Tetrahedron: *Asymmetry* 20 (2009) 1897–1902

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Efficient alcoholysis of 5,6-dihydro-1,10-phenanthroline-5,6-epoxide with ytterbium(III) triflate and subsequent enantioselective transesterification with lipases

Elke Schoffers *, Lars Kohler

Department of Chemistry, Western Michigan University, 3425 Wood Hall, Kalamazoo, MI 49008-5413, USA

ARTICLE INFO

Article history:
Received 22 June 2009
Accepted 16 July 2009
Available online 19 August 2009

ABSTRACT

New 5,6-dihydro-1,10-phenanthroline derivatives were prepared in high yield via ytterbium(III) triflate-catalyzed alcoholysis of the corresponding epoxide. Enzymatic transesterifications of racemic alkoxy alcohols afforded enantioselective separations with up to 99% ee. The lipase derived from *Burkholderia cepacia* (PSCI) was the most efficient, with *E*-values of up to 200. The steric effect of substituents in the 6-position on reaction time and enantioselectivities was assessed.

1. Introduction

1,10-Phenanthroline derivatives are well known for their chelation properties and have found numerous applications in analytical chemistry.[1] Regrettably, their development for asymmetric catalysis remains slow because of limited access to optically active material.[2,3] Herein we report a new method toward optically active B-ring-functionalized 1,10-phenanthroline derivatives. The first step involves Lewis acid-catalyzed ring opening of epoxide **1** with alcohols. The second step takes advantage of a lipase-mediated enantiodifferentiation.

We previously found that while both magnesium perchlorate and alumina catalyzed the ring opening of 1,10-phenanthroline-5,6-epoxide with nitrogen nucleophiles, the former was more effective.[4] However, neither one of the reagents promoted reactions with oxygen nucleophiles. Only two derivatives have been reported thus far under different conditions.[5,6]

Lanthanide trifluorosulfonates (triflates) have been applied to a range of reactions including aldol, Mannich, and Diels–Alder reactions.[7] Among them, ytterbium(III) triflate catalyzes epoxide conversions.[8–11] In our studies it became the reagent of choice for the formation of several chiral racemic alkoxy alcohol phenanthroline derivatives.

Enzymes have long been employed in organic chemistry and are instrumental in the preparation and separation of single stereoisomers. Their use in organic solvents dates back as far as 1908.[12] However, the prevalent use of aqueous solutions for biotransformations made the use of enzymes less appealing for synthetic chemists in subsequent decades. Meanwhile, enzymatic reactions in organic solvents, polar and non-polar, containing little to no water, have become a mainstay in biotransformations in large part due to the seminal contributions by Klibanov and co-workers.[13–15] The preparation of enantiomerically pure compounds is possible through enzymatic resolution of racemic mixtures or via asymmetrization of meso compounds. Enzymes may display a high degree of substrate specificity and yet accept structurally related, 'unnatural' compounds. Early examples of bulky aromatic and heterocyclic substrates include binaphthol **A** and quinoline **B** derivatives by Kazlauskas[16] and Hughes,[17] respectively (Fig. 1). Imperiali et al. reported the first successful biocatalysis to resolve a bipyridine scaffold **C**.[18] More recent publications describe the resolution

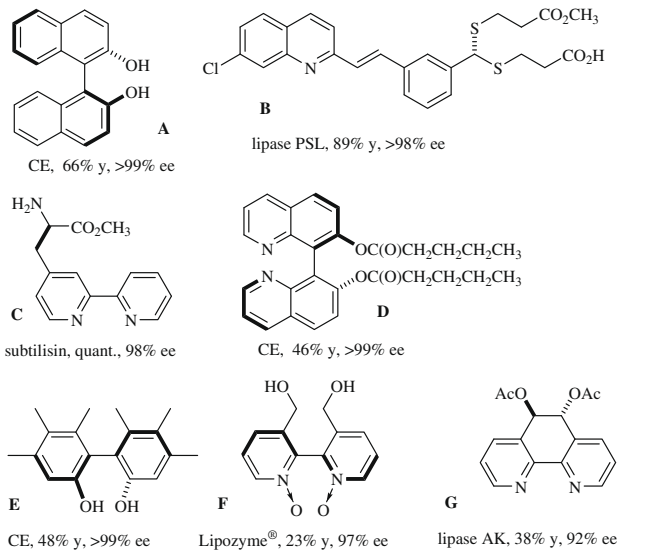


Figure 1. Selected resolution products for various enzymes, including cholesterol esterase (CE).

* Corresponding author. Tel.: +1 269 387 2265; fax: +1 269 387 2909.
E-mail address: Elke.Schoffers@wmich.edu (E. Schoffers).

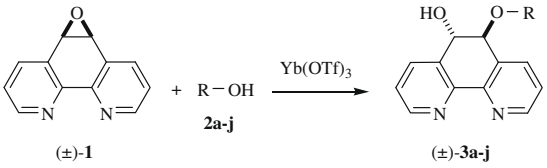
0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.07.021

of 8,8′-biquinoyl derivatives ('azaBINOL', **D**[19] and hexamethylbiphenol **E**[20] with cholesterol esterase (CE) as well as bipyridine *N*,*N*-dioxide **F**[21] and selected 1,10-phenanthroline congeners such as **G** with lipases, respectively.[6,22]

2. Results and discussion

2.1. Preparation of racemic *trans*-5,6-dihydro-1,10-phenanthroline derivatives (±)-3a–j

Epoxide (±)-**1**[5,23–25] was prepared using commercially available bleach and served as a starting material for the practical preparation of *trans*-5,6-dihydro-1,10-phenanthroline derivatives (±)-**3a**–**j**. Ytterbium(III) triflate was employed as a Lewis acid to activate the epoxide toward alcohols **2a**–**j** (Scheme 1).

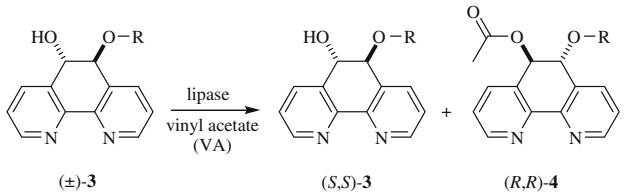


Scheme 1. Epoxide opening of (±)-**1** with alcohols **2a**–**j**.

A complete conversion was already achieved with 0.1 equiv of catalyst but resulted in significant amounts of side products. However, impurities were avoided with an increase of $Yb(OTf)_3$ to 0.5 equiv, giving rise to clean products in very good yields (81–99%). We developed two different procedures depending on the nucleophile used. Method A utilized inexpensive alcohols with low boiling points in large excess which served as nucleophile and solvent (**2a**–**e** and **2g**–**h**). Method B required 1.5 equiv of alcohol in small amounts of acetonitrile as a solvent (see **2i**, **j**). The results are summarized in Table 1 and reveal the generality of this reaction, including primary, secondary, tertiary, and unsaturated alcohols. In contrast, the reaction with phenol was unsuccessful.

2.2. Lipase-catalyzed resolution

Our work focused on two readily available Amano lipases, *Pseudomonas fluorescence* (AK) and *Burkholderia cepacia* (PSCI—PS immobilized on ceramic), to identify the best conditions for our newly-prepared 1,10-phenanthroline alkoxy alcohol derivatives (±)-**3** (Scheme 2).



Scheme 2. Enzymatic kinetic resolution of (±)-**3**.

A recent report has described the kinetic resolution of methoxy alcohol **3a** in a vinyl acetate (VA)/methanol mixture (Table 2, entry 1, $E = 44$). The corresponding acetate **4a** was obtained with 89% ee after 11 days, the remaining alcohol **3a** in 82% ee. The enantiomeric excess of the latter was improved to 97% via a second resolution in 35% yield. Our studies showed that a change in solvent from methanol to acetonitrile (ACN) provided better selectivities affording acetate (*R*,*R*)-**4a** in 96% ee (entry 2, $E = 147$). Prolonged conversion to 50% afforded both, the alcohol and acetate, in 94% ee (entry 3, $E = 115$). We also found that the same substrate could be resolved much faster with a different lipase, Amano PSCI. Alcohol **3a** was obtained in 99% ee after only 4 days (entry 4). The enantiopurity of acetate **4a** was improved from 70% to 82% ee by reducing the conversion rate to 51% after 2 days (entry 5) but the enantiopurity was lower than that with lipase AK (entry 2). We assigned the stereochemistry by comparing our product with the literature report for entry 1 in which the absolute configuration of methoxy alcohol **3a** was determined to have the (*S*,*S*)-configuration based on CD and NMR analyses.[6] The configuration of the remaining derivatives was identified assuming that the enzyme operates with the same stereochemical preference.

Table 1
$Yb(OTf)_3$-catalyzed reaction of (±)-**1** with alcohols **2a**–**j**

Entry	Nucleophile	Method[a]	Product (R=)	Yield (%)
1	Methanol **2a**	A	$-CH_3$, (±)-**3a**	98
2	Ethanol **2b**	A	$-C_2H_5$, (±)-**3b**	99
3	1-Propanol **2c**	A	$-C_3H_7$, (±)-**3c**	91
4	2-Propanol **2d**	A	$-CH(CH_3)_2$, (±)-**3d**	99
5	1-Butanol **2e**	A	$-C_4H_{10}$, (±)-**3e**	95
6	1-Butanol **2e**	B	$-C_4H_{10}$, (±)-**3e**	98
7	2-Butanol **2f**	B	$-CH(CH_3)C_2CH_5$, (±)-**3f**	92[b]
8	*tert*-Butanol **2g**	A	$-C(CH_3)_3$, (±)-**3g**	99
9	Allyl alcohol **2h**	A	$-CH_2-CH{=}CH_2$, (±)-**3h**	99
10	Benzyl alcohol **2i**	B	$-CH_2-C_6H_5$, (±)-**3i**	90
11	Cyclohexanol **2j**	B	$-C_6H_{11}$, (±)-**3j**	81

[a] Method A: Epoxide (0.510 mmol), alcohol (2.5 ml), $Yb(OSO_2CF_3)_3$ (0.5 equiv), 60–80 °C, 12–24 h. Method B: Epoxide (0.510 mmol), nucleophile (1.5 equiv), $Yb(OSO_2CF_3)_3$ (0.5 equiv), CH_3CN, 80 °C, 12–48 h.
[b] No separation of diastereomers.

Our specific rotations confirmed that lipases AK and PSCI preferentially operate on the (*R*,*R*)-isomer. A notable improvement in enantiodifferentiation with either enzyme was observed when the substituent at the 6-position changed from the methyl to the ethyl group (see entries 3/6 and 4/7). Entries 6 and 7 provide a direct comparison of the two lipases for the ethoxy substrate **3b**. Again, resolution with lipase AK was much slower (15 days) than that with PSCI (4 days) whereas *E*-values were over 200 for both resolutions. Based on these encouraging results we predominantly focused on the use of PSCI for the remaining substrates. It should be noted that substrates derived from primary alcohols show high enantioselectivities with *E*-values close to, or over, 200 (entries 6–8, 10, 13, and 14). This includes allyl alcohol adduct **3h**. Therefore, a slight increase in bulkiness from ethyl to *n*-propyl to *n*-butyl had little influence. Transformations with benzyl alcohol derivative **3i** were somewhat slower (6 days) with $E = 152$. Nonetheless, the corresponding products were isolated in very good yield and isomeric purity (entry 14; alcohol **3i** in 45% yield, 90% ee; acetate **4** in 48% yield, 96% ee). We observed that more sterically hindered substrates derived from secondary alcohols (isopropoxy and cyclohexyloxy derivatives **3d** and **3j**) showed an additional drop in *E*-values and required longer conversion times; 11 and 18 days, respectively (entries 9 and 15). Substrate **3g** which contains a very bulky *tert*-butoxy group showed negligible conversion with either enzyme.

3. Conclusion

In conclusion, we have developed a practical new method to convert 1,10-phenanthroline epoxide **1** into several alkoxyalcohol derivatives **3a**–**j** by using ytterbium triflate as catalyst. The racemic products **3** were subjected to lipase-mediated kinetic resolution. Major findings include that the use of acetonitrile (instead of methanol) in vinyl acetate significantly improves the enantiopurity of (*R*,*R*)-**4a** from 89% to 96% ee when lipase AK is employed. Moreover, our results show that lipase PSCI provides faster conversion rates with high enantioselectivities of up to 99% ee for most substrates. A total of 16 new single isomer 1,10-phenanthroline derivatives have been fully characterized.

Table 2
Enzymatic resolution[a] of alkoxy alcohol (±)-**3** with lipases AK and PSCI

Entry	Substrate (R)	Enzyme	Solvent	Time (days)	Temp (°C)	Conversion[b] (%)	% (*S*,*S*)-**3** (% ee_S)[c]	% (*R*,*R*)-**4** (% ee_P)[c]	*E*[b]
1[6]	$-CH_3$, (±)-**3a**	AK	VA/8% MeOH	11	45	48.0	48 (82)	48 (89)	44
2	$-CH_3$, (±)-**3a**	AK	VA/20% ACN	10	45	48.1	46 (89)	47 (96)	147
3	$-CH_3$, (±)-**3a**	AK	VA/20% ACN	10	45	50.0	46 (94)	47 (94)	115
4	$-CH_3$, (±)-**3a**	PSCI	VA/20% ACN	4	50	58.6	40 (99)	54 (70)	28
5	$-CH_3$, (±)-**3a**	PSCI	VA/20% ACN	2	50	51.2	44 (86)	50 (82)	28
6	$-C_2H_5$, (±)-**3b**	AK	VA/10% ACN	15	45	47.6	46 (89)	46 (98)	>200
7	$-C_2H_5$, (±)-**3b**	PSCI	VA/10% ACN	4	50	50.5	43 (99)	49 (97)	>200
8	$-C_3H_7$, (±)-**3c**	PSCI	VA/10% ACN	4	50	49.5	43 (96)	49 (98)	>200
9	$-CH(CH_3)_2$, (±)-**3d**	PSCI	VA/10% ACN	11	50	47.8	43 (86)	47 (94)	90
10	$-C_4H_{10}$, (±)-**3e**	PSCI	VA/10% ACN	4	50	49.5	42 (96)	47 (98)	>200
11	$-C(CH_3)_3$, (±)-**3g**	PSCI	VA/10% ACN	10	50	10.0[d]	N/A	N/A	N/A
12	$-C(CH_3)_3$, (±)-**3g**	AK	VA/10% ACN	10	45	2.0[d]	N/A	N/A	N/A
13	$-CH_2-CH=CH_2$ (±)-**3h**	PSCI	VA/10% ACN	4	50	49.5	44 (96)	47 (98)	>200
14	$-CH_2-C_6H_5$ (±)-**3i**	PSCI	VA/20% ACN	6	50	48.4	45 (90)	48 (96)	152
15	$-C_6H_{11}$, (±)-**3j**	PSCI	VA/10% ACN	18	50	46.8	45 (80)	46 (91)	52

[a] Substrate (±)-**3** (100 mg) was stirred with 500 mg lipase in 25 ml solvent.
[b] Conversion rates and *E*-values were determined from the enantiomeric excess of the substrate (*S*,*S*)-**3** and product (*R*,*R*)-**4**.[26]
[c] Determined via HPLC of isolated products.
[d] Determined via ^{1}H NMR.

4. Experimental

Commercial chemicals and reagents were obtained in >98% purity and used without further purification unless otherwise noted. Lipases were purchased from Aldrich or Amano Pharmaceuticals, Inc. Solvents were purchased as reagent grade for synthetic procedures and as HPLC grade for ee determination. The preparation of 1,10-phenanthroline-5,6-epoxide has been described in the literature.[5,23–25] Melting points were determined in open capillaries using a Thomas–Hoover Unimelt instrument. NMR spectra were recorded using a 400 MHz Jeol Eclipse nuclear magnetic resonance instrument. IR spectra were obtained from Bruker Equinox 55 and Perkin Elmer 1710 Fourier Transform Infrared Spectrometers. Elemental analyses were carried out by Numega Resonance Labs, Inc. in San Diego, CA. For HPLC analysis we used a Shimadzu instrument outfitted with a column (Chiralcel® OD-H), solvent delivery system (LC-20AT), detector (SPD-20A), autosampler (SIL-20A), and degasser (DGU-20A5). We used a Waters Micromass GCT instrument for HRMS measurements.

4.1. Determination of the enantiomeric excess and conversion

Enantiomerically enriched alcohols and acetates were separated using flash column chromatography (SiO_2; $CHCl_3$/MeOH = 99:1) and analyzed by chiral HPLC using a 70:30 mixture of isopropanol and hexane as eluent, 0.5 ml/min flow rate, and UV–vis detection at 266 nm. The enantiomeric excess was obtained by comparing the percentage areas of the (*S*,*S*)-enantiomer and the (*R*,*R*)-enantiomer. Substrate conversion was calculated using the enantiomeric excess of the substrate (ee_S) and the product (ee_P), $c = (ee_S)/(ee_P + ee_S)$.[26]

4.2. General procedure for the preparation of racemic alcohols (±)-3a–j

4.2.1. Method A

1,10-Phenanthroline-5,6-epoxide (100 mg, 0.510 mmol) and ytterbium(III) triflate (158 mg, 0.255 mmol) were dissolved in the appropriate alcohol (2.5 ml of **2a**–**e** or **2g**–**h**, see Table 1). After stirring the reaction mixture at 60–80 °C for 12–24 h the remaining alcohol was evaporated and the residue dissolved in chloroform (40 ml). Aqueous NaOH (10%, 3 ml) was added, the organic layer separated, and the aqueous layer extracted twice with $CHCl_3$ (10 ml). The combined organic layers were washed with brine (10 ml), dried with Na_2SO_4, filtered, and concentrated. The product was isolated by column chromatography (SiO_2; chloroform/1–3% methanol).

4.2.2. Method B

1,10-Phenanthroline-5,6-epoxide (100 mg, 0.510 mmol), ytterbium(III) triflate (158 mg, 0.255 mmol) and the appropriate alcohol (0.765 mmol of **2e**–**f** or **2i**–**j**, see Table 1) were dissolved in dry CH_3CN (0.5 ml). After stirring the reaction mixture at 80 °C for 12–24 h chloroform (40 ml) and aqueous NaOH (10%, 3 ml) were added. The organic layer was separated and the aqueous layer extracted twice with $CHCl_3$ (10 ml). The combined organic layers were washed with brine (10 ml), dried with Na_2SO_4, filtered, and concentrated. The product was isolated by column chromatography (SiO_2; chloroform/1–3% methanol).

4.3. Characterization of racemic alcohols (±)-3a–j

4.3.1. (±)-*trans*-5,6-Dihydro-6-methoxy-1,10-phenanthrolin-5-ol, (±)-3a [(±)-*trans*-5,6-dihydro-5-hydroxy-6-methoxy-1,10-phenanthroline]

Prepared according to Method A using methanol **2a**; 114 mg (98%); mp 196 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73–8.70 (2H, m), 7.99 (1H, app d, J = 7.7 Hz), 7.83 (1H, app d, J = 7.7 Hz), 7.34–7.30 (2H, m), 4.97 (1H, d, J = 9.5 Hz), 4.49 (1H, d, J = 9.5 Hz), 3.67 (3H, s), 3.15 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 150.2, 150.0, 149.7, 134.3, 134.2, 133.5, 131.9, 124.3, 124.0, 82.3, 71.4, 60.0; FT-IR (NaCl) ν/cm^{-1} 3242, 3065, 2991, 2934, 2828, 1583, 1566, 1467, 1429, 1419, 1355, 1217, 1186, 1130, 1086, 1041, 1032, 963, 880, 842, 806, 757, 746, 712, 626. This compound was previously prepared by Shen and Sullivan[5] in 60% yield by reacting epoxide **1** with sodium methoxide in methanol.

4.3.2. (±)-*trans*-5,6-Dihydro-6-ethoxy-1,10-phenanthrolin-5-ol, (±)-3b [(±)-*trans*-5,6-dihydro-6-ethoxy-5-hydroxy-1,10-phenanthroline]

Prepared via Method A using ethanol **2b**; 122 mg (99%); mp 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (2H, m), 8.02 (1H, app d, J = 7.7 Hz), 7.84 (1H, app d, J = 7.7 Hz), 7.36–7.32 (2H, m), 4.95 (1H, d, J = 10.2 Hz), 4.57 (1H, d, J = 10.3 Hz), 3.93–3.87 (2H, m), 2.97 (1H, br s), 1.37 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 150.0, 149.9, 149.8, 133.9, 133.7, 133.6, 132.7, 124.3, 124.0, 80.8, 71.6, 68.1, 15.6; FT-IR (KBr pellet) ν/cm^{-1} 3374, 3056, 2960, 2880, 1582, 1564, 1421, 1294, 1181, 1125, 1083,

1061, 1041, 796, 744. Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.45; H, 5.44; N, 11.76; HRMS (EI, *m/z*) calcd for $C_{14}H_{14}N_2O_2$ 242.1055, found 242.1058.

4.3.3. (±)-*trans*-5,6-Dihydro-6-propoxy-1,10-phenanthrolin-5-ol, (±)-3c (±)-*trans*-5,6-dihydro-5-hydroxy-6-propoxy-1,10-phenanthroline

Prepared according to Method A using 1-propanol **2c**; 119 mg (91%); mp 61 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72–8.69 (2H, m), 8.01 (1H, app d, J = 7.7 Hz), 7.84 (1H, app d, J = 7.7 Hz), 7.34–7.29 (2H, m), 4.96 (1H, d, J = 10.3 Hz), 4.55 (1H, d, J = 10.3 Hz), 3.78 (2H, t, J = 6.8 Hz), 3.25 (1H, br s), 1.74 (2H, app sextet, J = 7.1 Hz), 0.99 (3H, t, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 150.0, 149.9, 149.8, 133.8, 133.7, 133.6, 132.8, 124.2, 124.0, 81.0, 74.5, 71.7, 23.5, 10.7; FT-IR (KBr pellet) ν/cm^{-1} 3298, 3065, 2962, 2935, 2875, 1582, 1565, 1464, 1421, 1349, 1281, 1250, 1212, 1180, 1130, 1084, 1037, 965, 800, 746, 711, 624; HRMS (EI, *m/z*) calcd for $C_{15}H_{16}N_2O_2$ 256.1212, found 256.1222.

4.3.4. (±)-*trans*-5,6-Dihydro-6-isopropoxy-1,10-phenanthrolin-5-ol, (±)-3d [(±)-*trans*-5,6-dihydro-5-hydroxy-6-isopropoxy-1,10-phenanthroline]

Prepared according to Method A using 2-propanol **2d**; 129 mg (99%); mp 211 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75–8.71 (2H, m), 8.04 (1H, app d, J = 7.7 Hz), 7.85 (1H, app d, J = 7.7 Hz), 7.36–7.31 (2H, m), 4.90 (1H, dd, J = 2.9, 10.6 Hz), 4.62 (1H, d, J = 11.0 Hz), 3.99 (2H, septet, J= 6.1 Hz), 2.98 (1H, d, J = 2.9 Hz), 1.35 (6H, d, J = 6.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 149.9, 149.9, 149.8, 133.6, 133.5, 133.4, 124.2, 124.0, 78.7, 73.8, 71.7, 22.8, 22.7; FT-IR (KBr pellet) ν/cm^{-1} 3288, 3065, 2970, 2931, 2871, 1582, 1564, 1465, 1420, 1380, 1332 1212, 1177, 1124, 1080, 1069, 1038, 850, 800; HRMS (EI, *m/z*) calcd for $C_{15}H_{16}N_2O_2$ 256.1212, found 256.1219.

4.3.5. (±)-*trans*-5,6-Dihydro-6-butoxy-1,10-phenanthrolin-5-ol, (±)-3e [(±)-*trans*-5,6-dihydro-6-butoxy-5-hydroxy-1,10-phenanthroline]

The use of 1-butanol **2e** afforded 131 mg (95%) in Method A and 135 mg (98%) via Method B; mp 71 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75–8.72 (2H, m), 8.02 (1H, app dt, J = 1.3, 7.3 Hz), 7.84 (1H, app dt, J = 1.3, 7.7 Hz), 7.36–7.31 (2H, m), 4.96 (1H, d, J = 10.6 Hz), 4.56 (1H, d, J = 10.3 Hz), 3.88–3.79 (2H, m), 2.84 (1H, br s), 1.72 (2H, app quintet, J = 7.2 Hz), 1.46 (2H, app sextet, J = 7.3 Hz), 0.96 (3H, t, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 150.1, 150.0, 149.8, 133.8, 133.6, 132.7, 124.3, 124.0, 81.0, 72.8, 71.7, 32.3. 19.5, 14.0; FT-IR (KBr pellet) ν/cm^{-1} 3289, 3169, 3074, 2952, 2929, 2903, 2869, 1690, 1582, 1565, 1421, 1404, 1377, 1338, 1306, 1129, 1090, 1055, 1037, 791, 741; HRMS (EI, *m/z*) calcd for $C_{16}H_{18}N_2O_2$ 270.1368, found 270.1374.

4.3.6. (±)-*trans*-5,6-Dihydro-6-(2-butoxy)-1,10-phenanthrolin-5-ol, (±)-3f [(±)-*trans*-5,6-dihydro-6-(2-butoxy)-5-hydroxy-1,10-phenanthroline]

Prepared according to Method B using 2-butanol **2f** afforded 127 mg (92%) of a diastereomeric mixture; mp 178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75–8.72 (4H, m), 8.02 (2H, app d, J = 7.7 Hz), 7.87 (2H, app d, J = 7.7 Hz), 7.39–7.30 (4H, m), 4.94 (1H, d, J = 10.6 Hz), 4.90 (1H, d, J = 10.3 Hz), 4.66 (1H, d, J = 10.6 Hz), 4.63 (1H, d, J = 10.6 Hz), 3.82–3.71 (2H, m), 2.88 (2H, br s), 1.87–1.73 (2H, m), 1.67–1.54 (2H, m), 1.31 (3H, d, J = 6.2 Hz), 1.28 (3H, d, J = 6.2 Hz), 1.01 (3H, t, J = 7.5 Hz), 0.96 (3H, t, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 150.4, 149.9, 149.9, 149.8, 133.6, 133.5, 133.4, 133.4, 124.2, 124.0, 123.9, 79.2, 78.8, 78.4, 78.3, 72.2, 71.7, 30.0, 29.7, 20.0, 19.8, 10.2, 10.2; FT-IR (KBr, pellet) ν/cm^{-1} 3227, 3061, 2969, 2928, 1584, 1568, 1430, 1377, 1353, 1283, 1219, 1175, 1131, 1089, 1061, 1032, 905, 879, 845, 821, 762, 710. Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.95; H, 7.11; N, 10.51; HRMS (EI, *m/z*) calcd for $C_{16}H_{18}N_2O_2$ 270.1368, found 270.1373.

4.3.7. (±)-*trans*-5,6-Dihydro-6-*tert*-butoxy-1,10-phenanthrolin-5-ol, (±)-3g [(±)-*trans*-5,6-dihydro-6-*tert*-butoxy-5-hydroxy-1,10-phenanthroline]

Prepared according to Method A using *tert*-butanol (**2g**); 137 mg (99%); mp 219 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77–8.71 (2H, m), 8.04 (1H, app d, J = 7.7 Hz), 7.93 (1H, app d, J = 7.7 Hz), 7.36 (1H, dd, J = 4.8, 7.7 Hz), 7.32 (1H, dd, J = 4.8, 7.7 Hz), 4.80 (1H, d, J = 11.0 Hz), 4.73 (1H, d, J = 11.0 Hz), 2.75 (1H, br s), 1.37 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 150.0, 149.9, 149.6, 134.8, 133.9, 133.8, 133.3, 124.2, 123.6, 76.2, 73.9, 71.4, 28.9; FT-IR (KBr, pellet) ν/cm^{-1} 3207, 3072, 2972, 2929, 2851, 1584, 1564, 1469, 1417, 1392, 1369, 1349, 1287, 1232, 1190, 1126, 1075, 1045, 1022, 987, 906, 869, 807, 748; HRMS (EI, *m/z*) calcd for $C_{16}H_{18}N_2O_2$ 270.1368, found 270.1377.

4.3.8. (±)-*trans*-5,6-Dihydro-6-allyloxy-1,10-phenanthrolin-5-ol, (±)-3h [(±)-*trans*-5,6-dihydro-6-allyloxy-5-hydroxy-1,10-phenanthroline]

Prepared according to Method A using allyl alcohol (**2h**); 128 mg (99%); mp 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70–8.67 (2H, m), 8.01 (1H, app d, J = 7.7 Hz), 7.84 (1H, app d, J = 7.7 Hz), 7.33–7.28 (2H, m), 6.05–5.95 (1H, m), 5.37–5.32 (1H, m), 5.26–5.23 (1H, m), 5.00 (1H, d, J = 9.9 Hz), 4.65 (1H, d, J = 9.9 Hz), 4.36–4.33 (2H, m), 3.31 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 150.0, 149.9, 149.8, 134.2, 134.1, 134.0, 133.7, 132.5, 124.3, 124.0, 118.3, 80.2, 73.2, 71.6; FT-IR (KBr, pellet) ν/cm^{-1} 3160, 2871, 1581, 1563, 1465, 1419, 1354, 1216, 1180, 1134, 1084, 1038, 996, 934, 793, 757, 744, 624; HRMS (EI, *m/z*) calcd for $C_{15}H_{14}N_2O_2$ 254.1055, found 254.1070.

4.3.9. (±)-*trans*-5,6-Dihydro-6-benzyloxy-1,10-phenanthrolin-5-ol, (±)-3i [(±)-*trans*-5,6-dihydro-6-benzyloxy-5-hydroxy-1,10-phenanthroline]

Prepared according to Method B using benzyl alcohol **2i**; 140 mg (90%); mp 110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.75–8.73 (2H, m), 7.99 (1H, app d, J = 7.7 Hz), 7.86 (1H, app d, J = 7.7 Hz), 7.47–7.29 (7H, m), 5.02 (1H, d, J = 9.9 Hz), 4.92 (1H, ABq, J = 11.7 Hz), 4.84 (1H, ABq, J = 11.7 Hz), 4.75 (1H, d, J = 9.5 Hz), 2.92 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 150.2, 150.1, 149.8, 137.6, 134.1, 133.4, 132.2, 128.9, 128.4, 128.0, 124.3, 124.0, 80.5, 74.4, 71.7; FT-IR (KBr, pellet) ν/cm^{-1} 3416, 3054, 3027, 2912, 2857, 2820, 2713, 1581, 1564, 1453, 1421, 1400, 1350, 1293, 1212, 1185, 1125, 1085, 1069, 1039, 1009, 796, 758, 745, 701; HRMS (EI, *m/z*) calcd for $C_{19}H_{16}N_2O_2$ 304.1212, found 304.1214.

4.3.10. (±)-*trans*-5,6-Dihydro-6-cyclohexyloxy-1,10-phenanthrolin-5-ol, (±)-3j [(±)-*trans*-5,6-dihydro-6-cyclohexyloxy-5-hydroxy-1,10-phenanthroline]

Prepared according to the general procedure **B** using cyclohexanol **2j**; 122 mg (81%); mp 213 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76–8.71 (2H, m), 8.04 (1H, app d, J = 7.7 Hz), 7.87 (1H, app d, J = 7.7 Hz), 7.38–7.31 (2H, m), 4.91 (1H, br d, J = 10.3 Hz), 4.68 (1H, d, J = 11.0 Hz), 3.64–3.56 (1H, m), 2.96 (1H, br s), 2.19–1.20 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 149.9, 149.8, 133.6, 133.5, 133.4, 124.2, 124.0, 80.0, 78.7, 71.7, 33.3, 33.2, 25.7, 24.6, 24.5; FT-IR (KBr, pellet) ν/cm^{-1} 3327, 3069, 2926, 2854, 1581, 1564, 1451, 1417, 1382, 1355, 1342, 1285, 1253, 1130, 1084, 1072, 1035, 800, 745; HRMS (EI, *m/z*) calcd for $C_{18}H_{20}N_2O_2$ 296.1525, found 296.1529.

4.4. General procedure for lipase-catalyzed kinetic resolution of racemic alcohols (±)-3

A solution of racemic alcohol (±)-**3** (100 mg) in the appropriate solvent (see Table 2) was placed in a 50 ml round-bottomed flask. Lipase (500 mg) was added and the flask was closed with a glass stopper and sealed with Parafilm®. The suspension was stirred at 45 °C for lipase AK 'Amano' and at 50 °C for lipase PSCI 'Amano'. After approximately 50% substrate conversion (monitored by ^{1}H NMR) the reaction mixture was filtered through Celite, the solvent removed in vacuo, and the residue purified by column chromatography.

4.5. Characterization of enantiomerically enriched alcohols (*S,S*)-3a–e and (*S,S*)-3h–j

4.5.1. (*S,S*)-5,6-Dihydro-6-methoxy-1,10-phenanthrolin-5-ol, (*S,S*)-3a [(*S,S*)-5,6-dihydro-5-hydroxy-6-methoxy-1,10-phenanthroline]

40 mg (40%); ee = 99%; $[\alpha]_D^{25} = +108.4$ (*c* 0.43, methanol), literature:[22] ee = 97%; $[\alpha]_D^{20} = +93.2$ (*c* 0.43, methanol); chiral HPLC analysis: t_R = 13.7 min [(*S,S*)-enantiomer] and t_R = 9.9 min [(*R,R*)-enantiomer].

4.5.2. (*S,S*)-5,6-Dihydro-6-ethoxy-1,10-phenanthrolin-5-ol, (*S,S*)-3b [(*S,S*)-5,6-dihydro-6-ethoxy-5-hydroxy-1,10-phenanthroline]

43 mg (43%); ee = 99%; $[\alpha]_D^{25} = +75.2$ (*c* 1, methanol); chiral HPLC analysis: t_R = 12.1 min [(*S,S*)-enantiomer] and t_R = 9.0 min [(*R,R*)-enantiomer].

4.5.3. (*S,S*)-5,6-Dihydro-6-propoxy-1,10-phenanthrolin-5-ol, (*S,S*)-3c [(*S,S*)-5,6-dihydro-5-hydroxy-6-propoxy-1,10-phenanthroline]

43 mg (43%); ee = 96%; $[\alpha]_D^{25} = +96.9$ (*c* 1, methanol); chiral HPLC analysis: t_R = 12.9 min [(*S,S*)-enantiomer] and t_R = 8.8 min [(*R,R*)-enantiomer].

4.5.4. (*S,S*)-5,6-Dihydro-6-isopropoxy-1,10-phenanthrolin-5-ol, (*S,S*)-3d [(*S,S*)-5,6-dihydro-5-hydroxy-6-isopropoxy-1,10-phenanthroline]

43 mg (43%); ee = 86%; $[\alpha]_D^{25} = +43.4$ (*c* 1, methanol); chiral HPLC analysis: t_R = 11.3 min [(*S,S*)-enantiomer] and t_R = 8.6 min [(*R,R*)-enantiomer].

4.5.5. (*S,S*)-5,6-Dihydro-6-butoxy-1,10-phenanthrolin-5-ol, (*S,S*)-3e [(*S,S*)-5,6-dihydro-6-butoxy-5-hydroxy-1,10-phenanthroline]

42 mg (42%); ee = 96%; $[\alpha]_D^{25} = +100.9$ (*c* 1, methanol); chiral HPLC analysis: t_R = 12.7 min [(*S,S*)-enantiomer] and t_R = 8.7 min [(*R,R*)-enantiomer].

4.5.6. (*S,S*)-5,6-Dihydro-6-allyloxy-1,10-phenanthrolin-5-ol, (*S,S*)-3h ((*S,S*)-5,6-dihydro-6-allyloxy-5-hydroxy-1,10-phenanthroline)

44 mg (44%); ee = 96%; $[\alpha]_D^{25} = +103.3$ (*c* 1, methanol); chiral HPLC analysis: t_R = 12.1 min [(*S,S*)-enantiomer] and t_R = 9.2 min [(*R,R*)-enantiomer].

4.5.7. (*S,S*)-5,6-Dihydro-6-benzyloxy-1,10-phenanthrolin-5-ol, (*S,S*)-3i ((*S,S*)-5,6-dihydro-6-benzyloxy-5-hydroxy-1,10-phenanthroline)

45 mg (45%); ee = 90%; $[\alpha]_D^{25} = +95.9$ (*c* 1, methanol); chiral HPLC analysis: t_R = 14.8 min ((*S,S*)-enantiomer) and t_R = 11.9 min ((*R,R*)-enantiomer).

4.5.8. (*S,S*)-5,6-Dihydro-6-cyclohexyloxy-1,10-phenanthrolin-5-ol, (*S,S*)-3j [(*S,S*)-5,6-dihydro-6-cyclohexyloxy-5-hydroxy-1,10-phenanthroline]

45 mg (45%); ee = 80%; $[\alpha]_D^{25} = +43.9$ (*c* 1, methanol); chiral HPLC analysis: t_R = 12.2 min [(*S,S*)-enantiomer] and t_R = 8.9 min [(*R,R*)-enantiomer].

4.6. Characterization of enantiomerically enriched acetates (*R,R*)-4a–e and (*R,R*)-4h–j

4.6.1. (*R,R*)-5,6-Dihydro-6-methoxy-1,10-phenanthrolin-5-yl acetate, (*R,R*)-4a [(*R,R*)-5,6-dihydro-5-acetoxy-6-methoxy-1,10-phenanthroline]

56 mg (47%), ee = 96%; $[\alpha]_D^{25} = -303.4$ (*c* 0.4, methanol), literature:[22] ee = 98%; $[\alpha]_D^{20} = -163.8$ (*c* 0.4, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (1H, dd, *J* = 1.5, 4.8 Hz), 8.80 (1H, dd, *J* = 1.8, 4.8 Hz), 7.80 (1H, dd, *J* = 1.8, 7.7 Hz), 7.75 (1H, dd, *J* = 1.8, 7.7 Hz), 7.35 (1H, dd, *J* = 4.8, 7.3 Hz), 7.31 (1H, dd, *J* = 4.8, 7.6 Hz), 6.16 (1H, d, *J* = 4.8 Hz), 4.48 (1H, d, *J* = 4.8 Hz), 3.40 (3H, s), 2.00 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 151.1, 151.0, 150.9, 150.6, 137.7, 137.1, 129.8, 129.2, 124.1, 123.8, 78.0, 70.6, 57.7, 21.0; FT-IR (NaCl) ν/cm^{-1} 3065, 2995, 2939, 2831, 1740, 1585, 1569, 1469, 1433, 1374, 1298, 1233, 1132, 1093, 1041, 1026, 930, 821, 761, 748, 716, 627; chiral HPLC analysis: t_R = 11.6 min [(*S,S*)-enantiomer] and t_R = 24.2 min [(*R,R*)-enantiomer].

4.6.2. (*R,R*)-5,6-Dihydro-6-ethoxy-1,10-phenanthrolin-5-yl acetate, (*R,R*)-4b [(*R,R*)-5,6-dihydro-5-acetoxy-6-ethoxy-1,10-phenanthroline]

54 mg (46%), ee = 98%; $[\alpha]_D^{25} = -293.6$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82–8.78 (2H, m), 7.76 (2H, app d, *J* = 7.7 Hz), 7.36–7.30 (2H, m), 6.18 (1H, d, *J* = 5.5 Hz), 4.60 (1H, d, *J* = 5.1 Hz), 3.71–3.56 (2H, m), 2.04 (3H, s), 1.17 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.0, 150.9, 150.8, 137.1, 136.6, 130.7, 129.5, 124.1, 123.9, 76.7, 71.3, 66.0, 21.1, 15.4; FT-IR (NaCl) ν/cm^{-1} 3058, 2977, 2927, 2897, 1740, 1581, 1565, 1429, 1371, 1230, 1126, 1091, 1023, 975, 840, 759; chiral HPLC analysis: t_R = 10.0 min [(*S,S*)-enantiomer] and t_R = 21.9 min [(*R,R*)-enantiomer]. HRMS (EI, *m/z*) calcd for $C_{16}H_{16}N_2O_3$ 284.1161, found 284.1168.

4.6.3. (*R,R*)-5,6-Dihydro-6-propoxy-1,10-phenanthrolin-5-yl acetate, (*R,R*)-4c [(*R,R*)-5,6-dihydro-5-acetoxy-6-propoxy-1,10-phenanthroline]

57 mg (49%), ee = 98%; $[\alpha]_D^{25} = -292.1$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81–8.78 (2H, m), 7.76–7.74 (2H, m), 7.35–7.29 (2H, m), 6.18 (1H, d, *J* = 5.8 Hz), 4.59 (1H, d, *J* = 5.9 Hz), 3.59–3.47 (2H, m), 2.04 (3H, s), 1.61–1.49 (2H, m), 0.85 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.0, 150.8, 150.7, 137.0, 136.5, 130.8, 129.6, 124.0, 123.9, 76.9, 72.4, 71.3, 23.1, 21.1, 10.6; FT-IR (NaCl) ν/cm^{-1} 3056, 2965, 2936, 2877, 1741, 1580, 1565, 1465, 1429, 1371, 1335, 1230, 1129, 1084, 1038, 966, 812, 759, 712; chiral HPLC analysis: t_R = 9.7 min [(*S,S*)-enantiomer] and t_R = 21.0 min [(*R,R*)-enantiomer]. HRMS (EI, *m/z*) calcd for $C_{17}H_{18}N_2O_3$ 298.1317, found 298.1334.

4.6.4. (*R,R*)-5,6-Dihydro-6-isopropoxy-1,10-phenanthrolin-5-yl acetate, (*R,R*)-4d [(*R,R*)-5,6-dihydro-5-acetoxy-6-isopropoxy-1,10-phenanthroline]

55 mg (47%), ee = 94%; $[\alpha]_D^{25} = -185.8$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80–8.76 (2H, m), 7.80 (1H, app d, *J* = 7.7 Hz), 7.69 (1H, app d, *J* = 7.7 Hz), 7.35–7.28 (2H, m), 6.16 (1H, d, *J* = 7.3 Hz), 4.71 (1H, d, *J* = 7.3 Hz), 3.86 (1H, app septet, *J* = 6.1 Hz), 2.11 (3H, s), 1.22 (1H, d, *J* = 6.2 Hz), 1.16 (1H, d,

J = 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 150.8, 150.6, 150.5, 135.9, 135.7, 131.9, 129.9, 124.1, 124.0, 74.8, 72.3, 72.1, 22.6, 22.5, 21.1; FT-IR (NaCl) ν/cm^{-1} 3054, 2933, 2857, 1744, 1579, 1563, 1449, 1428, 1371, 1342, 1229, 1183, 1132, 1074, 1038, 960, 799, 746, 733, 621; chiral HPLC analysis: t_R = 9.7 min [(*S*,*S*)-enantiomer] and t_R = 22.3 min [(*R*,*R*)-enantiomer]. HRMS (EI, *m*/*z*) calcd for $C_{17}H_{18}N_2O_3$ 298.1317, found 298.1324.

4.6.5. (*R*,*R*)-5,6-Dihydro-6-butoxy-1,10-phenanthrolin-5-yl acetate, (*R*,*R*)-4e [(*R*,*R*)-5,6-dihydro-5-acetoxy-6-butoxy-1,10-phenanthroline]

54 mg (47%), ee = 98%; $[\alpha]_D^{25} = -240.5$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84–8.76 (2H, m), 7.79–7.72 (2H, m), 7.36–7.29 (2H, m), 6.17 (1H, d, J = 5.8 Hz), 4.59 (1H, d, J = 5.9 Hz), 3.64–3.51 (2H, m), 2.04 (3H, s), 1.55–1.46 (2H, m), 1.29 (2H, app sextet, J = 7.5 Hz), 0.85 (3H, t, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.0, 150.8, 150.7, 137.0, 136.5, 130.8, 129.6, 124.0, 123.9, 76.9, 71.3, 70.5, 31.9, 21.1, 19.3, 13.9; FT-IR (NaCl) ν/cm^{-1} 3059, 2959, 2933, 2872, 1742, 1580, 1564, 1465, 1428, 1371, 1230, 1127, 1090, 1024, 968, 759, 711; chiral HPLC analysis: t_R = 9.6 min [(*S*,*S*)-enantiomer] and t_R = 19.6 min [(*R*,*R*)-enantiomer]. HRMS (EI, *m*/*z*) calcd for $C_{18}H_{20}N_2O_3$ 312.1474, found 312.1481.

4.6.6. (*R*,*R*)-5,6-Dihydro-6-allyloxy-1,10-phenanthrolin-5-yl acetate, (*R*,*R*)-4h [(*R*,*R*)-5,6-dihydro-5-acetoxy-6-allyloxy-1,10-phenanthroline]

55 mg (47%), ee = 98%; $[\alpha]_D^{25} = -290.8$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84–8.78 (2H, m), 7.80–7.72 (2H, m), 7.37–7.29 (2H, m), 6.17 (1H, d, J = 5.5 Hz), 5.91–5.80 (1H, m), 5.25 (1H, dd, J = 1.5, 17.2 Hz), 5.21 (1H, app d, J = 10.6 Hz), 4.67 (1H, d, J = 5.1 Hz), 4.10 (2H, d, J = 5.5 Hz), 2.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 151.1, 151.0, 150.9, 137.4, 136.8, 134.0, 130.3, 129.4, 124.1, 123.9, 118.2, 75.6, 71.1, 71.0, 21.1; FT-IR (NaCl) ν/cm^{-1} 3061, 2992, 2922, 2866, 1740, 1580, 1565, 1429, 1371, 1335, 1230, 1129, 1074, 1025, 991, 969, 929, 811, 759, 747; chiral HPLC analysis: t_R = 11.4 min [(*S*,*S*)-enantiomer] and t_R = 28.0 min [(*R*,*R*)-enantiomer]. HRMS (EI, *m*/*z*) calcd for $C_{17}H_{16}N_2O_3$ 296.1161, found 296.1155.

4.6.7. (*R*,*R*)-5,6-Dihydro-6-benzyloxy-1,10-phenanthrolin-5-yl acetate, (*R*,*R*)-4i [(*R*,*R*)-5,6-dihydro-5-acetoxy-6-benzyloxy-1,10-phenanthroline]

55 mg (48%), ee = 96%; $[\alpha]_D^{25} = -280.8$ (*c* 1, methanol); mp 148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84–8.79 (2H, m), 7.77 (1H, app dd, J = 1.5, 7.7 Hz), 7.64 (1H, app dd, J = 1.5, 7.7 Hz), 7.38–7.24 (7H, m), 6.21 (1H, d, J = 5.1 Hz), 4.70 (1H, d, J = 5.5 Hz), 4.65 (1H, ABq, J = 12.1 Hz), 4.61 (1H, ABq, J = 12.1 Hz), 1.97 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 151.1, 151.0, 150.9, 137.6, 137.4, 137.1, 130.1, 129.3, 128.7, 128.2, 127.9, 124.1, 123.9, 75.5, 71.9, 70.9, 21.1; FT-IR (NaCl) ν/cm^{-1} 3060, 3032, 2925, 2869, 1740, 1580, 1565, 1454, 1429, 1371, 1229, 1129, 1071, 1027, 968, 810, 758, 745, 700; chiral HPLC analysis: t_R = 15.0 min [(*S*,*S*)-enantiomer] and t_R = 34.0 min [(*R*,*R*)-enantiomer]. HRMS (EI, *m*/*z*) calcd for $C_{21}H_{18}N_2O_3$ 346.1317, found 346.1307.

4.6.8. (*R*,*R*)-5,6-Dihydro-6-cyclohexyloxy-1,10-phenanthrolin-5-yl acetate, (*R*,*R*)-4j [(*R*,*R*)-5,6-dihydro-5-acetoxy-6-cyclohexyloxy-1,10-phenanthroline]

52 mg (46%), ee = 91%; $[\alpha]_D^{25} = -156.5$ (*c* 1, methanol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (2H, app d, J = 4.4 Hz), 7.81 (1H, app d, J = 7.7 Hz), 7.69 (1H, app d, J = 7.7 Hz), 7.35–7.28 (2H, m), 6.17 (1H, d, J = 7.4 Hz), 4.77 (1H, d, J = 7.3 Hz), 3.56–3.48 (1H, m), 2.11 (3H, s), 1.98–1.11 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 150.8, 150.7, 150.5, 150.4, 136.0, 135.8, 132.0, 129.9, 124.1, 124.0, 78.4, 74.6, 72.1, 32.8, 25.6, 24.3, 24.2, 21.1; FT-IR (NaCl) ν/cm^{-1} 3057, 2972, 2929, 1742, 1579, 1563, 1465, 1428, 1372, 1329, 1304, 1230, 1179, 1126, 1069, 1039, 976, 939, 802, 758, 747, 621; chiral HPLC analysis: t_R = 9.7 min ((*S*,*S*)-enantiomer) and t_R = 21.7 min ((*R*,*R*)-enantiomer). HRMS (EI, *m*/*z*) calcd for $C_{20}H_{22}N_2O_3$ 338.1630, found 338.1621.

Acknowledgments

The authors acknowledge support from Western Michigan University (WMU) and thank the National Institutes of Health (1R15GM67670-1) and the US Army (WS911QY-07-1-0003) for external funding. The authors also thank Dr. Andre R. Venter (WMU) and Kalexsyn, Inc. for help with HRMS measurements.

References

1. Thummel, R. P.; Chamchoumis, C. M. In *Advances in Nitrogen Heterocycles*; Moody, C. J., Ed.; JAI Press: Stamford, CT, 2000; pp 107–158.
2. Schoffers, E. *Eur. J. Org. Chem.* **2003**, 1145–1152.
3. Kwong, H.-L.; Yeung, H.-L.; Yeung, C.-T.; Lee, W.-S.; Lee, C.-S.; Wong, W.-L. *Coord. Chem. Rev.* **2007**, *251*, 2188–2222.
4. Schoffers, E.; Tran, S. D.; Mace, K. *Heterocycles* **2003**, *60*, 769–772.
5. Shen, Y.; Sullivan, B. P. *Inorg. Chem.* **1995**, *34*, 6235–6236.
6. Sanfilippo, C.; Nicolosi, G. *Tetrahedron: Asymmetry* **2008**, *19*, 2171–2176.
7. Kobayashi, S. In *Handbook on the Physics and Chemistry of Rare Earths*; Gschneider, K. A. J., Eyring, L., Eds.; Elsevier Science B. V., 2000; pp 315–375.
8. Likhar, P. R.; Kumar, M. P.; Bandyopadhyay, A. K. *Synlett* **2001**, 836-838.
9. Monasson, O.; Ginisty, M.; Bertho, G.; Gravier-Pelletier, C.; Le Merrer, Y. *Tetrahedron Lett.* **2007**, *48*, 8149–8152.
10. Serrano, P.; Llebaria, A.; Delgado, A. *J. Org. Chem.* **2002**, *67*, 7165–7167.
11. Tsuchiya, S.; Sunazuka, T.; Shirahata, T.; Hirose, T.; Kaji, E.; Omura, S. *Heterocycles* **2007**, *72*, 91–94.
12. Jones, B. J.; Desantis, G. *Acc. Chem. Res.* **1999**, *32*, 99–107.
13. Kirchner, G.; Scollar, M. P.; Klibanov, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072–7076.
14. Klibanov, A. M. *Acc. Chem. Res.* **1990**, *23*, 114–120.
15. Fitzpatrick, P.; Klibanov, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 3166–3171.
16. Kazlauskas, R. J. *J. Am. Chem. Soc.* **1989**, *111*, 4953–4959.
17. Hughes, D. L.; Bergan, J. J.; Amato, J. S.; Bhupathy, M.; Leazer, J. L.; McNamara, J. M.; Sidler, D. R.; Reider, P. J.; Grabowski, E. J. J. *J. Org. Chem.* **1990**, *55*, 6252–6259.
18. Imperiali, B.; Prins, T. J.; Fisher, S. L. *J. Org. Chem.* **1993**, *58*, 1613–1616.
19. Blakemore, P. R.; Milicevic, S. D.; Zakharov, L. N. *J. Org. Chem.* **2007**, *72*, 9368–9371.
20. Takemura, T.; Emoto, G.; Satoh, J.; Kobayashi, Y.; Yaginuma, C.; Takahashi, Y.; Utsukihara, T.; Horiuchi, C. A. *J. Mol. Catal. B: Enzym.* **2008**, *55*, 104–109.
21. Sanfilippo, C.; D'Antona, N.; Nicolosi, G. *Tetrahedron: Asymmetry* **2006**, *17*, 12–14.
22. Sanfilippo, C.; Nicolosi, G. *Tetrahedron: Asymmetry* **2007**, *18*, 1828–1832.
23. Antkowiak, R.; Antkowiak, W. Z. *Heterocycles* **1998**, *47*, 893–909.
24. Krishnan, S.; Kuhn, D. J.; Hamilton, G. A. *J. Am. Chem. Soc.* **1977**, *99*, 8121–8123.
25. Moody, C. J.; Rees, C. W.; Thomas, R. *Tetrahedron* **1992**, *48*, 3589–3602.
26. Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294–7299.