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Chiral zinc(II) and copper(II)-catalyzed asymmetric ring-opening reactions of *meso*-epoxides with aniline and indole derivatives

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ABSTRACT

The ring-opening reactions of *meso*-epoxides with aniline and indole derivatives proceeded smoothly in water in the presence of Zn(II) and Cu(II) surfactant-type catalysts to afford the corresponding products in moderate to high yields with good to excellent enantioselectivities. Opposite enantiomers were obtained by using Sc(III) and Zn(II) or Cu(II) with the same chiral ligand. Crystal structures of these catalysts may explain the reversal of the enantioselectivity. Some reactions were also tested in dichloromethane (DCM), and it was revealed that the reactions proceeded faster in water than in DCM. Finally, several nonlinear effect experiments suggested unique structure of these chiral catalysts.

1. Introduction

Most organic reactions have been carried out in organic solvents because most organic materials are not soluble in water and most reactive species are not stable in the presence of water. This is also the case for chiral catalysts, which are often unstable in the presence of water and thus are difficult to conduct catalytic asymmetric reactions in the presence of water. On the other hand, from an environmentally point of view, recent demand is development of benign chemical processes.[1] In this context, while several types of reactions in aqueous media have been reported,[2] organic solvents are required as co-solvents to dissolve organic materials in many cases. To overcome this problem, we developed Lewis acid–surfactant-combined catalysts (LASCs) to conduct organic reactions in water as the sole solvent. Hydrophobic substrates are taken into micellous emulsions created by LASCs and the hydrophobic substrates, where reactants, substrates, and the catalyst are concentrated, and the desired reactions proceed very efficiently.[3] Very recently, we have also shown that even hydrophilic substrates can be used in this system.[3e]

Catalytic asymmetric ring-opening reactions of *meso*-epoxides provide a useful method for the synthesis of chiral 1,2-bifunctional alcohols. Based on this method, a number of protocols have been developed for the synthesis of enantiomerically enriched 1,2-azido alcohols,[4] 1,2-amino alcohols,[5] 1,2-diol derivatives,[6] 1,2-cyano alcohols,[7] 1,2-mercaptoalcohols,[8] 1,2-halohydrines,[9] and 1,2-seleno alcohols.[10] Our group has mainly contributed to this field by exploiting efficient asymmetric reactions in water, and reported the first examples of chiral scandium and bismuth-catalyzed ring-opening reactions of *meso*-epoxides with aniline derivatives in water. We have also developed the first catalytic asymmetric ring-opening reactions of *meso*-epoxides with indole derivatives in water. In the course of our investigations to develop more efficient catalysts in water, we have discovered unique catalysis of zinc(II) and copper(II). We describe zinc(II) and copper(II) catalyzed asymmetric ring-opening reactions of *meso*-epoxides with aniline and indole derivatives in water.

2. Results and discussion

At the outset, we carried out the ring-opening reaction of *meso*-epoxide **1** with aniline in the presence of various metal surfactant-combined catalysts in water (Table 1). Sc(III), Zn(II), and Cu(II) catalysts gave the desired product **4a** in good to excellent yields with good to excellent enantioselectivities (entries 1, 7, 8). It is noted that opposite enantiomers were obtained by using Sc(III) and Zn(II) or Cu(II) with the same chiral ligand; while Sc(III) gave one enantiomer of the product, Zn(II) or Cu(II) gave the opposite enantiomer of the product. On the other hand, the reactions also proceeded in dichloromethane (DCM), and the Sc(III) and Zn(II) catalysts gave the desired product in 85% and 60% yields with 93% and 90% ees, respectively, although Cu(II) catalyst was not so effective.

We then carefully examined the reaction of *cis*-stilbene oxide (**1**) with aniline in the presence of 5 mol % of the Zn(II) or Cu(II) catalysts and 6 mol % of chiral bipyridine **3** in water and DCM at room

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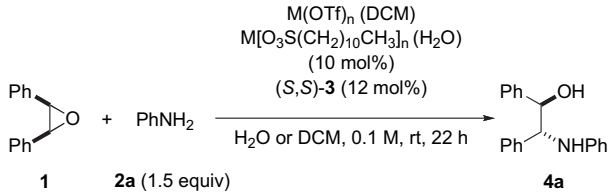
Table 1
Ring-opening reaction of *meso*-epoxide **1** with aniline



1 **2a** (1.5 equiv) **4a**

Entry	M	*n*	In H_2O		In DCM	
			Yield[a] (%)	ee[b] (%)	Yield[a] (%) **1**	ee[b] (%)
1	Sc	3	87	95 (1*S*,2*S*)	85	93 (1*S*,2*S*)
2	Y	3	9	62 (1*S*,2*S*)	—	—
3	Yb	3	27	82 (1*S*,2*S*)	—	—
4	In	3	6	32 (1*S*,2*S*)	—	—
5	Mn	2	6	81 (1*S*,2*S*)	—	—
6	Ni	2	Trace	—	—	—
7	Cu	2	82	80 (1*R*,2*R*)	18	80 (1*R*,2*R*)
8	Zn	2	97	92 (1*R*,2*R*)	60	90 (1*R*,2*R*)
9	Ag	1	Trace	—	—	—

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.

temperature. It is noted that $Zn[O_3S(CH_2)_{10}CH_3]_2$ or $Cu[O_3S(CH_2)_{10}CH_3]_2$ and **3** in water gave higher yields than $Zn(OTf)_2$ or $Cu(OTf)_2$ and **3** in DCM. In addition, $Zn[O_3S(CH_2)_{10}CH_3]_2$ or $Cu[O_3S(CH_2)_{10}CH_3]_2$ and **3** in water showed higher reactivity than $Zn(OTf)_2$ or $Cu(OTf)_2$ and **3** in DCM (Fig. 1).

After optimization of the reaction conditions, we surveyed substrate scope of several *meso*-epoxides and aniline derivatives using Zn(II) or Cu(II) as a catalyst (Table 2). While stilbene oxide derivatives showed good selectivities with various aniline derivatives (entries 1–8, 13–20), alkyl epoxide derivatives gave only moderate selectivities (entries 9–12, 21). It is interesting to find that $Cu(OTf)_2$ had almost no activity in DCM, but that $Zn(OTf)_2$ catalyzed the *meso*-epoxides ring-opening reactions in DCM (entries 22–29). The reactions proceeded slower in DCM than in water, while the desired products were obtained with good selectivities.

Next, we carried out the ring-opening reactions of *meso*-epoxides with indole derivatives using Sc(III), Zn(II), and Cu(II) catalysts in water and DCM (Table 3). Nitrogen-containing heterocycles and their derivatives are well-known structures in natural products and medicines.[11,12] The synthesis of chiral *N*-heteroaromatic derivatives in optically active form is especially important in this area. Gratifyingly, Sc(III) and Cu(II) gave the product in good yields with excellent enantioselectivities in water. In this reaction, enantiofacial selectivities between Sc(III) and Cu(II) were reversed, and the reaction proceeded sluggishly in the presence of Zn(II). On the other hand, when the reaction was carried out in DCM, only $Cu(OTf)_2$ gave the desired product in moderate yield with high enantioselectivity. We then examined several reaction conditions with the Cu(II) catalyst in water (Table 4). As for the equivalents of indole, 1.2 equiv gave the best yield and selectivity (entry 2). The concentration was found to give almost no influence on yield and selectivity (entries 2, 4–6). The yield dropped when the catalyst loading decreased (entries 2, 7–9). When 2 mol % of the catalyst was used, the desired product was obtained in 73% yield with 90% ee.

The reaction of *cis*-stilbene oxide (**1**) with indole (**5a**) also proceeded in the presence of 5 mol % of $Cu(OTf)_2$ catalysts and 6 mol % of chiral bipyridine **3** in DCM. While the reaction rate in DCM was almost the same as that in water (Fig. 2), the enantioselectivity was higher in water than in DCM.

Several examples of *meso*-epoxide ring-opening reactions with indole derivatives are shown in Table 5. In cases of stilbene oxide (**1**) with substituted indoles, the reactions proceeded smoothly in most cases to afford the corresponding indole adducts in moderate to good yields with excellent enantioselectivities (entries 3–6). As for *meso*-epoxides, aromatic ones reacted with indole (**5a**) to afford the desired compounds in moderate yields with good selectivities (entries 7–9). However, alkyl epoxide derivatives showed poor reactivity (entries 10, 11). On the other hand, when the reactions were conducted in DCM, the rates were slower than those in water, and the reaction mixtures were messy. In some cases, only a trace amount of the desired product was obtained (entries 15, 17, and 18).

To obtain information on the chiral Cu complex, X-ray crystal structural analysis was performed. Single crystals suitable for X-ray analysis were obtained from a (*S*,*S*)-**3**–$CuBr_2$ complex (Fig. 3). The complex adopts square pyramidal structure in which two pyridines and one hydroxyl group of **3** coordinated to copper in a tridentate manner. Formation of this structure may be a key for obtaining high enantioselectivity. In addition, difference of the structure between chiral scandium[2c] and copper may cause the difference of absolute configurations of the products.

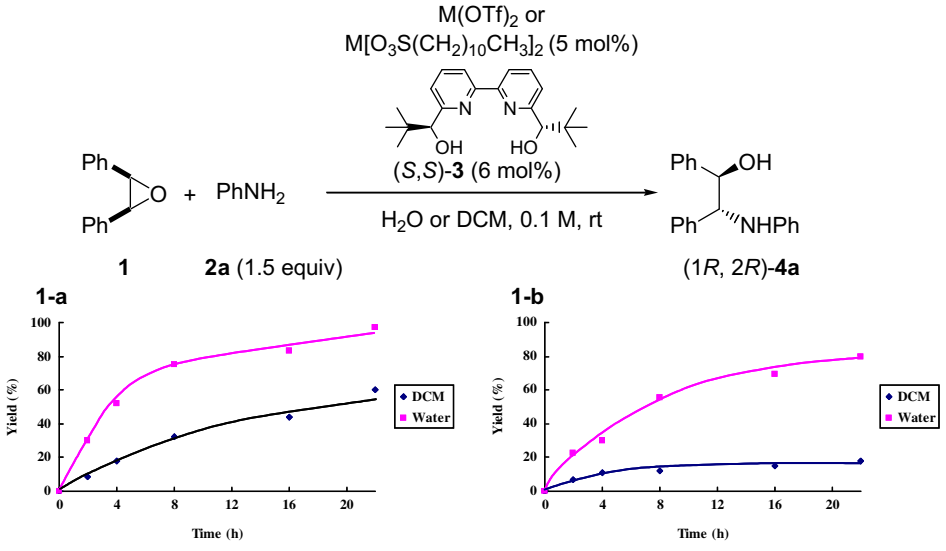
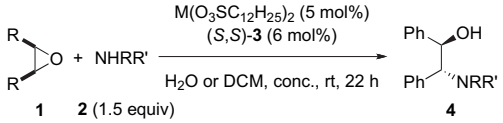


Figure 1. Plot of yield versus time for the ring-opening reactions of *cis*-stilbene oxide (**1**) with aniline (**2a**) in the presence of Zn(II) catalyst (**1**–**a**) or Cu(II) catalyst (**1**–**b**) and **3** in water (pink) and DCM (blue).

Table 2
Ring-opening reaction of *meso*-epoxides with aniline derivatives



Entry	R	NHRR′	Metal	Solvent	Conc (M)	Yield (%)[a]		ee (%)[b]
1	Ph	Aniline	Zn	H_2O	0.1	**4a**	97	92
2	Ph	2-Trifluoromethylaniline	Zn	H_2O	1.0	**4b**	100	92
3	Ph	1-Naphthylamine	Zn	H_2O	1.0	**4c**	55	95
4	Ph	*N*-Methylaniline	Zn	H_2O	1.0	**4d**	56	95
5	Ph	2-Methoxyaniline	Zn	H_2O	1.0	**4e**	43	91
6	3-MePh	Aniline	Zn	H_2O	1.0	**4f**	95	93
7	4-MePh	Aniline	Zn	H_2O	1.0	**4g**	82	93
8	4-BrPh	Aniline	Zn	H_2O	1.0	**4h**	44	90
9	Me	Aniline	Zn	H_2O	1.0	**4i**	80	54
10	Me	2-Naphthylamine	Zn	H_2O	1.0	**4j**	100	67
11[c]	$-(CH_2)_4-$	Aniline	Zn	H_2O	0.5	**4k**	94	66
12[c]	$-(CH_2)_4-$	2-Naphthylamine	Zn	H_2O	0.5	**4l**	77	79
13	Ph	Aniline	Cu	H_2O	1.0	**4a**	82	80
14	Ph	2-Trifluoromethylaniline	Cu	H_2O	1.0	**4b**	100	78
15	Ph	1-Naphthylamine	Cu	H_2O	1.0	**4c**	56	75
16	Ph	*N*-Methylaniline	Cu	H_2O	1.0	**4d**	88	91
17	Ph	2-Methoxyaniline	Cu	H_2O	1.0	**4e**	44	70
18	4-MePh	*N*-Methylaniline	Cu	H_2O	1.0	**4m**	78	90
19	4-BrPh	*N*-Methylaniline	Cu	H_2O	1.0	**4n**	72	92
20	2-Naphthyl	*N*-Methylaniline	Cu	H_2O	1.0	**4o**	81	90
21	$-(CH_2)_4-$	2-Naphthylamine	Cu	H_2O	0.5	**4l**	84	44
22	Ph	Aniline	Zn	DCM	0.1	**4a**	60	90
23	Ph	2-Trifluoromethylaniline	Zn	DCM	0.1	**4b**	92	90
24	Ph	1-Naphthylamine	Zn	DCM	0.1	**4c**	69	87
25	Ph	*N*-Methylaniline	Zn	DCM	0.1	**4d**	63	85
26	Ph	2-Methoxyaniline	Zn	DCM	0.1	**4e**	10	69
27	4-BrPh	Aniline	Zn	DCM	0.1	**4h**	20	86
28	$-(CH_2)_4-$	Aniline	Zn	DCM	0.1	**4k**	77	74
29	Me	Aniline	Zn	DCM	0.1	**4i**	74	70

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.
[c] Reaction was conducted at 10 °C.

We also conducted the reaction with Zn(II) and chiral bipyridine derivatives **7** and **8** (Table 6). Judging from these results, both hydroxyl groups are necessary for reactivity and selectivity. One hydroxyl group may be needed to coordinate to zinc and the other needed to coordinate to a substrate.

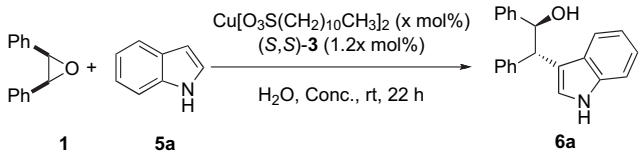
Finally, we examined non-linear effect (NLE) of these catalysts (Figs. 4 and 5). In Cu-catalyzed reactions, NLE was not observed both in water and in DCM. On the other hand, in Sc-catalyzed reactions, while NLE was not observed in water, positive NLE was appeared in DCM. These results suggest that monomeric structures of Cu catalysts both in water and DCM and Sc catalysts in water are predominant. Interestingly, when Sc–(*S*,*S*)-**3** and Sc–(*R*,*R*)-**3** complexes were prepared independently and combined appropriately to make catalysts with low ees in DCM, NLE was not observed (Fig. 6). It was assumed from these experiments that the Sc(III)–**3** complex would not dissociate after formation of the complex in DCM. On the other hand, formation of dimeric or oligomeric structure would be suppressed in water.

Table 3
Sc(III), Zn(II), and Cu(II)-catalyzed ring opening of *meso*-epoxide **1** with indole **5a**

Entry	Metal	*n*	In H_2O		In DCM	
			Yield[a] (%)	ee[b] (%)	Yield[a] (%)	ee (%)[b]
1	Sc	3	58	92 (1*R*,2*R*)	Trace[c]	—
2	Zn	2	8	80 (1*S*,2*S*)	Trace[c]	—
3	Cu	2	80	96 (1*S*,2*S*)	60	86 (1*S*,2*S*)

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.
[c] By-product was generated.

Table 4
Effect of concentrations and catalyst loadings



Entry	Indole (equiv)	Cone (M)	*x* (mol %)	Yield[a] (%)	ee[b] (%)
1	1.1	1.0	10	80	88
2	1.2	1.0	10	80	96
3	2.0	1.0	10	80	88
4	1.2	0.50	10	80	93
5	1.2	0.17	10	79	93
6	1.2	0.10	10	75	93
7	1.2	1.0	5	71	96
8	1.2	1.0	2	54 (73)[c]	92 (90)
9	1.2	1.0	1	48	86

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.
[c] Reaction time was 43 h.

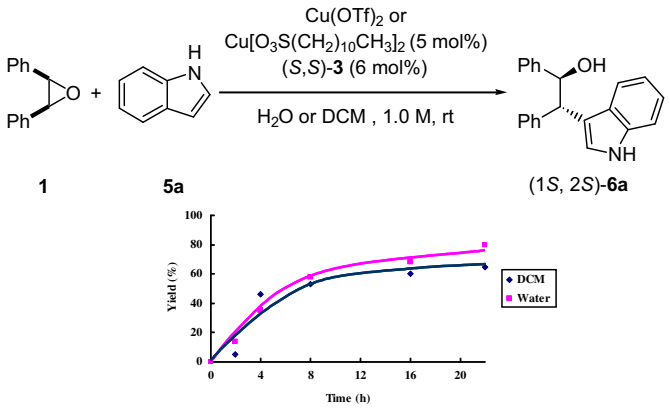
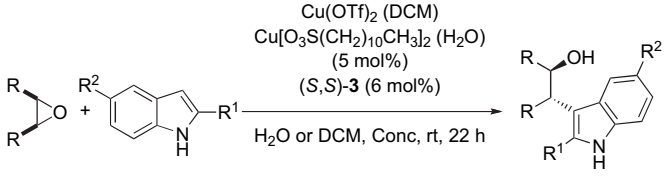


Figure 2. Plot of yield versus time for the ring-opening reactions of *cis*-stilbene oxide (**1**) with indole (**5a**) in the presence of Cu(II) catalyst and **3** in water (pink) and DCM (blue).

3. Conclusion

We have developed the ring-opening reaction of *meso*-epoxide with aniline and indole derivatives using surfactant-type chiral zinc and copper catalysts, and the desired ring-opening products were obtained in moderate to high yields with good to excellent enantioselectivities. Opposite enantiomers were obtained by using Sc(III) and Zn(II) or Cu(II) with the same chiral ligand; while Sc(III) gave one enantiomer of the product, Zn(II) or Cu(II) gave the opposite enantiomer of the product. Crystal structures of Sc(III) and Cu(II) catalysts may explain the reversal of the selectivity. Some reactions were tested not only in water but also in dichloromethane (DCM), and it was revealed that the reactions proceeded faster in water than in DCM. Catalytic activity of Zn(II) and Cu(II) as well as Sc(III) is remarkable for the reactions of *meso*-epoxides with anilines and indoles. Finally, several non-linear effect experiments suggested unique structure of these chiral catalysts.

Table 5
Ring opening of *meso*-epoxides with indole derivatives



Entry	R	R^1	R^2	Solvent	Concn (M)	Yield[a] (%)		ee[b] (%)
1	Ph	H	H	H_2O	1.0	**6a**	80	96 (1*S*,2*S*)
2[c]	Ph	H	H	H_2O	1.0	**6a**	71	96 (1*S*,2*S*)
3	Ph	H	OMe	H_2O	1.0	**6b**	45	92 (1*S*,2*S*)
4	Ph	H	Me	H_2O	1.0	**6c**	81	92 (1*S*,2*S*)
5	Ph	H	Br	H_2O	1.0	**6d**	58	90 (1*S*,2*S*)
6	Ph	Me	H	H_2O	0.1	**6e**	61	95 (1*S*,2*S*)
7	2-Naphthyl	H	H	H_2O	0.1	**6f**	43	87
8	4-MePh	H	H	H_2O	0.1	**6g**	43	84 (1*S*,2*S*)
9	4-Br-Ph	H	H	H_2O	0.5	**6h**	53	92 (1*S*,2*S*)
10	Me	H	H	H_2O	0.1	**6i**	Trace	—
11	$-(CH_2)_4-$	H	H	H_2O	0.1	**6j**	Trace	—
12	Ph	H	H	DCM	0.5	**6a**	60	92 (1*S*,2*S*)
13	Ph	H	OMe	DCM	0.5	**6b**	49	90 (1*S*,2*S*)
14	Ph	H	Me	DCM	0.5	**6c**	46	47 (1*S*,2*S*)
15	Ph	H	Br	DCM	0.5	**6d**	Trace	—
16	2-Naphthyl	H	H	DCM	0.5	**6f**	33	70
17	4-MePh	H	H	DCM	0.5	**6g**	Trace	—
18	$-(CH_2)_4-$	H	H	DCM	0.5	**6j**	Trace	—

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.
[c] The reaction was conducted in the presence of 2 mol % of the catalyst.

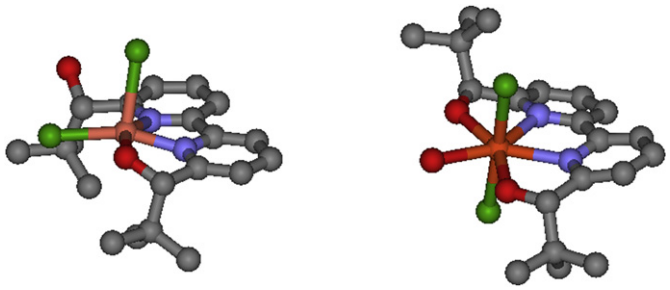
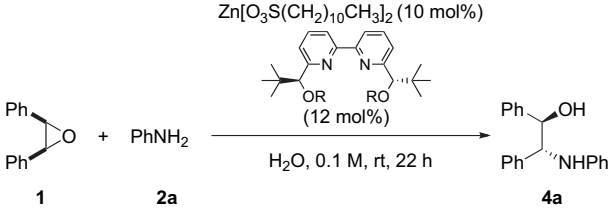


Figure 3. X-ray structure of [$CuBr_2$·**3**] (left) and [$ScBr_2$·H_2O·**3**]$^+$ moiety in the X-ray structure of [$ScBr_2$·H_2O·**3**]·Br·H_2O.[2c] Hydrogen atoms are omitted for clarity.

Table 6
Ring-opening reactions of *meso*-epoxide (**1**) with Zn(II) and chiral bipyridine derivatives



Entry	R		Yield[a] (%)	ee[b] (%)
1	H, H	**3**	97	92
2	H, Me	**7**	46	9
3	Me, Me	**8**	25	0

[a] Isolated yield.
[b] ee was determined by chiral HPLC analysis.

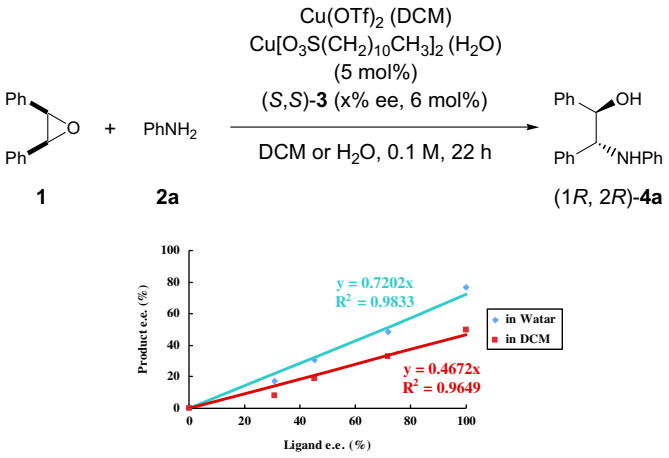


Figure 4. Non-linear effect experiments of ring-opening reaction of *cis*-stilbene (**1**) with aniline using Cu(II) catalyst in water (light blue) and in DCM (red).

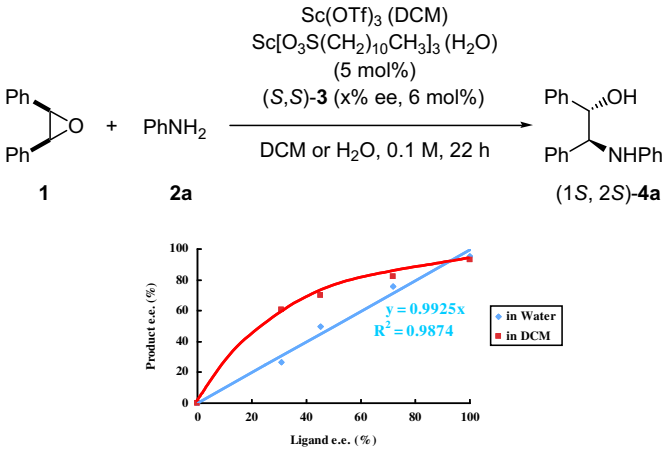


Figure 5. Non-linear effect experiments of ring-opening reaction of *cis*-stilbene with aniline using Sc(III) catalyst in water (light blue) and in DCM (red).

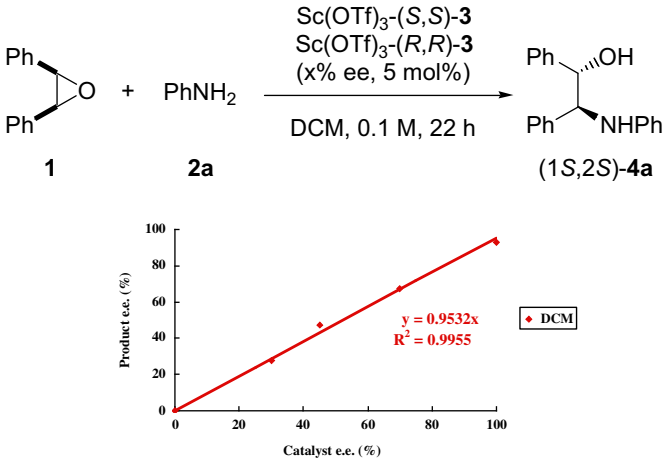


Figure 6. Non-linear effect experiments using pre-mixed catalysts in DCM.

4. Experimental section

4.1. General

IR spectra were measured with JASCO FT/IR-610 spectrometers. Data are represented as frequency of absorption (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA 400, LA-500, or LA-600 spectrometer in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) or chloroform served as internal standard (δ=0 or 7.26) for ^1H NMR and $CDCl_3$ as internal standard (δ=77.0) for ^{13}C NMR. Mass spectra were recorded on Brucker Daltonics BioTOF II spectrometer (ESI). Optical rotations were measured on a JASCO P1010 polarimeter using a 2 mL cell with 1 dm path length. Analytical high performance liquid chromatography (HPLC) was performed on a Shimadzu VP-series instrument equipped with a variant wavelength detector (D lump; 190–600 nm) using Daicel columns (0.46 cm ID×25 cm) as chiral stationary phase. Preparative thin-layer chromatography (TLC) was carried out using Wakogel B-5F. Column chromatography was carried out using Kanto silica gel 60 N (spherical, neutral, 40–100 mesh).

4.2. Materials

Chiral bipyridine ligand **3**, **7**, and **8** were prepared according to the reported procedure.[13] Aromatic epoxides were prepared by *m*CPBA oxidation of the corresponding *cis*-alkenes according to the reported procedures.[14,15] $M[O_3S(CH_2)_{10}CH_3]_n$ were prepared by reported procedures using MCl_n and $CH_3(CH_2)_{10}SO_3Na$ in water.[3b] All other compounds were commercially available and used as received except aniline and substituted anilines, which were distilled from calcium hydride before use.

4.2.1. Characterization of surfactant-type catalysts. Elementary analysis of $M[O_3S(CH_2)_{10}CH_3]_n$:

$Sc[O_3S(CH_2)_{10}CH_3]_3\cdot 3H_2O$ (white powder): Calcd C: 51.04, H: 9.64; found C: 51.31, H: 9.40.
$Zn[O_3S(CH_2)_{10}CH_3]_2\cdot 5H_2O$ (white powder): calcd C: 44.06, H: 9.24; found C: 44.61, H: 8.97.
$Cu[O_3S(CH_2)_{10}CH_3]_2\cdot 2H_2O$ (pale blue powder): calcd C: 48.17, H: 9.10; found C: 47.91, H: 8.93.

4.3. General procedure for *meso*-epoxide-opening reaction with anilines

A mixture of $Zn[O_3S(CH_2)_{10}CH_3]_2$ or $Cu[O_3S(CH_2)_{10}CH_3]_2$ and bipyridine ligand **3** in water was stirred for 1 h at room temperature. *meso*-Epoxide and aniline were then added to the mixture. The mixture was further stirred for 22–48 h at room temperature. The resulting mixture was quenched with satd $NaHCO_3$ aq and brine. The aqueous layer was extracted with dichloromethane (three times), and the combined organic layers were washed with brine, and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The residue was purified by preparative TLC (elution *n*-hexane/ethyl acetate=3/1) to give the corresponding amino alcohols.

4.3.1. Physical data of amino alcohols.

*4.3.1.1. (1R,2R)-1,2-Diphenyl-2-(phenylamino)-ethanol (**4a**).* ^1H NMR δ 2.75 (br s, 1H), 4.50 (d, J=5.5 Hz, 1H), 4.55 (br s, 1H), 4.85 (d, J=5.5 Hz, 1H), 6.56–6.58 (m, 1H), 6.57–6.58 (m, 1H), 6.83–6.84 (m, 1H), 7.06–7.08 (m, 2H), 7.18–7.28 (m, 10H); ^{13}C NMR δ 64.4, 77.9, 110.6, 114.1, 116.6, 118.1, 126.5, 127.2, 127.7, 128.1, 128.4, 128.7, 129.5, 129.7, 139.7, 140.5, 147.5; IR (KBr): 3406, 3065, 3031, 1616, 1513, 1492, 1342, 1164, 1121, 1068, 698 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{20}H_{20}NO$ $[M+H]^+$ 290.1545, found 290.1517; $[\alpha]_D^{26}$ +46.4 (*c* 1.00, CH_2Cl_2, 92% ee (1*R*,2*R*)); lit.[5d] $[\alpha]_D^{24}$ −45.2 (*c* 0.52, CH_2Cl_2, 92% ee (1*S*,2*S*)); HPLC (Daicel Chiralpak AD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=25.5 min (minor, (1*S*,2*S*)); t_R=29.8 min (major, (1*R*,2*R*))).

*4.3.1.2. 1,2-Diphenyl-2-(3-trifluorophenyl)-ethanol (**4b**).* ^1H NMR δ 2.75 (br s, 1H), 4.53 (d, J=6.2 Hz, 1H), 4.54 (br s, 1H), 4.88 (d,

J=6.2 Hz, 1H), 6.52–6.54 (m, 2H), 6.53–6.65 (m, 1H), 7.03–7.06 (m, 2H), 7.20–7.27 (m, 9H); ^{13}C NMR δ 64.8, 78.0, 114.2, 118.0, 126.6, 127.3, 127.5, 127.9, 128.2, 128.6, 129.0, 140.2, 140.6, 147.2; IR (KBr): 3407, 3058, 3028, 1502, 1453, 1317, 1262, 1155, 1051 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{21}H_{19}F_3NO$ [M+H]$^+$ 358.1418, found 358.1457; $[\alpha]_D^{26}$ +42.1 (*c* 0.99, CH_2Cl_2, 92% ee); HPLC (Daicel Chiralpak AD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=15.9 min (minor); t_R=18.5 min (major)).

*4.3.1.3. (1R,2R)-2-(Naphthalen-1-ylamino)-1,2-diphenylethanol (**4c**).* ^{1}H NMR δ 2.54 (br s, 1H), 4.68 (d, J=9.6 Hz, 1H), 4.99(d, J=9.6 Hz, 1H), 5.51 (br s, 1H), 6.27–6.28 (m, 1H), 7.06–7.41 (m, 14H), 7.72–7.77 (m, 1H), 7.96–7.97 (m, 1H); ^{13}C NMR δ 64.5, 78.2, 106.7, 117.7, 120.0, 124.0, 124.8, 125.6, 126.3, 126.5, 127.2, 127.5, 128.0, 128.3, 128.6, 128.7, 134.2, 139.9, 140.7, 142.1; IR (KBr): 3406, 3059, 3030, 1580, 1523, 1476, 1453, 1407, 1342, 1280, 1032, 768, 700 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{24}H_{22}NO$ [M+H]$^+$ 340.1701, found 340.1680; $[\alpha]_D^{26}$ +126.6 (*c* 1.07, CH_2Cl_2, 95% ee (1*R*,2*R*)); lit.[5d] $[\alpha]_D^{22}$ −144.9 (*c* 0.39, CH_2Cl_2, 91% ee (1*S*,2*S*)); HPLC (Daicel Chiralpak OD, eluent *n*-hexane/*i*-PrOH=4/1, flow rate 1.0 mL/min (major, (1*R*,2*R*)), t_R=11.4 min; t_R=21.0 min (minor, (1*S*,2*S*))).

*4.3.1.4. (1R,2R)-2-(N-Methyl-N-phenylamino)-1,2-diphenylethanol (**4d**).* ^{1}H NMR δ 2.70 (s, 3H), 3.95 (br s, 1H), 4.86 (d, J=9.7 Hz, 1H), 5.27(d, J=9.7 Hz, 1H), 6.88–6.90 (m, 1H), 6.90–7.00 (m, 4H), 7.11–7.27 (m, 8H), 7.36–7.38 (m, 2H); ^{13}C NMR δ 32.8, 71.6, 73.6, 117.7, 120.3, 127.6, 127.7, 127.8, 128.0, 128.2, 128.8, 129.1, 134.8, 140.7, 151.4; IR (KBr): 3423, 3060, 3030, 1597, 1561, 1451, 1320, 1188, 1079, 1055, 1030, 935, 754, 698 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{21}H_{22}NO$ [M+H]$^+$ 304.1701, found 304.1739; $[\alpha]_D^{26}$ −171.6 (*c* 0.99, CH_2Cl_2, 95% ee (1*R*,2*R*)); lit.[5d] $[\alpha]_D^{22}$ +171.7 (*c* 0.53, CH_2Cl_2, 96% ee, (1*S*,2*S*)); HPLC (Daicel Chiralpak ASH, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 0.8 mL/min, t_R=15.2 min (major, (1*R*,2*R*)); t_R=21.0 min (minor, (1*S*,2*S*))).

*4.3.1.5. (1R,2R)-2-(2-Methoxyphenylamino)-1,2-diphenylethanol (**4e**).* ^{1}H NMR δ 2.66 (br s, 1H), 3.85 (s, 3H), 4.50 (d, J=6.2 Hz, 1H), 4.86 (d, J=6.2 Hz, 1H), 5.12 (br s, 1H), 6.37–6.39 (m, 1H), 6.58–6.74 (m, 3H), 7.14–7.26 (m, 10H); ^{13}C NMR δ 55.6, 65.0, 78.3, 109.7, 111.8, 117.2, 121.1, 126.7, 127.3, 127.8, 128.0, 128.4, 137.1, 140.7, 147.4; IR (KBr): 3403, 3061, 3027, 1601, 1509, 1454, 1428, 1342, 1224, 1125, 1048, 1026, 768, 738, 700 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{21}H_{22}NO_2$ [M+H]$^+$ 320.1650, found 320.1665; $[\alpha]_D^{26}$ +51.9 (*c* 1.08, CH_2Cl_2, 95% ee (1*R*,2*R*)); lit.[5d] $[\alpha]_D^{22}$ −48.0 (*c* 0.54, CH_2Cl_2, 93% ee, (1*S*,2*S*)); HPLC (Daicel Chiralpak ASH, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 0.8 mL/min, t_R=20.4 min (minor, (1*S*,2*S*)); t_R=24.9 min (major, (1*R*,2*R*))).

*4.3.1.6. (1R,2R)-2-(Phenylamino)-1,2-di(m-tolyl)-ethanol (**4f**).* ^{1}H NMR δ 2.28 (s, 3H), 2.31 (s, 3H), 2.44 (br s, 1H), 4.48 (d, J=5.5 Hz, 1H), 4.55 (br s, 1H), 4.85 (d, J=5.5 Hz, 1H), 6.50–6.52 (m, 2H), 6.60–6.64 (m, 1H), 7.02–7.17 (m, 10H); ^{13}C NMR δ 21.4, 64.6, 77.9, 114.1, 117.8, 123.5, 124.3, 127.9, 128.1, 128.3, 128.4, 128.6, 129.0, 137.9, 138.2, 140.3, 140.6, 147.3; IR (KBr): 3406, 3049, 3021, 1602, 1503, 1430, 1317, 1267, 1155, 1048, 789, 749, 706 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{22}H_{24}NO$ [M+H]$^+$ 318.1858, found 318.1827; $[\alpha]_D^{27}$ +41.3 (*c* 0.05, CH_2Cl_2, 95% ee (1*R*,2*R*)); lit.[17] $[\alpha]_D^{23}$ +50.2 (*c* 0.89, CH_2Cl_2, 95% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak OD, eluent *n*-hexane/*i*-PrOH=9/1, flow rate 0.8 mL/min, t_R=12.1 min (major, (1*R*,2*R*)); t_R=15.9 min (minor, (1*S*,2*S*))).

*4.3.1.7. (1R,2R)-2-(Phenylamino)-1,2-di(p-tolyl)-ethanol (**4g**).* ^{1}H NMR δ 2.28 (s, 3H), 2.31 (s, 3H), 2.44 (br s, 1H), 4.48 (d, J=5.5 Hz, 1H), 4.55 (br s, 1H), 4.81 (d, J=5.5 Hz, 1H), 6.49–6.51 (m, 2H), 6.60–6.64 (m, 1H), 7.01–7.22 (m, 10H); ^{13}C NMR δ 21.1, 64.3, 77.8, 114.1, 117.8, 126.5, 127.2, 128.9, 129.0, 129.2, 137.0, 137.3, 137.4, 137.7, 147.7; IR (KBr): 3398, 3020, 2920, 1602, 1502, 1318, 1048, 819, 749, 691 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{22}H_{24}NO$ [M+H]$^+$ 318.1858, found 318.1827; $[\alpha]_D^{26}$ +74.4 (*c* 1.01, CH_2Cl_2, 95% ee (1*R*,2*R*)); lit.[5d] $[\alpha]_D^{24}$ −47.3 (*c* 0.54, CH_2Cl_2, 90% ee, (1*S*,2*S*)); HPLC (Daicel Chiralpak ADH, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=25.2 min (minor, (1*S*,2*S*)); t_R=30.6 min (major, (1*R*,2*R*))).

*4.3.1.8. (1R,2R)-2-(Phenylamino)-1,2-di(p-bromophenyl)ethanol (**4h**).* ^{1}H NMR δ 2.58 (br s, 1H), 4.40 (d, J=6.2 Hz, 1H), 4.52 (br s, 1H), 4.73 (d, J=6.2 Hz, 1H), 6.48–6.49 (m, 2H), 6.66–6.67 (m, 1H), 7.02–7.07 (m, 6H), 7.34–7.40 (m, 4H); ^{13}C NMR δ 64.3, 77.3, 114.2, 118.4, 121.5, 122.0, 128.3, 129.0, 129.1, 131.4, 131.7, 138.9, 139.3, 146.7; IR (KBr): 3398, 3049, 2363, 2344, 1601, 1501, 1486, 1430, 1403, 1315, 1071, 1008, 829, 751, 691 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{20}H_{18}Br_2NO$ [M+H]$^+$ 447.9735, found 447.9763; $[\alpha]_D^{26}$ +72.0 (*c* 1.01, CH_2Cl_2, 90% ee); HPLC (Daicel Chiralpak AD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=32.3 min (minor, (1*S*,2*S*)); t_R=41.5 min (major, (1*R*,2*R*))).

*4.3.1.9. (1R,2R)-3-(Phenylamino)-2-butanol (**4i**).* ^{1}H NMR δ 1.14 (d, J=6.9 Hz, 3H), 1.25 (d, J=6.9 Hz, 3H), 2.62 (br s, 1H), 3.29–3.34 (m, 1H), 3.61–3.65 (m, 1H), 6.66–6.74 (m, 3H), 7.15–7.23 (m, 2H); ^{13}C NMR δ 17.3, 19.5, 56.0, 71.3, 114.3, 118.2, 129.3, 147.8; IR (KBr): 3398, 2973, 2929, 1602, 1503, 1318, 1256, 750, 693 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{10}H_{16}NO$ [M+H]$^+$ 166.1232, found 166.1259; $[\alpha]_D^{25}$ −50.1 (*c* 0.99, CH_2Cl_2, 90% ee (1*R*,2*R*)); lit.[16] $[\alpha]_D^{25}$ −38.3 (*c* 0.95, benzene, >99.9% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak OD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=26.0 min (major (1*R*,2*R*)); t_R=29.9 min (minor (1*S*,2*S*))).

*4.3.1.10. 3-(1-Naphthylamino-1-yl)-2-butanol (**4j**).* ^{1}H NMR δ 1.21 (d, J=6.4 Hz, 3H), 1.28 (d, J=6.4 Hz, 3H), 2.60 (br s, 1H), 3.49–3.56 (m, 1H), 3.75–3.82 (m, 1H), 4.24 (br s, 1H), 6.68 (d, J=7.2 Hz, 1H), 7.20–7.44 (m, 4H), 7.75–7.82 (m, 2H); ^{13}C NMR δ 17.0, 19.8, 55.3, 71.4, 105.9, 117.9, 119.9, 124.0, 124.8, 125.7, 126.5, 128.7, 134.4, 142.6; IR (KBr): 3424, 2970, 2927, 1580, 1526, 1408, 1121, 1011, 769 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{14}H_{18}NO$ [M+H]$^+$ 216.1388, found 216.1400; $[\alpha]_D^{26}$ −64.6 (*c* 1.00, CH_2Cl_2, 67% ee); HPLC (Daicel Chiralpak AD, eluent *n*-hexane/*i*-PrOH=30/1, flow rate 1.0 mL/min, t_R=15.0 min (minor); t_R=17.0 min (major)).

*4.3.1.11. (1R,2R)-2-Phenylamino-1-cyclohexanol (**4k**).* ^{1}H NMR δ 1.10–1.08 (m, 1H), 1.27–1.43 (m, 3H), 1.40–1.43 (m, 2H), 1.70–1.78 (m, 2H), 3.00 (br s, 1H), 3.11–3.16 (m, 1H), 3.33–3.37 (m, 1H), 6.70–6.76 (m, 2H), 7.16–7.25 (m, 2H); ^{13}C NMR δ 24.2, 25.0, 31.5, 33.1, 60.2, 74.5, 114.4, 118.4, 129.3, 147.7; IR (KBr): 3394, 2924, 2858, 1599, 1513, 1497, 1449, 1321, 1052, 864, 741, 689 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{12}H_{18}NO$ [M+H]$^+$ 192.1388, found 192.1377; $[\alpha]_D^{26}$ −44.7 (*c* 0.99, CH_2Cl_2, 90% ee (1*R*,2*R*)); lit.[17] $[\alpha]_D^{25}$ −37.7 (*c* 0.54, CH_2Cl_2, 54% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak OD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=18.9 min (minor, (1*S*,2*S*)); t_R=22.3 min (major, (1*R*,2*R*))).

*4.3.1.12. 2-(1-Naphthylamino-1-yl)-1-cyclohexanol (**4l**).* ^{1}H NMR δ 1.05–1.10 (m, 1H), 1.29–1.44 (m, 3H), 1.69–1.78 (m, 2H), 2.11–2.23 (m, 2H), 2.85 (br s, 1H), 3.29–3.36 (m, 1H), 3.46–3.52 (m, 1H), 6.76 (d, J=7.2 Hz, 1H), 7.29–7.44 (m, 4H), 7.72–7.82 (m, 1H); ^{13}C NMR δ 24.2, 25.0, 31.5, 33.1, 60.2, 74.5, 114.4, 118.4, 129.3, 147.7; IR (KBr): 3515, 3399, 3049, 2922, 2855, 1576, 1537, 1489, 1446, 1411, 1282, 1064, 766 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{16}H_{20}NO$ [M+H]$^+$ 242.1545, found 242.1552; $[\alpha]_D^{26}$ −63.0 (*c* 0.99, CH_2Cl_2, 90% ee); HPLC (Daicel Chiralpak OD, eluent *n*-hexane/*i*-PrOH=19/1, flow rate 1.0 mL/min, t_R=18.9 min (minor); t_R=22.3 min (major)).

*4.3.1.13. 2-(N-Methyl-N-phenylamino)-1,2-di(p-tolyl)-ethanol (**4m**).* ^{1}H NMR δ 2.20 (s, 3H), 2.24 (s, 3H), 2.64 (s, 3H), 3.97 (br s, 1H), 4.85 (d, J=10.3 Hz, 1H), 5.23 (d, J=10.3 Hz, 1H), 6.85–6.93 (m, 5H), 7.00–7.04 (m, 4H), 7.21–7.29 (m, 4H); ^{13}C NMR δ 21.0, 32.4, 71.1,

73.3, 111.7, 120.2, 127.5, 128.6, 128.9, 129.1, 131.6, 137.2, 137.3, 137.6, 151.5; IR (KBr): 3422, 3023, 2918, 2882, 1597, 1501, 1451, 1379, 1318, 1180, 1032, 816, 751, 694 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{23}H_{26}NO$ $[M+H]^+$ 332.2014, found 332.1999; $[\alpha]_D^{26}$ −134.3 (*c* 1.00, CH_2Cl_2, 90% ee); HPLC (Daicel Chiralpak ASH, eluent *n*-hexane/*i*-PrOH=40/1, flow rate 1.0 mL/min, t_R=16.1 min (major); t_R=22.6 min (minor)).

*4.3.1.14. (1R,2R)-2-(N-Methyl-N-phenylamino)-1,2-di(4-bromophenyl)ethanol (**4n**).* ^{1}H NMR δ 2.67 (s, 3H), 3.88 (br s, 1H), 4.67 (d, *J*=9.6 Hz, 1H), 5.17 (d, *J*=9.6 Hz, 1H), 6.78–6.81 (m, 2H), 6.93–6.97 (m, 3H), 7.21–7.36 (m, 8H); ^{13}C NMR δ 32.8, 70.8, 73.7, 118.2, 121.1, 121.8, 122.0, 129.2, 130.3, 130.9, 131.3, 131.4, 132.4, 133.0, 139.4, 150.8; IR (KBr): 3425, 2883, 1699, 1594, 1490, 1380, 1311, 1185, 1069, 1009, 820, 753, 694 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{21}H_{20}Br_2NO$ $[M+H]^+$ 461.9891, found 461.9894; $[\alpha]_D^{27}$ −61.5 (*c* 1.02, CH_2Cl_2, 90% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ASH, eluent *n*-hexane/*i*-PrOH=40/1, flow rate 1.0 mL/min, t_R=26.8 min (major, (1*R*,2*R*)); t_R=31.3 min (minor, (1*S*,2*S*))).

*4.3.1.15. 2-(N-Methyl-N-phenylamino)-1,2-di(2-naphthyl-1-yl)-ethanol (**4o**).* ^{1}H NMR δ 2.76 (s, 3H), 3.88 (br s, 1H), 5.16 (d, *J*=9.6 Hz, 1H), 5.59 (d, *J*=9.6 Hz, 1H), 6.92–6.94 (m, 1H), 7.07–7.09 (m, 2H), 7.11–7.18 (m, 4H), 7.28–7.68 (m, 8H), 7.88–7.97 (m, 4H); ^{13}C NMR δ 32.9, 71.6, 73.7, 117.8, 120.5, 122.7, 125.1, 125.8, 127.5, 127.8, 127.9, 128.0, 129.2, 133.1, 134.5, 138.1, 151.3; IR (KBr): 3422, 3054, 1690, 1596, 1501, 1347, 1269, 1168, 1119, 859, 820, 749 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{29}H_{26}NO$ $[M+H]^+$ 404.2014, found 404.2005; $[\alpha]_D^{26}$ −60.2 (*c* 0.99, CH_2Cl_2, 90% ee); HPLC (Daicel Chiralpak ASH, eluent *n*-hexane/*i*-PrOH=40/1, flow rate 1.0 mL/min, t_R=44.4 min (major); t_R=50.1 min (minor)).

4.4. General procedure for *meso*-epoxide ring-opening reaction with indole

A mixture of $Cu[O_3S(CH_2)_{10}CH_3]_2$ and bipyridine ligand **3** in water was stirred for 1 h at room temperature. *meso*-epoxide and indole were then added to the mixture. The mixture was further stirred for 22–48 h at room temperature. The resulting mixture was quenched with satd $NaHCO_3$ aq and brine. The aqueous layer was extracted with dichloromethane (three times), and the combined organic layers were washed with brine, and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The residue was purified by preparative TLC (elution *n*-hexane/ethyl acetate=3/2) to give the product.

4.4.1. Physical data of the amino indole adducts.

*4.4.1.1. (1S,2S)-2-(1H-Indole-3-yl)-1,2-diphenylethanol (**6a**).* ^{1}H NMR δ 2.56 (br s, 1H), 4.55 (d, *J*=8.2 Hz, 1H), 5.28 (d, *J*=8.2 Hz, 1H), 6.99–7.20 (m, 14H), 7.42–7.43 (m, 1H), 8.09 (br s, 1H); ^{13}C NMR δ 52.0, 77.6, 111.1, 115.2, 119.3, 119.6, 122.2, 122.4, 126.3, 126.8, 127.3, 127.5, 127.9, 128.0, 128.6, 136.3, 141.7, 142.4; IR (KBr): 3348, 3026, 2873, 1490, 1457, 1340, 1224, 1042, 744, 698 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{22}H_{20}NO$ $[M+H]^+$ 314.1545, found 314.1578; $[\alpha]_D^{27}$ +61.3 (*c* 1.08, $CHCl_3$, 96% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{24}$ −63.4 (*c* 1.08, $CHCl_3$, 93% ee, (1*R*,2*R*)); HPLC (Daicel Chiralpak ODH, eluent *n*-hexane/*i*-PrOH=4/1, flow rate 0.8 mL/min, t_R=34.6 min (minor, (1*R*,2*R*)); t_R=48.3 min (major, (1*S*,2*S*))).

*4.4.1.2. (1S,2S)-2-(5-Methoxy-1H-indole-3-yl)-1,2-diphenylethanol (**6b**).* ^{1}H NMR δ 2.04 (br s, 1H), 3.72 (s, 3H), 4.53 (d, *J*=7.6 Hz, 1H), 5.33 (d, *J*=7.6 Hz, 1H), 6.77–6.82 (m, 2H), 7.08–7.30 (m, 12H), 8.02 (br s, 1H); ^{13}C NMR δ 52.0, 55.8, 77.3, 101.4, 111.7, 112.6, 115.0, 123.4, 126.3, 126.7, 127.3, 127.9, 128.0, 128.1, 128.6, 131.5, 141.9, 142.6, 154.1; IR (KBr): 3518, 3369, 3314, 3025, 1623, 1583, 1485, 1453, 1437, 1213, 1166, 1024, 926, 823, 808, 754, 727, 695 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{23}H_{22}NO_2$ $[M+H]^+$ 344.1651, found 344.1679; $[\alpha]_D^{28}$ +14.0 (*c* 0.96, $CHCl_3$, 92% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{24}$ −15.0 (*c* 0.96, $CHCl_3$, 92% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ADH, eluent *n*-hexane/*i*-PrOH=7/3, flow rate 1.0 mL/min, t_R=21.8 min (major, (1*S*,2*S*)); t_R=28.5 min (minor, (1*R*,2*R*))).

*4.4.1.3. (1S,2S)-2-(5-Methyl-1H-indole-3-yl)-1,2-diphenylethanol (**6c**).* ^{1}H NMR δ 2.34 (s, 3H), 2.49 (br s, 1H), 4.56 (d, *J*=8.3 Hz, 1H), 5.31(d, *J*=9.6 Hz, 1H), 6.97–6.99 (m, 1H), 7.06–7.30 (m, 13H), 8.03 (br s, 1H); ^{13}C NMR δ 21.5, 52.1, 77.7, 110.7, 113.5, 114.8, 119.0, 122.6, 124.0, 126.3, 126.8, 127.3, 127.9, 128.1, 128.6, 128.9, 134.7, 141.8, 142.4; IR (KBr): 3490, 3285, 3025, 1490, 1454, 1225, 1111, 1073, 1024, 797, 761, 729, 697, 647 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.1701, found 328.1715; $[\alpha]_D^{30}$ +33.7 (*c* 0.99, $CHCl_3$, 92% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{24}$ −137.6 (*c* 0.97, $CHCl_3$, 85% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ODH, eluent *n*-hexane/*i*-PrOH=7/3, flow rate 0.7 mL/min, t_R=29.6 min (major, (1*S*,2*S*)); t_R=36.9 min (minor, (1*R*,2*R*))).

*4.4.1.4. (1S,2S)-2-(5-Bromo-1H-indole-3-yl)-1,2-diphenylethanol (**6d**).* ^{1}H NMR δ 2.03 (br s, 1H), 4.51 (d, *J*=7.6 Hz, 1H), 5.27 (d, *J*=7.6 Hz, 1H), 7.06–7.34 (m, 13H), 7.47–7.48 (m, 1H), 8.18 (br s, 1H); ^{13}C NMR δ 51.6, 77.6, 79.0, 112.5, 112.9, 114.9, 121.9, 123.8, 125.1, 126.5, 126.6, 126.9, 127.4, 127.9, 128.0, 128.1, 128.2, 128.5, 129.4, 134.8, 141.4, 142.3; IR (KBr): 3396, 3347, 3243, 1603, 1491, 1455, 1332, 1048, 1034, 887, 798, 751, 741, 699 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{22}H_{19}BrNO$ $[M+H]^+$ 392.0630, found 392.0646; $[\alpha]_D^{30}$ +15.4 (*c* 1.00, $CHCl_3$, 95% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{22}$ −13.0 (*c* 0.43, $CHCl_3$, 90% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ODH, eluent *n*-hexane/*i*-PrOH=7/3, flow rate 1.0 mL/min, t_R=12.8 min (major, (1*S*,2*S*)); t_R=22.7 min (minor, (1*R*,2*R*))).

*4.4.1.5. (1S,2S)-2-(2-Methyl-1H-indole-3-yl)-1,2-diphenylethanol (**6e**).* ^{1}H NMR δ 2.03 (s, 3H), 2.54 (br s, 1H), 4.10 (d, *J*=7.2 Hz, 1H), 5.69 (d, *J*=7.2 Hz, 1H), 7.03–7.21 (m, 13H), 7.66 (d, *J*=7.2 Hz, 1H), 7.93 (br s, 1H); ^{13}C NMR δ; IR (KBr): 3400, 3058, 3027, 1617, 1491, 1458, 1387, 1303, 1246, 1185, 1079, 1051, 909, 740, 699 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.1701, found 328.1687; $[\alpha]_D^{30}$ +89.8 (*c* 1.09, $CHCl_3$, 95% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{22}$ −153.5 (*c* 0.68, $CHCl_3$, 98% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ADH, eluent *n*-hexane/*i*-PrOH=9/1, flow rate 1.0 mL/min, t_R=43.8 min (major, (1*S*,2*S*)); t_R=46.8 min (minor, (1*R*,2*R*))).

*4.4.1.6. 2-(1H-Indole-3-yl)-1,2-di(naphthalene-2-yl)ethanol (**6f**).* ^{1}H NMR δ 2.61 (br s, 1H), 4.91 (d, *J*=7.6 Hz, 1H), 5.64 (d, *J*=7.6 Hz, 1H), 6.96–6.99 (m, 1H), 7.12–7.7.15 (m, 1H), 7.31–7.46 (m, 9H), 7.59–7.74 (m, 8H), 8.12 (br s, 1H); ^{13}C NMR δ 51.8, 77.5, 111.1, 115.1, 119.7, 122.4, 122.8, 124.8, 125.4, 125.6, 125.7, 127.1, 127.5, 127.6, 127.8, 128.0, 132.2, 132.9, 133.1, 133.4, 136.3, 139.3, 139.9; IR (KBr): 3423, 3335, 3051, 2879, 1599, 1508, 1457, 1420, 1342, 1271, 1122, 1100, 1034, 908, 815, 745 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{30}H_{24}NO$ $[M+H]^+$ 414.1858, found 414.1858; $[\alpha]_D^{29}$ +74.1 (*c* 0.96, $CHCl_3$, 78% ee); HPLC (Daicel Chiralpak ADH, eluent *n*-hexane/*i*-PrOH=4/1, flow rate 1.0 mL/min, t_R=49.6 min (major); t_R=66.1 min (minor)).

*4.4.1.7. (1S,2S)-2-(1H-Indole-3-yl)-1,2-di-p-tolylethanol (**6g**).* ^{1}H NMR δ 2.21 (s, 3H), 2.26 (br s, 1H), 2.27 (s, 3H), 4.55 (d, *J*=7.6 Hz, 1H), 5.28 (d, *J*=7.6 Hz, 1H), 6.94 (d, *J*=8.3 Hz, 2H), 7.00–7.04 (m, 5H), 7.11–7.17 (m, 3H), 7.22–7.24 (m, 2H), 7.45 (d, *J*=6.9 Hz, 1H), 8.10 (br s, 1H); ^{13}C NMR δ 20.9, 21.1, 51.3, 60.4, 77.5, 111.0, 115.6, 119.4, 119.5, 122.2, 122.5, 126.7, 126.8, 127.0, 127.6, 128.5, 128.6, 128.8, 129.0, 135.6, 136.3, 136.8, 138.9, 139.5; IR (KBr): 3412, 3020, 2918, 1511, 1489, 1419, 1339, 1189, 1036, 813, 742, 576 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{24}H_{24}NO$ $[M+H]^+$ 342.1858, found 342.1822; $[\alpha]_D^{29}$ +43.8 (*c* 0.98, $CHCl_3$, 70% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{24}$ −54.5 (*c* 0.81, $CHCl_3$, 90% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ODH, eluent *n*-hexane/*i*-PrOH=4/1, flow rate 1.0 mL/min, t_R=23.4 min (major, (1*S*,2*S*)); t_R=27.9 min (minor, (1*R*,2*R*))).

*4.4.1.8. (1S,2S)-1,2-Bis(4-bromophenyl)-2-(1H-indole-3-yl)ethanol (**6h**).* ^{1}H NMR δ 2.60 (br s, 1H), 4.42 (d, J=8.3 Hz, 1H), 5.17 (d, J=8.3 Hz, 1H), 6.93 (d, J=8.9 Hz, 2H), 7.01–7.04 (m, 3H), 7.15–7.38 (m, 8H), 8.18 (br s, 1H); ^{13}C NMR δ 51.4, 76.8, 111.3, 114.1, 119.1, 119.8, 120.3, 121.3, 122.3, 122.5, 127.2, 128.4, 128.6, 130.3, 131.1, 131.3, 136.3, 140.3, 141.0; IR (KBr): 3411, 3055, 2892, 1702, 1591, 1486, 1456, 1405, 1339, 1100, 1071, 1040, 1009, 907, 833, 817, 781, 743 cm^{-1}; HRMS (ESI, Pos.): Calcd for $C_{22}H_{18}Br_2NO$ $[M+H]^+$ 471.9735, found 471.9711; $[\alpha]_D^{29}$ +78.7 (*c* 1.02, $CHCl_3$, 90% ee (1*S*,2*S*)); lit.[8d] $[\alpha]_D^{28}$ −28.9 (*c* 0.90, $CHCl_3$, 92% ee (1*R*,2*R*)); HPLC (Daicel Chiralpak ADH, eluent *n*-hexane/*i*-PrOH=7/3, flow rate 1.0 mL/min, t_R=14.9 min (major, (1*S*,2*S*)); t_R=18.7 min (minor, (1*R*,2*R*))).

4.5. Crystallization of [3·CuBr$_2$] complexes

Crystallization of [**3**·$CuBr_2$] complex was carried out as follows: To a solution of $CuBr_2$ (9.6 mg, 0.043 mmol) in DME (1.5 mL) was added **3** (14.1 mg, 0.043 mmol) at room temperature. The solution was stirred at 25 °C. Water (0.07 mL) was then added to the mixture, which was cooled to room temperature. After 3 days, crystals suitable for X-ray analysis were formed.

Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC-698334. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 J 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

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