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Asymmetric electrochemical oxidation of 1,2-diols, aminoalcohols, and aminoaldehydes in the presence of chiral copper catalyst

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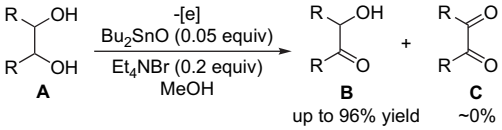
ABSTRACT

Asymmetric oxidation of 1,2-diols, aminoalcohols, and aminoaldehydes in the presence of copper(II) triflate and (*R*,*R*)-Ph-BOX was accomplished by electrochemical method using Br^- as a mediator. This oxidation was applicable to kinetic resolution of *racemic cis*-cycloalkane-1,2-diols, aminoalcohols, and aminoaldehydes to afford optically active compounds with good to high enantioselectivity.

1. Introduction

Selective oxidation of hydroxyl group to carbonyl group is a basic and important organic reaction. It was reported in 1974 that 1,2-diols are selectively oxidized to the corresponding α-ketoalcohols by utilizing a stoichiometric amount of dibutyltinoxide (Bu_2SnO), which forms dibutylstannylenes followed by brominolysis.[1] From the standpoint of green chemistry, we have reported efficient oxidation of 1,2-diols **A** by electrochemical method using a catalytic amount of Bu_2SnO and Br^- ion to afford α-ketoalcohols **B** in high yield without 1,2-diketones **C** (Eq. 1).[2]



(1)

More recently, we reported the first catalytic asymmetric oxidation of 1,2-diols **A′** to afford the corresponding optically active α-ketoalcohols **B′** in high enantioselectivity,[3] which is based on recognition of the diol-moiety by copper(II) ion associated with (*R*,*R*)-Ph-BOX complex[4] to form the activated intermediates **D′** followed by oxidation with NBS (Eq. 2). So far, to the best of our knowledge, catalytic asymmetric oxidation of **A′** to **B′** has not been known except for the two examples using semi-catalytic amount of chiral dioxiranes[5] or chiral hypervalent iodine.[6]

In continuing the study, we succeeded in kinetic resolution of **A′** by electrochemical oxidation. The concept we used in the asymmetric electrochemical oxidation of **A′** to optically active α-ketoalcohols **B′** is schematically represented in Scheme 1. Complex **D′** consisting diols **A′** and chiral copper catalyst Cu–**L*** was easily deprotonated by cathodically generated MeO^- to afford alkoxide anions **E′**, which reacted with anodically generated Br^+ to form *O*-brominated intermediates **F′**. MeO^- removed HBr from **F′** to afford **B′** and regenerate Cu–**L***. Although the mechanism for this oxidation is similar to that of the oxidation with NBS,[3] this electrochemical method is effective for some diols that NBS could not oxidize. In addition, this method is applicable to the asymmetric oxidation of aminoalcohols **G′** and aminoaldehydes **H′** to the corresponding optically active aminoesters.

2. Results and discussion

2.1. Accelerating effect based on recognition of the diol-moiety under the electrochemical oxidation condition

First, we tried electrochemical oxidation of phenylcyclohexane-*cis*-1,2-diol (*cis*-**1**) as a model compound to check for the accelerating effect based on recognition of *cis*-**1** with the Cu(II)–(*R*,*R*)-Ph-BOX complex. The electrochemical oxidation of *cis*-**1** in the presence of $Cu(OTf)_2$ and (*R*,*R*)-Ph-BOX predominantly afforded

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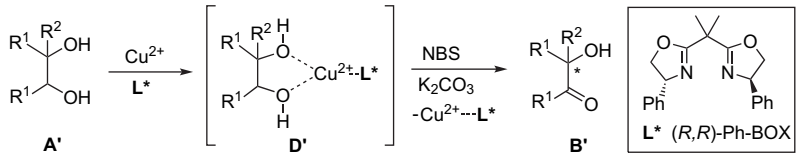
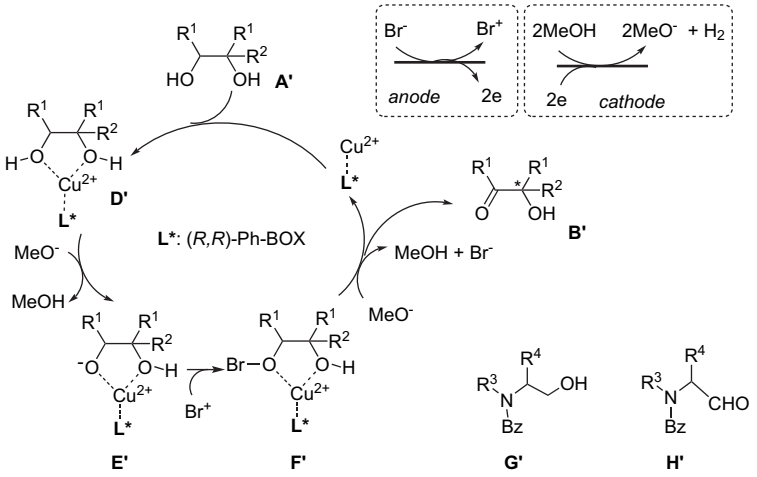
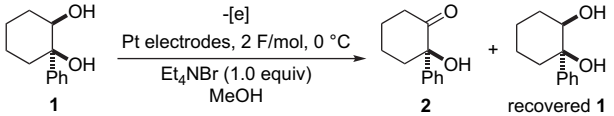


(2)



Scheme 1.

mono-oxidized product **2** (36% yield). However, the oxidation did not proceed in the absence of $Cu(OTf)_2$ and (*R*,*R*)-Ph-BOX (Eq. 3). These results suggest that *cis*-**1** might be recognized by the Cu(II)–(*R*,*R*)-Ph-BOX complex under this oxidation condition.

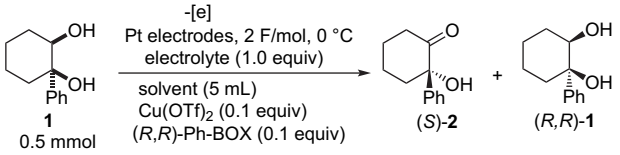


(3)

in the presence of $Cu(OTf)_2$ (0.1 equiv) and (*R*,*R*)-Ph-BOX (0.1 equiv)	36%	58%
in the presence of $Cu(OTf)_2$ (0.1 equiv)	3%	88%
in the absence of $Cu(OTf)_2$ and (*R*,*R*)-Ph-BOX	0%	100%

2.2. Effects of electrolytes and solvents on asymmetric oxidation

Next, we investigated electrolytes and solvents for the electrochemical oxidation that is applicable to kinetic resolution of *cis*-**1** (Eq. 4). The results are summarized in Table 1. A procedure for asymmetric electrochemical oxidation of *cis*-**1** is as follows: anodic oxidation of **1** was carried out using platinum electrodes (2×1 cm^2) in an undivided beaker-type cell containing 0.5 mmol of **1**, 1.0 equiv of electrolyte, 0.1 equiv of $Cu(OTf)_2$, 0.1 equiv of (*R*,*R*)-Ph-BOX, and solvent (5 mL). After passing through 2.0 F/mol of electricity at constant current (50 mA) at 0 °C and usual workup, optically active α-ketoalcohol (*S*)-**2** was obtained in 36% yield with moderate selectivity (*s*) value of 8 (Table 1, entry 1).[6–9] Comparable result was obtained by use of $CuBr_2$ instead of $Cu(OTf)_2$ (entries 1 and 2). Among the solvents tested, methanol was most suitable for this reaction (entries 1, 3, and 4). Although the counter cation of electrolytes had little effect on both yield and selectivity for the electrochemical reaction, Et_4NBr was slightly better than other bromide salts (entries 1 and 5–7). On the other hand, use of either Et_4NCl or Et_4NI did not yield the oxidation product (entries 8 and 9).



(4)

Table 1
Effect of electrolyte and solvent on electrochemical oxidation of **1**

Entry	Electrolyte	Solvent	(*S*)-**2**		(*R*,*R*)-**1**		*s*
			Yield (%)	ee (%)	Yield (%)	ee (%)	
1	Et_4NBr	MeOH	36	67	58	41	8
2[a]	Et_4NBr	MeOH	33	66	62	36	7
3	Et_4NBr	MeCN	Trace	—	91	—	—
4	Et_4NBr	CH_2Cl_2	8	13	79	2	1
5	Me_4NBr	MeOH	28	60	67	28	5
6	*n*-Pr_4NBr	MeOH	26	67	62	33	7
7	*n*-Bu_4NBr	MeOH	31	59	63	41	6
8	Et_4NCl	MeOH	Trace	—	94	—	—
9	Et_4NI	MeOH	0	—	Quant	—	—

[a] $CuBr_2$ (0.1 equiv) was used instead of $Cu(OTf)_2$ (0.1 equiv).

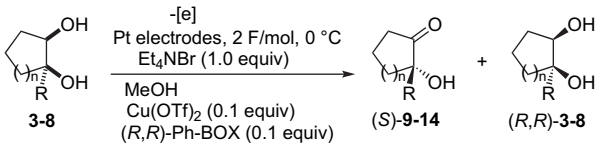
2.3. Asymmetric oxidation of several *cis*-cycloalkane-1,2-diols

Asymmetric electrochemical oxidation of several *cis*-cycloalkane-1,2-diol derivatives **3-8** is summarized in Table 2 (Eq. 5).[10] The *s* values of (*S*)-**9**–**11** varied significantly depending on the ring size (entries 1–3 in Table 2 and entry1 in Table 1). That is, the larger the ring size, the better the *s* value obtained. R substituent also influenced the *s* value (entries 4–6). Compound **8** with a cyclohexyl

Table 2
Electrochemical oxidation of *cis*-cycloalkane-1,2-diols **3**–**8**

Entry	Diol	*n*	R	(*S*)-Ketoalocohol		(*R*,*R*)-Diol		*s*
					Yield (%)	ee (%)	Yield (%)	ee (%)	
1	**3**	1	Ph	**9**	33	38	59	22	3
2	**4**	3	Ph	**10**	57	64	42	85	12
3	**5**	4	Ph	**11**	49	80	48	80	22
4	**6**	2	Bn	**12**	65	5	35	47	2
5	**7**	2	*i*-Pr	**13**	26	75	74	25	9
6	**8**	2	Cyclohexyl	**14**	21	81	76	18	11

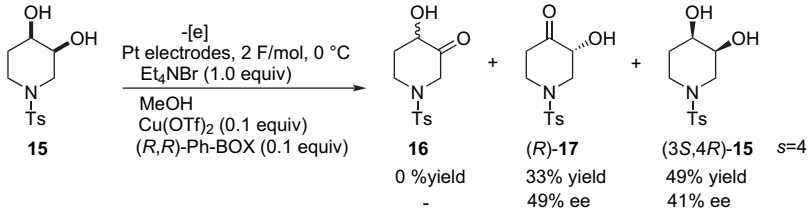
group was asymmetrically oxidized to afford (*S*)-**14** in higher selectivity (*s*=11, entry 6) than (*S*)-**12** with a benzyl group (*s*=2, entry 6) and (*S*)-**13** with an isopropyl group (*s*=9, entry 5).



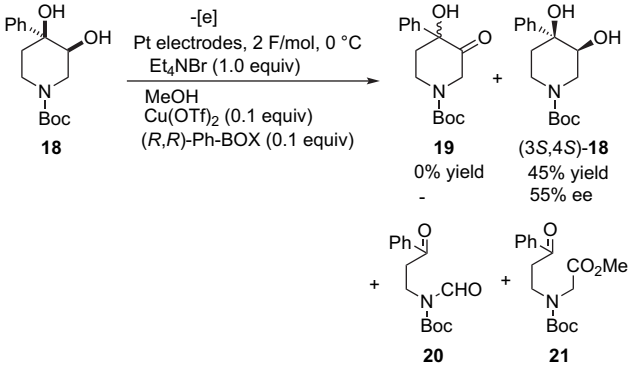
(5)

2.4. Oxidative kinetic resolution of piperidine-3,4-diols

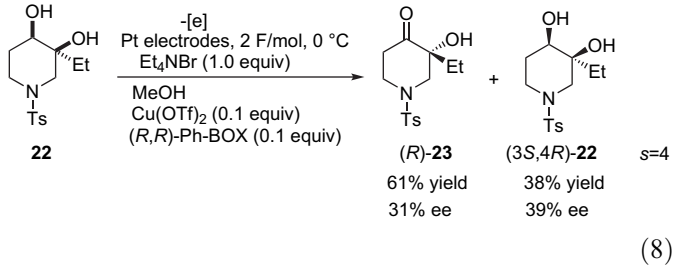
This electrochemical method, interestingly, was applicable to kinetic resolution of some piperidine-3,4-diols **15**, **18**, and **22** (Eqs. 6–8),[11] which were not oxidized with NBS.[3] The electrochemical oxidation of **15** afforded optically active ketoalcohol (*R*)-**17** and (3*S*,4*R*)-**15** in 49% ee and 41% ee, respectively, while **16** was not obtained (Eq. 6). The loss in the total yield (82%) in the reaction of **15** might be explained by the instability of 3-ketopiperidines under the oxidative conditions.[12] In fact, the oxidation of **18** afforded (3*S*,4*S*)-**18** in moderate enantioselectivity along with a small amount of further oxidized products **20** and **21** instead of **19** (Eq. 7). On the other hand, oxidation of **22** gave (*R*)-**23** and (3*S*,4*R*)-**22** with little loss in the total yield (Eq. 8).



(6)



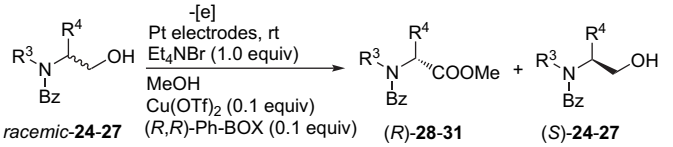
(7)



(8)

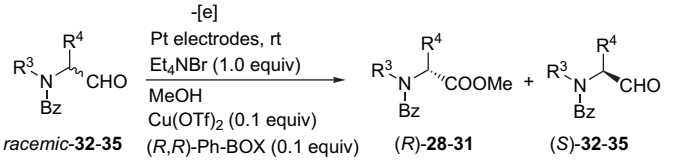
2.5. Oxidative kinetic resolution of *racemic* aminoalcohols and aminoaldehydes

Kinetic resolution of some *racemic* aminoalcohols **24**–**27** by electrochemical oxidation was tested (Eq. 9). The results are summarized in Table 3. In the oxidation of *racemic N*-benzoylpiperidinemethanol (**24**),[13] optically active α-aminoester (*R*)-**28** was obtained with low yield but with good enantioselectivity (6% yield, 71% ee) after passing through 5 F/mol[14] of electricity (entry 1). The oxidation of *racemic N*-benzoylated cyclic and acyclic aminoalcohols **25**–**27** afforded the corresponding (*R*)-aminoesters (*R*)-**29**–**31** (entries 2–4) with low electron efficiencies.



(9)

Since further improvement of the electron efficiency and yield was difficult, we tried oxidative kinetic resolution of *racemic N*-benzoylaminoaldehydes (**32**–**35**) (Eq. 10), which might be intermediates for the oxidation of aminoalcohols to aminoesters. The results are shown in Table 4. The oxidation of **32** proceeded more efficiently than that of aminoalcohol **24** to afford (*R*)-**28** with improved yield and good enantioselectivity after passing through 2.5 F/mol[14] of electricity (entry 1). Also, the oxidation of several aminoaldehydes (**33**–**35**) proceeded to afford (*R*)-**29**–**31** with improved yields and good enantioselectivities (entries 2–4).



(10)

2.6. Oxidation potentials

Oxidation potentials of materials used in these oxidations are given in Table 5. The most oxidizable species was Br^-, while $Cu(OTf)_2$ was hardly oxidizable (entries 1 and 2). Although oxidation potential of (*R*,*R*)-Ph-BOX was moderate, $Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex was stable under the oxidative conditions (entries 3 and 4). Diol *cis*-**1** formed a complex with $Cu(OTf)_2$–(*R*,*R*)-Ph-BOX, which was more oxidizable (entries 5 and 6). Similar tendencies were observed for aminoalcohol **24** and aminoaldehyde **32**(entries 9–12). On the other hand, such negative shifts were not observed in the oxidation potentials of ketoalcohol **2** and aminoester **28** (entries 7, 8, 13, and 14). Among these complexes, *cis*-**1**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX and **32**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complexes had the lowest oxidation potentials (entries 6 and 12).

2.7. Reaction mechanism for the asymmetric electrochemical oxidation of aminoalcohols and aminoaldehydes

On the basis of oxidation potentials described above, mechanisms for asymmetric electrochemical oxidation of aminoalcohols **G**′ and aminoaldehydes **H**′ are presented in Schemes 2 and 3,

Table 3
Electrochemical oxidation of *racemic* aminoalcohols **24**–**27**

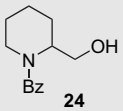
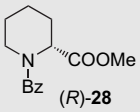
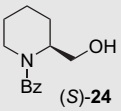
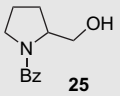
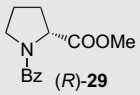
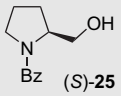
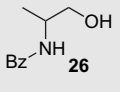
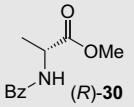
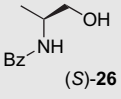
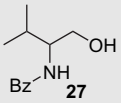
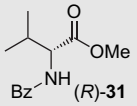
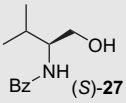
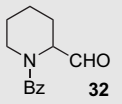
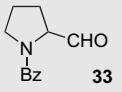
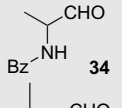
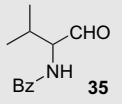
Entry	*racemic* Aminoalcohols	Electricity (F/mol)	Product (*R*)-**28**–**31**	Yield (%) [ee (%)]	Recovered (*S*)-**24**–**27**	Yield (%) [ee (%)]
1	 **24**	5	 (*R*)-**28**	6 [71]	 (*S*)-**24**	85 [2]
2	 **25**	3	 (*R*)-**29**	27 [70]	 (*S*)-**25**	50 [15]
3	 **26**	5	 (*R*)-**30**	27 [59]	 (*S*)-**26**	60 [6]
4	 **27**	10	 (*R*)-**31**	13 [22]	 (*S*)-**27**	88 [0]

Table 4
Electrochemical oxidation of *racemic* aminoaldehydes **32**–**35**

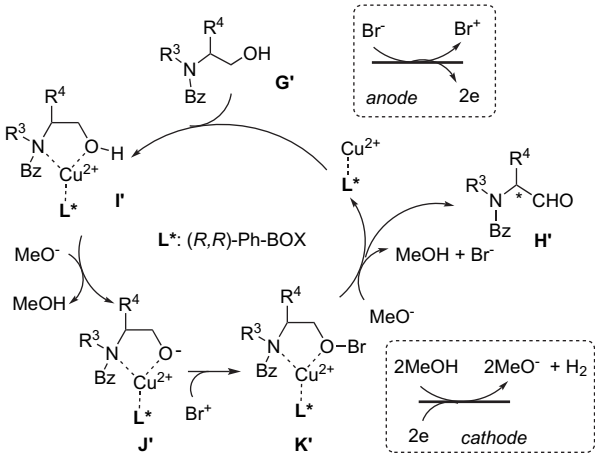
Entry	*racemic* Aminoalcohols	Electricity (F/mol)	(*R*)-Amino-esters	Yield (%) [ee (%)]	(S)-Amino-aldehydes	Yield (%) [ee (%)][a]
1	 **32**	2.5	(*R*)-**28**	19 [87]	(*S*)-**32**	66 [12]
2	 **33**	2	(*R*)-**29**	43 [86]	(*S*)-**33**	34 [27]
3	 **34**	1.5	(*R*)-**30**	50 [61]	(*S*)-**34**	18 [18]
4	 **35**	1.5	(*R*)-**31**	18 [64]	(*S*)-**35**	65 [12]

[a] Determined after transformation of (*S*)-**32**–**35** to (*S*)-**24**–**27**, respectively.

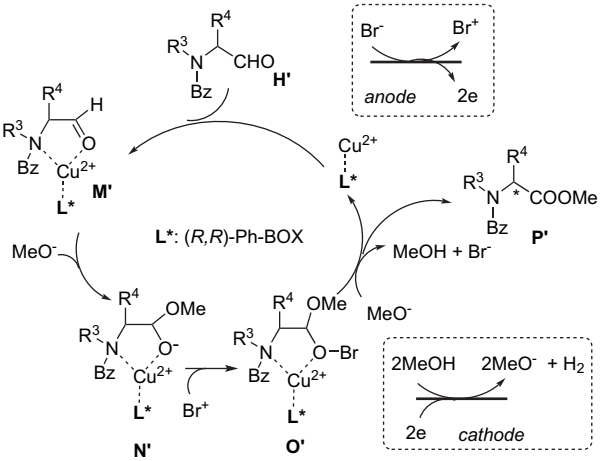
Table 5
Oxidation potentials

Entry	Material	Oxidation potential (V)[a]
1	Et_4NBr	1.15
2	$Cu(OTf)_2$	>3.0
3	(*R*,*R*)-Ph-BOX	2.07
4	$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	>3.0
5	Diol *cis*-**1**	2.10
6	*cis*-**1**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	1.80
7	Ketoalcohol **2**	2.20
8	**2**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	2.35
9	Aminoalcohol **24**	2.20
10	**24**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	2.10
11	Aminoaldehyde **32**	2.10
12	**32**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	1.75
13	Aminoester **28**	2.32
14	**28**–$Cu(OTf)_2$–(*R*,*R*)-Ph-BOX complex	2.65

[a] V versus $Ag/AgNO_3$.



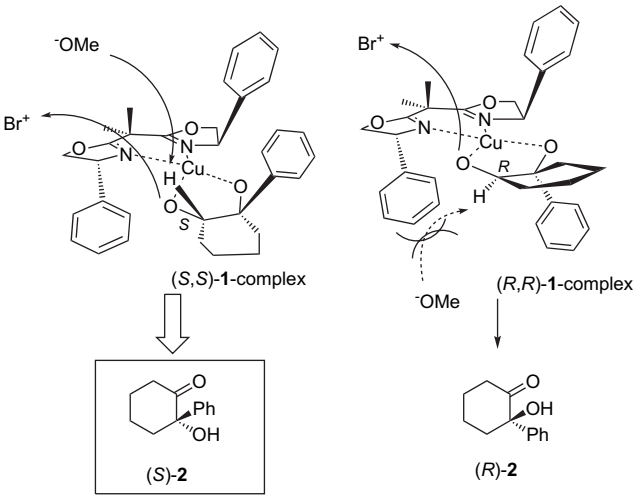
Scheme 2.



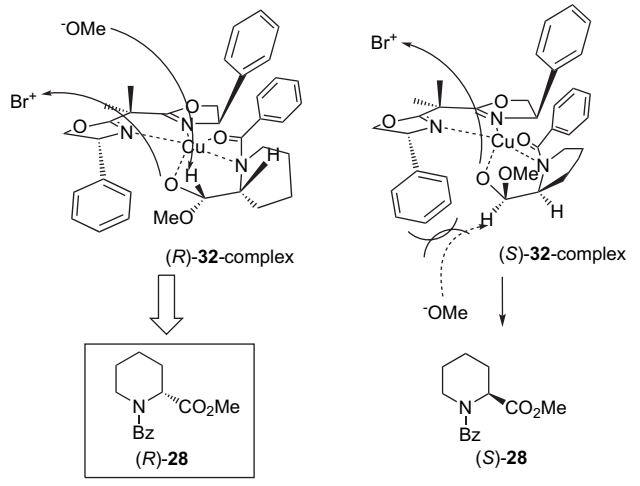
Scheme 3.

respectively. The electrochemical oxidation of **G**′ and **H**′ might proceed in a manner similar to that of diols as shown in Scheme 1. Anodically generated Br^+ and cathodically generated $2MeO^-$ react with complexes **I**′ and/or **M**′ to afford the corresponding optically active esters **P**′.

The stereochemical courses for kinetic resolution of *cis*-**1** and **32** catalyzed by Cu(II)–(*R*,*R*)-Ph-BOX are shown in Schemes 4 and 5. Although the activated intermediates (*R*,*R*)-**1**-complex and (*S*)-**32**-complex might be formed more easily than (*S*,*S*)-**1**-complex and (*R*)-**32**-complex, MeO^- as a base predominantly approaches the less crowded intermediate (*S*,*S*)-**1**-complex and (*R*)-**32**-complex to afford (*S*)-**2** and (*R*)-**28**.



Scheme 4. Plausible stereochemical course for kinetic resolution of *cis*-**1**.



Scheme 5. Plausible stereochemical course for kinetic resolution of *racemic*-**32** in MeOH.

3. Conclusion

In conclusion, this article describes an efficient procedure for the kinetic resolution of *racemic cis*-cycloalkane-1,2-diols, amino-alcohols, and aminoaldehydes in the presence of copper(II) triflate and (*R*,*R*)-Ph-BOX by electrochemical oxidation. Further study to improve the enantioselectivity is underway.

4. Experimental section

4.1. General

Electrochemical reactions were carried out by using DC Power Supply (GP 050-2) of Takasago Seisakusho, Inc. HPLC analyses were achieved by using an LC-10AT *VP* and an SPD-10A *VP* of Shimadzu Seisakusho Inc. Specific rotations were measured with Jasco DIP-1000. ^{1}H and ^{13}C NMR spectra were measured at 300 (or 400) and 75 (or 100) MHz on a Varian Gemini 300 spectrometer (or JEOL JNM-AL 400) with TMS as an internal standard. All melting points were measured on MICRO MELTING POINT APPARATUS (Yanaco) and are uncorrected. IR spectra were obtained on a Shimadzu FTIR-8100A. Mass spectra were obtained on a JEOL JMS-DX 303 instrument.

(*R*,*R*)-Ph-BOX, $Cu(OTf)_2$, Me_4NBr, Et_4NBr, *n*-Pr_4NBr, *n*-Bu_4NBr, Et_4NCl, and Et_4NI were commercially available.

4.2. Measurement of oxidation potentials

BAS CV-50W was used as a voltammetric analyzer. A solution of substrate (0.1 mmol) in MeCN (10 mL) containing 0.1 M Et_4NBF_4 was measured. Reference electrode was $Ag/AgNO_3$ in saturated aqueous KCl, working electrode was a glassy carbon, and counter electrode was a platinum wire. Scan rate was 100 mV/s.

4.3. Preparation of *cis*-cycloalkane-1,2-diols 3–8

OsO_4 (4%, 0.098 mmol) was added to a stirring solution of 1-phenylcyclohexene (32 mmol, 5.0 g) and 50% *N*-methylmorpholine-*N*-oxide (35.4 mmol) in THF/acetone/H_2O (1/1/1, 180 mL) at 0 °C. After stirring for 16 h, satd aqueous $NaHSO_3$ (120 mL) was added to the resulting mixture and the solution stirred for 1 h. The solution was evaporated in vacuo to give the residue, which was then dissolved in AcOEt. The organic portion was extracted with AcOEt and dried over $MgSO_4$. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (hexane/AcOEt=5/1) to afford **1** (93% yield).

4.4. Asymmetric electrochemical oxidation of 1: a typical procedure

Under an aerobic atmosphere, into an undivided electrolysis cell equipped with a platinum anode and cathode (1 cm×2 cm) was added a solution of $Cu(OTf)_2$ (18.1 mg, 0.05 mmol) and (*R*,*R*)-Ph-BOX (16.7 mg, 0.05 mmol) in MeOH (5 mL). This solution was stirred for 10 min. Into the solution were added 1-phenylcyclohexane-*cis*-1,2-diol (**1**, 96.1 mg, 0.5 mmol) and tetraethylammonium bromide (105.1 mg, 0.5 mmol), and 2 F/mol of electricity was passed at a constant rate of 50 mA (terminal voltage: ca. 10 V) through the solution as it was cooled with ice-water. The solvent was evaporated in vacuo to give the residue, which was then dissolved in AcOEt. The solution was poured into satd aqueous $Na_2S_2O_3$ (5 mL). The organic portion was extracted with AcOEt (10 mL×3) and dried over $MgSO_4$. The resulting solution was concentrated in vacuo. The residue was purified by silica gel column chromatography (*n*-hexane/AcOEt=10:1) to afford (*S*)-2-hydroxy-2-phenylcyclohexanone (**2**) as a white solid and recovered (1*R*,2*R*)-1-phenylcyclohexane-*cis*-1,2-diol (**1**) as a white solid.

*4.4.1. (S)-2-Hydroxy-2-phenylcyclohexanone (**2**)*

White solid; mp 74 °C; $[\alpha]_D^{29}$ +119.3 (*c* 1.2, $CHCl_3$, 67% ee); IR (neat) ν 3474, 2944, 2867, 1717, 1451, 1101 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62–1.95 (m, 4H), 2.00–2.10 (m, 1H), 2.38–2.60 (m, 2H), 2.95–3.05 (m, 1H), 4.50 (s, 1H), 7.26–7.42 (m, 5H); HR-EI (M^+) calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0972. The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 15 min for (*R*)-**2** and 19 min for (*S*)-**2**].

*4.4.2. (1R,2R)-1-Phenylcyclohexane-cis-1,2-diol (**1**)*[15]

White solid; mp 90 °C (lit.[15] mp 121–122 °C); $[\alpha]_D^{25}$ −3.7 (*c* 1.2, EtOH, 41% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35–1.95 (m, 9H), 2.62 (s, 1H), 3.92–4.04 (m, 1H), 7.22–7.28 (m, 1H), 7.38 (t, *J*=7.8 Hz, 2H), 7.51 (d, *J*=7.2 Hz, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 10 min for (1*S*,2*S*)-**1** and 13 min for (1*R*,2*R*)-**1**].

*4.4.3. (S)-2-Hydroxy-2-phenylcyclopentanone (**9**)*

Light-yellow oil (lit. 16 for racemate, mp 67 °C); $[\alpha]_D^{18}$ +57.4 (*c* 1.9, $CHCl_3$, 38% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79–1.94 (m, 1H),

2.00–2.16 (m, 1H), 2.16–2.31 (m, 1H), 2.40–2.58 (m, 3H), 2.88 (s, 1H), 7.27–7.46 (m, 5H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 16 min for (*R*)-**9** and 20 min for (*S*)-**9**].

4.4.4. (1*R*,2*R*)-1-Phenylcyclopentane-cis-1,2-diol (**3**) (lit. 17 for racemate)

White solid; mp 62–63 °C; $[\alpha]_D^{29}$ −7.2 (*c* 3.2, $CHCl_3$, 22% ee); IR (neat) *ν* 3400, 2967, 1447, 1092, 1055, 758, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.60–1.86 (m, 2H), 1.86–2.16 (m, 4H), 2.30 (br s, 1H), 2.80 (br s, 1H), 4.22 (t, *J*=7.5 Hz, 1H), 7.15–7.28 (m, 1H), 7.33 (t, *J*=7.5 Hz, 2H), 7.45 (d, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 15 min for (1*S*,2*S*)-**3** and 19 min for (1*R*,2*R*)-**3**].

4.4.5. (*S*)-2-Hydroxy-2-phenylcycloheptanone (**10**) (lit. 18 for racemate)

Light-yellow oil; $[\alpha]_D^{29}$ +123.4 (*c* 1.7, $CHCl_3$, 64% ee); ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.22–1.68 (m, 3H), 1.83–2.10 (m, 3H), 2.22–2.40 (m, 2H), 2.40–2.55 (m, 1H), 2.75–2.88 (m, 1H), 4.58 (s, 1H), 7.25–7.40 (m, 3H), 7.40–7.50 (m, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 20 min for (*S*)-**10** and 30 min for (*R*)-**10**].

4.4.6. (1*R*,2*R*)-1-Phenylcycloheptane-cis-1,2-diol (**4**)

White solid; mp 99–100 °C; $[\alpha]_D^{28}$ −1.9 (*c* 1.0, $CHCl_3$, 85% ee); IR (neat) *ν* 3400, 3023, 2930, 1460, 1019 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.40–1.78 (m, 7H), 1.78–2.15 (m, 4H), 2.90 (s, 1H), 4.00 (d, *J*=10.4 Hz, 1H), 7.22–7.32 (m, 1H), 7.32–7.47 (m, 2H), 7.47–7.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.0, 22.7, 26.6, 29.8, 39.1, 77.5, 78.9, 124.8, 126.9, 128.5, 148.3; HR-EI (M^+) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1300. The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 11 min for (1*S*,2*S*)-**4** and 13 min for (1*R*,2*R*)-**4**].

4.4.7. (*S*)-2-Hydroxy-2-phenylcyclooctanone (**11**)

Colorless oil; $[\alpha]_D^{29}$ +177.7 (*c* 2.0, $CHCl_3$, 80% ee); IR (neat) *ν* 3467, 2930, 2859, 1701, 1698, 1466, 1447, 1364, 1127 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.96–1.12 (m, 1H), 1.35–1.62 (m, 2H), 1.62–2.04 (m, 5H), 2.04–2.16 (m, 1H), 2.16–2.28 (m, 1H), 2.70–2.88 (m, 1H), 2.88–3.02 (m, 1H), 4.81 (s, 1H), 7.25–7.40 (m, 3H), 7.48 (d, *J*=6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 22.6, 24.2, 25.3, 30.1, 31.3, 36.0, 81.0, 126.0, 127.9, 128.5, 141.4, 216.6; HR-EI (M^+) calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1302. The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 20 min for (*S*)-**11** and 28 min for (*R*)-**11**].

4.4.8. (1*R*,2*R*)-1-Phenylcyclooctane-cis-1,2-diol (**5**)

White solid; mp 46–47 °C; $[\alpha]_D^{29}$ −8.3 (*c* 1.2, $CHCl_3$, 80% ee); IR (neat) *ν* 3400, 2923, 1601, 1447, 1028, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.20–1.92 (m, 11H), 2.00–2.15 (m, 1H), 2.24–2.40 (m, 1H), 2.98 (s, 1H), 4.40 (dd, *J*=3.0, 8.7 Hz, 1H), 7.22–7.32 (m, 1H), 7.39 (t, *J*=7.8 Hz, 2H), 7.54 (d, *J*=6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.3, 24.2, 26.8, 28.1, 30.8, 36.5, 75.6, 78.3, 125.4, 127.0, 128.4, 146.4; HR-EI (M^+) calcd for $C_{14}H_{20}O_2$ 220.1554, found 220.1454. The ee was determined by DAICEL Chiralpak AS (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 7 min for (1*S*,2*S*)-**5** and 13 min for (1*R*,2*R*)-**5**].

4.4.9. (*S*)-2-Hydroxy-2-benzylcyclohexanone (**12**)[19]

White solid; mp 55 °C; $[\alpha]_D^{29}$ +6.3 (*c* 1.7, $CHCl_3$, 5% ee); ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.60–1.80 (m, 2H), 1.80–1.95 (m, 2H), 2.14–2.47 (m, 2H), 2.50–2.60 (m, 1H), 2.70 (dt, *J*=6.0, 13.5 Hz, 1H), 2.97 (d, *J*=13.7 Hz, 1H), 3.14 (d, *J*=13.7 Hz, 1H), 3.85 (s, 1H), 7.18–7.36 (m, 5H). The ee was determined by DAICEL Chiralpak AD (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 254 nm, 9 min for (*S*)-**12** and 11 min for (*R*)-**12**].

4.4.10. (1*R*,2*R*)-1-Benzylcyclohexane-cis-1,2-diol (**6**)

White solid; mp 103–104 °C (lit. 20 for racemate, mp 107–108 °C); $[\alpha]_D^{29}$ −0.3 (*c* 1.0, $CHCl_3$, 47% ee); IR (neat) *ν* 3404, 2938 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.16–1.92 (m, 8H), 2.85 (d, *J*=13.5 Hz, 2H), 2.95 (d, *J*=13.5 Hz, 2H), 3.40–3.50 (m, 1H), 7.20–7.35 (m, 5H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (1*S*,2*S*)-**6** and 11 min for (1*R*,2*R*)-**6**].

4.4.11. (*S*)-2-Hydroxy-2-isopropylcyclohexanone (**13**) (lit. 21 for racemate)

Colorless oil; $[\alpha]_D^{29}$ +44.1 (*c* 0.4, $CHCl_3$, 75% ee); ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.70 (d, *J*=6.9 Hz, 3H), 1.01 (d, *J*=6.6 Hz, 3H), 1.55–1.80 (m, 4H), 2.06–2.18 (m, 1H), 2.18–2.32 (m, 1H), 2.32–2.43 (m, 1H), 2.43–2.53 (m, 2H), 3.81 (s, 1H). The ee was determined by DAICEL Chiralpak AS (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (80/1) (v/v), 1.0 mL/min, detection at 210 nm, 6.5 min for (*S*)-**13** and 7.5 min for (*R*)-**13**].

4.4.12. (1*R*,2*R*)-1-Isopropylcyclohexane-cis-1,2-diol (**7**)

White solid; mp 91–92 °C; IR (neat) *ν* 3400, 2940, 1449, 1071 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.91 (d, *J*=7.5 Hz, 3H), 0.94 (d, *J*=7.5 Hz, 3H), 1.12–1.30 (m, 3H), 1.40–1.80 (m, 7H), 2.08 (sep, *J*=7.1 Hz, 1H), 3.66 (dd, *J*=4.2, 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 16.2, 17.6, 20.6, 23.6, 28.0, 30.6, 32.8, 71.0, 75.4; HR-EI (M^+) calcd for $C_9H_{18}O_2$ 158.1307, found 158.1267. The ee of the 1-isopropylcyclohexane-*cis*-1,2-diol (**7**) was determined by HPLC of the corresponding 2-phenylcarbamoylated compound **7′** by usual method.

4.4.13. (1*R*,2*R*)-1-Hydroxy-1-isopropyl-2-phenylcarbamoyloxycyclohexane (**7′**)

Light-yellow oil; $[\alpha]_D^{27}$ +1.8 (*c* 1.0, $CHCl_3$, 25% ee); IR (neat) *ν* 3300, 2942, 2867, 1707, 1601, 1545, 1231, 1061 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.92 (d, *J*=7.2 Hz, 3H), 0.96 (d, *J*=7.2 Hz, 3H), 1.22–1.41 (m, 2H), 1.41–2.00 (m, 8H), 4.91 (dd, *J*=5.1, 10.2 Hz, 1H), 6.75 (s, 1H), 7.07 (t, *J*=6.9 Hz, 1H), 7.22–7.45 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 16.1, 17.5, 20.3, 23.7, 27.5, 28.5, 33.7, 75.2, 25.3, 118.5, 123.4, 129.0, 137.9, 152.8; HR-EI (M^+) calcd for $C_{16}H_{23}NO_3$ 277.1678, found 277.1677. The ee was determined by DAICEL Chiralpak AS (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (50/1) (v/v), 1.0 mL/min, detection at 254 nm, 16 min for (1*S*,2*S*)-**7′** and 19 min for (1*R*,2*R*)-**7′**].

4.4.14. (*S*)-2-Hydroxy-2-cyclohexylcyclohexanone (**14**)

Light-yellow oil (lit. 21 for racemate, mp 46–46.5 °C); $[\alpha]_D^{29}$ +91.9 (*c* 1.2, $CHCl_3$, 81% ee); ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.00–1.48 (m, 7H), 1.55–2.06 (m, 8H), 2.06–2.18 (m, 1H), 2.36–2.57 (m, 3H), 3.85 (s, 1H). The ee was determined by DAICEL Chiralpak AD (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (40/1) (v/v), 1.0 mL/min, detection at 210 nm, 8 min for (*S*)-**14** and 11 min for (*R*)-**14**].

4.4.15. (1*R*,2*R*)-1-Cyclohexylcyclohexane-cis-1,2-diol (**8**)

White solid; mp 109–110 °C; IR (neat) *ν* 3400, 2928, 1445, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.95–1.90 (m, 21H), 3.60–3.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.8, 23.7, 26.7, 26.9, 27.8, 29.5, 30.6, 43.6, 70.7, 75.2; HR-EI (M^+) calcd for $C_{12}H_{22}O_3$ 198.1620, found 198.1592. The ee of the 1-cyclohexylcyclohexane-*cis*-1,2-diol (**8**) was determined by HPLC of the corresponding 2-phenylcarbamoylated compound **8′**.

*4.4.16. (1R,2R)-1-Hydroxy-1-cyclohexyl-2-phenylcarbamoyloxycyclohexane (**8′**)*

White solid; mp 125 °C; $[\alpha]_D^{29}$ +3.5 (*c* 2.5, $CHCl_3$, 18% ee); IR (neat) *ν* 3308, 2938, 2855, 1736, 1608, 1549, 1447, 1325, 1237 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 0.90–1.90 (m, 20H), 4.89 (dd, *J*=4.8, 10.2 Hz, 1H), 6.76 (s, 1H), 7.07 (t, *J*=7.2 Hz, 1H), 7.28–7.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.5, 23.7, 26.1, 26.6, 26.8, 26.9, 27.4, 27.7, 30.2, 44.6, 75.0, 75.1, 118.5, 123.4, 129.1, 137.9, 152.7; HR-EI (M^+) calcd for $C_{19}H_{27}NO_3$ 317.1991, found 317.2000. The ee was determined by DAICEL Chiralpak AD (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (1*R*,2*R*)-**8′** and 12 min for (1*S*,2*S*)-**8′**].

*4.4.17. N-(p-Tolylsulfonyl)piperidine-(3S,4R)-diol (**15**)*

White solid; mp 112 °C (lit. 22 for racemate, mp 138–140 °C); $[\alpha]_D^{22}$ −7.1 (*c* 1.0, $CHCl_3$, 41% ee); IR (neat) *ν* 3350, 2926, 2872, 2359, 1929, 1732, 1661, 1599 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.77–1.95 (m, 2H), 2.08–2.18 (m, 1H), 2.18–2.36 (m, 1H), 2.44 (s, 3H), 2.94–3.10 (m, 3H), 3.10–3.23 (m, 1H), 3.70–3.82 (m, 1H), 3.82–3.94 (m, 1H), 7.33 (d, *J*=8.1 Hz, 2H), 7.65 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.5, 29.2, 41.9, 42.0, 67.4, 67.7, 127.6, 129.8, 143.8; HR-EI (M^+) calcd for $C_{12}H_{17}NO_4S$ 271.0878, found 271.0876. The ee was determined by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/ethanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 12 min for (3*R*,4*S*)-**15** and 16 min for (3*S*,4*R*)-**15**].

*4.4.18. (3R)-Hydroxy-N-(p-tolylsulfonyl)piperidine-4-one (**17**)*

Colorless solid; mp 114 °C; $[\alpha]_D^{19}$ +1.1 (*c* 0.75, $CHCl_3$, 49% ee); IR (neat) *ν* 3350, 2926, 2857, 1732, 1345 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 2.30–2.43 (m, 1H), 2.44 (s, 3H), 2.50–2.90 (m, 3H), 3.53 (br s, 1H), 4.10–4.25 (m, 1H), 4.28–4.45 (m, 2H), 7.35 (d, *J*=10.4 Hz, 2H), 7.69 (d, *J*=10.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.5, 38.7, 46.5, 52.5, 72.5, 100.6, 127.4, 127.7, 130.0, 133.5, 144.3; HR-EI (M^+) calcd for $C_{12}H_{15}NO_4S$ 269.0722, found 269.0719. The ee was determined by DAICEL Chiralcel OJ (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (3*S*)-**17** and 11 min for (3*R*)-**17**].

*4.4.19. N-(tert-Butoxycarbonyl)-3-phenylpiperidine-(3S,4S)-diol (**18**)*

Colorless solid; mp 101–103 °C; $[\alpha]_D^{22}$ −10.1 (*c* 0.2, $CHCl_3$, 55% ee); IR (neat) *ν* 3350, 2976, 2926, 2957, 2855, 1750, 1694, 1671, 1466, 1377, 1167 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.48 (s, 9H), 1.85–2.10 (m, 3H), 2.70–2.87 (m, 1H), 2.90–3.08 (m, 2H), 3.80–4.30 (m, 3H), 7.28 (t, *J*=7.6 Hz, 1H), 7.38 (t, *J*=7.6 Hz, 2H), 7.47 (d, *J*=7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 28.4, 37.9, 40.0, 44.4, 70.9, 74.3, 79.9, 125.0, 127.4, 128.6, 144.8, 154.8; HR-EI (M^+) calcd for $C_{16}H_{23}NO_4$ 293.1627, found 293.1616. The ee was determined by DAICEL Chiralcel OJ (4.6 mmø, 250 mm) [*n*-hexane/ethanol (15/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (3*S*,4*S*)-**18** and 11 min for (3*R*,4*R*)-**18**].

*4.4.20. N-(tert-Butoxycarbonyl)-N-(3-oxo-3-phenylpropyl)-formamide (**20**)*

Colorless oil; IR (neat) *ν* 2978, 2932, 2359, 2344, 1740, 1686, 1342, 1149 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.53 (s, 9H), 3.25 (t, *J*=7.5 Hz, 2H), 4.05 (t, *J*=7.5 Hz, 2H), 7.40–7.50 (m, 2H), 7.50–7.64 (m, 1H), 7.90–8.00 (m, 2H), 9.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 28.0, 29.7, 36.6, 36.9, 84.4, 128.1, 128.7, 133.3, 136.5, 163.0, 197.7; HR-EI (M^+) calcd for $C_{15}H_{19}NO_4$ 277.1314, found 277.1292.

*4.4.21. N-(tert-Butoxycarbonyl)-N-(3-oxo-3-phenylpropyl)glycine methyl ester (**21**)*

Colorless oil; IR (neat) *ν* 2976, 2359, 1752, 1705, 1682, 1367, 1213, 1169 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.41 and 1.47 (2s, 9H), 3.25–3.45 (m, 2H), 3.60–3.80 (m, 5H), 4.07 (d, *J*=14.4 Hz, 2H), 7.40–7.55 (m, 2H), 7.50–7.65 (m, 1H), 7.97 (d, *J*=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 28.2, 38.0, 44.4, 51.2, 51.9, 80.4, 128.1, 128.6, 133.2, 136.7, 155.2, 170.9, 199.2; HR-EI (M^+) calcd for $C_{17}H_{23}NO_5$ 321.1576, found 321.1571.

*4.4.22. (R)-3-Ethyl-3-hydroxy-N-(p-tolylsulfonyl)piperidine-4-one (**23**)*

White solid; mp 85–87 °C; $[\alpha]_D^{27}$ −11.2 (*c* 1.0, $CHCl_3$, 31% ee); IR (neat) *ν* 2855, 1718, 1339, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.87 (t, *J*=7.6 Hz, 3H), 1.85–2.00 (m, 1H), 2.00–2.15 (m, 1H), 2.31 (d, *J*=11.6 Hz, 1H), 2.40–2.62 (m, 2H), 2.43 (s, 3H), 2.82–2.97 (m, 1H), 3.72 (s, 1H, –OH), 4.03 (dd, *J*=2.8, 12.0 Hz, 1H), 4.08–4.20 (m, 1H), 7.34 (d, *J*=8.4 Hz, 2H), 7.65 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 6.6, 21.5, 29.5, 37.3, 46.9, 55.8, 78.0, 127.4, 129.9, 133.1, 144.2, 209.9; HR-EI (M^+) calcd for $C_{14}H_{19}NO_4S$ 297.1035, found 297.1022. The ee was determined by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/ethanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 18 min for (3*S*)-**23** and 19 min for (3*R*)-**23**].

*4.4.23. N-(p-Tolylsulfonyl)-3-ethylpiperidine-(3S,4R)-diol (**22**)*

White solid; mp 98–102 °C; $[\alpha]_D^{28}$ +3.6 (*c* 0.6, $CHCl_3$, 39% ee); IR (neat) *ν* 2967, 1464, 1335, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.94 (t, *J*=7.6 Hz, 3H), 1.58–1.80 (m, 2H), 1.70–1.82 (m, 1H), 1.88–2.00 (m, 1H), 2.00–2.40 (m, 2H, –OH), 2.44 (s, 3H), 2.71 (d, *J*=11.6 Hz, 1H), 2.70–2.82 (m, 1H), 3.11 (d, *J*=11.6 Hz, 1H), 3.18–3.30 (m 1H), 3.35–3.45 (m, 1H), 7.34 (d, *J*=8.0 Hz, 2H), 7.64 (d, *J*=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 7.0, 21.5, 27.7, 29.5, 43.2, 51.0, 70.5, 71.8, 127.6, 129.8, 132.9, 143.8; HR-EI (M^+) calcd for $C_{14}H_{21}NO_4S$ 299.1191, found 299.1181. The ee was determined by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/ethanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 19 min for (3*R*,4*S*)-**22** and 23 min for (3*S*,4*R*)-**22**].

4.5. A typical procedure for the preparation of *racemic* aminoalcohols

Sodium tetrahydroborate (120 mmol, 4.54 g) and calcium chloride (60 mmol, 6.66 g) were added to a stirred solution of *racemic N*-benzoylalanine methyl ester (*racemic*-**30**, 30 mmol, 6.22 g) in THF/MeOH (4/1, 150 mL) at 0 °C. The reaction mixture was stirred for 12 h. Water (50 mL) was added to the resulting mixture and the solution stirred for 15 min. The solution was evaporated in vacuo to give a residue, which was then dissolved in AcOEt. The organic portion was extracted with AcOEt and dried over $MgSO_4$. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (*n*-hexane/AcOEt=1/1) to afford **26** (85% yield).

4.6. A typical procedure for the preparation of *racemic* aminoaldehydes

To a solution of *N*-benzoyl-2-(hydroxymethyl)piperidine (*racemic*-**24**, 10 mmol, 2.19 g) and TEMPO (1 mmol, 156 mg) in CH_2Cl_2 (10 mL) was added $PhI(OAc)_2$ (11 mmol, 3.54 g). The reaction mixture was stirred for 1 h and then quenched with satd aqueous $Na_2S_2O_3$ (5 mL). The organic portion was extracted with CH_2Cl_2 and dried over $MgSO_4$. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (*n*-hexane/AcOEt=2/1) to afford **32** (73% yield).

*4.6.1. N-Benzoyl-2-piperidinecarbaldehyde (**32**)*[23]

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.30–1.90 (m, 5H), 2.16–2.20 (m, 1H), 3.02–3.21 (m, 1H), 3.60–3.80 (m, 1H), 5.30 (s, 1H), 7.43 (m, 5H), 9.66 (s, 1H).

*4.6.2. N-Benzoyl-2-pyrrolidinecarbaldehyde (**33**)*[23]

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$) *δ* 1.81–2.30 (m, 4H), 3.50–3.70 (m, 2H), 4.64–4.75 (m, 1H), 7.30–7.45 (m, 3H), 7.50–7.80 (m, 2H), 9.69 (s, 1H).

*4.6.3. N-(1-Formylethyl)benzamide (**34**)*[24]

Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (d, J=7.5 Hz, 3H), 4.70–4.81 (m, 1H), 6.83 (br s, 1H), 7.32–7.58 (m, 3H), 7.81–7.86 (m, 2H), 9.66 (s, 1H).

*4.6.4. N-(1-Formyl-2-methylpropyl)benzamide (**35**)*

White solid; mp 68–70 °C; IR (neat) ν 3320, 2967, 1732, 1647, 1536, 1314 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (d, J=6.9 Hz, 3H), 1.09 (d, J=6.9 Hz, 3H), 2.40–2.52 (m, 1H), 4.82–4.89 (m, 1H), 6.73 (br s, 1H), 7.44–7.59 (m, 3H), 7.83 (d, J=6.9 Hz, 2H), 9.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 19.0, 24.4, 63.6, 127.1, 128.6, 131.8, 140.0, 167.6, 199.8; HR-EI (M^+) calcd for $C_{12}H_{15}NO_2$ 205.1103, found 205.1098.

4.7. Asymmetric electrochemical oxidation of aminoalcohols

The oxidation was carried out according to the typical experimental procedure for the oxidation of **1**.

*4.7.1. N-Benzoyl-(2R)-(methoxycarbonyl)piperidine (**28**) (lit. 23 for racemate)*

Colorless oil; $[\alpha]_D^{26}$ +51.0 (*c* 0.40, $CHCl_3$, 87% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25–1.82 (m, 5H), 2.26–2.40 (m, 1H), 3.18–3.30 (m, 1H), 3.60–3.70 (m, 1H), 3.79 (s, 3H), 5.50–5.58 (m, 1H), 7.42 (m, 5H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (30/1) (v/v), 1.0 mL/min, detection at 254 nm, 25 min for (*R*)-**28** and 27 min for (*S*)-**28**].

*4.7.2. N-Benzoyl-(2S)-(hydroxymethyl)piperidine (**24**)*[4c]

White solid; mp 89–92 °C (lit. 25 for racemate, mp 93–95 °C); $[\alpha]_D^{26}$ −7.1 (*c* 2.0, $CHCl_3$, 12% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40–1.90 (m, 6H), 2.80–3.20 (m, 2H), 3.50–3.80 (m, 1H), 3.96 (dd, J=9.9, 10.5 Hz, 1H), 4.85 (br s, 1H), 7.41 (m, 5H). The ee was determined by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (30/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (*S*)-**24** and 34 min for (*R*)-**24**].

*4.7.3. N-Benzoyl-(2R)-methoxycarbonylpyrrolidine (N-Benzoyl-D-proline methyl ester) (**29**)*

White solid; mp 69–72 °C (lit. 26 for L-form, mp 89–90 °C); $[\alpha]_D^{21}$ +83.7 (*c* 0.5, $CHCl_3$, 86% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.80–2.11 (m, 3H), 2.14–2.40 (m, 1H), 3.50–3.60 (m, 1H), 3.62–3.71 (m, 1H), 3.78 (s, 3H), 4.66–4.70 (m, 1H), 7.30–7.45 (3H), 7.50–7.60 (m, 2H). The ee was determined by DAICEL Chiralpak AD (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (*R*)-**29** and 39 min for (*S*)-**29**].

*4.7.4. N-Benzoyl-(2S)-hydroxymethylpyrrolidine (**25**)*[27]

Colorless oil; $[\alpha]_D^{19}$ −21.1 (*c* 1.6, $CHCl_3$, 15% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57–1.95 (m, 4H), 2.12–2.25 (m, 1H), 3.42–3.58 (m, 2H), 3.70–3.83 (m, 2H), 4.37–4.46 (m, 1H), 4.90–4.98 (m, 1H), 7.38–7.55 (m, 5H). The ee was obtained by DAICEL Chiralpak AD (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (*R*)-**25** and 36 min for (*S*)-**25**].

*4.7.5. Methyl (2R)-(N-benzoyl)aminopropionate (N-benzoyl-D-alanine methyl ester) (**30**)*

Colorless oil (lit. 28 for L-form, mp 52–53 °C); $[\alpha]_D^{23}$ −23.3 (*c* 1.4, $CHCl_3$, 59% ee) [lit. 28 for L-form, $[\alpha]_D^{23}$ +38.6 (*c* 2.9, $CHCl_3$)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (d, J=6.9 Hz, 3H), 3.80 (s, 3H), 4.75–4.83 (m, 1H), 6.74 (br s, 1H), 7.41–7.55 (m, 3H), 7.80–7.85 (m, 2H). The ee was obtained by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 220 nm, 16 min for (*R*)-**30** and 17 min for (*S*)-**30**].

*4.7.6. (2S)-(N-Benzoyl)aminopropan-1-ol (**26**)*[29]

White solid; mp 110–112 °C (lit.[29] mp 132–133 °C); $[\alpha]_D^{26}$ −1.0 (*c* 0.9, $CHCl_3$, 18% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, J=6.6 Hz, 3H), 2.40–2.83 (br s, 1H), 3.60–3.68 (m, 1H), 3.72–3.80 (m, 1H), 4.322–4.35 (m, 1H), 6.44 (br s, 1H), 7.30–7.56 (m, 3H), 7.70–7.88 (m, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 220 nm, 8.3 min for (*S*)-**26** and 9.6 min for (*R*)-**26**].

*4.7.7. Methyl (2R)-(N-benzoyl)amino-3-methylbutyrate (N-benzoyl-D-valine methyl ester) (**31**)*

White solid; mp 94–96 °C (lit. 30 for *racemic* form, mp 86 °C); $[\alpha]_D^{20}$ −33.5 (*c* 0.5, $CHCl_3$, 64% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J=7.2 Hz, 3H), 1.03 (d, J=7.2 Hz, 3H), 2.22–2.35 (m, 1H), 3.78 (s, 3H), 4.78–4.82 (m, 1H), 6.62 (m, 1H), 7.43–7.56 (m, 3H), 7.82 (d, J=6.6 Hz, 2H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (50/1) (v/v), 1.0 mL/min, detection at 254 nm, 15 min for (*R*)-**31** and 20 min for (*S*)-**31**].

*4.7.8. (2S)-(N-Benzoyl)amino-3-methylbutan-1-ol (**27**)*[31]

White solid; mp 84–85 °C (lit.[31] mp 99 °C); $[\alpha]_D^{27}$ −4.5 (*c* 1.0, $CHCl_3$, 12% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, J=6.9 Hz, 3H), 1.02 (d, J=6.9 Hz, 3H), 1.95–2.06 (m, 1H), 2.90–3.22 (br s, 1H), 3.75–3.78 (m, 2H), 3.89–3.98 (m, 1H), 6.48 (br s, 1H), 7.39–7.56 (m, 3H), 7.77 (d, J=6.9 Hz, 2H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmø, 250 mm) [*n*-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 13 min for (*S*)-**27** and 22 min for (*R*)-**27**].

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