and Menthyl Diazoacetates* **18** *using Chiral Tetrahydro-methylenebis[oxazole]copper Catalysts*



18 **a** R^1 = (1*R*, 3*R*, 4*S*)-menthyl[a]) **b** R^1 = (1*S*, 3*S*, 4*R*)-menthyl[b]) **19** **20**

Entry	Catalyst generation[c])	Ligand	Diazo compound	Diastereo-selectivity[d]) **19/20**	Enantiomeric excess[d]) **19** [%]	**20** [%]	Configuration[e]) **19**	**20**
a	*A*	**2a**	**18a**	86:14	19	9	(1*R*,2*R*)	(1*R*,2*S*)
b	*A*	**2b**	**18a**	84:16	13	5	(1*R*,2*R*)	(1*R*,2*S*)
c	*A*	**2c**	**18a**	85:15	9	9	(1*R*,2*R*)	(1*R*,2*S*)
d	*A*	**2d**	**18a**	83:17	55	50	(1*R*,2*R*)	(1*R*,2*S*)
e	*A*	**11**	**18a**	82:18	34	56	(1*R*,2*R*)	(1*R*,2*S*)
f	*A*	**2e**	**18a**	86:14	19	5	(1*R*,2*R*)	(1*R*,2*S*)
g	*B*	**2e**	**18a**	87:13	96	97	(1*R*,2*R*)	(1*R*,2*S*)
h	*B*	*ent*-**2f**	**18b**	83:17	78	71	(1*S*,2*S*)	(1*S*,2*R*)
i	*A*	*ent*-**2f**	**18b**	83:17	90	90	(1*S*,2*S*)	(1*S*,2*R*)
k	*A*[f])	**1** (R=$Me_2C(OH)$)	**18b**	82:18	97	95	(1*S*,2*S*)	(1*S*,2*R*)
l	*B*[f])	**1** (R=$Me_2C(OH)$)	**18b**	82:18	97	95	(1*S*,2*S*)	(1*S*,2*R*)

[a]) (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl, from (–)-menthol.

[b]) (1*S*,2*R*,5*S*)-2-Isopropyl-5-methylcyclohexyl, from (+)-menthol.

[c]) *A*: Catalyst generated *in situ* from **2** and Cu^{I}(*t*-BuO); *B*: generated from the corresponding Cu^{II}complex **16** by reduction with 0.5 mol-equiv. of phenylhydrazine at room temperature (see the experimental procedures in [1c]).

[d]) Determined by GC analysis [1c].

[e]) Assignments according to [1c].

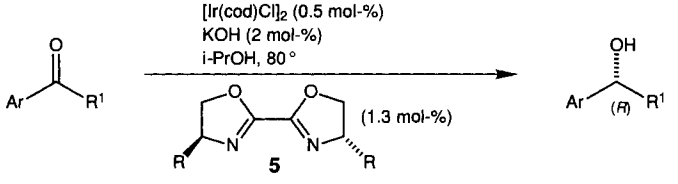
[f]) Results taken from [1c]. *A*: Catalyst generated *in situ* from **1** (R = $Me_2C(OH)$) and Cu^{I}(*t*-BuO)Cu; *B*: generated from the corresponding Cu^{II} complex **17** (R = $Me_2C(OH)$) by reduction with phenylhydrazine.

[4]) Prepared from L-serin methyl ester *via* protection as the corresponding 4,5-dihydro-2-phenyloxazole, followed by *Grignard* reaction with MeMgBr, deprotection with 6N HCl, and condensation with **10** (*cf. Scheme 1*).

The data in *Table 1* are in accordance with the findings of *Masamune* and coworkers [8] who reported excellent enantioselectivities in the cyclopropane formation from various olefins using the copper complex **16** (R = *t*-Bu) as catalyst. The selectivities induced by the $Me_2C(OH)$-substituted semicorrin **1** and the *t*-Bu-substituted bis[oxazole] **2e** are in the same range. However, in our hands, the semicorrin-based catalyst proved to be somewhat more reliable and less sensitive to variation of the reaction conditions.

Iridium-Catalyzed Transfer Hydrogenation of Ketones. – Screening of several transition-metal complexes with dihydrooxazole ligands of type **2** or **5** as potential hydrogenation catalysts did not reveal any apparent reactivity towards H_2. However, Ir^I complexes prepared *in situ* from $[Ir(cod)Cl]_2$ (cod = cycloocta-1,5-diene) and tetrahydrobi(oxazoles) **5** were found to catalyze transfer hydrogenations of ketones with i-PrOH [12] (*Table 2*). Alkyl aryl ketones were smoothly reduced at reflux temperature, affording optically active alcohols, whereas dialkyl ketones proved to be unreactive and gave only racemic products in low yields. The best results were obtained with the i-Pr-substituted ligand **5b** and isopropyl phenyl ketone as substrate (91% ee at 70% conversion, 87–88% ee at 93% conversion). These data compare favorably to the selectivities reported for other iridium catalysts [12a]. The corresponding iridium complexes derived from the neutral ligand **4** (R = i-Pr, R' = Me) or anionic ligands **1** and **2** did not show any significant catalytic activity.

Table 2. *Enantioselective Transfer Hydrogenation of Alkyl Aryl Ketones Catalyzed by [Tetrahydrobi(oxazole)]-iridium Complexes*[a])



Substrate		Ligand **5**	Reaction time [h]	Conversion [%]	Enantiomeric excess[b])[%]
Ar	R^1	R			
Ph	Me	**a** $PhCH_2$	3	89	47
Ph	Me	**b** Me_2CH	3	89	58
Ph	Me	**c** Me_3C	3	<5	–
4-$MeOC_6H_4$	Me	**b** Me_2CH	3	71	57
2-Naphthyl	Me	**b** Me_2CH	3	94	63
Ph	Me_2CH	**b** Me_2CH	3	70	91
Ph	Me_2CH	**b** Me_2CH	7	93	88

[a]) A solution of ligand **5** (1.3 mol-%, based on ketone) in i-PrOH was added to $[Ir(cod)Cl]_2$ (0.5 mol-%) under N_2. After stirring for 10 min at room temperature, 0.05M KOH (2 mol-%) in i-PrOH and ketone were added. The degassed solution (0.8M in ketone) was stirred at 80° *in vacuo* in an ampoule fitted with a *Teflon* stopper.

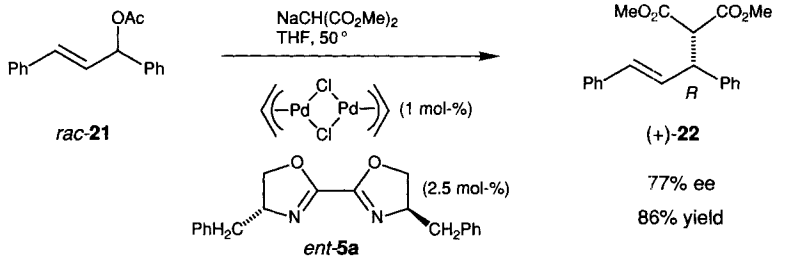
[b]) Determined by GC using a chiral capillary column (heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin; *OV-1701*-vinyl) [18].

Although [tetrahydrobi(oxazole)]iridium complexes so far cannot compete with the most efficient catalysts that have been developed for the enantioselective reduction of ketones [13], the substantial enantiomeric excesses induced by ligand **5b** demonstrate that the stereochemical course of a metal-catalyzed process can be strongly influenced by chiral tetrahydrobi(oxazoles) of this type.

Palladium-Catalyzed Allylic Alkylation. – As a further possible application of tetrahydrobi(oxazole) ligands, we decided to study transition-metal-catalyzed nucleophilic allylic substitution reactions [14–16]. The most promising enantioselective catalysts reported to date for this class of reactions are the chiral (ferrocenylphosphine)palladium complexes developed by *Hayashi* and coworkers [16] (for a study of [$Pd^{II}(\eta^3$-allyl)] complexes with chiral bidentate N-ligands, see [17]).

Some preliminary results obtained with [tetrahydrobi(oxazole)]palladium complexes are summarized in *Scheme 3*. In the presence of 2 mol-% of the complex prepared *in situ* from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand *ent*-**5a**, racemic 1,3-diphenylprop-2-enyl acetate reacted cleanly with the sodium salt of dimethyl malonate to afford diester (+)-**22** in 86% yield. The enantiomeric purity of the product ranged between 75 and 80% ee, as shown by ^{1}H-NMR spectroscopy in the presence of $[Eu(hfc)_3]$. The corresponding catalyst prepared from ligand **15** was also quite selective, although the reaction was rather slow in this case and did not go to completion (22% yield of (–)-**22**, 66% ee). Palladium complexes with the i-Pr- and *t*-Bu-substituted ligands **5b** and **5c** showed no apparent reactivity under these conditions.

Scheme 3



The significant enantiomeric excesses induced by ligands **5a** and **15** are encouraging, considering the fact that the selectivities obtained with ferrocenylphosphines and other chiral phosphine ligands in this particular transformation are distinctly lower (20–55% ee) [15][16]. However, sodium acetylacetonate, a nucleophile which in the (ferrocenylphosphine)palladium-catalyzed reaction with *rac*-**21** affords enantioselectivities up to 92% ee, failed to react in the presence of tetrahydro[bi(oxazole)]palladium catalysts. Extension of our studies to other nucleophiles and substrates is in progress.

Conclusion. – Our results, as well as independent studies from the laboratories of *Masamune* [8] and *Evans* [9], point to a considerable potential of chiral tetrahydrobi(oxazole) and tetrahydro-methylenebis[oxazole] ligands in enantioselective catalysis. As shown, a wide variety of such ligands can be readily prepared in enantiomerically pure form, starting from commercially available amino alcohols or amino acids. By proper selection of the substituents at the stereogenic centers, and by varying the chelate ring size and the electron donor and acceptor properties, the ligand structure can be adjusted to the requirements of a particular application. In this way, it should be possible to develop efficient enantioselective catalysts for many other metal-mediated processes.

Experimental. – *Selected Analytical Data of 4,4',5,5'-Tetrahydro-2,2'-methylenebis[oxazoles]* **2a–f**, **11** *and 4,4',5,5'-Tetrahydro-2,2'-bi(oxazoles)* **5a–c** *and* **15**.

2a. $[\alpha]_D^{23} = -62.7$ ($c = 1.26$, EtOH). IR ($CHCl_3$): 1660*s*, 1495*m*, 1470*m*, 1450*m*, 1385*m*, 1360*m*, 985*s*, 700*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.32–7.19 (*m*, 2 C_6H_5); 4.44 (*m*, H–C(4,4')); 4.23 (*dd*, $J = 8.5, 9.3$, H_a–C(5,5')); 4.02 (*dd*, $J = 7.2, 8.5$, H_b–C(5,5')); 3.32 (*t*, $J \approx 1.1$, C(2)CH_2C(2')); 3.11 (*dd*, $J = 5.3, 13.7$, 2 *H*CHPh); 2.67 (*dd*, $J = 9.6, 13.7$, 2 *H*CHPh). ^{13}C-NMR ($CDCl_3$, 75 MHz): 162.1 (C(2,2')); 137.8 (arom. C); 129.2, 128.5, 126.5 (arom. CH); 72.3 (C(5,5')); 67.5 (C(4,4')); 41.5 (CH_2Ph); 28.4 (C(2)CH_2C(2')).

2b. $[\alpha]_D^{23} = -147.6$ ($c = 1.20$, EtOH). IR ($CHCl_3$): 1670*s*, 1590*m*, 1480*m*, 1470*m*, 1390*m*, 1360*m*, 990*s*, 660*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.27 (*dd*, $J = 7.7, 9.1$, H_a–C(5,5')); 3.95 (*m*, H_b–C(5,5'), H–C(4,4')); 3.35 (*t*, $J = 1.0$, C(2)CH_2C(2')); 1.76 (*m*, 2 *C*HMe_2); 0.95 (*d*, $J = 6.7$, 2 CH_3); 0.88 (*d*, $J = 6.8$, 2 CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): 161.6 (C(2,2')); 72.2 (C(4,4')); 70.5 (C(5,5')); 32.5 (*C*HMe_2); 28.4 (C(2)CH_2C(2')); 18.6 (CH_3); 18.0 (CH_3).

2c. $[\alpha]_D^{23} = -127.7$ ($c = 1.02$, EtOH). IR ($CHCl_3$): 1665*s*, 1480*m*, 1460*m*, 1380*m*, 990*s*, 660*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.25 (*m*, H_a–C(5,5')); 4.09 (*m*, H_b–C(5,5'), H–C(4,4')); 3.34 (*s*, C(2)CH_2C(2')); 1.66–1.45 (*m*, 4 H), 1.30–1.10 (*m*, 2 H) (CH_2CHC(4,4')); 0.90 (*t*, $J = 7.4$, 2 CH_3CH_2); 0.82 (*d*, $J = 6.8$, 2 CH_3CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 161.5 (C(2,2')); 70.8 (C(4,4')); 70.1 (C(5,5')); 38.8 (*C*HMeEt); 28.4 (C(2)CH_2C(2')); 26.0 (CH_2Me); 14.2 (CH_3); 11.5 (CH_3).

2d. $[\alpha]_D^{23} = -121.6$ ($c = 0.96$, EtOH). IR ($CHCl_3$): 1660*s*, 1490*m*, 1470*m*, 1455*m*, 1385*m*, 1360*m*, 990*s*, 700*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.36–7.22 (*m*, 2 C_6H_5); 5.25 (br. *t*, $J \approx 9.0$, H–C(4,4')); 4.69 (*dd*, $J = 8.3$, 10.2, H_a–C(5,5')); 4.19 (*dd*, $J = 8.3$, 8.0, H_b–C(5,5')); 3.57 (*t*, $J = 1.1$, C(2)CH_2C(2')). ^{13}C-NMR ($CDCl_3$, 75 MHz): 163.0 (C(2,2')); 142.0 (arom. C); 128.7, 127.6, 126.7 (arom. CH); 75.4 (C(5,5')); 69.8 (C(4,4')); 28.4 (C(2)CH_2C(2')).

2e. M.p. 52°. $[\alpha]_D^{23} = -149.3$ ($c = 1.13$, EtOH). IR ($CHCl_3$): 1670*s*, 1470*m*, 1400*m*, 1485*m*, 1465*m*, 1000*m*, 985*m*, 710*m*, 660*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.20 (*dd*, $J = 8.7$, 10.2, H_a–C(5,5')); 4.09 (*dd*, $J = 7.7$, 8.6, H_b–C(5,5')); 3.88 (*m*, H–C(4,4')); 3.35 (*t*, $J = 1.1$, C(2)CH_2C(2')); 0.88 (*s*, 2 *t*-Bu). ^{13}C-NMR ($CDCl_3$, 75 MHz): 161.5 (C(2,2')); 75.8 (C(4,4')); 69.1 (C(5,5')); 33.7 (*C*Me_3); 28.4 (C(2)CH_2C(2')); 25.7 (CH_3).

ent-**2f**. M.p. 93–94°. $[\alpha]_D^{23} = +106.6$ ($c = 0.94$, EtOH). IR ($CHCl_3$): 3340*m* (br.), 1680*s*, 1470*m*, 1420*m*, 1390*m*, 1370*m*, 1240*m*, 1190*m*, 1165*m*, 1040*m*, 990*m*, 940*m*, 660*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 4.41 (*dd*, $J = 6.8$, 8.5, H_a–C(5,5')); 4.26 (*dd*, $J = 8.5$, 9.6, H_b–C(5,5')); 4.03 (*m*, H–C(4,4')); 3.30 (*t*, $J = 1.1$, C(2)CH_2C(2')); 3.15 (br. *s*, 2 OH); 1.30 (*s*, 2 CH_3); 1.15 (*s*, 2 CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): 164.3 (C(2,2')); 74.8 (C(4,4')); 71.5 (C–OH); 69.5 (C(5,5')); 28.2 (C(2)CH_2C(2')); 26.9 (CH_3); 25.5 (CH_3).

11. M.p. 111°. $[\alpha]_D^{23} = -77.2$ ($c = 1.04$, EtOH). IR ($CHCl_3$): 3340*m* (br.), 1675*s*, 1490*m*, 1455*m*, 1420*m*, 1395*m*, 1040*m*, 980*m*, 700*s*. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.37–7.24 (*m*, 2 C_6H_5); 5.52 (*d*, $J = 6.6$, H–C(5, 5')); 4.12 (*m*, H–C(4,4')); 3.94 (*dd*, $J = 2.8, 11.9$, 2 *H*CH(OH)); 3.65 (*dd*, $J = 3.3, 11.9$, 2 *H*CH(OH)); *ca.* 4.6–3.0 (v. br., 2 OH); 3.55 (*s*, C(2)CH_2C(2')). ^{13}C-NMR ($CDCl_3$, 75 MHz): 163.9 (C(2,2')); 139.9 (arom. C); 128.9, 128.6, 125.8 (arom. CH); 83.0 (C(5,5')); 75.9 (C(4,4')); 63.5 (CH_2OH); 28.5 (C(2)CH_2C(2')).

5a. M.p. 131–132°. $[\alpha]_D^{23} = -42.6$ ($c = 1.06$, EtOH). IR ($CHCl_3$): 1619*s*, 1600*w*, 1490*w*, 1450*w*, 1260*w*, 1135*s*, 1092*m*, 1030*w*, 945*s*, 700*m*. ^{1}H-NMR ($CDCl_3$, 300 MHz)[5]: 7.33–7.19 (*m*, C_6H_5); 4.66–4.55 (*m*, H–C(4)); 4.37 (*dd*, $J = 9.5, 8.7$, H_a–C(5)); 4.16 (*t*, $J \approx 8.4$, H_b–C(5)); 3.27 (*dd*, $J = 5.0, 13.9$, *H*CHPh); 2.71 (*dd*, $J = 9.2, 13.9$, *H*CHPh).

5b. M.p. 50°. $[\alpha]_D^{23} = -158.8$ ($c = 0.97$, $CHCl_3$). IR ($CHCl_3$): 1620*s*, 1475*w*, 1462*w*, 1382*w*, 1365*w*, 1336*w*, 1256*m*, 1140*m*, 1118*s*, 1106*m*, 1010*m* (br.), 941*m*, 855*w*. ^{1}H-NMR ($CDCl_3$, 200 MHz)[5]: 4.51–4.37 (*m*, 1 H), 4.18–4.03 (*m*, 2 H) (OCH_2CH); 1.95–1.73 (*m*, *H*CMe_2); 1.02 (*d*, $J = 6.7$, CH_3); 0.92 (*d*, $J = 6.8$, CH_3).

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[5]) Assignments and integrals refer to one of the two symmetric halves of the molecule.

5c. M.p. 190°. $[\alpha]_D^{23} = -164.4$ ($c = 0.99$, $CHCl_3$). IR ($CHCl_3$): 1621*s*, 1480*m*, 1368*m*, 1260*m*, 1235*w*, 1190*w*, 1135*s*, 1100*m*, 1062*w*, 1020*m*, 950*s*, 875*w*. ^{1}H-NMR ($CDCl_3$, 300 MHz)[5]: 4.38 (*dd*, $J = 8.8, 10.4$), 4.33 (*t*, $J = 8.8$), 4.08 (*dd*, $J = 8.9, 10.3$) (OCH_2CH); 0.95 (*s*, *t*-Bu).

15. M.p. 142–143°. $[\alpha]_D^{23} = -31.1$ ($c = 0.99$, EtOH). IR ($CHCl_3$): 3590*w*, 3281*m* (br.), 1620*s*, 1495*w*, 1455*m*, 1400*w* (br.), 1350*w*, 1260*s*, 1150*s*, 1136*s*, 1100*s*, 1030*m*, 950*m*, 910*m*, 880*w*, 860*w*, 805*m*, 700*s*, 680*m*, 660*m*, 620*w*. ^{1}H-NMR ($CDCl_3$, 200 MHz)[5]: 7.46–7.32 (*m*, C_6H_5); 5.75 (*d*, $J = 8.8$, H–C(5)); 4.35–4.27 (*m*, 1 H); 4.18–4.09 (*m*, 1 H); 3.83–3.63 (*m*, 2 H).

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