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Asymmetric Henry reaction catalyzed by a copper tridentate chiral schiff-base complex

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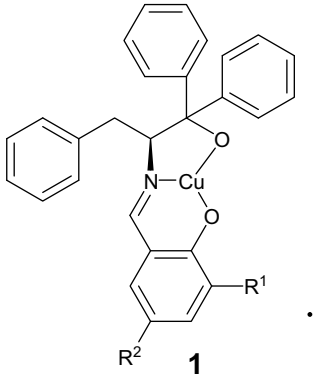
ABSTRACT

A series of copper-tridentate chiral Schiff-base complexes were prepared and employed in an asymmetric Henry reaction, affording the corresponding adducts in good yields and with high enantioselectivities (up to 96% ee).

1. Introduction

The Henry reaction[1] (or nitroaldol reaction) is one of the most important C–C bond forming reactions in organic synthesis. The resulting products of this reaction, a coupling between nitroalkanes and carbonyl groups, can be converted into many valuable building blocks depending on the different requirements in the synthesis of natural products and other useful compounds.[2] Recent efforts have been focused on the development of various metal-based catalysts by the groups of Shibasaki,[3] Trost,[4] Evans,[5] Palomo,[6] Jørgensen,[7] and others,[8,12] and organocatalysts[9] for the asymmetric Henry reaction.[10]

Chiral Schiff-bases have frequently been used in catalytic asymmetric synthesis.[11] Recently, we have reported that novel copper Schiff-base complexes **1k** and **1l** (Fig. 1),[12] which could be easily prepared from a natural amino acid, can catalyze asymmetric Henry reactions under mild conditions. However, both the yields (43–90%) and the enantioselectivities (45–86%) need to be improved.[12] In order to promote these results and acquire some information on the relationship between the structure of a complex and its enantioselectivity in the Henry reaction, we have been making continuous efforts to modify the ligands for the Henry reaction.



1

1a: R^1=Me, R^2=H
1b: R^1=H, R^2=Me
1c: R^1=Et, R^2=H
1d: R^1=i-Pr, R^2=H
1e: R^1=t-Bu, R^2=H
1f: R^1=H, R^2=t-Bu
1g: R^1=MeO, R^2=H
1h: R^1=H, R^2=MeO
1i: R^1=Cl, R^2=H
1j: R^1=H, R^2=Cl
1k: R^1=R^2=H
1l: R^1=R^2=t-Bu

Figure 1. The structure of the catalytic complexes.

2. Results and discussion

Initial studies have been focused on the reaction using different complexes **1a**–**1l** (Fig. 1). In our former work,[12] two types of catalysts **1k** and **1l** were employed in the asymmetric Henry reaction, which contained 3,5-di-*tert*-butylated substituents **1l** and without any substituent on the phenol ring **1k**. The experimental results (Table 1, entries 11 and 12) showed that the substituents on the phenol ring had a great influence on the enantioselectivity but little influence on the reaction yield. On the other hand, nitromethane did not react with the imine group of the ligand in this complex **1**. Intrigued by this result, a variety of catalysts with different substituents on the phenol rings were then prepared and screened by the asymmetric Henry reaction. In this reaction, ethanol was chosen as a solvent since we had employed it as the reaction solvent previously.[12] All the experimental results are listed in Table 1. From Table 1, it was found that the steric hindrance of the substituent on the phenol ring of the ligand affected the enantioselectivity. For instance, when the substituent was a methyl group (Fig. 1, **1a** and **1b**), both the yields and enantioselectivities were enhanced (Table 1, entries 1 and 2). Especially, when the methyl group was located at the *ortho* position of phenol ring, the highest ee value 92% can be obtained, which showed that substitution on the *ortho*-position (R^1) would affect the reaction to a greater extent than on the *para*-position (R^2). Slightly increasing the volume of the R^1 substituent from methyl group to ethyl group (Fig. 1, **1c**) resulted in a little decrease both in the yield and ee

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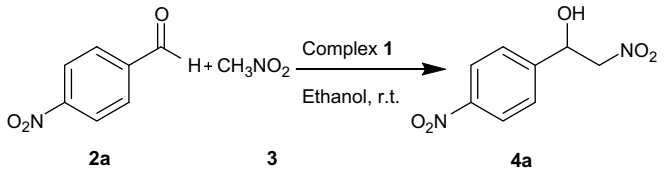
Table 1
The optimization of the catalytic complexes[a]



2a 3 4a

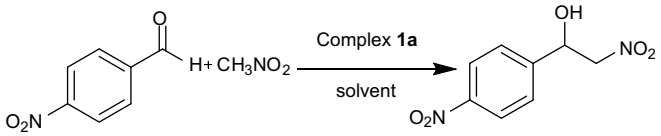
Entry	Complex	Yield[b] (%)	ee[c] (%)	Config[d]
1	**1a**	86	92	*S*
2	**1b**	81	84	*S*
3	**1c**	83	70	*S*
4	**1d**	86	88	*S*
5	**1e**	82	72	*S*
6	**1f**	87	70	*S*
7	**1g**	99	54	*S*
8	**1h**	82	74	*S*
9	**1i**	88	88	*S*
10	**1j**	86	83	*S*
11[e]	**1k**	85	78	*S*
12[e]	**1l**	85	64	*S*

[a] All reactions were performed with 0.5 mmol of 4-nitro-benzaldehyde and 2.5 mmol nitromethane in the presence of 2.5 mmol % of complex **1** at room temperature.
[b] Isolated yields.
[c] Determined by chiral HPLC using a OD–H column.
[d] The absolute configurations of products were determined by comparison with the literature[5] values.
[e] Refer to our previous work.[12]

(Table 1, entry 3). Increasing the steric hindrance further (Fig. 1, **1d**, **1e**, and **1f**) led to lower yields and ee values (Table 1, entries 4–6). For the *tert*-butyl substitution, the ee value decreased in spite of the substitution at the *para* position because of the great hindrance of the *tert*-butyl group. Thus, these studies indicated that a suitable *steric* hindrance was necessary for obtaining both high yield and ee; the methyl group meets this requirement. On the other hand, the electronic effect also has an influence on the reaction. For instance, the substitution of a strong electron-donating methoxyl group on the phenol ring (Fig. 1, **1g** and **1h**) led to a obvious decrease in the ee values although this substitution had little influence on the reaction yields (Table 1, entries 7 and 8). When the R^1 or R^2 group was an electron-withdrawing group, such as a chloro group (Fig. 1, **1i** and **1j**), a slight electronic effect was observed in this situation and a normal reaction yield was obtained (Table 1, entries 9 and 10). After optimization for different substitutions, complex **1a** was seen to be the best catalyst among those screened in this reaction.

After the selection of the catalyst, solvents, additives, temperatures, and the catalyst loading were tested in the asymmetric Henry reaction between 4-nitro-benzaldehyde and nitromethane. Generally, the protonic solvents were superior to the non-protonic ones (Table 2, entries 1–11). Moreover, among different protonic solvents, ethanol was established as the best for this reaction system (Table 2, entry 1, 86% yield, 92% ee). When 10 mg of 4 Å sieves was added, the reaction rate accelerated while the corresponding product was obtained in high yield but with very low ee (Table 2, entry 12). When the reaction temperature was decreased from room temperature to −5 °C, the reaction took longer time and gave the corresponding product in a lower yield with almost the same ee value (Table 2, entry 13). In contrast, increasing the reaction temperature accelerated the reaction rate, but reduced the ee value (Table 2, entry 14). Therefore, room temperature is an optimal reaction temperature. Afterwards, different catalyst loadings were tested, and the results showed that 2.5 mol % catalyst loading was the best quantity for this reaction (entries 1, 15, and 16). Overall, the optimized conditions include catalyst complex **1a**, the reaction

Table 2
Effects of solvent and temperature on the asymmetric Henry reaction under the catalysis of complex 1a[a]

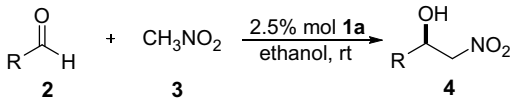


2a 3 4a

Entry	Solvent	*T* (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	Ethanol	rt	24	86	92
2	Toluene	rt	24	37	72
3	CH_2Cl_2	rt	24	43	38
4	CH_3CN	rt	24	41	62
5	THF	rt	24	50	46
6	Et_2O	rt	24	60	68
7	*n*-Hexane	rt	24	87	62
8	CH_3OH	rt	24	79	36
9	*t*-Butanol	rt	24	81	72
10	*n*-Propanol	rt	24	84	88
11	*i*-Propanol	rt	24	88	84
12[d]	Ethanol	rt	10	99	4
13	Ethanol	−5	48	49	92
14	Ethanol	50	6	90	84
15[e]	Ethanol	rt	24	78	86
16[f]	Ethanol	rt	24	81	86

[a] All reactions were performed with 0.5 mmol of 4-nitro-benzaldehyde and 2.5 mmol of nitromethane in the presence of 2.5 mol % of complex **1a** in 2 mL of solvent at the appointed temperature.
[b] Isolated yields by the column chromatography.
[c] Determined by HPLC on a OD-H column.
[d] 100 mg of 4 Å sieve was added.
[e] 1.25 mol % of complex **1a** was added.
[f] 5 mol % of complex **1a** was added.

Table 3
Enantioselective Henry reaction of nitromethane with various aldehydes catalyzed by complex **1a**[a]



2 **3** **4**

a: R = 4-NO_2Ph
b: R = 2-NO_2Ph
c: R = 4-ClPh
d: R = 3-ClPh
e: R = 2-ClPh
f: R = Ph
g: R = 4-MePh
h: R = 2-MePh
i: R = 4-MeOPh
j: R = 2-MeOPh
k: R = 1-Naphthyl
l: R = $PhCH_2$
m: R = *i*-Bu
n: R = Pr

Entry	Product	Time (h)	Yield[b] (%)	ee[c] (%)	Config[d]
1	**4a**	24	86	92	*S*
2	**4b**	24	87	92	*S*
3	**4c**	24	81	90	*S*
4	**4d**	24	82	91	*S*
5	**4e**	24	85	96	*S*
6	**4f**	24	76	91	*S*
7	**4g**	48	67	91	*S*
8	**4h**	24	81	95	*S*
9	**4i**	36	72	84	*S*
10	**4j**	24	83	93	*S*
11	**4k**	48	80	91	*S*
12	**4l**	48	71	81	—[e]
13	**4m**	72	76	85	*S*
14	**4n**	96	70	85	*S*

[a] Reactions were performed with 0.5 mmol of aldehyde and 2.5 mmol of nitromethane in the presence of 2.5 mol % of complex **1a** in 2 mL of ethanol at room temperature.
[b] Isolated yields after the column chromatography purifications.
[c] Determined by HPLC using chiral OD-H or OJ-H column.
[d] The absolute configurations of products were determined by comparison with the literature[5,6,8a,8q] values.
[e] The absolute configuration is not determined.

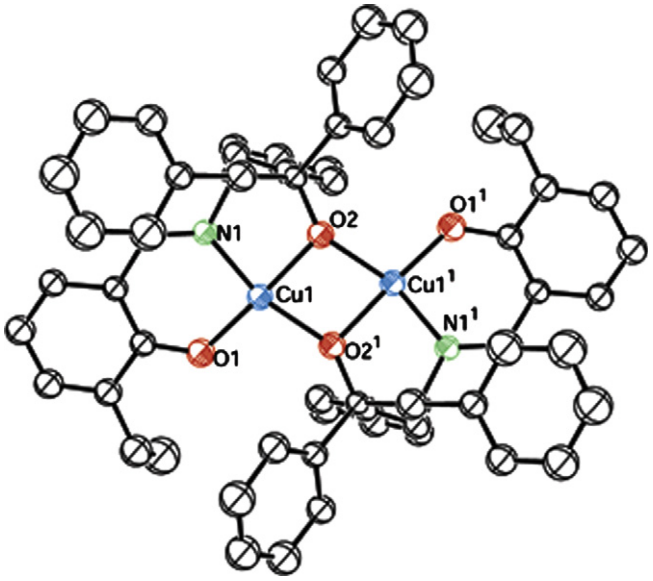


Figure 2. The crystal structure of complex **1c**, selected bond lengths: Cu1–N1 = 1.897 Å, Cu1–O1 = 1.881 Å, Cu1–O2 = 1.943 Å, Cu1–O21 = 1.944 Å.

carried out at room temperature and the reaction solvent being ethanol.

With the optimized conditions in hand, the scope of the substrate was extended. A variety of aldehydes were employed as substrates to react with nitromethane, giving the corresponding products with high yields and ee values, as shown in Table 3. The data clearly showed that complex **1a** and the optimized reaction conditions can be applied in a wide scope of substrates, including different kinds of aromatic and aliphatic aldehydes. The aromatic aldehydes could undergo an asymmetric Henry reaction smoothly with good yields and ee values. The steric hindrance had little influence on this reaction (Table 3, entries 1–11). The ones with electron-withdrawing group gave higher yields (entries 1–5 vs entries 7–10). The substrates with *ortho*-substituent (entries 2, 5, 8, and 10) gave higher enantioselectivities than other ones. The aliphatic aldehydes could also react with nitromethane well and give the corresponding products with the yields of 71–76% and ee values of 81–85% regardless of the branch on the chain (Table 3, entries 12–14).

We also prepared a single crystal of complex **1c** and measured its X-ray structure (Fig. 2, Tables 4 and 5). Complex **1c** crystallized in the chiral space group $P4_32_12$,[13] as shown in Figure 2. The asymmetric unit comprises a copper atom and a chiral Schiff-base molecule. Each Cu(II) is bounded to an N atom, two O atoms from one Schiff-base and another O atom from another Schiff-base, completing a distorted square planar coordination geometry. Two adjacent Cu atoms are linked together via two O toms from two adjacent Schiff-bases, forming a dimer.

Table 4
Crystal data

Compound	**1c**
Empirical formular	$C_{60}H_{54}Cu_2N_2O_4$
Formular wt	994.13
Crystal system	Tetragonal
Space group	$P4_32_12$
a (Å)	10.4050(15)
b (Å)	10.4050(15)
c (Å)	46.987(9)
α (°)	90.00
β (°)	90.00
γ (°)	90.00
V (Å^3)	5087.0(15)
Z	4
T (K)	293(2)
ρ_{calc} (g cm^{-3})	1.289
F(000)	2072
μ (mm^{-1})	0.885
data/parameters	2673/141
R_1 [$I > 2\sigma(I)$]	0.0846
wR_2	0.1963
Goodness-of-fit	1.055
Largest difference in peak and hole (e A^3)	1.369, −1.486
Crystal size (mm)	
X	0.213
Y	0.213
Z	0.502

Table 5
Bond lengths and angles

Bond lengths and angles	
Cu(1)–O(1)	1.881(7)
Cu(1)–N(1)	1.898(8)
Cu(1)–O(2)	1.944(6)
Cu(1)–O(2)	1.944(6)
O(1)–Cu(1)–N(1)	95.0(3)
O(1)–Cu(1)–O(2)	172.1(3)
N(1)–Cu(1)–O(2)	83.7(3)
O(1)–Cu(1)–O(2)	103.5(3)
N(1)–Cu(1)–O(2)	159.3(3)
O(2)–Cu(1)–O(2)	79.3(3)

3. Conclusion

In conclusion, the efficiency of an asymmetric Henry reaction was enhanced by the modification of the catalytic ligands on the basis of natural α-amino acids. To the best of our knowledge, this is the first time that the substituents on the phenol ring have been reported to have a great influence on the yield and enantioselectivity of the Henry reaction. However, these substituents are far from the stereogenic carbon atom of our Schiff-base ligands. The structure of the single crystal of catalyst **1c** has been measured, which could be useful for the design of new catalysts for asymmetric Henry reactions. Further studies on asymmetric synthesis are still in progress in our group.

4. Experimental

4.1. General remarks

The aldehydes were all purified through distillation at low pressure or recrystallization. Solvents were dried according to standard procedure and distilled prior to use. Most reagents, such as nitromethane, phenylalanine, hydroxybenzene groups, and copper acetate monohydrate, were used as received from commercial sources. Complexes were prepared by a series of reactions. All reactions were carried out under indicated conditions. NMR spectra were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C using $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Infrared spectra and mass spectra were obtained. The enantiomeric excess of the Henry products was determined by HPLC on Chiralcel OD-H or OJ-H column.

5. Preparation for complex 1

5.1. General experimental procedure for the preparation of salicylaldehyde derivatives

To a solution of the corresponding phenol (10 mmol) in 10 mL ethanol was added 3.0 g of NaOH (75 mmol) in 15 mL water. The

resulting solution was heated to 80 °C, and the dropwise addition of chloroform was started. After the reaction began, further heating was unnecessary. A total of 2.36 g. (20 mmol) of chloroform were added so as to maintain gentle refluxing. Stirring was continued for 1 h after all the chloroform had been added. The ethanol was removed by reduced pressure, and 1 M HCl was added to neutralize the excess NaOH until pH 2–3. The residue was then extracted with ethyl acetate three times. The combined organic extracts were dried using anhydrous Na_2SO_4 and evaporated under reduced pressure; the mixture was then purified by column chromatography over silica gel to afford salicylaldehyde derivatives **5** with high purity.

5.2. Preparation for (*S*)-ethyl-2-amino-3-phenylpropanoate

The starting material, L-phenylalanine, is commercially available. A solution of the L-phenylalanine (3 g, 18.3 mmol) in 20 mL ethanol was cooled by ice water. After cooling, 4.6 mL of $SOCl_2$ was added dropwise. The resulting solution was then refluxed for 4 h. Evaporation of the solvent gave a white solid, which was treated with saturated aqueous Na_2CO_3 until pH 8–9, after which it was extracted with ethyl acetate (10 mL × 3). The combined organic extracts were dried using anhydrous Na_2SO_4 and evaporated under reduced pressure, which gave the (*S*)-ethyl-2-amino-3-phenylpropanoate (3.395 g, 96% yield).

5.3. Preparation for (*S*)-2-amino-1,1,3-triphenylpropan-1-ol

In a three-necked round-bottomed flask fitted with a reflux condenser, under a nitrogen atmosphere, 1.5 g (62 mmol) furbished Mg and 20 mL anhydrous diethyl ether, which was treated with sodium prior to use, were added. The stir was started and a solution of bromobenzene (4.34 mL, 42 mmol) in 5 mL diethyl ether was added dropwise. After the reaction began, the solution maintained slightly boils through the control of the velocity of addition. After the addition, the resulting solution was heated under reflux for 0.5 h. The heating equipment was switched off and the addition of the above (*S*)-2-ethyl-2-amino-3-phenylpropanoate (2 g, 10.4 mmol) in 10 mL diethyl ether was started. Another reflux of 0.5 h was needed, after which, the resulting solution was cooled in ice water and saturated NH_4Cl aqueous was added until no more white precipitate was produced. The solution was filtered and the liquid was extracted by diethyl ether (25 mL × 3). The combined organic extracts were dried using anhydrous Na_2SO_4 and evaporated under reduced pressure to give yellow solid. The solid was then recrystallized in 30 mL methanol, which gave a white solid (*S*)-2-amino-1,1,3-triphenylpropan-1-ol (2.556 g, 81% yield).

5.4. General procedure for the preparation for chiral Schiff-base 6

To a solution of 0.5 mmol of the above (*S*)-2-amino-1,1,3-triphenylpropan-1-ol in 5 mL methanol was added 0.55 mmol of the above **5**. The solution was refluxed for 4 h. The methanol was removed under reduced pressure. The residue was purified by chromatography (4.76% EtOAc in petroleum) to give, the resulting chiral Schiff-base as a yellow solid, in high yield (>98%).

5.4.1. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-methylphenol 6a

$[\alpha]_D^{25} = -53.2$ (*c* 0.81, CH_2Cl_2). IR (film cm^{-1}): 3060, 3028, 2926, 1623, 1450, 744, 700. ^1H NMR ($CDCl_3$, δ ppm): 2.23 (s, 3H), 2.86 (dd, *J* = 10.2, 13.5 Hz, 1H), 3.01 (br, 1H), 3.01 (d, *J* = 13.5 Hz, 1H), 4.35 (d, *J* = 10.2 Hz, 1H), 6.68 (m, 2H), 6.96(d, *J* = 7.2 Hz, 2H), 7.19 (m, 8H), 7.39 (m, 2H), 7.49 (m, 2H), 7.56 (s, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 12.83 (br, 1H). ^{13}C NMR: 15.5, 37.6, 78.9, 79.9, 117.8, 118.3, 125.8, 126.1, 126.3, 127.0, 127.2, 128.4, 128.5, 128.6, 129.4, 129.9, 133.6, 139.1, 144.3, 145.7, 159.0, 167.0. HRMS: calcd for $C_{29}H_{27}NO_2$: 421.2042, found 421.2036.

5.4.2. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-4-methylphenol 6b

$[\alpha]_D^{25} = -72.0$ (*c* 1.01, CH_2Cl_2). IR (film cm^{-1}): 3480, 3061, 2924, 2868, 1631, 1492, 1279, 909, 736, 702. ^1H NMR ($CDCl_3$, δ ppm): 2.18 (s, 3H), 2.85 (dd, *J* = 10.2, 13.5 Hz, 1H), 2.93 (br, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 4.33 (d, *J* = 10.2 Hz), 6.65 (s, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 6.9 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 7.14 (m, 3H), 7.25 (m, 4H), 7.38 (m, 2H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.54 (s, 1H), 7.64 (d, *J* = 7.5 Hz, 2H), 12.41 (br, 1H). ^{13}C NMR: 20.3, 37.6, 78.9, 79.9, 116.6, 118.2, 126.1, 126.3, 126.4, 127.1, 127.2, 127.8, 128.4, 128.5, 128.6, 129.8, 131.7, 133.4, 139.1, 144.3, 145.5, 158.4, 166.8. HRMS: calcd for $C_{29}H_{27}NO_2$: 421.2042, found 421.2038.

5.4.3. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-ethylphenol 6c

$[\alpha]_D^{25} = -50.2$ (*c* 0.96, CH_2Cl_2). IR (film cm^{-1}): 3438, 3052, 3029, 2967, 2933, 2876, 1622, 1451, 748, 700. ^1H NMR ($CDCl_3$, δ ppm): 1.22 (m, 3H), 2.65 (m, 2H), 2.88 (dd, *J* = 2.6, 12.2 Hz, 1H), 3.01 (m, 2H), 4.35 (dd, *J* = 2.6, 9.9 Hz, 1H), 6.71 (m, 2H), 6.92 (m, 2H), 7.16 (m, 5H), 7.38 (m, 3H), 7.48 (m, 2H), 7.58 (s, 1H), 7.66 (m, 2H), 12.80 (br, 1H). ^{13}C NMR: 13.8, 14.1, 22.5, 23.1, 37.6, 78.8, 79.9, 115.3, 117.8, 118.4, 121.0, 126.1, 126.3, 126.4, 127.0, 127.1, 127.2, 128.4, 128.5, 128.6, 129.4, 129.9, 130.1, 131.8, 131.9, 139.1, 144.3, 145.6, 153.5, 158.7, 167.1. HRMS: calcd for $C_{30}H_{29}NO_2$: 435.2198, found 435.2192.

5.4.4. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-isopropylphenol 6d

$[\alpha]_D^{25} = -53.2$ (*c* 0.81, CH_2Cl_2). IR (film cm^{-1}): 3440, 3062, 3029, 2962, 2931, 2872, 1622, 1449, 748, 700. ^1H NMR ($CDCl_3$, δ ppm): 1.23 (m, 6H), 2.87 (m, 1H), 3.01 (m, 2H), 3.34 (d, *J* = 12.9 Hz, 1H), 4.36 (dd, *J* = 1.7, 9.9 Hz, 1H), 6.72 (t, *J* = 3.0 Hz, 2H), 6.97 (d, *J* = 1.3 Hz, 2H), 7.19 (m, 8H), 7.39 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.59 (s, 1H), 7.66 (d, *J* = 7.5 Hz, 2H), 12.88 (br, 1H). ^{13}C NMR: 22.5, 22.6, 22.7, 16.3, 27.1, 37.6, 78.7, 79.9, 115.4, 117.9, 118.4, 121.1, 126.1, 126.3, 126.4, 126.5, 126.8, 127.0, 127.2, 128.4, 128.5, 128.6, 129.1, 129.3, 129.9, 136.2, 139.2, 144.3, 145.7, 152.9, 158.1, 167.2. HRMS: calcd for $C_{31}H_{31}NO_2$: 449.2355, found 449.2348.

5.4.5. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-*tert*-butylphenol 6e

$[\alpha]_D^{25} = -71.0$ (*c* 0.97, CH_2Cl_2). IR (film cm^{-1}): 3063, 3029, 2960, 1622, 1436, 909, 734, 702. ^1H NMR ($CDCl_3$, δ ppm): 1.40 (s, 9H), 2.90 (dd, *J* = 10.0, 13.7 Hz, 1H), 3.03 (m, 2H), 4.34 (dd, *J* = 1.8, 10.0 Hz, 1H), 6.68 (d, *J* = 2.7 Hz, 2H), 6.97 (t, *J* = 3.8 Hz, 2H), 7.13 (m, 4H), 7.23 (m, 4H), 7.39 (m, 2H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.60 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 2H), 13.09 (br, 1H). ^{13}C NMR: 29.5, 34.9, 37.6, 78.7, 80.0, 117.9, 118.5, 126.1, 126.3, 126.4, 127.0, 127.2, 128.4, 128.5, 128.6, 129.7, 129.7, 129.9, 130.0, 137.2, 129.2, 144.3, 145.7, 160.0, 167.5. HRMS: calcd for $C_{32}H_{33}NO_2$: 463.2511, found 463.2503.

5.4.6. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-4-*tert*-butylphenol 6f

$[\alpha]_D^{25} = -71.3$ (*c* 0.88, CH_2Cl_2). IR (film cm^{-1}): 3473, 3029, 2959, 1631, 1492, 1262, 742, 700. ^1H NMR ($CDCl_3$, δ ppm): 1.26 (s, 9H), 2.86 (dd, *J* = 10.2, 13.5 Hz, 1H), 2.98 (br, 1H), 3.06 (d, *J* = 13.5 Hz, 1H), 4.36 (d, *J* = 8.7 Hz, 1H), 6.83 (d, *J* = 9.1 Hz, 2H), 6.97 (d, *J* = 6.4 Hz, 2H), 7.16 (t, *J* = 7.1 Hz, 3H), 7.26 (m, 5H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.56 (s, 1H), 7.66 (d,

J = 7.7 Hz, 2H), 12.33 (br, 1H). ^{13}C NMR: 14.3, 31.4, 31.5, 34.0, 37.7, 78.7, 80.0, 116.4, 117.9, 126.2, 126.4, 127.1, 127.2, 128.1, 128.4, 128.5, 128.6, 129.90, 129.94, 139.2, 141.5, 144.3, 145.6, 158.3, 167.2. HRMS: calcd for $C_{32}H_{33}NO_2$: 463.2511, found 463.2506.

5.4.7. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-methoxyphenol 6g

$[\alpha]_D^{25} = -56.1$ (c 0.67, CH_2Cl_2). IR (film cm^{-1}): 3501, 3062, 3028, 2935, 1628, 1467, 1254, 909, 734, 702. ^{1}H NMR ($CDCl_3$, δ ppm): 2.86 (dd, J = 10.2, 12.9 Hz, 1H), 2.93 (br, 1H), 3.04 (d, J = 12.9 Hz, 1H), 3.87 (s, 3H), 4.34 (dd, J = 1.7, 10.2 Hz, 1H), 6.47 (dd, J = 0.6, 7.2 Hz, 1H), 6.67 (t, J = 8.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 6.97 (dd, J = 0.8, 7.2 Hz, 2H), 7.13 (m, 4H), 7.24 (m, 3H), 7.38 (t, J = 7.6 Hz, 2H), 7.48 (d, J = 7.6 Hz, 2H), 7.54 (s, 1H), 7.65 (dd, J = 0.9, 8.0 Hz, 2H), 13.26 (br, 1H). ^{13}C NMR: 37.6, 56.1, 78.7, 79.9, 114.1, 118.1, 118.3, 123.1, 125.6, 125.9, 126.1, 126.2, 126.4, 127.1, 127.2, 128.37, 128.4, 128.5, 128.6, 128.64, 128.8, 129.2, 129.9, 139.0, 144.2, 145.3, 148.3, 151.2, 166.7. HRMS: calcd for $C_{29}H_{27}NO_3$: 437.1991, found 437.1983.

5.4.8. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-4-methoxyphenol 6h

$[\alpha]_D^{25} = -54.0$ (c 0.68, CH_2Cl_2). IR (film cm^{-1}): 3389, 3027, 2928, 1633, 1492, 1269, 744, 700. ^{1}H NMR ($CDCl_3$, δ ppm): 2.84 (dd, J = 10.2, 13.2 Hz, 1H), 2.92 (br, 1H), 3.04 (d, J = 13.2 Hz, 1H), 3.68 (s, 3H), 4.34 (dd, J = 1.5, 10.2 Hz, 1H), 6.37 (d, J = 2.7 Hz, 1H), 6.83 (t, J = 3.5 Hz, 1H), 6.96 (dd, J = 1.2, 6.9 Hz, 2H), 7.15 (m, 4H), 7.26 (m, 4H), 7.39 (m, 2H), 7.50 (m, 3H), 7.64 (d, J = 7.2 Hz, 2H), 12.13 (br, 1H). ^{13}C NMR: 37.4, 55.8, 78.8, 79.8, 115.3, 117.4, 118.1, 119.2, 126.0, 126.2, 126.3, 127.0, 127.1, 128.2, 128.26, 128.34, 128.36, 128.4, 128.5, 128.7, 129.7, 138.9, 144.1, 145.3, 151.9, 154.6, 166.3. HRMS: calcd for $C_{29}H_{27}NO_3$: 437.1991, found 437.1985.

5.4.9. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-6-chlorophenol 6i

$[\alpha]_D^{25} = -58.1$ (c 0.90, CH_2Cl_2). IR (film cm^{-1}): 3385, 3061, 3028, 2932, 1629, 1449, 736, 701. ^{1}H NMR ($CDCl_3$, δ ppm): 2.87 (dd, J = 9.9, 12.9 Hz, 1H), 2.90 (br, 1H), 3.04 (d, J = 12.9 Hz, 1H), 4.37 (dd, J = 1.7, 9.9 Hz, 1H), 6.67 (t, J = 7.7 Hz, 1H), 6.76 (dd, J = 1.4, 7.7 Hz, 1H), 6.96 (dd, J = 1.4, 6.9 Hz, 2H), 7.15 (m, 3H), 7.25 (m, 3H), 7.32 (m, 2H), 7.40 (t, J = 7.7 Hz, 2H), 7.48 (t, J = 7.8 Hz, 3H), 7.64 (d, J = 7.5 Hz, 2H), 13.77 (br, 1H). ^{13}C NMR: 37.5, 78.5, 79.8, 118.6, 119.1, 121.7, 126.1, 126.2, 126.6, 127.2, 127.4, 128.5, 128.6, 128.7, 129.8, 130.1, 132.9, 138.8, 144.0, 145.2, 157.5, 166.0. HRMS: calcd for $C_{28}H_{24}ClNO_2$: 441.1496, found 441.1491.

5.4.10. 2-(((*S*)-1-Hydroxy-1,1,3-triphenylpropan-2-ylimino)-methyl)-4-chlorophenol 6j

$[\alpha]_D^{25} = -33.5$ (c 0.78, CH_2Cl_2). IR (film cm^{-1}): 3482, 3060, 3028, 2930, 1632, 1479, 1276, 745, 700. ^{1}H NMR ($CDCl_3$, δ ppm): 2.84 (m, 2H), 3.06 (d, J = 13.7 Hz, 1H), 4.35 (t, J = 5.0 Hz, 1H), 6.82 (m, 2H), 6.96 (m, 2H), 7.16 (m, 4H), 7.26 (m, 4H), 7.40 (m, 2H), 7.47 (m, 3H), 7.63 (m, 2H), 12.71 (br, 1H). ^{13}C NMR: 37.5, 78.9, 79.9, 118.5, 119.2, 123.3, 126.2, 126.3, 126.7, 127.2, 127.4, 128.5, 128.6, 128.7, 129.8, 130.6, 130.6, 132.4, 138.8, 144.1, 145.2, 159.4, 165.4. HRMS: calcd for $C_{28}H_{24}ClNO_2$: 441.1496, found 441.1489.

5.5. General procedure for complex 1

To a solution of 0.5 mmol of chiral Schiff-base **6** in 10 mL of methanol, 0.6 mmol of $Cu(OAc)_2{\cdot}H_2O$ were added. The solution was stirred in the room temperature for 2 h after which 20 mmol of NaOH were added. Another 6 h of stirring time was needed. The methanol was evaporated under reduced temperature. To the residue was added 10 mL of brine and extracted by benzene (10 mL × 3). The combined organic extracts were dried using anhydrous Na_2SO_4, and evaporated under reduced pressure to give a dark green solid **1**.

5.5.1. Typical experimental procedure for an enantioselective Henry reaction

To a mixture of complex **1a** (0.0125 mmol) and ethanol (2 mL) at a given temperature was added 2.5 mmol of nitromethane. The mixture was allowed to stir for 2 h, and **2** (0.5 mmol) was added. After being stirred for the indicated time, the mixture was quenched by diluted HCl (0.5 mL, 1 M), and then ethanol was evaporated in vacuo. The residue was then extracted with acetic ethyl ester (2 mL) for three times. Purification by column chromatography afforded the desired Henry product **4**. The ee value was determined by HPLC on Chiralcel OD-H or OJ-H column.

5.5.2. (*S*)-1-(4-Nitrophenyl)-2-nitroethanol 4a

Compound **4a** was prepared according to the general procedure and purified by column chromatography (16.7% EtOAc in petroleum ester) to give an off-white solid (86% yield). Mp: 83–85 °C; IR (film cm^{-1}): 3401, 2919, 1555, 1416, 1382, 1349, 1086, 856, 754, 727, 697. ^{1}H NMR ($CDCl_3$, δ ppm): 3.20 (br, 1H), 4.60 (m, 2H), 5.61 (m, 1H), 7.64 (d, 2H, J = 8.6 Hz), 8.27 (d, 2H, J = 8.6 Hz). ^{13}C NMR: 70.1, 80.7, 124.3, 127.1, 145.1, 148.3. HRMS: calcd for $C_8H_8N_2O_5$: 212.0433, found 212.0443. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (80:20 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 22.9 min, major enantiomer t_r = 27.8 min; 92% ee; $[\alpha]_D^{25} = +35.9$ (c 1.01, CH_2Cl_2).

5.5.3. (*S*)-1-(2-Nitrophenyl)-2-nitroethanol 4b

Compound **4b** was prepared according to the general procedure and purified by column chromatography (16.7% EtOAc in petroleum ester) to give a brown solid (87% yield). Mp: 79–81 °C; IR (film cm^{-1}): 3537, 1587, 1533, 1422, 1380, 1365, 1091, 1071, 866. ^{1}H NMR ($CDCl_3$, δ ppm): 3.24 (br, 1H), 4.56 (dd, 1H, J = 9, 13.8 Hz), 4.88 (dd, 1H, J = 2.1, 13.8 Hz), 6.06 (d, 1H, J = 9 Hz), 7.56 (t, 1H, J = 7.8 Hz), 7.76 (t, 1H, J = 7.8 Hz), 7.96 (d, 1H, J = 8.3 Hz), 8.09 (d, 1H, J = 8.3 Hz). ^{13}C NMR: 66.8, 80.1, 124.9, 128.7, 129.7, 134.3, 134.5, 147.0. HRMS: calcd for $C_8H_8N_2O_5$: 212.0433, found 212.0452. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (90:10 hexanes–isopropanol, 0.7 mL/min, 215 nm); minor enantiomer t_r = 21.2 min, major enantiomer t_r = 23.8 min; 92% ee; $[\alpha]_D^{25} = +139.7$ (c 0.61, CH_2Cl_2).

5.5.4. (*S*)-1-(4-Chlorophenyl)-2-nitroethanol 4c

Compound **4c** was prepared according to the general procedure and purified by column chromatography (10% EtOAc in petroleum ester) to give a colorless oil (81% yield). IR (film cm^{-1}): 3446, 2924, 2255, 1557, 1493, 1379, 1090, 1015, 909, 829, 735, 651, 530; ^{1}H NMR ($CDCl_3$, δ ppm): 3.19 (br, 1H), 4.48 (dd, 1H, J = 3.4, 13.4 Hz), 4.57 (dd, 1H, J = 9.2, 13.4 Hz), 5.44 (dd, 1H, J = 3.4, 9.2 Hz), 7.34 (d, 2H, J = 8.6Hz), 7.38 (d, 2H, J = 8.6 Hz). ^{13}C NMR: 70.4, 81.1, 127.4, 129.3, 134.9, 136.7. HRMS: calcd for $C_8H_8ClNO_3$: 201.0193, found 201.0194. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD–H column (85:15 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 18.4 min, major enantiomer t_r = 22.6 min; 90% ee; $[\alpha]_D^{25} = +20.5$ (c 1.12, CH_2Cl_2).

5.5.5. (*S*)-1-(3-Chlorophenyl)-2-nitroethanol 4d

Compound **4d** was prepared according to the general procedure and purified by column chromatography (10% EtOAc in petroleum ester) to give a colorless oil (82% yield). IR (film cm^{-1}): 3563, 1597, 1557, 1477, 1422, 1378, 910, 739. ^{1}H NMR ($CDCl_3$, δ ppm): 2.92 (br, 1H), 4.51 (dd, 1H, J = 3.4, 13.6 Hz), 4.59 (dd, 1H, J = 8.9, 13.6 Hz),

5.46 (dd, 1H, J = 3.4, 8.9 Hz), 7.35 (m, 4H). ^{13}C NMR: 70.4, 81.1, 124.2, 126.3, 129.2, 130.4, 135.1, 140.2. HRMS: calcd for $C_8H_8ClNO_3$: 201.0193, found 201.0195. Enantiomeric excess was determined by HPLC[8q] with a Chiralcel OD-H column (85:15 hexanes: isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 25.9 min, major enantiomer t_r = 31.7 min; 91% ee; $[\alpha]_D^{25} = +82.1$ (c 0.57, CH_2Cl_2).

5.5.6. (*S*)-1-(2-Chlorophenyl)-2-nitroethanol 4e

Compound **4e** was prepared according to the general procedure and purified by column chromatography (10% EtOAc in petroleum ester) to give a colorless oil (85% yield). IR (film cm^{-1}): 3589, 2924, 2256, 1557, 1473, 1442, 1416, 1379, 1344, 1285, 1211, 1131, 1086, 1037, 905, 734, 650, 610. ^{1}H NMR ($CDCl_3$, δ ppm): 3.17 (br, 1H), 4.44 (dd, 1H, J = 9.5, 13.5 Hz), 4.65 (dd, 1H, J = 2.5, 13.5 Hz), 5.82 (dd, 1H, J = 2.5, 9.5 Hz), 7.32 (m, 3H), 7.64 (m, 1H). ^{13}C NMR: 68.0, 79.4, 127.6, 127.7, 129.8, 130.0, 131.6, 135.7. HRMS: calcd for $C_8H_8ClNO_3$: 201.0193, found 201.0188. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OJ-H column (98:2 hexanes–isopropanol, 0.8 mL/min, 215 nm); minor enantiomer t_r = 72.8 min, major enantiomer t_r = 77.2 min; 96% ee; $[\alpha]_D^{25} = +46.3$ (c 1.07, CH_2Cl_2).

5.5.7. (*S*)-1-Phenyl-2-nitroethanol 4f

Compound **4f** was prepared according to the general procedure and purified by column chromatography (12.5% EtOAc in petroleum ester) to give a colorless oil (76% yield). IR (film cm^{-1}): 3535, 3032, 2920, 1554, 1495, 1453, 1418, 1379, 1290, 1212, 1066, 895, 764, 702, 608. ^{1}H NMR ($CDCl_3$, δ ppm): 3.24 (br, 1H), 4.49 (m, 1H), 4.59 (m, 1H), 5.44 (dd, 1H, J = 3.2, 9.5 Hz), 7.40 (m, 5H). ^{13}C NMR: 71.0, 81.2, 126.0, 129.0, 129.0, 138.3. HRMS: calcd for $C_8H_9NO_3$: 167.0582, found 167.0579. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (85:15 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 19.9 min, major enantiomer t_r = 22.4 min; 91% ee; $[\alpha]_D^{25} = +38.1$ (c 0.98, CH_2Cl_2).

5.5.8. (*S*)-2-Nitro-1-*p*-tolylethanol 4g

Compound **4g** was prepared according to the general procedure and purified by column chromatography (12.5% EtOAc in petroleum ester) to give a yellow oil (67% yield). IR (film cm^{-1}): 3548, 3028, 2924, 1555, 1516, 1418, 1378, 1287, 1208, 1077, 910, 819, 734. ^{1}H NMR ($CDCl_3$, δ ppm): 2.36 (s, 3H), 2.71 (br, 1H), 4.48 (dd, 1H, J = 2.9, 13.4 Hz), 4.60 (dd, 1H, J = 9.6, 13.4 Hz), 5.42 (dd, 1H, J = 2.9, 9.6 Hz), 7.20 (d, 2H, J = 7.8 Hz), 7.28 (m, 2H). ^{13}C NMR: 21.2, 71.0, 81.3, 126.0, 129.8, 135.3, 139.0. HRMS: calcd for $C_9H_{11}NO_3$: 181.0739, found 181.0746. Enantiomeric excess was determined by HPLC[8n] with a Chiralcel OD-H column (85:15 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 18.6 min, major enantiomer t_r = 22.8 min; 91% ee; $[\alpha]_D^{25} = +23.4$ (c 1.12, CH_2Cl_2).

5.5.9. (*S*)-2-Nitro-1-o-tolylethanol 4h

Compound **4h** was prepared according to the general procedure and purified by column chromatography (10.0% EtOAc in petroleum ester) to give a yellow oil (81% yield). IR (film cm^{-1}): 3551, 3024, 2925, 1557, 1490, 1462, 1418, 1379, 1285, 1218, 1069, 900, 769, 678, 616. ^{1}H NMR ($CDCl_3$, δ ppm): 2.40 (s, 3H), 2.69 (br, 1H), 4.44 (dd, 1H, J = 2.5, 13.2 Hz), 4.56 (dd, 1H, J = 9.5, 13.2 Hz), 5.69 (dd, 1H, J = 2.5, 9.5 Hz), 7.24 (m, 3H), 7.51 (m, 1H). ^{13}C NMR: 18.8, 67.9, 80.2, 125.6, 126.7, 128.6, 130.8, 134.6, 136.4. HRMS: calcd for $C_9H_{11}NO_3$: 181.0739, found 181.0751. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (85:15 hexanes–isopropanol, 0.7 mL/min, 215 nm); minor enantiomer t_r = 11.2 min, major enantiomer t_r = 15.8 min; 95% ee; $[\alpha]_D^{25} = +51.2$ (c 1.01, CH_2Cl_2).

5.5.10. (*S*)-1-(4-Methoxyphenyl)-2-nitroethanol 4i

Compound **4i** was prepared according to the general procedure and purified by column chromatography (12.5% EtOAc in petroleum ester) to give a yellow oil (72% yield). IR (film cm^{-1}): 3464, 2934, 1553, 1514, 1462, 1420, 1379, 1304, 1249, 1178, 1076, 1030, 896, 834, 784, 731, 693. ^{1}H NMR ($CDCl_3$, δ ppm): 2.93 (br, 1H), 3.80 (s, 3H), 4.46 (dd, 1H, J = 3.2, 13.1 Hz), 4.58 (dd, 1H, J = 9.5, 13.1 Hz), 5.38 (dd, 1H, J = 3.2, 9.5 Hz), 6.91 (d, 2H, J = 8.6 Hz), 7.31 (d, 2H, J = 8.6 Hz). ^{13}C NMR: 55.4, 70.8, 81.3, 114.5, 129.4, 130.4, 160.1. HRMS: calcd for $C_9H_{11}NO_4$: 197.0688, found 197.0693. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (90:10 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 38.7 min, major enantiomer t_r = 48.9 min, 84% ee; $[\alpha]_D^{25} = +29.0$ (c 2.03, CH_2Cl_2).

5.5.11. (*S*)-1-(2-Methoxyphenyl)-2-nitroethanol 4j

Compound **4j** was prepared according to the general procedure and purified by column chromatography (14.3% EtOAc in petroleum ester) to give a slight yellow oil (83% yield). IR (film cm^{-1}): 3538, 3011, 2944, 1556, 1492, 1347, 1290, 1073, 1026, 910, 859, 735, 616. ^{1}H NMR ($CDCl_3$, δ ppm): 3.13 (d, 1H, J = 5.7 Hz), 3.89 (s, 3H), 4.58 (dd, 1H, J = 8.9, 13.0 Hz), 4.66 (dd, 1H, J = 3.3, 13.0 Hz), 5.63–5.66 (m, 1H), 6.92 (m, 1H), 7.03 (m, 1H), 7.34 (m, 1H), 7.45 (m, 1H). ^{13}C NMR: 55.4, 67.8, 79.9, 110.6, 121.1, 126.1, 127.2, 129.8, 156.1. HRMS: calcd for $C_9H_{11}NO_4$: 197.0688, found 197.0691. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (90:10 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 20.9 min, major enantiomer t_r = 23.9 min; 93% ee; $[\alpha]_D^{25} = +43.6$ (c 1.05, CH_2Cl_2).

5.5.12. (*S*)-1-(1-Naphthyl)-2-nitroethanol 4k

Compound **4k** was prepared according to the General Procedure and purified by column chromatography (16.7% EtOAc in petroleum ester) to give a yellow solid (80% yield). IR (film cm^{-1}): 3558, 3062, 2922, 1552, 1513, 1418, 1378, 1277, 1204, 1097, 911, 802, 780, 738, 650, 622. ^{1}H NMR ($CDCl_3$, δ ppm): 2.92 (br, 1H), 4.66 (m, 2H), 6.26 (m, 1H), 7.55 (m, 3H), 7.76 (m, 1H), 7.87 (m, 2H), 8.02 (m, 1H). ^{13}C NMR: 68.3, 80.8, 121.9, 123.9, 125.5, 126.1, 127.0, 129.3, 129.3, 129.6, 133.68, 133.73. HRMS: calcd for $C_{12}H_{11}NO_3$: 217.0739, found 217.0736. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OD-H column (85:15 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 24.3 min, major enantiomer t_r = 32.7 min; 91% ee; $[\alpha]_D^{25} = +24.1$ (c 1.06, CH_2Cl_2).

5.5.13. (*S*)-1-Nitro-3-phenylpropan-2-ol 4l

Compound **4l** was prepared according to the general procedure and purified by column chromatography (14.3% EtOAc in petroleum ester) to give a colorless oil (71% yield). IR (film cm^{-1}): 3431, 2924, 1554, 1453, 1422, 1383, 1089, 756, 702. ^{1}H NMR ($CDCl_3$, δ ppm): 2.60 (br, 1H), 2.81 (dd, 1H, J = 6.4, 14.0 Hz), 2.89 (dd, 1H, J = 7.4, 14.0 Hz), 4.36 (dd, 1H, J = 7.2, 12.3 Hz), 4.43 (dd, 1H, J = 2.7, 12.3 Hz), 4.53 (dd, 1H, J = 4.8, 8.4 Hz), 7.28 (m, 5H). ^{13}C NMR: 40.5, 69.6, 79.8, 127.4, 128.7, 129.0, 136.0. HRMS: calcd for $C_9H_{11}NO_3$: 181.0739, found 181.0741. Enantiomeric excess was determined by HPLC[12] with a Chiralcel OD–H column (90:10 hexanes–isopropanol, 0.5 mL/min, 215 nm); minor enantiomer t_r = 30.5 min, major enantiomer t_r = 38.6 min; 81% ee; $[\alpha]_D^{25} = -43.4$ (c 2.17, CH_2Cl_2).

5.5.14. (*S*)-4-Methyl-1-nitropentan-2-ol 4m

Compound **4m** was prepared according to the General Procedure and purified by column chromatography (14.3% EtOAc in petroleum ester) to give a colorless oil (76% yield). IR (film cm^{-1}): 3416, 2960, 1557, 1467, 1384, 1296, 1206, 1144, 1089, 1045, 891, 848, 735, 646. ^{1}H NMR ($CDCl_3$, δ ppm): 1.00 (m, 6H),

1.80 (m, 1H), 2.34 (br, 1H), 4.11 (m, 1H), 4.45 (m, 2H). ^{13}C NMR: 21.8, 23.1, 24.3, 42.5, 67.1, 81.1. HRMS: calcd for $C_6H_{13}NO_3$: 147.0895, found 147.0889. Enantiomeric excess was determined by HPLC[5] with a Chiralcel OJ-H column (98:2 hexanes–isopropanol, 0.6 mL/min, 215 nm); minor enantiomer t_r = 35.0 min, major enantiomer t_r = 38.4 min; 85% ee; $[\alpha]_D^{25} = -1.9$ (*c* 2.31, CH_2Cl_2).

5.5.15. (*S*)-1-Nitropentan-2-ol 4n[6b]

Compound **4n** was prepared according to the general procedure and purified by column chromatography (14.3% EtOAc in petroleum ester) to give a colorless oil (70% yield). IR (film cm^{-1}): 3444, 3022, 2964, 2936, 1555, 1464, 1421, 1382, 1285, 1216, 1132, 1085, 1025, 758, 669. ^{1}H NMR ($CDCl_3$, δ ppm): 0.97 (t, 3H, *J* = 6.9 Hz), 1.51 (m, 4H), 2.52 (br, 1H), 4.35 (m, 1H), 4.42 (m, 2H). ^{13}C NMR: 13.8, 18.5, 35.9, 68.6, 80.8. HRMS: calcd for $C_5H_{11}NO_3$: 133.0739, found 133.0735. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (98:2 hexanes–isopropanol, 0.6 mL/min, 215 nm); minor enantiomer t_r = 34.4 min, major enantiomer t_r = 36.3 min; 85% ee; $[\alpha]_D^{25} = -15.8$ (*c* 2.12, CH_2Cl_2).

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13. Bruker SMART CCD diffractometer, structure was solute by direct method, refined on F_2. Crystallographic data for the structure reported in this Letter have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition numbers: CCDC 672046. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EW, UK (Fax: Int code+(1223) 336-033; E-mail: deposit@ccdc.cam.ac.uk).