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Catalytic asymmetric nitroaldol (Henry) reactions with copper(II)/cyclopropane-based bisoxazoline complexes

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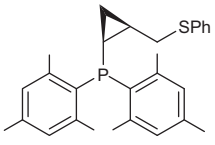
ABSTRACT

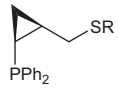
A series of cyclopropane-based bisoxazolines were synthesized from (*R*)- and (*S*)-amino alcohols, and applied to copper-catalyzed enantioselective nitroaldol reactions between nitromethane and various aldehydes. The reactions generated β-hydroxy nitroalkanes in high yields (97%) and with good enantioselectivities (up to 87% ee). The effects of the oxazoline stereocenters constructed in the Henry reactions were also studied.

1. Introduction

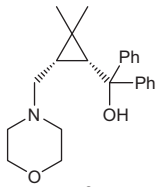
Chiral bisoxazolines have emerged as one of the most attractive ligands for asymmetric catalysis,[1] because they offer an advantageous combination of structural diversity, convenient synthesis, and excellent enantioselectivity for a wide range of reactions. Although a large variety of chiral bisoxazolines have been prepared from malonate,[2] tartrate,[3] ferrocene or cyclohexane,[4] biphenyl or binaphthyl,[5] pyridine[6], and other derivatives, formidable challenges remain in terms of the design and evaluation of novel bisoxazoline ligands. Such challenges increase the requirements for chiral catalysis. Cyclopropane-based ligands can exhibit high enantioselectivity for many catalytic reactions because of their highly variable platform and unusual bond angles; these ligands also offer a well-ordered chiral environment.[7] Apart from our own efforts,[8] however, very few efficient chiral cyclopropane-based ligands **1**–**5** have been reported,[7,8] motivating us to incorporate cyclopropanes into bisoxazoline ligands to explore their potential utility in asymmetric catalytic reactions.



1



2a: R= Et
2b: R= Me



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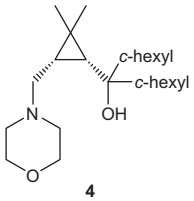

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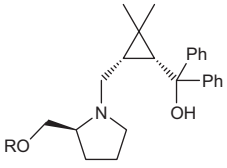

5a: R= TBS
5b: R= TBDPS

The asymmetric nitroaldol (Henry) reaction has become a powerful synthetic tool for the enantioselective construction of carbon–carbon bonds. The resulting β-hydroxy nitroalkanes provide efficient access to valuable bifunctional compounds, such as β-amino alcohols and α-hydroxy carboxylic acids.[9] Given its significance, researchers have developed numerous asymmetric protocols, which involve the use of BINOL,[10] bisoxazolidines,[11] cinchona alkaloids,[12] dinuclear zinc complexes,[13] amino alcohols,[8e,14] diamine,[15] chiral Schiff bases, and tetrahydro-bisisoquinoline ligands.[16] To the best of our knowledge, only a few reports on bisoxazoline catalysts for Henry reactions have been published.[17] We previously reported the application of novel cyclopropane-based bisoxazolines **8a**–**8d** in catalytic enantioselective Diels–Alder additions.[18] To screen the effects of the configuration of the 4-substituent on the oxazoline and to develop novel chiral catalysts without privileged structures in asymmetric Henry reactions, we herein synthesized two new compounds **8e** and **8f**, which were the enantiomers of **8a** and **8d**, respectively, and describe in full detail the synthesis of chiral cyclopropane-based bisoxazolines and their applications as chiral ligands in copper-catalyzed asymmetric Henry reactions.

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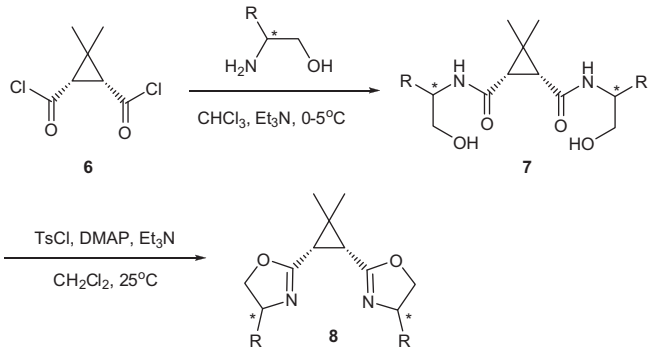
2. Results and discussion

Bisoxazoline ligands **8a**–**8f** were prepared by following the method reported by Evans (Scheme 1).[19] Dicarbonyl chloride **6** was first converted into new dihydroxy cyclopropane diamides **7a**–**7f** with (*R*)- and (*S*)-amino alcohols; subsequent reaction with *p*-toluenesulfonyl chloride and triethylamine in the presence of a catalytic amount of 4-(dimethylamino) pyridine produced **8a**–**8f**.



a: R=*i*-Pr (*S*), **b:** R=*t*-Bu (*S*), **c:** R=Bn (*S*), **d:** R=Ph (*S*), **e:** R=*i*-Pr (*R*), **f:** R=Ph (*R*)

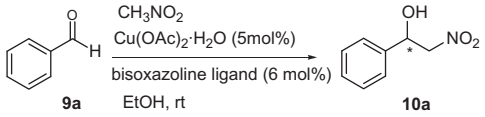
Scheme 1. Synthesis of chiral cyclopropane-based bisoxazoline ligands **8a**–**8f**.

Ligands **8a**–**8f** were evaluated in copper-catalyzed Henry reactions between nitromethane and benzaldehyde **9a** (Table 1).[17a] The results indicated that varying the substitution on the oxazoline ring had considerable effects on the enantioselectivity of the reactions. The bisoxazoline ligands with an *i*-Pr group **8a** presented higher ee values than did **8c** with a Bn group (entry 1 vs entry 3); the more hindered ligands **8b** and **8d** decreased the enantioselectivity greatly (entries 2 and 4). Furthermore, the absolute configuration of the Henry adducts could be controlled by the configuration of the 4-substituent on the oxazoline, **8a** with an (*S*)-*i*-Pr group furnished (*R*)-enantiomers, while **8e** with an (*R*)-*i*-Pr group generated (*S*)-enantiomers. Thus, bisoxazoline ligand **8e** was the ligand of choice, yielding a nitro alcohol product with 64% ee (entry 5).

The Henry reaction of benzaldehyde with nitromethane was tested to determine the optimal conditions for asymmetric catalytic reactions (Table 2). The ee values of product **10a** remained almost unchanged in the three solvents examined (entries 1–3). Although replacing $Cu(OAc)_2{\cdot}H_2O$ with $Cu(OAc)_2$ slightly improved the enantioselectivity (entry 4 vs entry 2), the use of $Cu(OTf)_2$ yielded no product (entry 5). The addition of 4 Å molecular sieves or base promoters, such as pyridine and triethyl-amine, was not beneficial to the enantioselectivity; instead a loss of enantioselectivity was observed (entries 6–8). Further optimization of this process showed that the reaction may be performed with lower catalyst loading (3 mol %; entry 10). The temperature had a significant effect on the ee values; lowering the temperature of the reaction from 25 °C to 0 °C considerably increased the ee values (entry 4 vs entry 11). These experiments demonstrated that the best results can be obtained with 6 mol % of ligand **8e** and 5 mol % of $Cu(OAc)_2$ in isopropanol at 0 °C (entry 11).

With the optimal ligand and conditions identified, we explored the scope of the reactions (Table 3). In general, good to high enantiomeric excesses (69–87% ee) were observed at 0 °C with various aldehydes. Strong electron withdrawing groups, such as NO_2 or F, significantly reduced enantioselectivity (entries 6 and 7). Except for **9f** and **9g**, other *ortho*-, *meta*-, and *para*-substituted benzaldehydes presented consistently good enantiomeric excesses (81–87% ee, entries 2–5 and 8–14). In particular, a noteworthy result

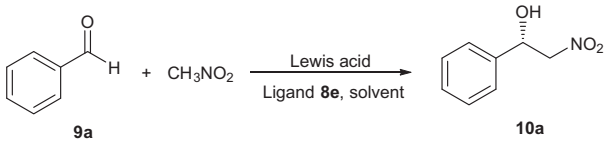
Table 1
Ligand survey of the Henry reactions[a]



Entry	Ligand	Time (h)	Yield[b] (%)	ee[c] (%)	Config[d]
1	(*S*,*S*)-**8a**	72	91	62	(*R*)
2	(*S*,*S*)-**8b**	98	66	6	—
3	(*S*,*S*)-**8c**	72	90	46	(*R*)
4	(*S*,*S*)-**8d**	72	58	4	—
5	(*R*,*R*)-**8e**	48	74	64	(*S*)
6	(*R*,*R*)-**8f**	48	72	4	—

[a] All reactions were performed at room temperature on a 0.5 mmol scale with 6 mol % of ligand and 5 mol % of $Cu(OAc)_2{\cdot}H_2O$.
[b] Values are isolated yields after chromatographic purification.
[c] Enantiomeric excess was determined by HPLC using a Chiracel OD-H column.
[d] The absolute configuration was assigned by comparing their specific rotations with data from the literature.[17a]

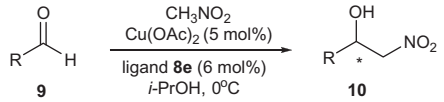
Table 2
Optimization of the reaction conditions between nitromethane and benzaldehyde[a]



Entry	Lewis acid	Catalyst (mol %)	Temp (°C)	Solvent	Additive	Yield[b] (%)	ee[c] (%)
1	$Cu(OAc)_2{\cdot}H_2O$	5	25	EtOH	—	74	64
2	$Cu(OAc)_2{\cdot}H_2O$	5	25	*i*-PrOH	—	74	66
3	$Cu(OAc)_2{\cdot}H_2O$	5	25	MeOH	—	70	62
4	$Cu(OAc)_2$	5	25	*i*-PrOH	—	75	72
5	$Cu(OTf)_2$	5	25	*i*-PrOH	—	0	—
6	$Cu(OAc)_2$	5	25	*i*-PrOH	MS	72	69
7	$Cu(OAc)_2$	5	25	*i*-PrOH	Et_3N	82	55
8	$Cu(OAc)_2$	5	25	*i*-PrOH	Pyridine	80	57
9	$Cu(OAc)_2$	10	25	*i*-PrOH	—	72	68
10	$Cu(OAc)_2$	3	25	*i*-PrOH	—	70	71
11	$Cu(OAc)_2$	5	0	*i*-PrOH	—	70	85
12	$Cu(OAc)_2{\cdot}H_2O$	5	0	EtOH	—	50	82

[a] All reactions were performed on a 0.5 mmol scale in aldehyde.

Table 3
Henry reactions of nitromethane with various aldehydes[a]



Entry	R	Product	Yield[b] (%)	ee[c] (%)
1	Ph	**10a**	70	85
2	3-ClC_6H_4	**10b**	95	81
3	4-ClC_6H_4	**10c**	96	82
4	3-BrC_6H_4	**10d**	80	81
5	4-BrC_6H_4	**10e**	88	81
6	2-FC_6H_4	**10f**	84	73
7	4-$NO_2C_6H_4$	**10g**	91	68
8	2-$CH_3OC_6H_4$	**10h**	96	82
9	3-$CH_3OC_6H_4$	**10i**	95	81
10	4-$CH_3OC_6H_4$	**10j**	63	86
11	2-$CH_3C_6H_4$	**10k**	93	83
12	3-$CH_3C_6H_4$	**10l**	65	86
13	4-$CH_3C_6H_4$	**10m**	97	83
14	4-$EtOC_6H_4$	**10n**	70	87
15	2,4-$(MeO)_2C_6H_3$	**10o**	90	79
16	3,5-$(MeO)_2C_6H_3$	**10p**	96	83
17	2,6-$(MeO)_2C_6H_3$	**10q**	97	84
18	2-Naphthyl	**10r**	96	73
19	*n*-C_7H_{15}	**10s**	60	69
20	PhCH=CH	**10t**	75	77
21	Cyclohexyl	**10u**	65	74

[a] All reactions were performed at 0 °C on a 0.5 mmol scale with 6 mol % of ligand and 5 mol % of $Cu(OAc)_2$ in isopropanol.
[b] Values are isolated yields after chromatographic purification.
[c] Enantiomeric excess was determined by HPLC using Chiracel OD-H, Chiralpak AS-H or AD-H columns. The absolute configuration was assigned by comparing their specific rotations or the HPLC elution order with data from the literature.

(87% ee) was obtained with 4-ethoxybenzaldehyde. Even for the two substituted benzaldehydes, **9o**–**9q**, good enantioselectivities were achieved (entries 15–17). The other aromatic aldehydes, such as 2-naphthaldehyde and cinnamaldehyde, also showed good ee values (entries 18 and 20). The substrate scope was not limited to aromatic aldehydes; aliphatic aldehydes **9s** and **9u** were effective substrates, generating nitroaldol products with 69% ee and 74% ee, respectively (entries 19 and 21).

3. Conclusion

A series of cyclopropane-based chiral bisoxazolines **8a**–**8f** have been conveniently prepared from (*R*)- and (*S*)-amino alcohols. Using the ligands without any additives, the Henry reactions gave the corresponding β-nitro alcohols in good to high enantioselectivities (up to 87% ee) from various aldehydes; even with low catalyst loading (3 mol %), good enantioselectivities were obtained. In particular, the two enantiomers of β-nitro alcohols could be obtained; bisoxazoline **8a** with an (*S*)-*i*-Pr group furnished the (*R*)-enantiomers; while **8e** with an (*R*)-*i*-Pr group generated the (*S*)-enantiomers. The application of these bisoxazolines in other asymmetric catalytic reactions is currently under investigation.

4. Experimental

4.1. General

All reactions were performed under an argon atmosphere. Solvents were dried according to standard procedures and distilled before use. All reagents were purchased commercially and used without further purification, unless stated otherwise. *cis*-3,3-Dimethylcyclopropane dicarbonyl chloride **6** was prepared following the methods in the literature.[20a,b] Melting points were recorded using a Cole-Parmer Melt-Temp apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Low- and high-resolution mass spectra were obtained with an ESI mass spectrometer or an Agilent instrument using the TOF MS technique. Optical rotations were measured on a Perkin–Elmer PE-341 polarimeter. Enantiomeric excesses (ee) were determined by chiral HPLC analyses using chiral columns (Chiralcel OD-H, Chiralpak AS-H or AD-H), and elution with isopropanol–hexanes.

4.2. General procedure for the preparation of dihydroxy cyclopropane diamides 7[19]

To a cold (0 °C) solution of amino alcohol (22.5 mmol) and Et_3N (10 mL, 72 mmol) in $CHCl_3$ (60 mL), a solution of dimethyl cyclopropane dicarbonyl chloride (1.8 g, 9 mmol) was slowly added in $CHCl_3$ (30 mL). The reaction mixture was allowed to warm to room temperature and was stirred for 24 h. The mixture was then washed with saturated brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (MeOH/EtOAc) to produce solid white powder **7**.

4.2.1. (1*R*,2*S*)-*N*,*N*′-Bis[(1*S*)-1-hydroxymethyl-2-methyl-propyl]-3,3-dimethyl-1,2-cyclopropanediamide 7a

White solid powder. Yield: 62%. Mp: 121–122 °C. $[\alpha]_D^{20} = -30.0$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, DMSO) δ: 8.62 (d, *J* = 8.7 Hz, 1H), 8.33 (d, *J* = 9.0 Hz, 1H), 4.56 (t, *J* = 5.4 Hz, 1H), 4.51 (t, *J* = 5.7 Hz, 1H), 3.67–3.58 (m, 2H), 3.38–3.29 (m, 4H), 1.88–1.77 (m, 2H), 1.74 (s, 2H), 1.21 (s, 3H), 1.17 (s, 3H), 0.85–0.80 (m, 12H); ^{13}C NMR (75 MHz, DMSO) δ: 169.8, 169.7, 61.5, 56.0, 55.91, 55.90, 34.83, 34.78, 28.7, 28.0, 27.9, 24.2, 19.85, 19.79, 17.8, 17.7, 15.7. EI MS (70 eV) *m*/*z*: 328 $[M]^+$, 298, 226, 140, 69, 41. HRMS: Calcd for $C_{17}H_{32}N_2O_4$ $[M]^+$ 328.2362. Found: 328.2366.

4.2.2. (1*R*,2*S*)-*N*,*N*′-Bis[(1*S*)-1-hydroxymethyl-2,2-dimethylpropyl]-3,3-dimethyl-1,2-cyclopropane-diamide 7b

White solid powder. Yield: 66%. Mp: 190–192 °C. $[\alpha]_D^{20} = -29.6$ (*c* 2.0, $CHCl_3$). ^1H NMR (300 MHz, DMSO) δ: 8.65 (d, *J* = 9.0 Hz, 1H), 8.27 (d, *J* = 9.6 Hz, 1H), 4.40 (t, *J* = 5.7 Hz, 1H), 4.34 (t, *J* = 5.1 Hz, 1H), 3.68–3.52 (m, 4H), 3.34–3.23 (m, 2H), 1.78 (s, 2H), 1.23 (s, 3H), 1.20 (s, 3H), 0.86 (s, 9H), 0.84 (s, 9H). ^{13}C NMR (75 MHz, DMSO) δ: 169.97, 169.95, 61.04, 61.02, 59.11, 59.07, 34.9, 33.7, 33.4, 28.8, 27.1, 27.0, 24.4, 16.1. EI MS (70 eV) *m*/*z*: 356 $[M]^+$, 326, 299, 240, 140, 57, 43. Anal. Calcd $C_{19}H_{36}N_2O_4$: C, 64.01; H, 10.18; N, 7.86. Found: C, 63.80; H, 10.03; N, 7.67.

4.2.3. (1*R*,2*S*)-*N*,*N*′-Bis[(1*S*)-2-hydroxy-1-phenyl-methylethyl]-3,3-dimethyl-1,2-cyclopropanediamide 7c

White solid powder. Yield: 67%. Mp 142–143 °C. $[\alpha]_D^{20} = -39.2$ (*c* 2.0, $CHCl_3$). ^1H NMR (300 MHz, DMSO) δ: 8.75 (d, *J* = 8.1 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.26–7.13 (m, 10H), 4.76 (t, *J* = 5.7 Hz, 1H), 4.73 (t, *J* = 4.2 Hz, 1H), 3.97–3.89 (m, 2H), 3.40–3.24 (m, 4H), 2.89–2.80(m, 2H), 2.65–2.50 (m, 2H), 1.60 (d, *J* = 3.0 Hz, 2H), 1.12 (s, 3H), 0.84 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ: 169.4, 169.3, 139.31, 139.27, 129.2, 128.2, 128.1, 126.00, 125.97, 63.0, 62.6, 53.1, 52.7, 36.8, 36.7, 34.6, 34.3, 28.5, 24.3, 15.1. EI MS (70 eV) *m*/*z*: 424 $[M]^+$, 394, 274, 140, 91, 60, 41. Anal. Calcd $C_{25}H_{32}N_2O_4$: C, 70.73; H, 7.60; N, 6.60. Found: C, 70.66; H, 7.52; N, 6.53.

4.2.4. (1*R*,2*S*)-*N*,*N*′-Bis[(1*S*)-2-hydroxy-1-phenylethyl]-3,3-dimethyl-1,2-cyclopropanediamide 7d

White solid powder. Yield: 46%. Mp 135–137 °C. $[\alpha]_D^{20} = +64.8$ (*c* 2.0, $CHCl_3$). ^1H NMR (300 MHz, DMSO) δ: 9.11 (d, *J* = 8.1 Hz, 1H), 9.01 (d, *J* = 8.4 Hz, 1H), 7.32–7.18 (m, 10H), 4.92–4.78 (m, 4H), 3.57–3.47 (m, 4H), 1.82 (s, 2H), 1.23 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ: 169.5, 169.3, 141.21, 141.17, 128.14, 128.12, 127.1, 127.0, 126.8, 65.0, 64.9, 55.4, 55.2, 34.7, 34.3, 28.7,

24.7, 15.6. EI MS (70 eV) *m*/*z*: 366 [M-2CH$_3$]$^+$, 347, 260, 243, 229, 140, 106, 96, 41. Anal. Calcd $C_{23}H_{28}N_2O_4$: C, 69.67; H, 7.12; N, 7.07. Found: C, 69.62; H, 7.07; N, 7.04.

4.2.5. (1*R*,2*S*)-*N*,*N*′-Bis[(1*R*)-1-hydroxymethyl-2-methylpropyl]-3,3-dimethyl-1,2-cyclopropanediamide 7e

White solid powder. Yield: 64%. Mp 121–122 °C. $[\alpha]_D^{25} = +35.0$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO) δ: 8.64 (d, *J* = 8.7 Hz, 1H), 8.32 (d, *J* = 9.0 Hz, 1H), 4.56 (t, *J* = 5.4 Hz, 1H), 4.50 (t, *J* = 5.7 Hz, 1H), 3.67–3.58 (m, 2H), 3.39–3.27 (m, 4H), 1.99–1.77 (m, 2H), 1.74 (s, 2H), 1.21 (s, 3H), 1.17 (s, 3H), 0.85–0.73 (m, 12H). ^{13}C NMR (75 MHz, DMSO) δ: 170.62, 170.56, 61.9, 56.4, 35.21, 35.16, 28.9, 28.44, 28.40, 24.9, 20.18, 20.15, 18.18, 18.14, 16.1. MS *m*/*z*: 329 [M+H]$^+$, 311, 226, 208, 152, 140, 132. HRMS: Calcd for $C_{17}H_{33}N_2O_4$ [M+H]$^+$ 329.2440. Found: 329.2435.

4.2.6. (1*R*,2*S*)-*N*,*N*′-Bis[(1*R*)-2-hydroxy-1-phenylethyl]-3,3-dimethyl-1,2-cyclopropanediamide 7f

White solid powder. Yield: 45%. Mp 137–138 °C. $[\alpha]_D^{25} = -77.5$ (*c* 2.0, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO) δ: 9.13 (d, *J* = 8.1 Hz, 1H), 9.03 (d, *J* = 8.1 Hz, 1H), 7.27–7.21 (m, 10H), 4.89–4.82 (m, 2H), 3.63–3.47 (m, 6H), 1.81 (s, 2H), 1.18 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ: 169.6, 169.4, 141.2, 141.1, 128.2, 128.1, 127.1, 127.0, 126.8, 65.0, 64.8, 55.4, 55.3, 34.7, 34.3, 28.6, 24.8, 15.6. HRMS: Calcd for $C_{23}H_{29}N_2O_4$ [M+H]$^+$ 397.2127. Found: 397.2124.

4.3. General procedure for the preparation of cyclopropane-based bisoxazoline ligands 8[19]

To a solution of dihydroxy diamide **7** (9.0 mmol), Et_3N (5.52 mL, 39.6 mmol) and a catalytic amount of 4-(dimethylamino)pyridine (0.121 g, 0.99 mmol) in CH_2Cl_2 (72 mL), a solution of *p*-toluenesulfonyl chloride (3.433 g, 18 mmol) in CH_2Cl_2 (42 mL) was added slowly. The reaction mixture was then stirred at room temperature for 27 h. The mixture was then diluted with CH_2Cl_2 (200 mL), and washed with saturated aqueous NH_4Cl, Na_2CO_3 and brine successively. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a pale yellow viscous oil. The residue was purified by neutral Al_2O_3 column chromatography (pet ether/EtOAc) to afford **8** as colorless oil or white solid.

4.3.1. (1*R*,2*S*)-1,2-Bis[4(*S*)-isopropyloxazolin-2-yl]-3,3-dimethylcyclopropane 8a

Colorless oil. Yield: 82%. $[\alpha]_D^{20} = -131.3$ (*c* 1.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.23–4.10 (m, 2H), 3.88–3.79 (m, 4H), 1.80 (d, *J* = 3.6 Hz, 2H), 1.76–1.65 (m, 2H), 1.42 (s, 3H), 1.23 (s, 3H), 0.97 (t, *J* = 7.2 Hz, 6H), 0.87 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.7, 163.2, 72.5, 72.2, 69.5, 69.4, 32.7, 32.5, 28.3, 26.6, 26.4, 24.4, 19.1, 19.0, 18.5, 18.1, 16.7. EI MS (70 eV) *m*/*z*: 292[M]$^+$, 277, 249, 163, 136, 69, 41. HRMS: Calcd for $C_{17}H_{28}N_2O_2$ [M]$^+$ 292.2151. Found: 292.2149.

4.3.2. (1*R*,2*S*)-1,2-Bis[4(*S*)-*tert*-butyloxazolin-2-yl]-3,3-dimethylcyclopropane 8b

White solid. Yield: 52%. Mp 42–43 °C, $[\alpha]_D^{20} = -135.8$ (*c* 2.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.15–4.04 (m, 2H), 3.92–3.75 (m, 4H), 1.82 (d, *J* = 4.8 Hz, 2H), 1.43 (s, 3H), 1.23 (s, 3H), 0.90 (s, 9H), 0.87 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.9, 163.2, 76.2, 75.7, 68.0, 67.9, 33.5, 28.5, 27.1, 26.4, 26.1, 25.9, 24.6, 16.8. EI MS (70 eV), *m*/*z*: 320 [M]$^+$, 305, 279, 263, 205, 163, 136, 123, 57, 41. HRMS: Calcd for $C_{19}H_{32}N_2O_2$ [M]$^+$ 320.2464. Found: 320.2462.

4.3.3. (1*R*,2*S*)-1,2-Bis[4(*S*)-benzyloxazolin-2-yl]-3,3-dimethylcyclopropane 8c

Colorless oil. Yield: 39%. $[\alpha]_D^{20} = -56.5$ (*c* 0.78, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.30–7.16 (m, 10H), 4.37–4.30 (m, 2H), 4.11–4.05 (m, 2H), 3.88–3.81 (m, 2H), 3.15–2.99 (m, 2H), 2.61–2.53 (m, 2H), 1.81 (d, *J* = 0.9 Hz, 2H), 1.44 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.1, 163.8, 138.4, 138.2, 129.1, 129.0, 128.43, 128.37, 126.32, 126.27, 71.0, 67.6, 67.5, 41.8, 41.6, 28.3, 26.5, 26.4, 24.6, 16.6. EI MS (70 eV), *m*/*z*: 388 [M]$^+$, 297, 163, 91, 67, 41. HRMS: Calcd for $C_{25}H_{28}N_2O_2$ [M]$^+$ 388.2151. Found: 388.2150.

4.3.4. (1*R*,2*S*)-1,2-Bis[4(*S*)-phenyloxazolin-2-yl]-3,3-dimethylcyclopropane 8d

Colorless oil. Yield: 45%. $[\alpha]_D^{20} = -152.3$ (*c* 2.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.34–7.11 (m, 10H), 5.19–5.12 (m, 2H), 4.58–4.48 (m, 2H), 3.99–3.90 (m, 2H), 1.96 (d, *J* = 10.2 Hz, 2H), 1.58 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.0, 164.5, 142.7, 142.6, 128.6, 128.4, 127.3, 127.2, 127.0, 126.7, 74.1, 70.2, 70.0, 28.4, 26.8, 26.3, 25.1, 16.8. EI MS (70 eV), *m*/*z*: 360 [M]$^+$, 345, 276, 242, 120, 104, 91, 43, 29. HRMS: Calcd for $C_{23}H_{24}N_2O_2$ [M]$^+$ 360.1838. Found: 360.1853.

4.3.5. (1*R*,2*S*)-1,2-Bis[4(*R*)-isopropyloxazolin-2-yl]-3,3-dimethylcyclopropane 8e

Colorless oil. Yield: 70%. $[\alpha]_D^{25} = +126.5$ (*c* 2.4, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.20–4.09 (m, 2H), 3.88–3.79 (m, 4H), 1.84–1.65 (m, 4H), 1.42 (s, 3H), 1.23 (s, 3H), 0.96 (t, *J* = 6.96 Hz, 6H), 0.87 (t, *J* = 6.87 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.7, 163.2, 72.6, 72.3, 69.6, 69.4, 32.8, 32.6, 28.4, 26.6, 26.4, 24.5, 19.1, 19.0, 18.5, 18.1, 16.7; EI MS *m*/*z*: 293 [M+H]$^+$, 226, 208, 185, 168, 152, 140. HRMS: Calcd for $C_{17}H_{29}N_2O_2$ [M+H]$^+$ 293.2229. Found: 293.2197.

4.3.6. (1*R*,2*S*)-1,2-Bis[4(*R*)-phenyloxazolin-2-yl]-3,3-dimethylcyclopropane 8f

Colorless oil. Yield: 53%. $[\alpha]_D^{25} = +160.2$ (*c* 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.35–7.12 (m, 10H), 5.19–5.12 (m, 2H), 4.58–4.48 (m, 2H), 3.99–3.90 (m, 2H), 1.96 (d, *J* = 2.1 Hz, 2H), 1.58 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.9, 164.5, 142.6, 142.5, 128.5, 128.3, 127.3, 127.1, 126.9, 126.7, 74.0, 70.1, 69.8, 28.3, 26.7, 26.2, 25.1, 16.8. EI MS *m*/*z*: 360 [M]$^+$, 345, 276, 199, 184, 155, 104, 91, 83, 56. HRMS: Calcd for $C_{23}H_{24}N_2O_2$ [M]$^+$ 360.1838. Found: 360.1842.

4.4. General procedure for the asymmetric Henry reaction[17a]

Ligand **8** (0.03 mmol) was mixed with $Cu(OAc)_2$ (4.54 mg, 0.025 mmol) under an argon atmosphere. Isopropanol (1.0 mL) was then added, and the mixture was stirred for 1 h. To the resulting clear solution, nitromethane (0.3 mL, 5 mmol) and the aldehyde (0.5 mmol) were added via syringe. Stirring was continued at 0 °C until TLC-control indicated the complete consumption of the aldehyde. The reaction mixture was diluted with saturated aqueous NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The volatile components were removed under reduced pressure and the crude products were purified by column chromatography to give the desired products. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H, Chiralpak AD-H, or AS-H column, and the absolute configurations of the nitroaldol products were assigned by comparing their specific rotations or the HPLC elution order with data from the literature.

4.4.1. (*S*)-2-Nitro-1-phenylethanol 10a[17a]

Colorless oil. Yield 70%. $[\alpha]_D^{20} = +47.9$ (*c* 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.41–7.33 (m, 5H), 5.46–5.41 (m, 1H), 4.63–4.46 (m, 2H), 2.93 (d, *J* = 3.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 138.1, 128.8, 128.7, 125.8, 81.0, 70.8. HRMS (TOF): Calcd for $C_8H_9NNaO_3$ [M+Na]$^+$: 190.0480, Found: 190.0476. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column

(80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.3 min, major (*S*)-enantiomer t_R = 10.3 min; 85% ee.

4.4.2. (*R*)-2-Nitro-1-phenylethanol 10a[17a]

Colorless oil. Yield 91%. $[\alpha]_D^{20} = -29.6$ (*c* 1.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.41–7.33 (m, 5H), 5.46–5.41 (m, 1H), 4.63–4.46 (m, 2H), 2.93 (d, *J* = 3.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 138.1, 128.8, 128.7, 125.8, 81.0, 70.8. HRMS (TOF): Calcd for $C_8H_9NNaO_3$ $[M+Na]^+$: 190.0480, Found: 190.0474. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); major (*R*)-enantiomer t_R = 8.7 min, minor (*S*)-enantiomer t_R = 10.5 min; 62% ee.

4.4.3. (*S*)-1-(3-Chlorophenyl)-2-nitroethanol 10b[21a]

Colorless oil. Yield 95%. $[\alpha]_D^{20} = +27.3$ (*c* 1.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.42–7.25 (m, 4H), 5.46–5.41 (m, 1H), 4.61–4.47 (m, 2H), 3.09 (d, *J* = 3.94 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 140.0, 134.7, 130.2, 128.9, 126.1, 124.0, 80.8, 70.1. HRMS (TOF): Calcd for $C_8H_8ClNNaO_3$ $[M+Na]^+$: 224.0090, Found: 224.0089. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.4 min, major (*S*)-enantiomer t_R = 10.3 min; 81% ee.

4.4.4. (*S*)-1-(4-Chlorophenyl)-2-nitroethanol 10c[17a]

Colorless oil. Yield 96%. $[\alpha]_D^{20} = +30.4$ (*c* 0.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.39–7.26 (m, 4H), 5.45–5.40 (m, 1H), 4.60–4.45 (m, 2H), 3.08 (d, *J* = 3.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 136.5, 134.6, 129.0, 127.3, 80.8, 70.2. HRMS (TOF): Calcd for $C_8H_8ClNKO_3$ $[M+K]^+$: 239.9830, Found: 239.9824. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.1 min, major (*S*)-enantiomer t_R = 9.8 min; 82% ee.

4.4.5. (*S*)-1-(3-Bromophenyl)-2-nitroethanol 10d[21b]

Colorless oil. Yield 80%. $[\alpha]_D^{20} = +23.4$ (*c* 1.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.58–7.25 (m, 4H), 5.46–5.41 (m, 1H), 4.61–4.47 (m, 2H), 3.03 (d, *J* = 3.9 Hz, 1H), ^{13}C NMR (75 MHz, $CDCl_3$) δ: 140.3, 131.8, 130.5, 129.0, 124.5, 122.8, 80.8, 70.1. HRMS (TOF): Calcd for $C_8H_8BrNNaO_3$ $[M+Na]^+$: 267.9585, Found: 267.9572. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 9.0 min, major (*S*)-enantiomer t_R = 11.6 min; 81% ee.

4.4.6. (*S*)-1-(4-Bromophenyl)-2-nitroethanol 10e[15a]

White solid. Yield 88%. $[\alpha]_D^{20} = +25.8$ (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.56–7.52 (m, 2H), 7.31–7.26 (m, 2H), 5.46–5.41 (m, 1H), 4.61–4.46 (m, 2H), 2.90 (d, *J* = 3.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 137.0, 132.2, 127.6, 123.0, 80.9, 70.3. HRMS (TOF): Calcd for $C_8H_8BrNKO_3$ $[M+K]^+$: 283.9325, Found: 283.9319. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.9 min, major (*S*)-enantiomer t_R = 11.3 min; 81% ee.

4.4.7. (*S*)-1-(2-Fluorophenyl)-2-nitroethanol 10f[21c]

Colorless oil. Yield 84%. $[\alpha]_D^{20} = +37.6$ (*c* 1.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.56–7.53 (m, 1H), 7.37–7.32 (m, 1H), 7.26–7.19 (m, 1H), 7.11–7.05 (m, 1H), 5.74 (dd, *J* = 8.0, 4.15 Hz, 1H), 4.65–4.54 (m, 2H), 3.07 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.9, 157.7, 130.4, 127.5, 125.0, 115.5, 79.6, 65.4. HRMS (TOF): Calcd for $C_8H_8FNNaO_3$ $[M+Na]^+$: 208.0386, Found: 208.0387. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (95:5 *n*-hexanes/isopropanol, 0.8 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 23.3 min, major (*S*)-enantiomer t_R = 24.6 min; 73% ee.

4.4.8. (*S*)-1-(4-Nitrophenyl)-2-nitroethanol 10g[15a]

White solid. Yield 91%. $[\alpha]_D^{20} = +20.0$ (*c* 1.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.29–8.24 (m, 2H), 7.63 (d, *J* = 8.6 Hz, 2H), 5.62 (dd, *J* = 7.7, 4.6 Hz, 1H), 4.66–4.55 (m, 2H), 3.20 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 148.1, 144.9, 126.9, 124.2, 80.6, 69.9. HRMS (TOF): Calcd for $C_8H_8N_2NaO_5$ $[M+Na]^+$: 235.0331, Found: 235.0322. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 12.8 min, major (*S*)-enantiomer t_R = 15.3 min; 68% ee.

4.4.9. (*S*)-1-(2-Methoxyphenyl)-2-nitroethanol 10h[17a]

Yellow oil. Yield 96%. $[\alpha]_D^{20} = +40.9$ (*c* 1.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.44 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.36–7.30 (m, 1H), 7.04–7.00 (m, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 5.63 (d, *J* = 6.8 Hz, 1H), 4.68–4.53 (m, 2H), 3.88 (s, 3H), 3.14 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.0, 129.8, 127.2, 125.9, 121.1, 110.5, 79.8, 67.8, 55.4. HRMS (TOF): Calcd for $C_9H_{11}NNaO_4$ $[M+Na]^+$: 220.0586, Found: 220.0572. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.0 min, major (*S*)-enantiomer t_R = 9.0 min; 82% ee.

4.4.10. (*S*)-1-(3-Methoxyphenyl)-2-nitroethanol 10i[21a]

Colorless oil. Yield 95%. $[\alpha]_D^{20} = +29.5$ (*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.33–7.26 (m, 1H), 6.96–6.86 (m, 3H), 5.42 (d, *J* = 9.3 Hz, 1H), 4.62–4.46 (m, 2H), 3.81 (s, 3H), 2.97 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.8, 139.8, 129.9, 118.0, 114.2, 111.4, 81.0, 70.7, 55.2. HRMS (TOF): Calcd for $C_9H_{11}NNaO_4$ $[M+Na]^+$: 220.0586, Found: 220.0584. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 13.9 min, major (*S*)-enantiomer t_R = 18.2 min; 81% ee.

4.4.11. (*S*)-1-(4-Methoxyphenyl)-2-nitroethanol 10j[21a]

Colorless oil. Yield 63%. $[\alpha]_D^{20} = +29.4$ (*c* 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.34–7.29 (m, 2H), 6.94–6.90 (m, 2H), 5.40 (dd, *J* = 9.5, 3.2 Hz, 1H), 4.64–4.45 (m, 2H), 3.81 (s, 3H), 2.75 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.0, 130.2, 127.3, 114.4, 81.2, 70.6, 55.3. HRMS (TOF): Calcd for $C_9H_{11}NNaO_4$ $[M+Na]^+$: 220.0586. Found: 220.0577. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 11.2 min, major (*S*)-enantiomer t_R = 13.6 min; 86% ee.

4.4.12. (*S*)-1-(2-Methylphenyl)-2-nitroethanol 10k[17a]

Colorless oil. Yield 93%. $[\alpha]_D^{20} = +41.4$ (*c* 1.3, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.52–7.49 (m, 1H), 7.27–7.17 (m, 3H), 5.69–5.64 (m, 1H), 4.57–4.39 (m, 2H), 2.78–2.77 (m, 1H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 136.2, 134.4, 130.7, 128.5, 126.6, 125.5, 80.1, 67.8, 18.7. HRMS (TOF): Calcd for $C_9H_{11}NNaO_3$ $[M+Na]^+$: 204.0637. Found: 204.0632. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (85:15 *n*-hexanes/isopropanol, 0.8 mL/min, 215 nm); minor (*R*)-enantiomer t_R = 7.7 min, major (*S*)-enantiomer t_R = 11.8 min; 83% ee.

4.4.13. (*S*)-1-(3-Methylphenyl)-2-nitroethanol 10l[15a]

Colorless oil. Yield 65%. $[\alpha]_D^{20} = +36.4$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.31–7.15 (m, 4H), 5.42–5.37 (m, 1H), 4.62–4.45 (m, 2H), 2.89 (d, *J* = 3.8 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 138.7, 138.1, 129.5, 128.8, 126.5, 122.9, 81.1, 70.9, 21.2. HRMS (TOF): Calcd for $C_9H_{11}NNaO_3$ $[M+Na]^+$:

204.0637. Found: 204.0634. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 7.4 min, major (*S*)-enantiomer t_R = 8.4 min; 86% ee.

4.4.14. (*S*)-1-(4-Methylphenyl)-2-nitroethanol 10m[15a]

White solid. Yield 97%. $[\alpha]_D^{20} = +37.4$ (*c* 1.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.29–7.19 (m, 4H), 5.42 (dd, *J* = 9.44, 3.10 Hz, 1H), 4.64–4.45 (m, 2H), 2.77 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 138.9, 135.1, 129.6, 125.8, 81.2, 70.9, 21.1. HRMS (TOF): Calcd for $C_9H_{11}NNaO_3$ $[M+Na]^+$: 204.0637, Found: 204.0635. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 8.8 min, major (*S*)-enantiomer t_R = 10.7 min; 83% ee.

4.4.15. (+)-1-(4-Ethoxyphenyl)-2-nitroethanol 10n

White solid. Yield 70%. $[\alpha]_D^{20} = +32.5$ (*c* 1.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.31–7.26 (m, 2H), 6.93–6.88 (m, 2H), 5.42–5.36 (m, 1H), 4.63–4.44 (m, 2H), 4.03 (q, *J* = 7.0 Hz, 2H), 2.76 (dd, *J* = 3.6, 1.1 Hz, 1H). 1.41 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.2, 130.1, 127.2, 114.8, 81.1, 70.5, 63.5, 14.6. HRMS (TOF): Calcd for $C_{10}H_{13}NNaO_4$ $[M+Na]^+$: 234.0742. Found: 234.0736. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor enantiomer t_R = 8.9 min, major enantiomer, t_R = 10.1 min; 87% ee.

4.4.16. (+)-1-(2,4-Dimethoxyphenyl)-2-nitroethanol 10o

Pale yellow solid. Yield 90%. $[\alpha]_D^{20} = +34.7$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.33–7.26 (m, 1H), 6.53–6.47 (m, 2H), 5.55 (dd, *J* = 7.2, 5.3 Hz, 1H), 4.63–4.53 (m, 2H), 3.85 (s, 3H), 3.81 (s, 3H), 3.07 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.1, 157.1, 128.0, 118.5, 104.6, 98.7, 80.0, 67.6, 55.38, 55.36. HRMS (TOF): Calcd for $C_{10}H_{13}NNaO_5$ $[M+Na]^+$: 250.0691. Found: 250.0694. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor enantiomer t_R = 9.7 min, major enantiomer t_R = 13.3 min; 79% ee.

4.4.17. (*S*)-1-(3,5-Dimethoxyphenyl)-2-nitroethanol 10p[15e]

White solid. Yield 96%. $[\alpha]_D^{20} = +24.4$ (*c* 1.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 6.54 (d, *J* = 2.2 Hz, 2H), 6.43 (t, *J* = 2.2 Hz, 1H), 5.42–5.36 (m, 1H), 4.63–4.47 (m, 2H), 3.80 (s, 6H), 2.84 (d, *J* = 3.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.1, 140.5, 103.8, 100.5, 81.1, 70.9, 55.3. HRMS (TOF): Calcd for $C_{10}H_{13}NNaO_5$ $[M+Na]^+$: 250.0691. Found: 250.0695. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); major (*S*)-enantiomer t_R = 8.0 min, minor (*R*)-enantiomer t_R = 9.6 min; 83% ee.

4.4.18. (−)-1-(2,6-Dimethoxyphenyl)-2-nitroethanol 10q

White solid. Yield 97%. $[\alpha]_D^{20} = -9.2$ (*c* 1.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.26 (dd, *J* = 10.0, 8.4 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 2H), 5.97–5.89 (m, 1H), 4.85 (dd, *J* = 11.9, 10.0 Hz, 1H), 4.46 (dd, *J* = 11.9, 3.6 Hz, 1H), 4.12 (d, *J* = 11.4 Hz, 1H), 3.88 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.8, 130.2, 113.4, 104.2, 79.8, 65.3, 55.8. HRMS (TOF): Calcd for $C_{10}H_{13}NNaO_5$ $[M+Na]^+$: 250.0691. Found: 250.0686. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); major enantiomer t_R = 14.0 min, minor enantiomer t_R = 20.0 min, 84% ee.

4.4.19. (*S*)-1-(2-Naphthyl)-2-nitroethanol 10r[21a]

Pale yellow solid. Yield 96%. $[\alpha]_D^{20} = +32.3$ (*c* 1.3, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.85–7.83 (m, 4H), 7.52–7.40 (m, 3H), 5.57 (d, *J* = 6.9 Hz, 1H), 4.68–4.51 (m, 2H), 3.04 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 135.4, 133.3, 133.1, 128.8, 128.0, 127.7, 126.59, 126.56, 125.2, 123.1, 81.0, 71.0. HRMS (TOF): Calcd for $C_{12}H_{11}NNaO_3$ $[M+Na]^+$: 240.0637, Found: 240.0639. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); minor (*R*)-enantiomer t_R = 23.4 min, major (*S*)-enantiomer t_R = 33.4 min; 73% ee.

4.4.20. (*S*)-1-Nitrononan-2-ol 10s[1d]

Colorless oil. Yield 60%. $[\alpha]_D^{20} = +6.2$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 4.47–4.29 (m, 3H), 2.66 (d, *J* = 4.7 Hz, 1H), 1.57–1.29 (m, 12H), 0.89 (m, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 80.6, 68.7, 33.7, 31.6, 29.2, 29.0, 25.1, 22.5, 13.9. HRMS (TOF): Calcd for $C_9H_{19}NNaO_3$ $[M+Na]^+$: 212.1263. Found: 212.1266. Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (98:2 *n*-hexanes/isopropanol, 1.0 mL/min, 210 nm); major (*S*)-enantiomer t_R = 7.0 min, minor (*R*)-enantiomer t_R = 7. 8 min; 69% ee.

4.4.21. (*S,E*)-1-Nitro-4-phenyl-3-buten-2-ol 10t[21a]

Pale yellow solid. Yield 75%. $[\alpha]_D^{20} = +3.7$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.41–7.26 (m, 5H), 6.79 (dd, *J* = 16.0, 1.2 Hz, 1H), 6.15 (dd, *J* = 15.9, 6.3 Hz, 1H), 5.09–5.03 (m, 1H), 4.56–4.47 (m, 2H), 2.62 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 135.5, 133.7, 128.7, 128.5, 126.7, 124.9, 79.8, 69.6. HRMS (TOF): Calcd for $C_{10}H_{11}NNaO_3$ $[M+Na]^+$: 216.0637, Found: 216.0635. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (80:20 *n*-hexanes/isopropanol, 1.0 mL/min, 230 nm); major (*S*)-enantiomer t_R = 18.6 min, minor (*R*)-enantiomer t_R = 21.3 min; 77% ee.

4.4.22. (*S*)-1-Cyclohexyl-2-nitroethanol 10u[17a]

Colorless oil. Yield 65%. $[\alpha]_D^{20} = +13.7$ (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 4.52–4.38 (m, 2H), 4.13–4.06 (m, 1H), 2.60 (d, *J* = 5.2 Hz, 1H), 1.81–1.77 (m, 3H), 1.71–1.65 (m, 2H), 1.24–1.20 (m, 1H) 1.17–1.07 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 79.3, 72.8, 41.3, 28.5, 27.8, 26.0, 25.8, 25.6. HRMS (TOF): Calcd for $C_8H_{15}NNaO_3$ $[M+Na]^+$: 196.0950, Found: 196.0943. Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 *n*-hexanes/isopropanol, 1.0 mL/min, 210 nm); minor (*R*)-enantiomer t_R = 8.1 min, major (*S*)-enantiomer t_R = 8.9 min; 74% ee.

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