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Synthesis of novel chiral bisoxazoline ligands with a norbornadiene backbone: use in the copper-catalyzed enantioselective Henry reaction

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Abstract: Novel chiral bisoxazoline ligands based on norbornadiene were synthesized and used for the asymmetric Henry reaction. Various aromatic aldehydes were converted into chiral β-nitro alcohols with high yields and moderate to acceptable enantioselectivities under the optimized reaction conditions.

Key words: Asymmetric synthesis, Henry reaction, chiral bisoxazolines, nitroaldol, copper

1. Introduction

In recent years, chiral bisoxazoline-metal complexes have proven to be versatile chiral catalysts able to catalyze a wide range of reactions.[1−4] The short and efficient synthesis of bisoxazoline ligands, the flexibility in ligand design, coordination to a large number of transition metals, and excellent enantioselectivity in many reactions make these ligands indispensable in asymmetric catalysis.

The nitroaldol or Henry reaction is one of the important C − C bond forming reactions in organic chemistry.[5−7] It involves the addition of a nitroalkane having an α-hydrogen atom to a carbonyl compound to form a β-nitro alcohol that can be transformed into valuable oxygen- and nitrogen-containing derivatives. Despite the early discovery of the Henry reaction in 1895, catalyst-controlled asymmetric versions of this reaction were undocumented until 1992.[8] Since then, various chiral catalytic systems were developed involving the use of BINOL,[8−10] bisoxazolines,[11−26] bisoxazolidines,[27,28] cinchona alkaloids,[29−31] zinc complexes,[32−34] salen-cobalt[35] and salen-chromium[36] complexes, amino alcohols,[37−43] diamines,[44−49] chiral Schiff bases,[50−56] and tetrahydro-bisisoquinoline ligands.[57,58]

To the best of our knowledge, there is still a limited number of papers on the synthesis of chiral bisoxazoline ligands forming five-[22] and seven-membered[19] chelates with metals and their application in the asymmetric Henry reaction. Herein we report the synthesis of novel bisoxazoline ligands **1a**−**e** and **2** forming seven-membered metal chelates where the oxazoline groups are attached to the sp^2 carbon backbone and their use in the copper-catalyzed asymmetric Henry reaction (Figure).

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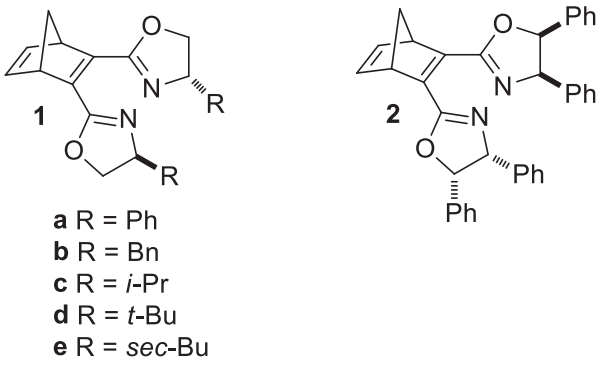
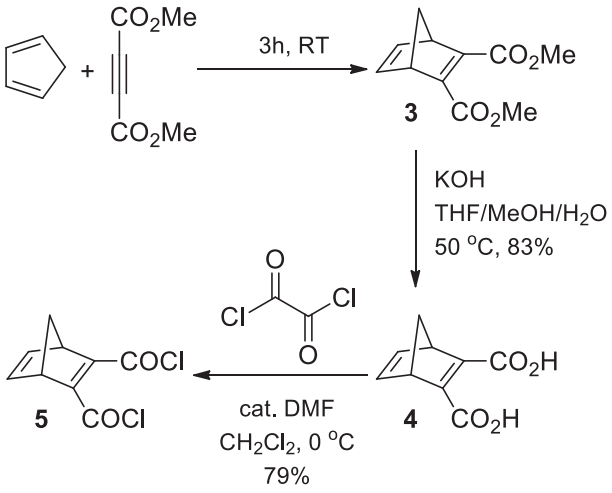


Figure. Structures of norbornadiene based chiral bisoxazoline ligands **1a**−**e** and **2**.

2. Results and discussion

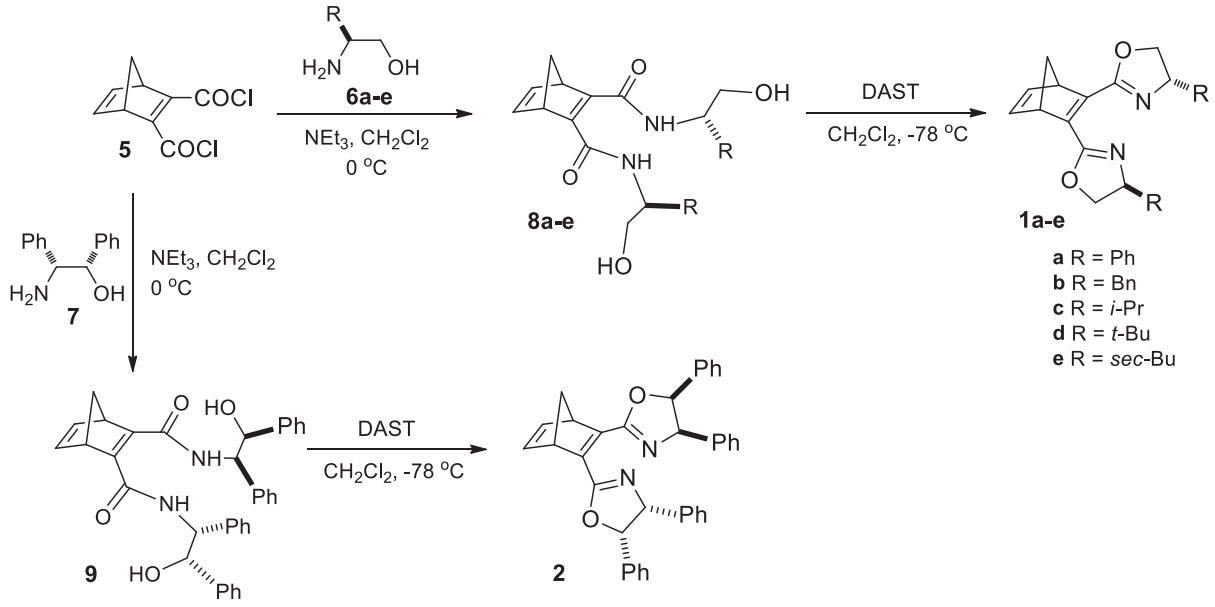
2.1. Preparation of the bisoxazoline ligands 1a − e and 2

The synthesis of diacyl chloride **5** used in the preparation of the chiral bisoxazoline ligands **1a**−**e** and **2** starts with the reaction of cyclopentadiene and dimethyl acetylenedicarboxylate. The Diels–Alder reaction of these compounds at room temperature yielded the diester **3** quantitatively.[59] Heating compound **3** in THF/MeOH/H_2O in the presence of KOH at 50 °C gave dicarboxylic acid **4** in 83% yield. Finally, compound **4** was treated with oxalyl chloride in the presence of a catalytic amount of DMF at 0 °C to give diacyl chloride **5** in 79% yield according to the literature[60] with some modifications as indicated in the experimental part (Scheme 1).



Scheme 1. Synthesis of diacyl chloride **5**.

Diacyl chloride **5** was treated with various chiral β-amino alcohols **6a**−**e** and **7** in the presence of triethylamine at 0 °C to afford bis(hydroxy amides) **8a**−**e** and **9** in 65%−96% yields according to the procedure published by Evans et al.[61] Their subsequent reaction with diethylaminosulfur trifloride (DAST) at −78 °C yielded bisoxazoline ligands **1a**−**e** and **2** in 45%−88% yields (Scheme 2).



Scheme 2. Synthesis of bisoxazoline ligands **1a**−**e** and **2** from diacyl chloride **5**.

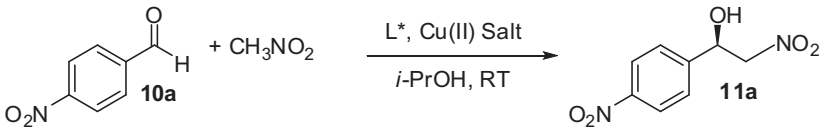
2.2. Copper-catalyzed asymmetric Henry reaction

Initially the reactivity and selectivity of chiral bisoxazoline ligands **1a**−**e** and **2** in the copper-catalyzed Henry reaction were investigated (Table 1). The reaction between *p*-nitrobenzaldehyde and nitromethane in the presence of 6 mol% ligand and 5 mol% of $Cu(OAc)_2$ was chosen as a model system.[19] The reactions were carried out at room temperature in 2-propanol and completed in 2–6 days. The first results showed that varying the substituents on the oxazoline ring had remarkable effects on the enantioselectivity of the reactions. The chiral bisoxazoline ligand **1a** with a –Ph group resulted in the lowest ee value among all ligands (entry 1). Ligand **1b** with a –Bn group presented higher enantioselectivity than did **1c** with an *i*-Pr group (entry 2 vs. 3). Ligand **1d** with a sterically hindered *t*-Bu group and ligand **2b** with two stereogenic centers on the oxazoline ring decreased the enantioselectivity dramatically (entries 4 and 6). The highest ee value was obtained with ligand **1e** with a *sec*-Bu group, which was the ligand of choice yielding a nitroaldol product **11a** with 44% ee (entry 5).

In order to find the optimal conditions for the copper-catalyzed Henry reaction, the catalyst loading was changed. Lowering the catalyst amount from 5 mol% to 3 mol% or increasing it to 10 mol% slightly decreased the enantioselectivity (entries 7 and 8). On the other hand, the addition of triethylamine as a base promoter lowered the enantioselectivity substantially (entry 9). Replacing $Cu(OAc)_2$ with $Cu(OTf)_2$ or with $Cu(OAc)_2 \cdot H_2O$ did not help to increase the enantioselectivity of the Henry reactions (entries 10 and 11).

The best solvent for the asymmetric Henry reaction was found to be 2-propanol (Table 2, entry 1). The other polar protic solvents (MeOH and EtOH) resulted in lower ee values (entries 2 and 3). Moreover, polar aprotic solvents (Et_2O, THF, CH_2Cl_2 etc.) presenting lower ee values were also not suitable for this reaction (entries 4−9). As a result, the best reaction conditions for the enatioselective Henry reaction was obtained by using 6 mol% ligand **1e** and 5 mol% $Cu(OAc)_2$ in 2-propanol at room temperature.

Table 1. Optimization of the reaction conditions.[a]



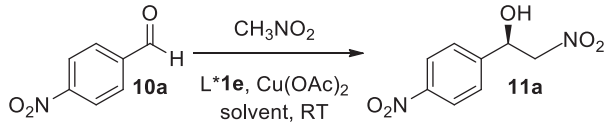
Entry	Ligand	Cu Salt	Cu Salt (mol %)	NEt_3	Time (days)	Yield[b] (%)	ee[c] (%)
1	**1a**	$Cu(OAc)_2$	5	-	6	48	4
2	**1b**	$Cu(OAc)_2$	5	-	2	93	22
3	**1c**	$Cu(OAc)_2$	5	-	2	66	16
4	**1d**	$Cu(OAc)_2$	5	-	2	44	8
5	**1e**	$Cu(OAc)_2$	5	-	2	80	44
6	**2**	$Cu(OAc)_2$	5	-	4	97	8
7	**1e**	$Cu(OAc)_2$	3	-	2	81	42
8	**1e**	$Cu(OAc)_2$	10	-	2	91	40
9	**1e**	$Cu(OAc)_2$	5	+	2	97	14
10	**1e**	$Cu(OTf)_2$	5	-	3	73	17
11	**1e**	$Cu(OAc)_2 \cdot H_2O$	5	-	3	97	36

[a] All reactions were performed at room temperature on a 0.2 mmol scale with 2 mmol nitromethane in 2-propanol.

[b] Values are isolated yields after chromatographic purification.

[c] Enantiomeric excess was determined by HPLC using a Chiralcel OD-H column.

Table 2. Solvent survey for the enantioselective Henry reaction.[a]



Entry	Solvent	Time (days)	Yield[b] (%)	ee[c] (%)
1	*i*-PrOH	2	80	44
2	MeOH	3	24	26
3	EtOH	3	98	36
4	Et_2O	3	82	32
5	1,4-Dioxane	3	98	36
6	THF	6	85	30
7	CH_2Cl_2	3	16	30
8	$CHCl_3$	3	82	23
9	Toluene	6	62	26

[a] All reactions were performed at room temperature on a 0.2 mmol scale with 2 mmol nitromethane, 6 mol % of ligand **1e** and 5 mol % of $Cu(OAc)_2$.

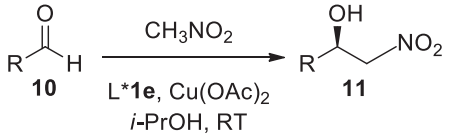
[b] Values are isolated yields after chromatographic purification.

[c] Enantiomeric excess was determined by HPLC using a Chiralcel OD-H column.

After optimizing the reaction conditions, the asymmetric Henry reaction was performed with various aromatic aldehydes (Table 3). In general, the reactions were slow, but better enantiomeric excesses were obtained with these aldehydes than with *p*-nitrobenzaldehyde (54% − 67% ee, entries 2 − 11 vs. entry 1). *Ortho*-, *meta*-, and *para*-methoxybenzaldehydes (**10c** − **e**) showed acceptable enantioselectivities (61% − 67% ee, entries 3 − 5), whereas it was slightly lower for *p*-ethoxybenzaldehyde (**10f**) (54% ee, entry 6). Benzaldehydes having electron

withdrawing groups except for **10a** did not decrease the enantioselectivitiy much (entries 8 and 9). Benzaldehyde (**10b**) with 63% ee showed better enantioselectivity than 1-naphthaldehyde (**10j**) and cinnamaldehyde (**10k**) (entry 2 vs. entries 10 and 11).

Table 3. Henry reaction of nitromethane with various aldehydes.[a]



Entry	R	Product	Time (days)	Yield[b] (%)	ee[c] (%)
1	4-$NO_2C_6H_4$	**11a**	2	80	44
2	Ph	**11b**	7	80	63
3	2-$MeOC_6H_4$	**11c**	13	69	61
4	3-$MeOC_6H_4$	**11d**	13	98	67
5	4-$MeOC_6H_4$	**11e**	13	71	60
6	4-$EtOC_6H_4$	**11f**	7	85	54
7	4-MeC_6H_4	**11g**	7	97	60
8	4-ClC_6H_4	**11h**	14	19	56
9	3-BrC_6H_4	**11i**	13	89	62
10	1-Naphthyl	**11j**	7	98	54
11	PhCH=CH	**11k**	7	95	60

[a] All reactions were performed at room temperature on a 0.2 mmol scale with 2 mmol nitromethane, 6 mol % of ligand **1e** and 5 mol % of $Cu(OAc)_2$ in 2-propanol.

[b] Values are isolated yields after chromatographic purification.

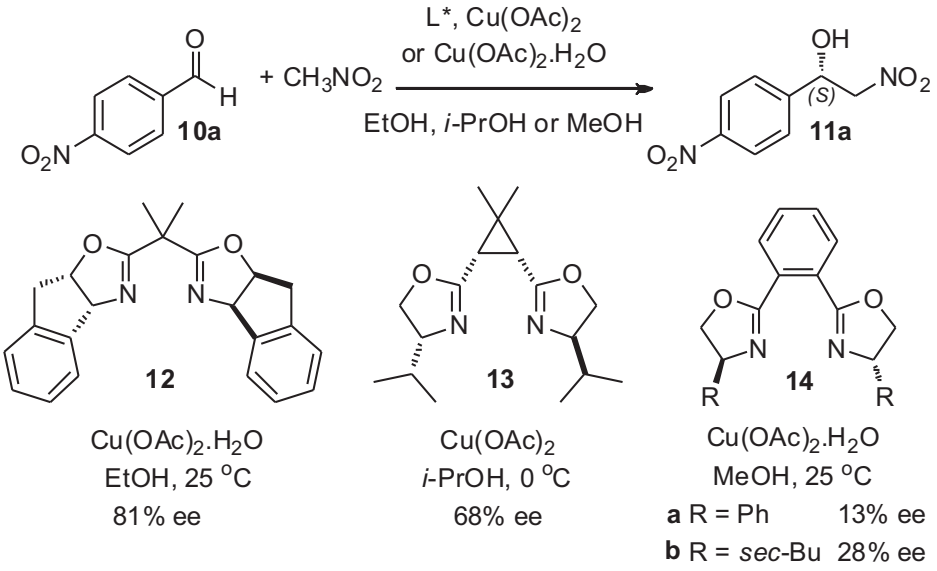
[c] Enantiomeric excess was determined by HPLC using a Chiralcel OD-H column.

The moderate to acceptable enantiomeric excesses obtained in the copper-catalyzed Henry reaction might be the result of distortion in the C_2-symmetry of the ligands **1a**$-$**e** and **2**. The norbornadiene backbone not only enlarges the chelate but also breaks the C_2-symmetry apparent by the signal doubling of the ligands in the ^{1}H and ^{13}C NMR spectra.

Although bisoxazoline ligands forming six-membered metal chelates result in excellent enantioselectivity in the copper-catalyzed Henry reactions, their seven-membered derivatives exhibit rather lower enantioselectivity. For example, the reaction of *p*-nitrobenzaldeyde (**10a**) with nitromethane presents 81% ee, when inda-box ligand **12** forming six-membered metal chelate is used (Scheme 3).[12] However, cyclopropane based ligand **13** forming seven-membered metal chelate results in lower stereoselectivity (68% ee).[19] Moreover, when a bisoxazoline ligand forming seven-membered metal chelate with two oxazoline groups attached to sp^2 carbon atoms (ligands **14a** and **14b**), stereoselectivity of the copper-catalyzed Henry reaction further decreased to 13% and 28% ee respectively.[23] Our norbornadiene based bisoxazoline ligands **1a**$-$**e** and **2** are examples of ligands forming seven-membered metal chelate having two oxazoline groups attached to sp^2 carbon atoms. Under the guidance of these studies, it might be argued that these type of ligands show lower stereoselectivity but still ligand **1e** with 44% ee exhibits higher enantioselectivity than ligands **14a** and **14b** in the enantioselective Henry reaction between *p*-nitrobenzaldehyde (**10a**) and nitromethane (Table 1, entry 5 vs. Scheme 3).

In conclusion, a series of novel chiral bisoxazoline ligands **1a**$-$**e** and **2** having a norbornadiene backbone were synthesized in five steps in 45%$-$88% yields. They were used as chiral ligands in the copper-catalyzed

asymmetric Henry reaction. With the optimized reaction conditions, various β-nitro alcohols **11a**$-$**k** were obtained with 44%$-$67% enantiomeric excesses. Application of the bisoxazoline ligands **1a**$-$**e** and **2** in other asymmetric catalytic reactions is currently under investigation.



Scheme 3. Comparison of the enantioselectivity of ligands **12**,[12] **13**,[19] and **14**[23] in the copper-catalyzed Henry reaction of p-nitrobenzaldehyde (**10a**) with nitromethane.

3. Experimental

3.1. General

Reagents obtained from commercial suppliers were used without further purification unless otherwise noted. Preparation of bisoxazoline ligands and β-nitro alcohols was performed in flame-dried glassware under a static pressure of nitrogen. Solvents were dried prior to use following standard procedures. Technical grade solvents for chromatography (hexane and ethyl acetate) were distilled before use. Reactions were monitored by thin layer chromatography using Merck silica gel 60 Kieselgel F254 TLC (aluminum sheets 20 $\times$ 20 cm) and column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) from Merck using the indicated solvents. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker-Biospin (DPX-400) instrument. AB signals in the ^{1}H NMR spectra were denoted by the symbol "$^{\diamond}$". Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 FT-IR spectrometer. Enantiomeric ratios were determined by analytical HPLC analysis on a Shimadzu LC-20A Prominence instrument with a chiral stationary phase using Daicel OD-H columns (n-hexane:i-propanol mixtures as solvent). Optical rotations were measured on a Rudolph Research Analytical Autopol III polarimeter. Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus and were not corrected. High resolution mass spectrometry (HRMS) was performed using an Agilent Technologies 6224 TOF LC/MS instrument.

3.2. Procedure for the preparation of bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarbonyl dichloride (5)

To a dichloromethane suspension (325 mL) of compound **4** and DMF (0.6 mL, 7.8 mmol) at 0 °C was added oxalyl chloride (15.4 mL, 180 mmol) slowly via a syringe. The reaction mixture was stirred at this temperature

until a clear solution was obtained. Subsequently, the solvent was evaporated under reduced pressure and the residue was distilled under vacuum (bp 88 °C; Lit:[60] bp 85–87 °C/0.45 mmHg) to give analytically pure diacyl chloride **5** (16.8 g, 79%, pale yellow oil).

3.3. General procedure for the preparation of bis(hydroxy amides) 8 and 9[61]

To a solution of β-amino alcohol (10.0 mmol) in CH_2Cl_2 (25 mL) at 0 °C was added triethylamine (25 mmol). Then a dichloromethane solution (5 mL) of compound **5** (5.0 mmol) was added dropwise to the reaction mixture at this temperature. The ice bath was removed and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was extracted with HCl (1 N, 8 mL), $NaHCO_3$ solution (8 mL), and H_2O (3 × 20 mL) consecutively. The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure to afford crude bis(hydroxy amide) as a white solid.

3.3.1. (1*R*,4*S*)-*N*²,*N*³-bis((*S*)-2-hydroxy-1-phenylethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (8a):

White solid; mp 79−80 °C (R_f = 0.30 ethyl acetate:methanol = 99:1). Yield: 96%. Purified by column chromatography using ethyl acetate:methanol = 95:5. $[\alpha]_D^{18}$ = +4.3 (c = 0.440 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 7.9 Hz, 1H, NH), 8.27 (d, J = 6.6 Hz, 1H, NH), 7.29−7.20 (m, 10H, Ar-H), 6.89−6.85 (m, 2H, 5-H, 6-H), 5.11−5.06 (m, 2H, NCH), 3.96 (br. s, 2H, 1-H, 4-H), 3.85−3.77 (m, 4H, OCH_2), 2.11 (d, J = 6.8 Hz, 1H, 7-H$_A$), 1.96 (d, J = 6.8 Hz, 1H, 7-H$_B$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 165.1 [165.0], 154.4 [153.3], 142.6 [142.1], 138.9 [138.9], 129.1 [129.0], 128.0 [128.0], 127.0, 71.4, 66.8 [66.6], 56.4 [56.1], 54.6, [54.5]. IR (ATR): ν 3305, 3028, 2939, 2872, 1638, 1596, 1521, 1495, 1454, 1291, 1070, 1028, 756, 698 cm^{-1}. HRMS (ESI$^+$): m/z calcd for $C_{25}H_{26}N_2O_4H$: 419.1971; found: 419.2005 $[M+H]^+$.

3.3.2. (1*R*,4*S*)-*N*²,*N*³-bis((*S*)-1-hydroxy-3-phenylpropan-2-yl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (8b):

White solid, mp 52−53 °C (R_f = 0.33 ethyl acetate:methanol = 99:1). Yield: 82%. Purified by column chromatography using ethyl acetate:methanol = 95:5. $[\alpha]_D^{19}$ = −81.6 (c = 0.690 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, J = 7.7 Hz, 1H, NH), 7.83 (d, J = 7.3 Hz, 1H, NH), 7.25−7.21 (m, 4H, Ar-H), 7.18−7.14 (m, 6H, Ar-H), 6.79 (br. s, 2H, 5-H, 6-H), 4.17−4.14 (m, 2H, NCH), 3.84 (s, 1H, 1-H), 3.80 (s, 1H, 4-H), 3.64$^\diamond$ (dt, J = 11.2, 3.2 Hz, 2H, OCH), 3.52$^\diamond$ (ddd, J = 11.2, 5.3, 1.8 Hz, 2H, OCH), 2.84 (dd, J = 7.2, 4.9 Hz, 4H, CH_2), 2.02$^\diamond$ (d, J = 6.8 Hz, 1H, 7-H$_A$), 1.91$^\diamond$ (d, J = 6.8 Hz, 1H, 7-H$_B$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.3 [165.1], 153.9 [153.3], 142.5 [141.9], 137.9 [137.9], 129.5 [129.5], 128.8 [128.8], 126.9 [126.9], 71.2, 64.4 [64.2], 54.4 [54.4], 53.6, 37.2; IR (ATR): ν 3309, 3026, 2939, 2871, 1636, 1594, 1523, 1496, 1454, 1292, 1033, 743, 698 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{27}H_{30}N_2O_4H$: 447.2284; found: 447.2308 $[M+H]^+$.

3.3.3. (1*R*,4*S*)-N^2,N^3-bis((*S*)-1-hydroxy-3-methylbutan-2-yl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (8c):

White solid, mp 86−87 °C (R_f = 0.22 ethyl acetate:methanol = 99:1). Yield: 65%. $[\alpha]_D^{18} = -78.5$ (c = 0.275 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J = 8.3 Hz, 1H, NH), 7.75 (d, J = 7.8 Hz, 1H, NH), 6.90−6.86 (m, 2H, 5-H, 6-H), 3.93 (br. s, 2H, 1-H, 4-H), 3.77−3.71 (m, 2H, NCH), 3.68−3.57 (m, 4H, OCH_2), 2.11$^\diamond$ (d, J = 7.0 Hz, 1H, 7-H_A), 1.96$^\diamond$ (d, J = 7.0 Hz, 1H, 7-H_B), 1.92−1.82 (m, 2H, CH), 0.91 (d, J = 8.0 Hz, 6H, CH_3), 0.90 (d, J = 6.8 Hz, 3H, CH_3), 0.88 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$)δ: 165.9 [165.7], 153.9 [153.2], 142.6 [142.1], 71.3, 64.1 [63.9], 57.8 [57.8], 54.5, 29.4 [29.4], 19.7 [19.7], 19.1 [19.0]; IR (ATR): ν 3428, 3268, 2963, 2935, 2869, 1632, 1574, 1532, 1461, 1317, 1291, 1024, 712, 607 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{19}H_{30}N_2O_4H$: 351.2284; found: 351.2298 $[M+H]^+$.

3.3.4. (1*R*,4*S*)-N^2,N^3-bis((*S*)-1-hydroxy-3,3-dimethylbutan-2-yl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (8d):

White solid, mp 185−186 °C (R_f = 0.12 ethyl acetate:methanol = 99:1). Yield: 73%. The reaction was performed at 0 °C and after the addition of diacyl chloride **5**, the reaction mixture was stirred at this temperature for 30 min. Extraction was done according to the general method. Purified by column chromatography using ethyl acetate:methanol = 95:5. $[\alpha]_D^{20} = -46.7$ (c = 0.75 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86 (d, J = 9.0 Hz, 1H, NH), 7.58 (d, J = 8.5 Hz, 1H, NH), 6.93−6.91$^\diamond$ (m, 1H, 5-H_A) 6.89−6.87$^\diamond$ (m, 1H, 6-H_B), 3.94 (br. s, 2H, 1-H, 4-H), 3.86−3.77 (m, 4H, NCH, OCH), 3.56−3.49 (m, 2H, OCH), 2.14$^\diamond$ (d, J= 6.8 Hz, 1H, 7-H_A), 1.98$^\diamond$ (d, J = 6.8 Hz, 1H, 7-H_B), 0.92 [s, 9H, $C(CH_3)_3$], 0.91 [s, 9H, $C(CH_3)_3$]; ^{13}C NMR (100 MHz, $CDCl_3$)δ: 166.4 [166.0], 153.7 [153.1], 142.8 [142.0], 71.2, 63.3 [63.3], 60.3 [60.3], 54.6 [54.5], 33.9 [33.8], 27.2; IR (ATR): ν 3475, 3384, 3246, 2964, 1633, 1595, 1540, 1366, 1294, 1050, 726, 693 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{21}H_{34}N_2O_4H$: 379.2597; found: 379.2620 $[M+H]^+$.

3.3.5. (1*R*,4*S*)-N^2,N^3-bis((2S)-1-hydroxy-3-methylpentan-2-yl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (8e):

White solid, mp 118−119 °C (R_f = 0.38 ethyl acetate:methanol = 95:5). Yield: 77%. Purified by column chromatography using ethyl acetate:methanol = 95:5. $[\alpha]_D^{19} = -84.4$ (c = 0.205 g/100 mL, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, J = 8.2 Hz, 1H, NH), 7.80 (d, J = 8.1 Hz, 1H, NH), 6.94−6.90 (m, 2H, 5-H, 6-H), 3.97 (br. s, 2H, 1-H, 4-H), 3.88−3.82 (m, 2H, NCH), 3.73−3.63 (m, 4H, OCH_2), 2.16$^\diamond$ (br. dt, J = 6.8, 1.3 Hz, 1H, 7-H_A), 2.01$^\diamond$ (br. dt, J = 6.8, 1.4 Hz, 1H, 7-H_B), 1.73−1.62 (m, 2H, CH_2CH_3), 1.62−1.42 (m, 2H, CH_2CH_3), 1.23−1.09 (m, 2H, $CHCH_3$), 0.93 (d, J = 6.8 Hz, 3H, CH_3), 0.92 (d, J = 6.8 Hz, 3H, CH_3), 0.89 (t, J = 7.4 Hz, 3H, CH_2CH_3), 0.88 (t, J = 7.3 Hz, 3H, CH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$)δ: 165.8 [165.6], 153.8 [153.2], 142.5 [142.1], 71.3, 63.5, 56.5 [56.5], 54.4, 35.9, 25.8, 15.7, 11.6 [11.5]; IR (ATR): ν 3349, 2963, 2933, 2874, 1588, 1571, 1509, 1375, 1292, 1069, 1043, 1032, 762, 707, 600 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{21}H_{34}N_2O_4H$: 379.2597; found: 379.2560 $[M+H]^+$.

3.3.6. (1*R*,4*S*)-N^2,N^3-Bis((1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxamide (9):

White solid, mp 97−98 °C (R_f = 0.71 ethyl acetate:*n*-hexane = 3:1). Yield: 75%. $[\alpha]_D^{19}$ = +112.0 (c = 0.515 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ :8.73 (d, J = 7.8 Hz, 1H, NH), 8.25 (d, J = 8.4 Hz, 1H, NH), 7.18−7.08 (m, 12H, Ar-H), 7.02−6.94 (m, 8H, Ar-H) 6.89$^\diamond$ (dd, J = 4.7, 3.2 Hz, 1H, 5-H$_A$), 6.84$^\diamond$ (dd, J = 4.7, 3.2 Hz, 1H, 6-H$_A$), 5.30−5.26 (m, 2H, NCH), 5.08 (d, J = 4.2 Hz, 1H, OCH), 5.04 (d, J = 4.2 Hz, 1H, NCH) 3.94 (br. s, 1H, 1-H), 3.89 (br. s, 1H, 4-H) 2.06$^\diamond$ (d, J = 6.8 Hz, 1H, 7-H$_A$), 1.96$^\diamond$ (d, J = 6.8 Hz, 1H, 7-H$_B$); ^{13}C-NMR (100 MHz, $CDCl_3$)δ: 164.4 [164.4], 154.5 [153.0], 142.6 [142.0], 140.0 [139.9], 137.1 [136.9], 128.3, 128.3 [128.3], 128.2 [128.2], 127.9, 127.9 [127.8], 126.8 [126.7], 77.1 [77.1], 71.2, 60.1 [59.7], 54.5 [54.4]; IR (ATR): ν 3304, 3029, 1641, 1596, 1496, 1452, 1293, 1090, 1058, 1028, 758, 698 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{37}H_{34}N_2O_4H$: 571.2591; found: 571.2624 $[M+H]^+$.

3.4. General procedure for the preparation of bisoxazoline ligands 1 and 2[62]

To a dichloromethane solution (4 mL) of bis(hydroxy amide) (0.25 mmol) in a flame-dried Schlenk tube at –78 °C was added diethylaminosulfur trifluoride (0.1 mL, 0.75 mmol). After stirring at this temp. for 10 min, CH_2Cl_2 (20 mL) was added and the mixture was washed with saturated aqueous $NaHCO_3$ (10 mL) and H_2O (15 mL) consecutively. The organic phase was dried over $MgSO_4$ and concentrated in vacuo to yield the crude product. Purification by column chromatography (ethyl acetate:n-hexane = 1:1) resulted in isolation of the bisoxazoline ligand as yellow oil, which was directly used for catalysis.

3.4.1. (1*R*,4*S*)-2,3-Bis((*S*)-4′-phenyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (1a):

Yellow oil (R_f = 0.42 ethyl acetate:*n*-hexane = 1:1). Yield: 45%. $[\alpha]_D^{19}$ = −50.7 (c = 0.623 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$)δ: 7.30−7.20 (m, 10H, Ph), 6.93 (br. t, J = 2.0 Hz, 2H, 5-H, 6-H), 5.25 (t, J = 8.4 Hz, 1H, 4′-H), 5.22 (t, J = 8.4 Hz, 1H, 4′-H), 4.65 (dd, J = 8.4, 10.2 Hz, 1H, 5′-H), 4.62 (dd, J = 8.4, 10.2, 1H, 5′-H), 4.12 (t, J = 8.4 Hz, 1H, 5′-H), 4.08 (t, J = 8.4 Hz, 1H, 5′-H), 4.07 (br. t, J = 1.6 Hz, 2H, 1-H, 4-H), 2.30$^\diamond$ (dt, J = 6.8, 1.6 Hz, 1H, 7-H$_A$), 2.03$^\diamond$ (dt, J = 6.8, 1.6 Hz, 1H, 7-H$_B$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 162.8 [162.8], 147.2 [147.1], 142.6 [142.6], 142.3 [142.2], 128.8, 127.7, 127.0 [127.0], 75.0, 72.0, 70.1, 55.3 [55.3]; IR (ATR): ν 2955, 2924, 2857, 1741, 1652, 1453, 1364, 1235, 1031, 1011, 754, 698 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{25}H_{22}N_2O_2H$: 383.1759; found: 383.1754 $[M+H]^+$.

3.4.2. (1*R*,4*S*)-2,3-Bis((*S*)-4-benzyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (1b)

Yellow oil (R_f = 0.56 ethyl acetate:*n*-hexane = 2:1). Yield: 86%. $[\alpha]_D^{19}$ = −36.4 (c = 0.535 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32−7.28 (m, 5H, Ar-H), 7.23−7.20 (m, 5H, Ar-H), 6.95 (br. s, 2H, 5-H, 6-H), 4.54−4.42 (m, 2H, 4′-H), 4.24 (t, J = 9.0 Hz, 1H, 5′-H), 4.20 (t, J = 9.0 Hz, 1H, 5′-H), 4.07−3.99 (m, 4H, 5′-H, 1-H, 4-H), 3.23−3.15 (m, 2H, CH_2Ph), 2.71−2.63 (m, 2H, CH_2Ph), 2.27$^\diamond$ (dd, J = 1.5, 6.8 Hz, 1H, 7-H$_A$), 2.06$^\diamond$ (dd, J = 1.5, 6.8 Hz, 1H, 7-H$_B$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 162.0 [162.0], 147.0 [146.7], 142.5 [142.5], 138.1 [138.0] 129.4 [129.4], 128.7 [128.7], 126.7, 72.0 [71.8] 71.9, 67.9 [67.8], 55.3 [55.1], 41.8 [41.7]; IR (ATR): ν 2926, 1630, 1602, 1495, 1453, 1296, 1236, 1031, 1008, 956, 734, 698 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{27}H_{26}N_2O_2H$: 411.2072; found: 411.2067 $[M+H]^+$.

3.4.3. (1*R*,4*S*)-2,3-Bis((*S*)-4′-isopropyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (1c):

Yellow oil (R_f = 0.74, ethyl acetate:*n*-hexane = 2:1). Yield: 78%. $[\alpha]_D^{19} = -41.5$ (c = 0.908 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ : 6.88 − 6.86$^\diamond$ (m, 1H, 5-H), 6.85 − 6.83$^\diamond$ (m, 1H, 6-H), 4.25 − 4.17 (m, 2H, 4′-H), 3.99 − 3.89 (m, 6H, 5′-H, 1-H, 4-H), 2.20$^\diamond$ (br. d, J = 6.7 Hz, 1H, 7-H$_A$), 1.96$^\diamond$ (br. d, J = 6.7 Hz, 1H, 7-H$_B$), 1.79 − 1.70 (m, 2H, C*H*CH$_3$), 0.93 (d, J = 6.8 Hz, 3H, CH$_3$), 0.91 (d, J = 6.8 Hz, 3H, CH$_3$), 0.84 (d, J = 6.8 Hz, 3H, CH$_3$), 0.81 (d, J = 6.8 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 161.5 [161.4], 146.8 [146.7], 142.7 [142.6], 72.7 [72.7] 71.9, 70.1, 55.3 [55.2], 32.9 [32.8], 19.2 [19.1], 18.3 [18.2]; IR (ATR): ν 2962, 2927, 2872, 1628, 1592, 1364, 1216, 668 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{19}H_{26}N_2O_2H$: 315.2072; found: 315.2067 $[M+H]^+$.

3.4.4. (1*R*,4*S*)-2,3-Bis((*S*)-4′-*t*-butyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (1d):

Yellow oil (R_f = 0.48, ethyl acetate:*n*-hexane = 2:1). Yield: 60%. $[\alpha]_D^{19} = -71.4$ (c = 0.440 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.88 − 6.86$^\diamond$ (m, 1H, 5-H$_A$), 6.83 − 6.81$^\diamond$ (m, 1H, 6-H$_B$), 4.20 − 4.13 (m, 2H, 4′-H), 4.02 (t, 1H, 5′-H), 4.01 − 3.97 (m, 2H, 5′-H, 1-H), 3.92 − 3.86 (m, 3H, 5′-H, 4-H), 2.20$^\diamond$ (d, J = 6.6 Hz, 1H, 7-H$_A$), 1.95$^\diamond$ (d, J = 6.6 Hz, 1H, 7-H$_B$); 0.86 (s, 9H, CH$_3$), 0.83 (s, 9H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 161.4 [161.2], 146.7 [146.6], 142.8 [142.5], 76.4 [76.2] 71.9, 68.8 [68.7], 55.2 [55.1], 34.3 [34.1], 26.1 [26.1]; IR (ATR): ν 2955, 2870, 1636, 1478, 1363, 1296, 1236, 1010, 751 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{21}H_{30}N_2O_2H$: 343.2385; found: 343.2380 $[M+H]^+$.

3.4.5. (1*R*,4*S*)-2,3-Bis((4*S*)-4-sec-butyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (1e):

Yellow oil (R_f = 0.26, ethyl acetate:*n*-hexane = 1:1). Yield: 80%. $[\alpha]_D^{19} = -79.8$ (c = 0.440 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ : 6.95 − 6.93$^\diamond$ (m, 1H, 5-H$_A$), 6.92 − 6.90$^\diamond$ (m, 1H, 6-H$_B$), 4.27 (dd, J = 9.8, 8.0 Hz, 1H, 5′-H), 4.24 (dd, J = 9.7, 7.8 Hz, 1H, 5′-H), 4.18 − 4.09 (m, 2H, 4′-H), 4.03 − 3.96 (m, 4H, 5′-H, 1-H, 4-H), 2.27$^\diamond$ (br. dt, J = 6.6, 1.7 Hz, 1H, 7-H$_A$), 2.02$^\diamond$ (br. dt, J = 6.7, 1.3 Hz, 1H, 7-H$_B$), 1.74 − 1.63 (m, 2H, C*H*CH$_3$), 1.61 − 1.48 (m, 2H, C*H*$_2$CH$_3$), 1.24 − 1.13 (m, 2H, C*H*$_2$CH$_3$), 0.94 (t, J = 7.4 Hz, 3H, CH$_2$C*H*$_3$), 0.93 (t, J = 7.4 Hz, 3H, CH$_2$C*H*$_3$), 0.85 (d, J = 6.8 Hz, 3H, CHC*H*$_3$), 0.81 (d, J = 6.8 Hz, 3H, CHC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 161.4 [161.3], 146.6 [146.5], 142.6 [142.5], 71.8, 71.0, 69.5 [69.5], 55.1 [55.1], 39.0 [38.9], 26.3 [26.2], 14.4 [14.3], 11.8; IR (ATR): ν 2961, 2930, 2875, 1634, 1460, 1379, 1296, 1236, 1092, 1010, 960, 751 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{21}H_{30}N_2O_2H$: 343.2385; found: 343.2380 $[M+H]^+$.

3.4.6. (1*R*,4*S*)-2,3-Bis((4*R*,5*S*)-4′,5′-diphenyl-4′,5′-dihydrooxazol-2′-yl)bicyclo[2.2.1]hepta-2,5-diene (2)

Yellow oil (R_f = 0.42, ethyl acetate:*n*-hexane = 1:3). Yield: 88%. $[\alpha]_D^{19} = +30.0$ (c = 0.400 g/100 mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$)δ: 7.25 − 7.17 (m, 20H, Ar-H), 7.08 − 7.07 (m, 2H, 5-H, 6-H), 5.30 (d, J = 8.3 Hz, 1H, 4′-H), 5.26 (d, J = 8.3 Hz, 1H, 4′-H), 5.11 (d, J = 7.0 Hz, 1H, 5′-H), 5.09 (d, J = 7.0 Hz, 1H, 5′-H), 4.25 − 4.24 (m, 2H, 1-H, 4-H), 2.50$^\diamond$ (d, J = 6.7 Hz, 1H, 7-H$_A$), 2.18$^\diamond$ (d, J = 6.7 Hz, 1H,

7-H$_B$); ^{13}C NMR (100 MHz, $CDCl_3$)δ: 162.3 [162.2], 147.2 [147.2], 142.8 [142.6], 141.7 [141.6], 140.2 [140.1], 128.8, 128.3 [128.3], 127.8, 127.0, [126.9], 125.9 [125.9], 89.5, 79.0, 72.2, 55.5 [55.5]; IR (ATR): ν 3063, 3029, 2940, 1633, 1495, 1454, 1295, 1270, 1006, 963, 757, 698 cm^{-1}; HRMS (ESI$^+$): m/z calcd for $C_{37}H_{30}N_2O_2H$: 535.2385; found: 535.2380 $[M+H]^+$.

3.5. General procedure for the catalytic Henry reaction[19]

To $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) in a flame-dried Schlenk tube was added a 2-propanol solution (0.4 mL) of bisoxazoline ligand **1e** (4.1 mg, 0.012 mmol) under nitrogen atmosphere at room temperature. After stirring for 1 h, aldehyde (0.2 mmol) and nitromethane (0.122 g, 0.11 mL, 2 mmol) were added via syringe. The reaction was stirred at room temperature until TLC control indicated complete consumption of the aldehyde. The solvent was removed under reduced pressure and the crude product was purified by column chromatography to give the desired nitro alcohol. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, and the absolute configurations of the nitroaldol products were assigned by comparing their specific rotations and the HPLC retention times with data from the literature.

3.5.1. (*R*)-1-(4-Nitrophenyl)-2-nitroethanol (11a)[12]

(44% ee, Entry 1, Table 3): Yield 80%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:3. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 12.56 min, minor (*S*)-enantiomer t_R = 15.59 min; $[\alpha]_D^{19} = -13.2$ (c = 0.365 g/100 mL, $CHCl_3$).

3.5.2. (*R*)-2-Nitro-1-phenylethanol (11b)[12]

(63% ee, Entry 2, Table 3): Yield 80%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 8.31 min, minor (*S*)-enantiomer t_R = 9.97 min; $[\alpha]_D^{19} = -26.6$ (c = 0.365 g/100 mL, $CHCl_3$).

3.5.3. (*R*)-1-(2-Methoxyphenyl)-2-nitroethanol (11c)[12]

(61% ee, Entry 3, Table 3): Yield 69%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 7.44 min, minor (*S*)-enantiomer t_R = 8.56 min; $[\alpha]_D^{19} = -37.5$ (c = 0.325 g/100 mL, $CHCl_3$).

3.5.4. (*R*)-1-(3-Methoxyphenyl)-2-nitroethanol (11d)[58]

(67% ee, Entry 4, Table 3): Yield 98%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 12.61 min, minor (*S*)-enantiomer t_R = 16.24 min; $[\alpha]_D^{19} = -31.5$ (c = 0.305 g/100 mL, $CHCl_3$).

3.5.5. (*R*)-1-(4-Methoxyphenyl)-2-nitroethanol (11e)[58]

(60% ee, Entry 5, Table 3): Yield 71%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 11.41 min, minor (*S*)-enantiomer t_R = 14.05 min; $[\alpha]_D^{19} = -47.7$ (c = 0.350 g/100 mL, $CHCl_3$).

3.5.6. (−)-1-(4-Ethoxyphenyl)-2-nitroethanol (11f)[19]

(54% ee, Entry 6, Table 3): Yield 85%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major enantiomer t_R = 8.76 min, minor enantiomer t_R = 9.99 min; $[\alpha]_D^{19} = -13.8$ (c = 0.600 g/100 mL, $CHCl_3$).

3.5.7. (*R*)-1-(4-Methylphenyl)-2-nitroethanol (11g)[58]

(60% ee, Entry 7, Table 3): Yield 97%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 8.65 min, minor (*S*)-enantiomer t_R = 10.55 min; $[\alpha]_D^{19} = -27.2$ (c = 0.585 g/100 mL, $CHCl_3$).

3.5.8. (*R*)-1-(4-Chlorophenyl)-2-nitroethanol (11h)[12]

(57% ee, Entry 8, Table 3): Yield 19%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 7.80 min, minor (*S*)-enantiomer t_R = 9.50 min; $[\alpha]_D^{19} = -7.1$ (c = 0.350 g/100 mL, $CHCl_3$).

3.5.9. (*R*)-1-(3-Bromophenyl)-2-nitroethanol (11i)[63]

(62% ee, Entry 9, Table 3): Yield 89%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:4. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 8.84 min, minor (*S*)-enantiomer t_R = 11.39 min; $[\alpha]_D^{19} = -26.7$ (c = 0.445 g/100 mL, $CHCl_3$).

3.5.10. (*R*)-1-(1-Naphthyl)-2-nitroethanol (11j)[12]

(54% ee, Entry 10, Table 3): Yield 98%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:3. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow rate 1.0 mL/min, λ = 230 nm); major (*R*)-enantiomer t_R = 10.30 min, minor (*S*)-enantiomer t_R = 16.32 min; $[\alpha]_D^{18} = -4.3$ (c = 0.255 g/100 mL, $CHCl_3$).

3.5.11. (*R,E*)-1-Nitro-4-phenyl-3-buten-2-ol (11k)[58]

(60% ee, Entry 11, Table 3): Yield 95%. Purified by column chromatography using ethyl acetate:*n*-hexane = 1:3. HPLC (Chiralcel OD-H column, column temperature 20 °C, solvent *n*-hexane:*i*-propanol = 80:20, flow

rate 1.0 mL/min, λ = 230 nm); minor (*S*)-enantiomer t_R = 19.83 min, major (*R*)-enantiomer t_R = 22.66 min; $[\alpha]_D^{19} = -17.0$ (c = 0.235 g/100 mL, $CHCl_3$).

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References

1. Ghosh, A. K.; Packiarajan, M.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1–45.
2. Rasappan, R.; Laventine, D.; Reiser, O. *Coord. Chem. Rev.* **2008**, *252*, 702–714.
3. Desimoni, G.; Faita, G.; Jorgensen, K. A. *Chem. Rev.* **2011**, *111*, Pr284-Pr437.
4. Stanley, L. M.; Sibi, M. P. In *Privileged Chiral Ligands and Catalysts*; Zhou, Q.-L., Ed. Wiley: Weinheim, Germany, 2011, pp. 171–219.
5. Luzzio, F. A. *Tetrahedron* **2001**, *57*, 915–945.
6. Boruwa, J.; Gogoi, N.; Saikia, P. P.; Barua, N. C. *Tetrahedron: Asymmetry* **2006**, *17*, 3315–3326.
7. Palomo, C.; Oiarbide, M.; Laso, A. *Eur. J. Org. Chem.* **2007**, 2561–2574.
8. Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418–4420.
9. Arai, T.; Yamada, Y. M. A.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *Chem. Eur. J.* **1996**, *2*, 1368–1372.
10. Choudary, B. M.; Ranganath, K. V. S.; Pal, U.; Kantam, M. L.; Sreedhar, B. *J. Am. Chem. Soc.* **2005**, *127*, 13167–13171.
11. Christensen, C.; Juhl, K.; Jorgensen, K. A. *Chem. Commun.* **2001**, 2222–2223.
12. Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692–12693.
13. Christensen, C.; Juhl, K.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **2002**, *67*, 4875–4881.
14. Du, D. M.; Lu, S. F.; Fang, T.; Xu, J. X. *J. Org. Chem.* **2005**, *70*, 3712–3715.
15. Toussaint, A.; Pfaltz, A. *Eur. J. Org. Chem.* **2008**, 4591–4597.
16. Lee, J. M.; Kim, J.; Shin, Y.; Yeom, C. E.; Lee, J. E.; Hyeon, T.; Kim, B. M. *Tetrahedron: Asymmetry* **2010**, *21*, 285–291.
17. Lang, K.; Park, J.; Hong, S. *J. Org. Chem.* **2010**, *75*, 6424–6435.
18. Reddy, B. V. S.; George, J. *Tetrahedron: Asymmetry* **2011**, *22*, 1169–1175.
19. Mao, J. Y.; Nie, X.; Wang, M.; Wang, Q.; Zheng, B.; Bian, Q. H.; Zhong, J. C. *Tetrahedron: Asymmetry* **2012**, *23*, 965–971.
20. Yuryev, R.; Liese, A. *Synlett* **2009**, 2589–2592.
21. Maggi, R.; Lanari, D.; Oro, C.; Sartori, G.; Vaccaro, L. *Eur. J. Org. Chem.* **2011**, 5551–5554.
22. Balaraman, K.; Vasanthan, R.; Kesavan, V. *Synthesis* **2012**, *44*, 2455–2462.
23. Ginotra, S. K.; Singh, V. K. *Org. Biomol. Chem.* **2007**, *5*, 3932–3937.
24. Zhou, Z. M.; Li, Z. H.; Hao, X. Y.; Zhang, J.; Dong, X.; Liu, Y. Q.; Sun, W. W.; Cao, D.; Wang, J. L. *Org. Biomol. Chem.* **2012**, *10*, 2113–2118.
25. Kato, T.; Marubayashi, K.; Takizawa, S.; Sasai, H. *Tetrahedron: Asymmetry* **2004**, *15*, 3693–3697.
26. Angulo, B.; Garcia, J. I.; Herrerias, C. I.; Mayoral, J. A.; Minana, A. C. *J. Org. Chem.* **2012**, *77*, 5525–5532.
27. Liu, S. L.; Wolf, C. *Org. Lett.* **2008**, *10*, 1831–1834.

28. Spangler, K. Y.; Wolf, C. *Org. Lett.* **2009**, *11*, 4724–4727.
29. Li, H. M.; Wang, B. M.; Deng, L. *J. Am. Chem. Soc.* **2006**, *128*, 732–733.
30. Palacio, C.; Connon, S. J. *Org. Lett.* **2011**, *13*, 1298–1301.
31. Zielinska-Blajet, M.; Skarzewski, J. *Tetrahedron: Asymmetry* **2011**, *22*, 351–355.
32. Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621–2623.
33. Trost, B. M.; Yeh, V. S. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 861–863.
34. Bulut, A.; Aslan, A.; Dogan, O. *J. Org. Chem.* **2008**, *73*, 7373–7375.
35. Kogami, Y.; Nakajima, T.; Ikeno, T.; Yamada, T. *Synthesis* **2004**, 1947–1950.
36. Zulauf, A.; Mellah, M.; Schulz, E. *J. Org. Chem.* **2009**, *74*, 2242–2245.
37. Palomo, C.; Oiarbide, M.; Mielgo, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 5442–5444.
38. Palomo, C.; Oiarbide, M.; Laso, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 3881–3884.
39. Klein, G.; Pandiaraju, S.; Reiser, O. *Tetrahedron Lett.* **2002**, *43*, 7503–7506.
40. Zhong, Y. W.; Tian, P.; Lin, G. Q. *Tetrahedron: Asymmetry* **2004**, *15*, 771–776.
41. Kohn, U.; Schulz, M.; Gorls, H.; Anders, E. *Tetrahedron: Asymmetry* **2005**, *16*, 2125–2131.
42. Guo, Z. L.; Zhong, S.; Li, Y. B.; Lu, G. *Tetrahedron: Asymmetry* **2011**, *22*, 238–245.
43. Zheng, B.; Wang, M.; Li, Z. Y.; Bian, Q. H.; Mao, J. Y.; Li, S. N.; Liu, S. Z.; Wang, M. A.; Zhong, J. C.; Guo, H. C. *Tetrahedron: Asymmetry* **2011**, *22*, 1156–1160.
44. Arai, T.; Watanabe, M.; Fujiwara, A.; Yokoyama, N.; Yanagisawa, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 5978–5981.
45. Arai, T.; Watanabe, M.; Yanagisawa, A. *Org. Lett.* **2007**, *9*, 3595–3597.
46. Bandini, M.; Piccinelli, F.; Tommasi, S.; Umani-Ronchi, A.; Ventrici, C. *Chem. Commun.* **2007**, 616–618.
47. Sanjeevakumar, N.; Periasamy, M. *Tetrahedron: Asymmetry* **2009**, *20*, 1842–1847.
48. Noole, A.; Lippur, K.; Metsala, A.; Lopp, M.; Kanger, T. *J. Org. Chem.* **2010**, *75*, 1313–1316.
49. Kodama, K.; Sugawara, K.; Hirose, T. *Chem. Eur. J.* **2011**, *17*, 13584–13592.
50. Gan, C. S.; Lai, G. Y.; Zhang, Z. H.; Wang, Z. Y.; Zhou, M. M. *Tetrahedron: Asymmetry* **2006**, *17*, 725–728.
51. Colak, M.; Aral, T.; Hosgoren, H.; Demirel, N. *Tetrahedron: Asymmetry* **2007**, *18*, 1129–1133.
52. Colak, M.; Demirel, N. *Tetrahedron: Asymmetry* **2008**, *19*, 635–639.
53. Xin, D. Y.; Ma, Y. D.; He, F. Y. *Tetrahedron: Asymmetry* **2010**, *21*, 333–338.
54. Wei, Y.; Yao, L.; Zhang, B.; He, W.; Zhang, S. Y. *Tetrahedron* **2011**, *67*, 8552–8558.
55. Lai, G. Y.; Wang, S. J.; Wang, Z. Y. *Tetrahedron: Asymmetry* **2008**, *19*, 1813–1819.
56. Ozturk, G.; Colak, M.; Demirel, N. *Chirality* **2011**, *23*, 374–378.
57. Ji, Y. Q.; Qi, G.; Judeh, Z. M. A. *Eur. J. Org. Chem.* **2011**, 4892–4898.
58. Ji, Y. Q.; Qi, G.; Judeh, Z. M. A. *Tetrahedron: Asymmetry* **2011**, *22*, 929–935.
59. Michieletto, I.; Fabris, F.; De Lucchi, O. *Tetrahedron: Asymmetry* **2000**, *11*, 2835–2841.
60. Nishikubo, T.; Kameyama, A.; Kishi, K.; Nakajima, T. *Macromolecules* **1994**, *27*, 1087–1092.
61. Evans, D. A.; Peterson, G. S.; Johnson, J. S.; Barnes, D. M.; Campos, K. R.; Woerpel, K. A. *J. Org. Chem.* **1998**, *63*, 4541–4544.
62. van Lingen, H. L.; van Delft, F. L.; Storcken, R. P. M.; Hekking, K. F. W.; Klaassen, A.; Smits, J. J. M.; Ruskowska, P.; Frelek, J.; Rutjes, F. P. J. T. *Eur. J. Org. Chem.* **2005**, 4975–4987.
63. Vazquez-Villa, H.; Reber, S.; Ariger, M. A.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 8979–8981.