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Chiral Primary Amine Catalyzed Asymmetric Epoxidation of α-Substituted Acroleins

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1,1-Disubstituted terminal alkenes remain challenging substrates in asymmetric epoxidation reactions. In this study, chiral primary amines are shown to catalyze the asymmetric epoxidation of α-substituted acroleins, a versatile type of 1,1-disubstituted terminal alkene. Among various chiral primary amines explored, the chiral primary-tertiary vicinal diamine derived from *trans*-1,2-diphenylethane-1,2-diamine is identified as the optimal catalyst, which, in combination with 5-sulfosalicyclic acid (5-SSA), exhibits good catalytic activity (up to 95% yield) and enantioselectivity (up to 88% *ee*). Aqueous 2 M sodium chloride was found to be the optimal reaction media.

Introduction

1,1-Disubstituted terminal alkenes have been regarded as challenging substrates in asymmetric epoxidation reactions.[1] In particular, catalytic asymmetric epoxidation of α-substituted acroleins has not been achieved so far. One conceivable way to address this type of substrate is the well-utilized imminium catalysis.[2] Unfortunately, typical secondary amine based iminium catalysis has been much less effective with α-substituted enones and enals, a result that is mainly ascribed to the sterically demanding nature of α-substituents in the iminium intermediates. Accordingly, iminium-catalyzed epoxidation reactions have been largely limited to α-unsubstituted enones and enals.[3] Catalytic enantioselective reaction with α-substituted enones and enals still represents an elusive target in iminium chemistry. In this regard, α-substituted acroleins are particularly challenging substrates when the difficulties in stereocontrol with β-unsubstituted enals are considered in the context of iminium-enamine catalysis.[2a]

On the other hand, chiral primary amines have recently appeared as efficient aminocatalysts that enable transformations with sterically congested substrates beyond the reach of secondary amines.[4] The use of chiral primary amines has made possible the iminium activation of α-acyloxy acroleins or α-substituted enones toward enantioselective Diels–Alder reactions,[5] [2+2] cycloaddition reactions,[6] and epoxidation[3f] or peroxidation reactions.[3g,3h] We also established chiral primary-tertiary diamines as effective catalysts for enamine activation of both ketones and aldehydes,[7] and this catalysis has now been further expanded to include iminium activation of α-acyloxy acroleins.[5f] More recently, Pihko and co-workers reported that achiral, bulky anilines could catalyze the epoxidation of α-branched acroleins with *tert*-butyl hydroperoxide (TBHP) as the oxidant.[8] Upon the submission of this manuscript, List and co-workers reported a catalytic system that combined chiral primary amines and chiral phosphoric acids for the asymmetric epoxidation of α-substituted enals with excellent enantioselectivity.[9] Nevertheless, a simple, asymmetric catalytic system is still highly desirable. Herein, we wish to report an asymmetric epoxidation of α-substituted acroleins catalyzed by simple chiral primary-tertiary diamines.

Results and Discussions

Initial Trials with Primary Amine Catalysts

Following Pihko's report,[8] we first tested a series of chiral anilines in the epoxidation of 2-benzylacrylaldehyde (**1a**) with TBHP. Aniline-oxazoles such as **3a**–**c** were readily synthesized according to the published procedures.[10] Catalysis by the chiral aniline-oxazoles gave moderate activity, but rather poor enantioselectivity (Scheme 1). Extensive explorations with the aniline derivatives did not lead to satisfactory improvement, and the best enantioselectivity (34% *ee*) was obtained only when a chiral counteranion strategy was applied (catalyst **4**, Scheme 1).[11]

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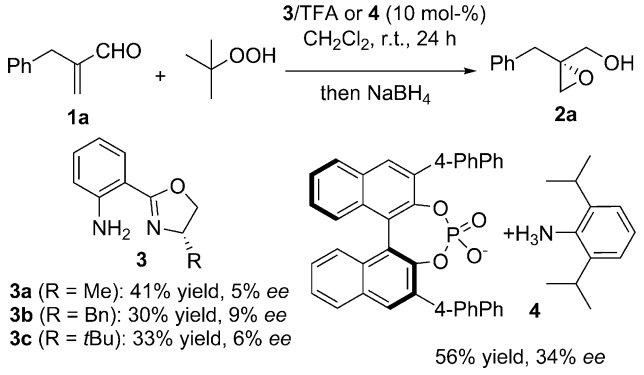
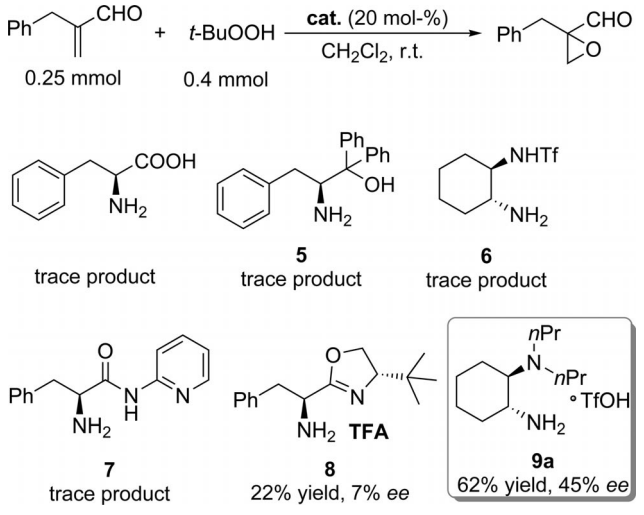


Scheme 1. Chiral aniline catalyzed asymmetric epoxidation reaction of 2-benzylacrylaldehyde.

Other types of chiral primary amines were then screened. To our delight, the chiral primary-tertiary diamine Brønsted acid conjugate catalyst **9a** in combination with trifluoromethanesulfonic acid (TfOH), previously developed in our group,[7a] was found to be the optimal primary amino catalyst for the epoxidation reactions. With 20 mol-% of **9a**/TfOH, the reaction afforded 62% yield and 45% *ee*. In contrast, other chiral pimary amine catalysts, such as amino acids, amino alcohol **5**, amino sulfamide **6**, and amino amide **7**, were nearly inactive for the reaction (Scheme 2).

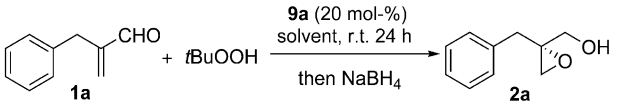


Scheme 2. Screening of different chiral primary amines.

Initial Optimization of the Epoxidation Reaction Catalyzed by 9a

With **9a**/TfOH conjugate as catalyst, the essential reaction conditions were first determined. As shown in Table 1, the reaction proceeded smoothly in nearly all the organic solvents examined with moderate yield and enantioselectivity (Table 1, entries 1–6). Gratifying, the catalytic activity could be significantly improved (Table 1, entry 7, 73% yield, 47% *ee*) with water as solvent, which was then selected as the optimal solvent for subsequent studies.

Table 1. Initial optimization of the epoxidation of 2-benzylacrylaldehyde catalyzed by **9a**.



Entry[a]	Acid[b]	Solvent	Yield [%][c]	*ee* [%][d]
1	TfOH	toluene	59	43
2	TfOH	*n*-hexane	53	46
3	TfOH	THF	27	37
4	TfOH	MeOH	75	41
5	TfOH	CH_3CN	41	39
6	TfOH	CH_2Cl_2	62	45
7	**TfOH**	**H_2O**	**73**	**47**
8	2,4-DNBS	H_2O	59	37
9	DBSA	H_2O	57	32
10	*p*TSA	H_2O	52	28
11	TFA	H_2O	61	10
12	CH_3CO_2H	H_2O	10	<5
13	*m*$NO_2C_6H_4CO_2H$	H_2O	15	10
14	$H_3PW_{12}O_{40}$	H_2O	32	9
15	$Zn(OAc)_2$	H_2O	trace	–
16	–	H_2O	trace	–

[a] Reagents and conditions: 2-benzylacrylaldehyde (73 mg, 0.5 mmol), TBHP (0.8 mmol), solvent (0.5 mL), catalyst (20 mol-%), r.t. [b] 2,4-DNBS: 2,4-dinitrobenzenesulfonic acid; DBSA: 4-dodecylbenzenesulfonic acid. [c] Isolated yield. [d] Determined by HPLC after reduction by $NaBH_4$.

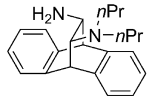
Bearing in mind the dramatic effect of acidic additives in the catalysis of **9a**,[7] we next examined a range of acidic additives to further improve the activity and stereoselectivity. Not unexpectedly, the reaction barely occurred in the absence of any acidic additives (Table 1, entry 16). In general, the use of stronger acids led to better results (Table 1, entries 7–13), and optimal results were obtained with the most acidic additive TfOH (Table 1, entry 7). The unexpected low yield and stereoselectivity exhibited in the presence of $H_3PW_{12}O_{40}$ may be ascribed to its poor solubility in water (Table 1, entry 14). A Lewis acid, $Zn(OAc)_2$, was also tested, but the reaction did not occur (Table 1, entry 15).

Screening of Primary-Tertiary Diamine Catalysts

Under the initial optimized conditions (in H_2O, TfOH), a series of chiral primary-tertiary diamines bearing different skeletons and substituents were synthesized (see the Supporting Information for details) and assessed in the model reaction (Figure 1). As revealed in Table 2, several general observations can be summarized: (a) Vicinal primary-tertiary diamine is the optimal bifunctional catalytic motif for this reaction. The use of other diamines such as primary-secondary diamines **9c**, **10a**, or **11h** (Table 2, entries 3, 6 and 18), gave inferior results or was inactive in the case of primary-primary diamine **9b** (Table 2, entry 2); (b) Among the diamine skeletons examined (**9**–**13**), those based on *trans*-1,2-diphenylethane-1,2-diamine stand out with generally better activity and stereoselectivity (Table 2, entries 11–18); (c) Side chains of the tertiary amine moieties have a significant impact on both activity and enantioselectivity.

9a: $R^1 = R^2 = n$Pr
9b: $R^1 = R^2 = H$
9c: $R^1 = Et$, $R^2 = H$
9d: $R^1 = R^2 = Me$
9e: $R^1 = R^2 = nC_{10}H_{21}$

10a: $R^1 = Bn$, $R^2 = H$, $R^3 = Me$
10b: $R^1 = Bn$, $R^2 = R^3 = Et$
10c: $R^1 = Bn$, R^1, $R^2 = -(CH_2)_4-$
10d: $R^1 = Bn$, R^1, $R^2 = -(CH_2)_6-$
10e: $R^1 = i$Pr, $R^2 = -(CH_2)_6-$



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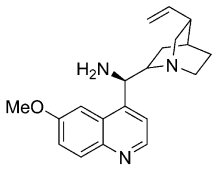

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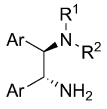
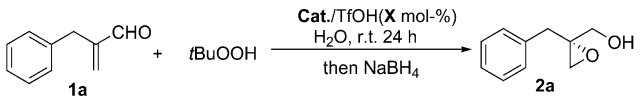


11a: Ar = Ph, $R^1 = R^2 = Me$
11b: Ar= Ph, $R^1 = R^2 = Et$
11c: Ar = Ph, $R^1 = R^2 = n$Pr
11d: Ar = Ph, $R^1 = R^2 = n$Bu
11e: Ar = Ph, $R^1 = R^2 = nC_6H_{13}$
11f: Ar = Ph, $R^1 = R^2 = BnCH_2CH_2$
11g: Ar = Ph, R^1, $R^2 = (CH_2)_5$
11h: Ar = Ph, $R^1 = H$, $R^2 = n$Bu
11i: Ar = 4-MeOPh, $R^1 = R^2 = n$Pr
11j: Ar = 2-MeOPh, $R^1 = R^2 = n$Pr (1*S*,2*S*)
11k: Ar= 2-OHPh, $R^1 = R^2 = n$Pr (1*S*,2*S*)
11l: Ar = 4-ClPh, $R^1 = R^2 = n$Pr (1*S*,2*S*)
11m: Ar = 3,4-Cl_2Ph, $R^1 = R^2 = n$Pr (1*S*,2*S*)
11n: Ar = 4-CF_3Ph, $R^1 = R^2 = n$Pr (1*S*,2*S*)
11o: Ar = 3,5-$(CF_3)_2$Ph, $R^1 = R^2 = n$Pr (1*S*,2*S*)

Figure 1. Selected primary-tertiary diamines.

Table 2. Screening of chiral primary-tertiary diamines.



1a 2a

Entry[a]	Amine	X	Yield [%][b]	*ee* [%][c]
1	**9a**	20	73	47
2	**9b**	20	<10	–
3	**9c**	20	63	45
4	**9d**	20	77	46
5	**9e**	20	87	15
6	**10a**	20	54	56
7	**10b**	20	60	57
8	**10c**	20	62	59
9	**10d**	20	64	53
10	**10e**	20	59	45
11	**11a**	10	83	43
12	**11b**	10	83	49
13	**11c**	**10**	**87**	**58**
14	**11d**	10	80	53
15	**11e**	10	61	30
16	**11f**	10	79	37
17	**11g**	10	<10	–
18	**11h**	10	49	31
19	**12**	10	77	25
20	**13**	10	60	5

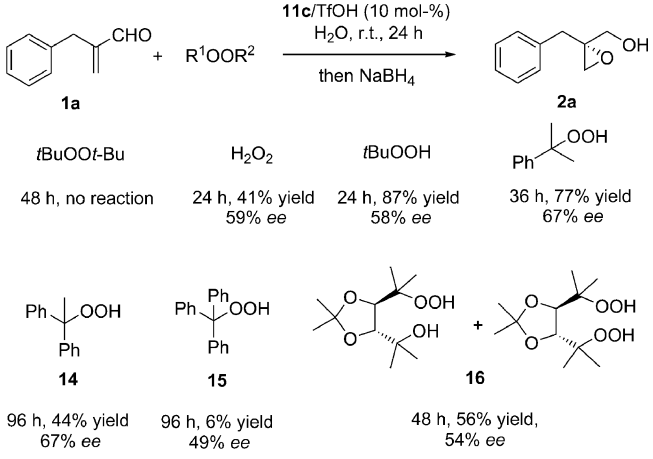
[a] Reagents and conditions: 2-benzylacrylaldehyde (73 mg, 0.5 mmol), TBHP (0.8 mmol), water (0.5 mL), X mol-% catalyst, r.t. [b] Isolated yield. [c] Determined by HPLC after reduction by $NaBH_4$.

In an extreme case, simply switching of the acyclic dialkylated group (e.g., **11c**) to a cyclic pyrrolidinyl group (**11g**) makes the catalyst almost inactive (Table 2, entry 17). Finally, *trans*-1,2-diphenylethane-1,2-diamine derived primary-tertiary diamine **11c** was identified as the optimal catalyst in this round of screening. The reaction in the presence of 10 mol-% **11c**/TfOH gave 87% yield and 58% *ee* (Table 2, entry 13); hence, this system was chosen for further optimization.

Further Optimization

With **11c**/TfOH established as the optimal catalyst, the reaction was further optimized by examining different oxidants, aqueous salt effects, acidic additives, and electronic effects.

Oxidant: A range of oxidants, mostly peroxides, have been examined (Scheme 3). All the hydroperoxides tested could react with 2-benzylacrylaldehyde (**1a**) to afford the desired epoxide product **2a**, and the use of cumene hydroperoxide (CMHP) as the oxidant was found to give a significantly improved enantioselectivity (67% *ee*) albeit with a slightly lower yield (Scheme 3). No further improvement on enantioselectivity could be attained with either more bulky hydroperoxides such as **14** and **15**, or chiral hyroperoxides such as **16**. With a balance of activity and stereoselectivity, CMHP was chosen as the oxidant for further optimization.

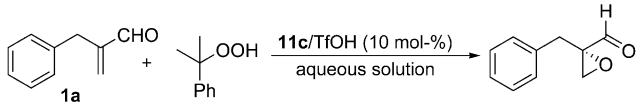


Scheme 3. Screening of oxidants.

Aqueous Salt Effect: Salt additives are well-known to have a dramatic effect on the reactivity and stereoselectivity for reactions in aqueous media.[12] Interestingly, the reactions were accelerated considerably, along with a modest increase of enantioselectivity, when conducted in salt solution, and the use of 2 M NaCl solution was found to give the best improvement. In this medium, the reaction proceeded to 94% conversion with 71% *ee* in 16 h in the presence of 10 mol-% catalyst (Table 3, entry 5). Other aqueous solutions were also examined and were found to exhibit mixed salt effects. For example, in aqueous LiCl solution, which is a typical salting-out salt like NaCl, the activity was seriously diminished (Table 3, entry 7), suggesting that the

salting-out effect is not the only working factor in this system. In a control experiment under neat conditions, the reaction proceeded much faster but, unfortunately, with reduced enantioselectivity (Table 3, entry 10), highlighting the beneficial nature of aqueous media for stereocontrol in this case.

Table 3. Salt effect in **11c**/TfOH catalyzed epoxidation of **1a**.

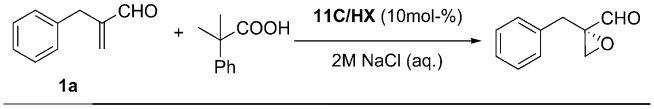


Entry[a]	Solvent	Time [h]	Conv. [%][b]	*ee* [%][c]
1	H_2O	16 (36)	39 (83)[d]	67
2	NaCl (0.5 M)	16 (36)	45 (91)[d]	68
3	NaCl (1 M)	16 (36)	60 (95)[d]	70
4	NaCl (1.5 M)	16 (24)	84 (97)[d]	70
5	**NaCl (2 M)**	**16**	**94**	**71**
6	brine	16	91	71
7	LiCl (2 M)	24	10	–
8	NaF (2 M)	16	96	69
9	KBr (2 M)	16	78	66
10	neat	5	95	55

[a] Reagents and conditions: 2-benzylacrylaldehyde (73 mg, 0.5 mmol), CMHP (0.8 mmol), H_2O (0.5 mL), catalyst (10 mol-%), r.t. [b] Determined by GC, >90% selectivity for the desired epoxide product. [c] Determined by HPLC after reduction by $NaBH_4$. [d] Conversion after the time given in parentheses in the time column.

Reidentification of Optimal Acidic Additives: Previously, we have observed that the addition of a second weak acid could significantly improve the catalysis of pimary-tertiary diamines such as **9a**/TfOH.[7] Considering this, we also examined the effect of a second weak acid in the current reaction (10 mol-% **11c** in 2 M NaCl) to further improve the enantioselectivity. Although the activity was decreased with an added weak acid such as 1,1′-bi-2-naphthol (BINOL), it is interesting to note that the addition of silica gel (column chromatography grade, 200–400 mesh) exhibited a modest but reproducible increase in enantioselectivity (Table 4, entry 4, 73% *ee*). During this study, we also noticed that Brønsted acids bearing bi/multi acidic moieties, such as salicyclic acid, were also an applicable type of acidic additive in addition to TfOH. By tuning the acidity of salicyclic acid, we were able to identify an optimal Brønsted acid, 5-sulfosalicyclic acid (5-SSA) (Table 4, entries 5–7), which gave a slightly better enantioselectivity than that obtained with TfOH (Table 4, entry 7 vs. entry 1). The silica gel effect also worked with 5-SSA (Table 4, entry 8). With a **11c**/5-SSA/silica gel combination, we could obtain 96% conversion and 79% *ee*, which is the best enantioselectivity so far achieved at temperatures in the range of 0 °C to room temperature (Table 4, entry 9). Further lowering the reaction temperature only led to seriously reduced activity without any noticeable improvement in enantioselectivity.

Table 4. Screening of acidic additives under aqueous conditions.

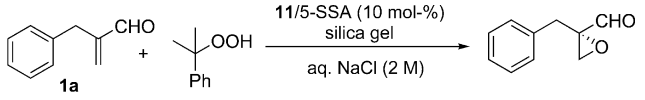


Entry[a]	Acid combination[b]	Time [h]	Conv. [%][c]	*ee*[%][d]
1	TfOH	16	94	71
2	TfOH/(*R*)-BINOL	16	44	70
3	TfOH/(*S*)-BINOL	16	56	70
4	TfOH, silica gel (20 mg)	16	95	73
5	salicyclic acid	36	80	53
6	2-SBA	24	94	72
7	5-SSA	24	94	75
8	5-SSA, silica gel (20 mg)	18	92	76
9[e]	5-SSA, silica gel (20 mg)	24	96	79

[a] Reagents and conditions: 2-benzylacrylaldehyde (73 mg, 0.5 mmol), CMHP (0.8 mmol), solvent (0.5 mL), catalyst (10 mol-%), r.t. [b] 2-SBA: 2-sulfobenzoic acid; 5-SSA: 5-sulfosalicyclic acid. [c] Determined by GC, >90% selectivity for the desired epoxide product. [d] Determined by HPLC after reduction by $NaBH_4$. [e] The reaction was first performed at 0 °C for 6 h and then warmed to r.t. for 18 h.

Electronic Tuning of Catalyst 11: With the established optimal conditions in hand, we then focused on electronic tuning of diamine catalyst **11** with the aim of achieving better stereocontrol. It is known that electronic tuning is a viable approach for catalyst development because it can be adjusted without significantly perturbing the structure, and dramatic electronic effects have also been reported in a number of organocatalytic systems.[13] Unfortunately, no improvement of the enantioselectivity was obtained in the present reaction with catalyst **11** bearing either electron-donating groups (**11i**–**k**, Table 5, entries 1–3) or electron-withdrawing groups (**11l**–**o**, Table 5, entries 4–7). However, notable electronic effects on the activity have been observed in this study, wherein catalyst **11l**–**o** with electron-withdrawing groups generally exhibited a higher activity than those (**11i**–**k**) with electron-donating groups. Overall, the parent diamine **11c** remained the optimal catalyst.

Table 5. Electronic effect of *trans*-1,2-diarylethane-1,2-diamines **11**.

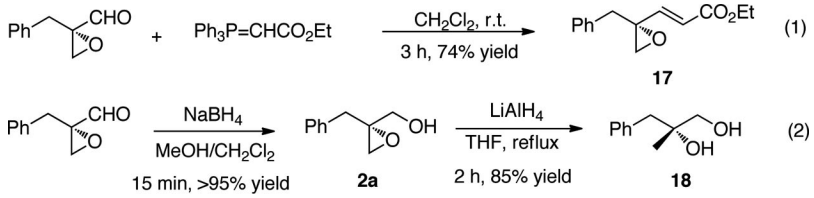


Entry[a]	Amine	Time [h]	Conv. [%][b]	*ee* [%][c]
1	**11i**	48	83	68
2	**11j**	48	75	63
3	**11k**	48	43	39
4	**11l**	24	90	59
5	**11m**	24	91	70
6	**11n**	24	95	66
7	**11o**	24	89	55

[a] Reagents and conditions: 2-benzylacrolein (0.5 mmol), CMHP (0.8 mmol), aqueous NaCl (2 M, 0.5 mL), catalyst (10 mol-%), silica gel (20 mg), 0 °C (6 h), then r.t. [b] Determined by GC, >90% selectivity for the desired epoxide product. [c] Determined by HPLC after reduction by $NaBH_4$.

Substrate Scope

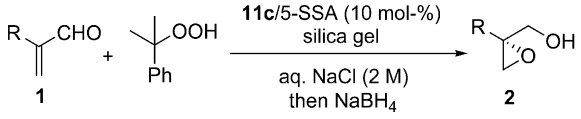
Under the optimal conditions (10 mol-% of **11c**/5-SSA/silica gel in 2 M NaCl, with CMHP and at 0 °C to r.t.), we next probed the scope of the epoxidation reaction for a vari-



Scheme 4. Transformation of epoxide products.

ety of α-branched acroleins. All the α-alkyl-substituted acroleins reacted smoothly to generate the desired epoxides in good yields (79–95%) and enantioselectivities (32–88% *ee*, Table 6). The aromatic substituents of the α-benzylacroleins have some effect on the enantioselectivity, and the best enantiomeric excess (88% *ee*) was obtained with 2-OMe substituted benzylacroleins such as **1g** and **1j** (Table 6, entries 7 and 10). A reasonable enantioselectivity (75% *ee*) was also obtained with non-benzylic substituted acrolein **1l** (Table 6, entry 12). The reaction works smoothly with allylic alcohol type acrolein **1k** to give the desired epoxide **2k** in high yield (95% yield), but low enantioselectivity (32% *ee*, Table 6, entry 11). α-Alkoxyl and acryloxyl-substituted acroleins such as **1m** and **1n** were found to be inert substrates for the current reactions. Finally, the epoxidation reaction of α,β-disubstituted enals, such as (*E*)-2-methyl-3-phenylacrylaldehyde, was tried under the current system, however, the reaction did not proceed at all. The absolute configuration of products (e.g., **2a**) was determined to be *R* by comparison of their optical rotation values with those of known compounds.[14]

Table 6. Substrate scope of **11c**/5-SSA-catalyzed epoxidation reactions.



Entry[a]	1	R	Time [h]	2	Yield [%][b]	*ee* [%][c]
1	**1a**	Bn	24	**2a**	90 (96)	79
2	**1b**	4-Me$C_6H_4CH_2$	36	**2b**	85 (94)	78
3	**1c**	4-Cl$C_6H_4CH_2$	36	**2c**	87 (95)	82
4	**1d**	4-MeO$C_6H_4CH_2$	24	**2d**	88 (96)	76
5	**1e**	1-NaphCH_2	24	**2e**	91 (97)	79
6	**1f**	2-Cl$C_6H_4CH_2$	24	**2f**	88 (96)	81
7	**1g**	2-MeO$C_6H_4CH_2$	24	**2g**	89 (94)	88
8	**1h**	3-MeO$C_6H_4CH_2$	24	**2h**	89 (97)	75
9	**1i**	2,4-Cl_2 $C_6H_3CH_2$	24	**2i**	79	78
10	**1j**	2,4-$(MeO)_2C_6H_3CH_2$	24	**2j**	94	88
11	**1k**	BnOCH_2	24	**2k**	95	32
12	**1l**	Bn$(CH_2)_3$	36	**2l**	85 (96)	75
13	**1m**	BnO	48	**2m**	no reaction	–
14	**1n**	PhCOO	48	**2n**	no reaction	–

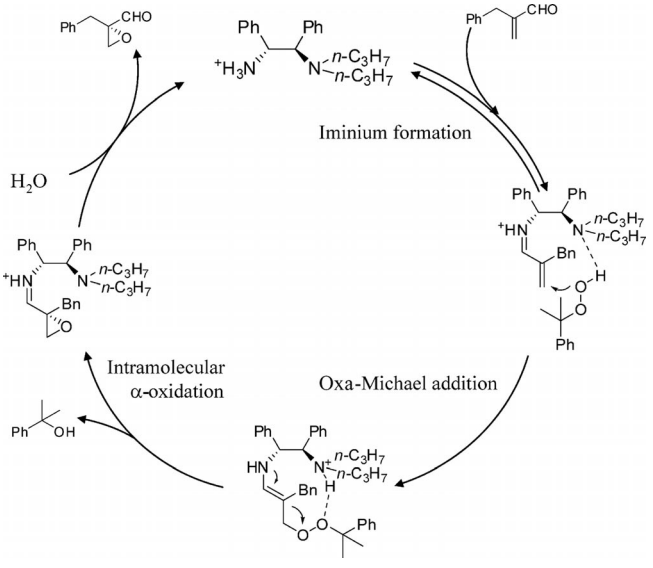
[a] Reagents and conditions: α-branched acrolein (0.5 mmol), cumene hydroperoxide (0.8 mmol), aqueous NaCl (2 M, 0.5 mL), catalyst (10 mol-%), silica gel (20 mg), 0 °C (6 h) then r.t. [b] Isolated yield. Conversion determined by GC is given in parenthesis. [c] Determined by HPLC after reduction by $NaBH_4$.

Synthetic Transformations of Epoxidation Products

The epoxide aldehyde obtained from the reaction mixture could be readily transformed into chiral α,β-unsaturated ester **17** by a standard olefination reaction without further purification [Scheme 4, Equation (1)]. The chiral epoxides could also be elaborated into 1,2-diols containing a chiral quaternary center such as **18**, which is an important building block in many natural products and bioactive synthetic molecules,[15] by reduction with $LiAlH_4$ [Scheme 4, Equation (2)]. In both reactions, the stereocenters of the chiral epoxide products were maintained.

Proposed Transition State

A catalytic cycle is proposed based on experimental observations and preliminary analysis. The reaction occurs through iminium-activated oxa-Michael addition followed by an enamine-mediated intramolecular α-oxidation, which is the stereo-determining step. The hydrolysis of the iminium intermediate then releases the product and completes the cycle. In this catalytic scenario, the N–H···O hydrogen bonding between the protonated tertiary amine and hydroperoxide is critical for stereocontrol (Scheme 5).



Scheme 5. Proposed catalytic cycle.

Conclusions

We have developed a chiral primary amine **11c**/5-sulfosalicyclic acid catalyzed enantioselective epoxidation of α-substituted acroleins with up to 95% yield and 88% *ee* in aqueous salt solution (2 M NaCl). The current study provides the simple chiral primary-tertiary diamine **11c** as a promising lead for further developments along these lines.

Experimental Section

General Information: Commercial reagents were used as received, unless otherwise indicated. ^{1}H and ^{13}C NMR spectra were recorded with a 300 MHz instrument, as noted, and were internally referenced to the residual protic solvent signals. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical mutiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). HPLC analysis was performed using Chiralcel columns. Catalysts **4**–**10** and **13** are known compounds.[4,7]

Synthesis of 3b. General Procedure: Synthesized according to the published procedure.[9] To a 100 mL flask, under Argon, was added anhydrous $ZnCl_2$ (133 mg, 1 mmol), chlorobenzene (30 mL), 2-aminobenzonitrile (1.18 g, 10 mmol), and (*S*)-2-amino-3-phenylpropan-1-ol (1.51 g, 10 mmol), and the mixture was heated to reflux for 3 d. After cooling to r.t., H_2O (50 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by flash column chromatography to afford **3b** (1.64 g, 65% yield) as a white solid. $[\alpha]_D^{20}$ = +47.8 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.62–2.69 (m, 1 H, $PhCH_2$), 2.99–3.06 (m, 1 H, $PhCH_2$), 3.89–3.94 (t, *J* = 4.5 Hz, 1 H, OCH_2), 4.13–4.19 (t, *J* = 9.0 Hz, 1 H, OCH_2), 4.45–4.55 (m, 1 H, NCH), 5.99 (br., 2 H, NH_2), 6.55–6.59 (m, 2 H, ArH), 7.07–7.21 (m, 6 H, PhH, ArH), 7.57–7.60 (d, *J* = 8.1 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.3, 68.2, 70.3, 109.0, 115.7, 116.0, 126.5, 128.6, 129.3, 129.7, 132.1, 138.4, 148.7, 164.1 ppm. HRMS: calcd. for $C_{16}H_{16}N_2O$: 252.1263; found 252.1262.

Catalysts **3a** and **3c** were synthesized following the same procedure.

(*S*)-2-(4-Methyl-4,5-dihydrooxazol-2-yl)aniline (3a): Synthesized from (*S*)-2-aminopropan-1-ol and 2-aminobenzonitrile in 64% yield as a colorless oil. $[\alpha]_D^{20}$ = +14.4 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33–1.35 (d, *J* = 6.3 Hz, 3 H, Me), 3.82–3.88 (m, 1 H, NCH), 4.37–4.43 (m, 2 H, OCH_2), 6.08 (br., 2 H, NH_2), 6.63–6.70 (m, 2 H, ArH), 7.17–7.22 (m, 1 H, ArH), 7.68–7.71 (dd, *J* = 7.8, 1.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 62.1, 72.3, 109.2, 115.6, 116.0, 129.6, 131.9, 148.6, 163.5 ppm. HRMS: calcd. for $C_{10}H_{12}N_2O$: 176.0950; found 176.0951.

(*S*)-2-(4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)aniline (3c): Synthesized form (*S*)-2-amino-3,3-dimethylbutan-1-ol and 2-aminobenzonitrile in 67% yield as a white solid. $[\alpha]_D^{20}$ = +29.2 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (s, 9 H, *t*Bu), 4.08–4.14 (m, 2 H, OCH_2), 4.20–4.24 (m, 1 H, NCH), 6.14 (br., 2 H, NH_2), 6.62–6.71 (m, 2 H, ArH), 7.16–7.22 (m, 1 H, ArH), 7.65–7.68 (dd, *J* = 8.1, 1.5 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.9, 33.8, 66.9, 76.4, 109.2, 115.6, 115.9, 129.6, 131.9, 148.7, 163.5 ppm. HRMS: calcd. for $C_{13}H_{18}N_2O$: 218.1419; found 218.1417.

Synthesis of Catalyst 11c. General Procedure: The mono acetyl protected diamine was synthesized according to the published procedure.[16] To a solution of *N*-[(1*R*,2*R*)-2-amino-1,2-diphenylethyl]-acetamide (1.27 g, 5 mmol) in H_2O (1 mL) and CH_3CN (50 mL), was added propionaldehyde (2 mL, 30 mmol). After stirring for 20 min at r.t., $NaCNBH_3$ (630 mg, 10 mmol) was added and the resulting solution was stirred for another 20 min. Acetic acid (1 mL) was added and, after 2 h, the solvent was removed under reduced pressure. Aqueous NaOH (1 M, 50 mL) was added and the product was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, washed with brine (20 mL), dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by flash column chromatography and directly used for the next step.

To the product obtained above was added aqueous HCl (4 M, 50 mL) and the solution was heated to reflux for 24 h. CH_2Cl_2 (60 mL) and H_2O (30 mL) were added and K_2CO_3 was added until pH 12 was reached. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography to afford catalyst **11c** as a colorless oil (1.26 g, 85% yield). $[\alpha]_D^{20}$ = –21.9 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94–0.99 (t, *J* = 7.5 Hz, 6 H, Me), 1.53–1.62 (m, 4 H, CH_2), 2.04 (br., 2 H, NH_2), 2.08–2.14 (m, 2 H, CH_2), 2.57–2.61 (m, 2 H, CH_2), 3.77–3.81 (d, *J* = 10.5 Hz, 1 H, CH), 4.41–4.45 (d, *J* = 10.5 Hz, 1 H, CH), 6.99–7.20 (m, 10 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.8, 51.9, 55.9, 71.0, 126.6, 126.7, 127.4, 127.9, 128.1, 129.7, 136.0, 143.6 ppm. HRMS: calcd. for $C_{20}H_{28}N_2$ 296.2252; found 296.2254.

Catalysts **11a**, **11b**, and **11d**–**j** were synthesized according to same procedure.

(1*R*,2*R*)-*N*^{1},*N*^{1}-Dimethyl-1,2-diphenylethane-1,2-diamine (11a): The catalyst was synthesized according to the general procedure as a pale-yellow solid in 40% overall yield. $[\alpha]_D^{20}$ = –43.2 (*c* = 0.5, $CDCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.08–2.16 (br., 2 H, NH_2), 2.20 (s, 6 H, Me), 3.58–3.66 (d, *J* = 10.6 Hz, 1 H, CH), 4.37–4.46 (d, *J* = 10.6 Hz, 1 H, CH), 6.93–7.04 (m, 3 H, ArH), 7.04–7.18 (m, 5 H, ArH), 7.18–7.25 (d, *J* = 7.9 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.0, 55.7, 75.4, 126.8, 126.9, 127.3, 128.0, 128.1, 129.8, 134.0, 143.4 ppm. HRMS: calcd. for $C_{16}H_{20}N_2$ 240.1626; found 240.1628.

(1*R*,2*R*)-*N*^{1},*N*^{1}-Diethyl-1,2-diphenylethane-1,2-diamine (11b): The needle-like catalyst was synthesized according to the general procedure in 55% overall yield. $[\alpha]_D^{20}$ = –20.8 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05–1.10 (t, *J* = 7.1 Hz, 6 H, Me), 2.03–2.14 (m, 2 H, CH_2), 2.36 (br., 2 H, NH_2), 2.67–2.78 (m, 2 H, CH_2), 3.76–3.79 (d, *J* = 10.6 Hz, 1 H, CH), 4.35–4.38 (d, *J* = 10.5 Hz, 1 H, CH), 6.92–7.17 (m, 10 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 43.5, 55.8, 70.4, 126.7, 126.8, 127.4, 128.0, 128.1, 129.6, 136.1, 143.3 ppm. HRMS: calcd. for $C_{18}H_{24}N_2$ 268.1939; found 268.1943.

(1*R*,2*R*)-*N*^{1},*N*^{1}-Dibutyl-1,2-diphenylethane-1,2-diamine (11d): The catalyst was synthesized according to the standard procedure in 45% overall yield. $[\alpha]_D^{20}$ = –45.6 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96–0.99 (t, *J* = 7.2 Hz, 6 H, Me), 1.30–1.57 (m, 8 H, CH_2), 2.03–2.13 (m, 4 H, CH_2 and NH_2), 2.61–2.68 (m, 2 H, CH_2), 3.78–3.82 (d, *J* = 10.8 Hz, 1 H, CH), 4.41–4.45 (d, *J* = 10.8 Hz, 1 H, CH), 7.00–7.07 (m, 3 H, ArH), 7.09–7.16 (m, 5 H, ArH), 7.21–7.26 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 20.8, 31.1, 49.7, 55.8, 70.7, 126.7, 126.8, 127.4,

128.0, 129.7, 135.8, 143.6 ppm. HRMS: calcd. for $C_{22}H_{32}N_2$ [M + H] 325.2644; found 325.2651.

(1*R*,2*R*)-N^1,N^1-Dihexyl-1,2-diphenylethane-1,2-diamine (11e): The catalyst was synthesized according to the standard procedure in 72% overall yield. $[\alpha]_D^{20}$ = –39.6 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89–0.95 (t, *J* = 7.2 Hz, Me), 1.34 (m, 12 H, CH_2), 1.54 (m, 4 H, CH_2), 2.05–2.11 (m, 2 H, CH_2), 2.21 (br., 2 H, NH_2), 2.62–2.69 (m, 2 H, CH_2), 3.77–3.81 (d, *J* = 10.8 Hz, 1 H, CH), 4.40–4.44 (d, *J* = 10.8 Hz, 1 H, CH), 6.99–7.16 (m, 8 H, ArH), 7.21–7.25 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.7, 27.3, 28.8, 31.9, 50.1, 55.9, 70.9, 126.6, 126.7, 127.4, 127.9, 128.1, 129.7, 136.0, 143.7 ppm. HRMS: calcd. for $C_{26}H_{40}N_2$ 380.3191; found 380.3193.

(1*R*,2*R*)-1,2-Diphenyl-N^1,N^1-bis(3-phenylpropyl)ethane-1,2-diamine (11f): The needle-like catalyst was synthesized according to the standard procedure in 60% overall yield. $[\alpha]_D^{20}$ = +19.8 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84–1.92 (m, 4 H, CH_2), 2.03 (br., 2 H, NH_2), 2.14–2.22 (m, 2 H, CH_2), 2.57–2.82 (m, 6 H, CH_2), 3.77–3.81 (d, *J* = 10.5 Hz, 1 H, CH), 4.37–4.40 (d, *J* = 10.5 Hz, 1 H, CH), 6.90–6.93 (m, 2 H, ArH), 7.03–7.13 (m, 6 H, ArH), 7.18–7.33 (m, 12 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.6, 33.8, 49.6, 55.8, 71.0, 125.8, 126.7, 126.8, 127.5, 128.0, 128.4, 128.5, 129.7, 135.6, 142.4, 143.4 ppm. HRMS: calcd. for $C_{32}H_{37}N_2$ [M + H] 449.2957; found 449.2958.

(1*R*,2*R*)-1,2-Diphenyl-2-(piperidin-1-yl)ethanamine (11g): The catalyst was synthesized according to the standard procedure in 90% overall yield as a white solid. $[\alpha]_D^{20}$ = –29.2 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37–1.39 (m, 2 H, CH_2), 1.54–1.58 (m, 2 H, CH_2), 1.87–1.99 (m, 2 H, NH_2), 2.13–2.16 (d, *J* = 7.8 Hz, 1 H, CH_2), 2.39 (br., 1 H, CH_2), 2.73–2.77 (d, *J* = 11.1 Hz, CH_2), 3.17–3.20 (d, *J* = 7.8 Hz, 1 H, CH), 3.24–3.27 (m, 1 H, CH_2), 4.12–4.14 (d, *J* = 7.8 Hz, 1 H, CH), 7.19–7.29 (m, 10 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 25.3, 31.1, 49.0, 68.6, 78.2, 79.9, 126.7, 126.8, 127.4, 128.0, 128.3, 128.4, 140.3, 144.0 ppm. HRMS: calcd. for $C_{19}H_{24}N_2$ 280.1939; found 280.1944.

(1*R*,2*R*)-N^1-Butyl-1,2-diphenylethane-1,2-diamine (11h): The needle-like catalyst was synthesized according to the standard procedure in 45% overall yield. $[\alpha]_D^{20}$ = +69.3 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81–0.85 (t, *J* = 7.2 Hz, Me), 1.21–1.44 (m, 4 H, CH_2), 1.73 (br., 3 H, NH_2 and NH), 2.29–2.46 (m, 2 H, CH_2), 3.69–3.72 (d, *J* = 7.2 Hz, 1 H, CH), 3.96–3.99 (d, *J* = 7.2 Hz, 1 H, CH), 7.11–7.25 (m, 10 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 20.4, 32.4, 47.5, 61.9, 69.9, 126.9, 127.0, 127.8, 128.0, 128.1, 141.7, 143.6 ppm. HRMS: calcd. for $C_{18}H_{24}N_2$ 268.1939; found 268.1936.

(1*R*,2*R*)-1,2-Bis(4-methoxyphenyl)-N^1,N^1-dipropylethane-1,2-diamine (11i): The needle-like catalyst was synthesized according to the standard procedure in 49% overall yield. $[\alpha]_D^{20}$ = –14.4 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93–0.99 (m, 6 H, Me), 1.54–1.59 (m, 4 H, CH_2), 2.01–2.20 (m, 2 H, CH_2), 2.28 (br., 2 H, NH_2), 2.53–2.58 (m, 2 H, CH_2), 3.68–3.72 (m, 7 H, OMe and CH), 4.33–4.36 (d, *J* = 10.6 Hz, 1 H, CH), 6.64–6.69 (m, 4 H, ArH), 6.91–6.94 (m, 2 H, ArH), 7.11–7.14 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.8, 51.9, 55.0, 55.1, 55.3, 70.3, 76.6, 112.8, 113.4, 128.3, 129.0, 130.6, 135.9, 158.1, 158.2 ppm. HRMS: calcd. for $C_{22}H_{32}N_2O_2$ 356.2464; found 356.2469.

(1*S*,2*S*)-1,2-Bis(2-methoxyphenyl)-N^1,N^1-dipropylethane-1,2-diamine (11j): (1*S*,2*S*)-1,2-Bis(2-methoxyphenyl)ethane-1,2-diamine was synthesized according to the published procedure.[17] $[\alpha]_D^{20}$ = +79.0 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (br., 4 H, NH_2), 3.79 (s, 6 H, OMe), 4.46 (s, 2 H, CH), 6.75–6.85 (m, 4 H, ArH), 7.09–7.15 (m, 2 H, ArH), 7.21–7.24 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 55.5, 110.3, 120.3, 127.6, 128.1, 132.1, 156.9 ppm. HRMS: calcd. for $C_{16}H_{20}N_2O_2$ 272.1525; found 272.1521. The optical purity of the (1*S*, 2*S*)-1,2-bis(2-methoxyphenyl) ethane-1,2-diamine was determined as >99% *ee* by HPLC with chiral column after acetylation. **11j** was synthesized according to the standard procedure in 57% overall yield. $[\alpha]_D^{20}$ = +73.2 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93–0.98 (t, *J* = 7.2 Hz, 6 H, Me), 1.53–1.63 (m, 4 H, CH_2), 2.04–2.10 (m, 2 H, CH_2), 2.18 (br., 2 H, NH_2), 2.54–2.63 (m, 2 H, CH_2), 3.67 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 4.75 (s, 2 H, CH), 6.63–6.74 (m, 4 H, ArH), 6.70–7.02 (m, 2 H, ArH), 7.15–7.21 (dd, *J* = 4.2, 10.5 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 21.8, 52.0, 55.2, 55.3, 110.2, 119.2, 120.4, 126.3, 127.3, 127.5, 128.6, 129.6, 131.4, 157.2, 158.0 ppm. HRMS: calcd. for $C_{22}H_{32}N_2O_2$ 356.2464; found 356.2468.

2,2′-[(1*S*,2*S*)-1-Amino-2-(dipropylamino)ethane-1,2-diyl]diphenol (11k): The catalyst was synthesized by treatment of **11j** with BBr_3 in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90–0.96 (t, *J* = 7.2 Hz, 6 H, Me), 1.51–1.63 (m, 4 H, CH_2), 2.24–2.32 (m, 2 H, CH_2), 2.76–2.95 (m, 4 H, CH_2 and NH_2), 4.17–4.26 (m, 2 H, CH), 6.75–6.95 (m, 6 H, ArH), 7.18–7.26 (m, 2 H, ArH), 13.40 (br., 2 H, OH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 20.1, 54.5, 61.6, 70.4, 77.2, 118.3, 118.7, 119.4, 119.5, 121.3, 128.7, 129.6, 129.8, 133.2, 156.1, 157.6 ppm. HRMS: calcd. for $C_{20}H_{28}N_2O_2$ 328.2151; found 328.2154.

(1*S*,2*S*)-1,2-Bis(4-chlorophenyl)-N^1,N^1-dipropylethane-1,2-diamine (11l): (1*S*,2*S*)-1,2-Bis(4-chlorophenyl)ethane-1,2-diamine was synthesized according to the published procedure.[18] $[\alpha]_D^{20}$ = +33.8 (*c* = 0.5, MeOH). ^{1}H NMR (300 MHz, D_2O): δ = 3.22 (br., 4 H, NH_2), 4.94 (s, 2 H, CH), 7.09 (d, *J* = 8.4 Hz, 4 H, ArH), 7.29 (d, *J* = 8.4 Hz, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.3, 129.3, 129.4, 129.6, 135.4. **11l** was synthesized by the same method used to generate **11c** in 60% overall yield. $[\alpha]_D^{20}$ = –15.6 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93–0.98 (t, *J* = 7.5 Hz, 6 H, Me), 1.51–1.60 (m, 4 H, CH_2), 2.02–2.08 (m, 2 H, CH_2), 2.10 (br., 2 H, NH_2), 2.50–2.60 (m, 2 H, CH_2), 3.68–3.72 (d, *J* = 10.5 Hz, 1 H, CH), 4.36–4.40 (d, *J* = 10.5 Hz, 1 H, CH), 6.91–6.94 (m, 2 H, ArH), 7.07–7.15 (m, 6 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.7, 51.8, 55.3, 70.3, 127.8, 128.2, 129.4, 130.8, 132.5, 132.6, 134.1, 142.0 ppm. HRMS: calcd. for $C_{20}H_{27}Cl_2N_2$ [M + H] 365.1551; found 365.1556.

(1*S*,2*S*)-1,2-Bis(3,4-dichlorophenyl)-N^1,N^1-dipropylethane-1,2-diamine (11m): (1*S*,2*S*)-1,2-Bis(3,4-dichlorophenyl)ethane-1,2-diamine was synthesized according to the published procedure.[18] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52 (br., 4 H, NH_2), 4.01 (s, 2 H, CH), 7.04–7.08 (m, 2 H, ArH), 7.34–7.37 (d, *J* = 8.1 Hz, 2 H, ArH), 7.42 (d, *J* = 2.1 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 60.9, 126.4, 128.9, 130.3, 131.3, 132.6, 143.3 ppm. The needle-like catalyst **11m** was synthesized according to the standard procedure in 55% overall yield. $[\alpha]_D^{20}$ = –28.4 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94–0.98 (t, *J* = 7.2 Hz, 6 H, Me), 1.53–1.60 (m, 4 H, CH_2), 2.03–2.08 (m, 2 H, CH_2), 2.10 (br., 2 H, NH_2), 2.49–2.56 (m, 2 H, CH_2), 3.63–3.66 (d, *J* = 10.5 Hz, 1 H, CH), 4.34–4.38 (d, *J* = 10.5 Hz, 1 H, CH), 6.83–6.86 (dd, *J* = 8.1, 1.8 Hz, 2 H, ArH), 6.96–6.70 (dd, *J* = 8.4, 2.1 Hz, 1 H, ArH), 7.10 (s, 1 H, ArH), 7.17–7.24 (m, 2 H, ArH), 7.40 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.7, 51.78, 54.9, 69.9, 127.6, 128.7, 129.7, 129.9, 130.0, 130.9, 131.1, 131.2, 131.9, 132.3, 135.6, 143.6 ppm. HRMS: calcd. for $C_{20}H_{24}Cl_4N_2$ [M + H] 433.0772; found 433.0767.

(1*S*,2*S*)-N^1,N^1-Dipropyl-1,2-bis[4-(trifluoromethyl)phenyl]ethane-1,2-diamine (11n): The catalyst was synthesized according to the standard procedure in 61% overall yield. $[\alpha]_D^{20}$ = +17.4 (*c* = 0.5, EtOH). ^{1}H

NMR (300 MHz, $CDCl_3$): δ = 0.95–1.00 (t, J = 7.5 Hz, 6 H, Me), 1.51–1.63 (m, 4 H, CH_2), 2.03–2.12 (m, 2 H, CH_2), 2.16 (br., 2 H, NH_2), 2.54–2.64 (m, 2 H, CH_2), 3.81–3.85 (d, J = 10.5 Hz, 1 H, CH), 4.51–4.55 (d, J = 10.5 Hz, 1 H, CH), 7.10–7.13 (d, J = 7.8 Hz, 2 H, ArH), 7.32–7.44 (m, 6 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 21.7, 51.8, 55.4, 70.4, 124.5, 124.6, 125.0, 125.1, 128.4, 129.7 ppm. HRMS: calcd. for $C_{22}H_{27}F_6N_2$ [M + H] 433.2078; found 433.2071.

(1*S*,2*S*)-1,2-Bis[3,5-bis(trifluoromethyl)phenyl]-*N*^{1},*N*^{1}-dipropylethane-1,2-diamine (11o): The catalyst was synthesized according to the standard procedure as a white solid in 55% overall yield. $[\alpha]_D^{20}$ = +9.6 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90–0.94 (t, J = 7.2 Hz, 6 H, Me), 1.47–1.57 (m, 4 H, CH_2), 2.03–2.10 (m, 2 H, CH_2), 2.15 (br., 2 H, NH_2), 2.53–2.63 (m, 2 H, CH_2), 3.73–3.76 (d, J = 10.2 Hz, 1 H, CH), 4.58–4.62 (d, J = 10.2 Hz, 1 H, CH), 7.32 (s, 2 H, ArH), 7.51 (s, 1 H, ArH), 7.58 (s, 3 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 21.6, 51.8, 55.6, 71.2, 121.3, 124.9, 128.3, 129.2, 130.6, 130.7, 131.0, 131.2, 131.5, 131.6, 138.1, 145.6 ppm. HRMS: calcd. for $C_{24}H_{25}F_{12}N_2$ [M + H] 569.1826; found 569.1819.

Synthesis of Catalyst 12: The chiral primary-primary diamine was synthesized according to the published procedure.[19] ^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (br., 4 H, NH_2), 2.66 (t, J = 1.5 Hz, 2 H, CH), 4.03 (s, 2 H, CH), 7.13–7.16 (m, 4 H, ArH), 7.28–7.33 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 53.6, 62.3, 124.1, 126.1, 126.3, 126.4, 138.9, 142.1 ppm. The optical purity of the primary-primary diamine was determined as 98.5% *ee* by HPLC with a chiral column after acetylation. Catalyst **12** was synthesized following the same method used for **11c** in 73% overall yield from the primary-primary diamine. $[\alpha]_D^{20}$ = –83.2 (c = 0.5, MeOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.72–0.76 (t, J = 7.4 Hz, 6 H, Me), 1.27–1.36 (m, 6 H, NH_2 and CH_2), 2.18–2.20 (m, 2 H, CH_2), 2.29–2.33 (m, 2 H, CH_2), 2.47–2.49 (m, 1 H, CH), 2.93–2.95 (m, 1 H, CH), 4.04 (d, J = 7.2 Hz, 1 H, CH), 4.37 (d, J = 5.1 Hz, 1 H, CH), 7.06–7.11 (m, 4 H, ArH), 7.23–7.32 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.6, 21.4, 47.0, 53.3, 53.5, 54.8, 72.6, 123.2, 123.8, 125.4, 125.7, 125.8, 126.0, 126.2, 140.1, 141.1, 142.4, 144.0 ppm. HRMS: calcd. for $C_{22}H_{28}N_2$ 320.2252; found 320.2251.

Typical Experimental Procedure for 11c/5-SSA-Catalyzed Epoxidation: Catalyst **11c** (14.8 mg, 0.05 mmol), 5-sulfosalicycic acid dihydrate (12.7 mg, 0.05 mmol), and silica gel (20 mg) were mixed in aqueous NaCl (2 M, 0.5 mL) and stirred for 15 min at 0 °C. 2-Benzylacrylaldehyde[20] (73 mg, 0.5 mmol) and cumene hydroperoxide (0.8 mmol) were added and the mixture was stirred at 0 °C for 6 h, then at r.t. for 18 h. GC monitoring indicated that the conversion of 2-benzylacrylaldehyde was 96%. The mixture was diluted with CH_2Cl_2/MeOH (20 mL, 4:1, v/v), and $NaBH_4$ (57 mg, 1.5 mmol) was added. The solution was stirred for 15 min, then aqueous $NaHCO_3$ (3%, 20 mL) was added. After 15 min, the organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL). The organic layers were combined, dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by careful flash column chromatography to afford the desired product **2a** as a colorless oil (74 mg, 90% yield). $[\alpha]_D^{20}$ = +16.8 (c = 0.5, MeOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.86 (br., 1 H, OH), 2.65–2.67 (d, J = 4.2 Hz, 1 H, $PhCH_2$), 2.84–2.89 (m, 2 H, $PhCH_2$ and CH_2), 3.05–3.10 (m, 1 H, CH_2), 3.56–3.61 (m, 1 H, CH_2), 3.71–3.75 (m, 1 H, CH_2), 7.20–7.33 (m, 5 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.3, 49.6, 59.9, 62.9, 126.8, 128.5, 129.6, 136.1 ppm. HRMS: calcd. for $C_{10}H_{12}O_2$ 164.0837; found 164.0839. The enantioselectivity was determined by HPLC with an AD-H chiral column (*i*PrOH/*n*-hexane, 3:97; 1.0 mL/min; 210 nm; 25 °C), t_R = 17.7 min (minor), t_R = 19.3 min (major), 79% *ee*. The absolute configuration was determined as *R* by comparison with the known compound.[13]

Other epoxidation products are new compounds.

(*R*)-[2-(4-Methylbenzyl)oxiran-2-yl]methanol (2b): Colorless oil. 78% *ee*. $[\alpha]_D^{20}$ = +19.2 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.73 (br., 1 H, OH), 2.32 (s, 3 H, Me), 2.65–2.66 (d, J = 4.5 Hz, 1 H, $PhCH_2$), 2.80–3.06 (m, 3 H, $PhCH_2$ and CH_2), 3.55–3.62 (m, 1 H, CH_2), 3.70–3.76 (m, 1 H, CH_2), 7.10–7.17 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 37.9, 49.6, 60.0, 62.8, 129.2, 129.4, 132.9, 136.4 ppm. HRMS: calcd. for $C_{11}H_{14}O_2$ 178.0994; found 178.0996.

(*R*)-[2-(4-Chlorobenzyl)oxiran-2-yl]methanol (2c): Colorless oil. 82% *ee*. $[\alpha]_D^{20}$ = 13.4 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.65 (br., 1 H, OH), 2.66–2.67 (d, J = 4.9 Hz, 1 H, $PhCH_2$), 2.85–2.90 (m, 2 H, $PhCH_2$ and CH_2), 3.05–3.10 (m, 1 H, CH_2), 3.58–3.62 (m, 1 H, CH_2), 3.72–3.76 (m, 1 H, CH_2), 7.21–7.33 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.3, 49.6, 59.9, 62.8, 126.8, 128.5, 129.6, 136.0 ppm. HRMS: calcd. for $C_{10}H_{11}ClO_2$ 198.0448; found 198.0447.

(*R*)-[2-(4-Methoxybenzyl)oxiran-2-yl]methanol (2d): Colorless oil. 76% *ee*. $[\alpha]_D^{20}$ = +8.4 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.70–1.74 (m, 1 H, OH), 2.64–2.65 (d, J = 4.9 Hz, 1 H, $PhCH_2$), 2.79–3.04 (m, 3 H, CH_2 and $PhCH_2$), 3.55–3.62 (m, 1 H, CH_2), 3.70–3.75 (m, 1 H, CH_2), 3.79 (s, 3 H, OMe), 6.82–6.86 (m, 2 H, ArH), 7.12–7.14 (d, J = 11.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.4, 49.6, 55.2, 60.0, 62.8, 113.9, 128.0, 130.5, 158.5 ppm. HRMS: calcd. for $C_{11}H_{14}O_3$ 194.0943; found 194.0945.

(*R*)-[2-(Naphthalen-1-ylmethyl)oxiran-2-yl]methanol (2e): Colorless oil. 78% *ee*. $[\alpha]_D^{20}$ = 14.6 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.86–1.89 (t, J = 2.4 Hz, 1 H, OH), 2.53–2.55 (d, J = 4.8 Hz, 1 H, $PhCH_2$), 2.85–2.87 (d, J = 4.8 Hz, 1 H, $PhCH_2$), 3.36–3.68 (m, 2 H, CH_2), 3.71–3.81 (m, 2 H, $PhCH_2$), 7.34–7.43 (m, 2 H, ArH), 7.48–7.56 (m, 2 H, ArH), 7.78 (d, J = 5.4 Hz, 1 H, ArH), 7.85 (d, J = 5.4 Hz, 1 H, ArH), 8.08 (d, J = 5.7 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.5, 49.9, 59.9, 63.5, 124.0, 125.4, 125.7, 126.2, 127.7, 128.1, 128.8, 132.2, 132.6, 133.8 ppm. HRMS: calcd. for $C_{14}H_{14}O_2$ 214.0994; found 214.0996.

(*R*)-[2-(2-Chlorobenzyl)oxiran-2-yl]methanol (2f): Colorless oil. 81% *ee*. $[\alpha]_D^{20}$ = +43.2 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.97 (br., 1 H, OH), 2.57–2.58 (d, J = 4.3 Hz, 1 H, $PhCH_2$), 2.86–2.88 (d, J = 5.4 Hz, 1 H, $PhCH_2$), 3.06–3.27 (m, 2 H, CH_2), 3.63–3.82 (m, 2 H, CH_2), 7.16–7.37 (m, 4 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.9, 49.5, 59.4, 63.2, 126.8, 128.4, 129.5, 132.0, 133.8, 134.6 ppm. HRMS: calcd. for $C_{10}H_{11}ClO_2$ 198.0448; found 198.0450.

(*R*)-[2-(2-Methoxybenzyl)oxiran-2-yl]methanol (2g): Colorless oil. 88% *ee*. $[\alpha]_D^{20}$ = +35.8 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.12–2.17 (m, 1 H, OH), 2.67–2.69 (d, J = 4.8 Hz, 1 H, $PhCH_2$), 2.80–2.87 (m, 2 H, CH_2 and $PhCH_2$), 3.06–3.10 (d, J = 14.1 Hz, 1 H, CH_2), 3.48–3.55 (m, 1 H, CH_2), 3.64–3.70 (m, 1 H, CH_2), 3.81 (m, 3 H, OMe), 6.83–6.91 (m, 2 H, ArH), 7.14–7.24 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.9, 49.0, 54.0, 58.6, 61.7, 109.0, 119.3, 123.1, 126.8, 130.1, 156.0 ppm. HRMS: calcd. for $C_{11}H_{15}O_3$ [M + H] 195.1021; found 195.1029.

(*R*)-[2-(3-Methoxybenzyl)oxiran-2-yl]methanol (2h): Colorless oil. 75% *ee*. $[\alpha]_D^{20}$ = +8.8 (c = 0.5, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.99–2.03 (m, 1 H, OH), 2.68 (d, J = 4.5 Hz, 1 H, $PhCH_2$), 2.87 (m, 2 H, CH_2 and $PhCH_2$), 3.04 (d, J = 14.4 Hz, 1 H, CH_2), 3.55 (m, 1 H, CH_2), 3.72 (m, 1 H, CH_2), 3.82 (s, 3 H, OMe), 6.75–6.82 (m, 3 H, ArH), 7.11–7.22 (m, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.3, 49.8, 55.2, 60.0, 62.7, 112.1, 115.4, 121.9, 129.5, 137.6, 159.6 ppm. HRMS: calcd. for $C_{11}H_{14}O_3$ 194.0943; found 194.0941.

(*R*)-[2-(2,4-Dichlorobenzyl)oxiran-2-yl]methanol (2i): Colorless oil. 78% *ee*. $[\alpha]_D^{20}$ = +11.0 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.83 (br., 1 H, OH), 2.52–2.54 (d, *J* = 4.5 Hz, 1 H, $PhCH_2$), 2.86–2.87 (d, *J* = 4.5 Hz, 1 H, $PhCH_2$), 3.66–3.22 (m, 2 H, CH_2), 3.63–3.80 (m, 2 H, CH_2), 7.17–7.24 (m, 2 H, ArH), 7.38–7.39 (d, *J* = 1.5 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.2, 49.4, 59.1, 63.3, 127.1, 129.2, 132.3, 132.8, 133.5, 135.3 ppm. HRMS: calcd. for $C_{10}H_{10}Cl_2O_2$ 232.0058; found 232.0053.

(*R*)-[2-(2,4-Dimethoxybenzyl)oxiran-2-yl]methanol (2j): Colorless oil. 88% *ee*. $[\alpha]_D^{20}$ = +36.6 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12–2.18 (m, 1 H, OH), 2.66–2.69 (d, *J* = 7.8 Hz, 1 H, $PhCH_2$), 2.78–2.83 (m, 2 H, CH_2 and $PhCH_2$), 3.01–3.05 (m, 1 H, CH_2), 3.51–3.58 (m, 1 H, CH_2), 3.66–3.72 (m, 1 H, CH_2), 3.80 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 6.43–6.46 (m, 2 H, ArH), 7.06–7.08 (d, *J* = 8.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.6, 50.3, 55.3, 60.2, 63.1, 98.5, 104.3, 116.8, 131.8, 158.3, 159.9 ppm. HRMS: calcd. for $C_{12}H_{16}O_4$ 224.1049; found 224.1050.

(*R*)-[2-(Benzyloxymethyl)oxiran-2-yl]methanol (2k): Colorless oil. 32% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.09–2.13 (t, *J* = 2.4 Hz, 1 H, OH), 2.75–2.77 (d, *J* = 4.8 Hz, 1 H, $PhCH_2$), 2.88–2.90 (d, *J* = 4.8 Hz, 1 H, $PhCH_2$), 3.60–3.67 (m, 2 H, CH_2), 3.70–3.92 (m, 2 H, CH_2), 4.51–4.61 (m, 2 H, CH_2), 7.27–7.38 (m, 5 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.8, 58.6, 62.2, 70.8, 73.5, 127.8, 127.9, 128.5, 137.6 ppm. HRMS: calcd. for $C_{14}H_{14}O_2Na$ [M + Na] 237.0891; found 237.0901.

(*R*)-[2-(3-Phenylpropyl)oxiran-2-yl]methanol (2l): Colorless oil. 75% *ee*. $[\alpha]_D^{20}$ = +15.0 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56–1.83 (m, 5 H, OH and CH_2), 2.60–2.67 (m, 3 H, CH_2 and $PhCH_2$), 2.87 (d, *J* = 4.5 Hz, 1 H, $PhCH_2$), 3.59–3.66 (m, 1 H, CH_2), 3.74–3.80 (m, 1 H, CH_2), 7.15–7.18 (m, 3 H, ArH), 7.26–7.31 (m, 2 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.4, 31.4, 35.9, 49.7, 59.6, 62.8, 126.0, 128.3, 128.4, 141.8 ppm. HRMS: calcd. for $C_{12}H_{16}O_2$ 192.1150; found 192.1149.

(*R*,*E*)-Ethyl 3-(2-Benzyloxiran-2-yl)acrylate (17): A reaction mixture of the model reaction (0.5 mmol scale) was poured into H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). After drying with Na_2SO_4, the solvent was concentrated to about 5 mL and freshly prepared Wittig reagent $Ph_3P{=}CH_2CO_2Et$ (1 mmol) was added. After 4 h, the mixture was concentrated and purified by flash chromatography on silica gel to afford the desired product **17** as a colorless oil (86 mg, 74% yield). The enantioselectivity was determined to be 76% *ee* by HPLC. $[\alpha]_D^{20}$ = –25.4 (*c* = 0.5, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13–1.19 (m, 3 H, Me), 2.72–2.88 (m, 2 H, $PhCH_2$), 3.37 (s, 2 H, CH_2), 4.20 (m, 2 H, OCH_2), 6.28 (d, *J* = 15 Hz, 1 H, CH), 6.90 (d, *J* = 15 Hz, 1 H, CH), 7.18–7.38 (m, 5 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 39.3, 55.0, 57.6, 60.6, 122.4, 126.9, 128.5, 129.6, 135.5, 146.4, 166.0 ppm. HRMS: calcd. for $C_{14}H_{16}O_3$ 232.1099; found 232.1097.

(*R*)-2-Methyl-3-phenylpropane-1,2-diol (18): A mixture of epoxide alcohol **2a** (0.5 mmol, 76% *ee*) and $LiAlH_4$ (1 mmol) in THF (10 mL) was heated to reflux for 2 h. After cooling to r.t., the reaction was quenched with sat. aqueous Na_2SO_4. The solid was filtered and washed with Et_2O (3×). The filtrates were concentrated and purified by flash column chromatography to afford product **18** as a white solid (67 mg, 85% yield based on epoxide aldehyde). $[\alpha]_D^{20}$ = +6.4 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 3 H, Me), 1.95 (s, 1 H, OH), 2.07 (d, *J* = 6.0 Hz, 1 H, OH), 2.75–2.88 (q, *J* = 13.2 Hz, 2 H, $PhCH_2$), 3.39–3.50 (m, 2 H, CH_2), 7.21–7.30 (m, 5 H, PhH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5, 44.7, 69.2, 73.0, 126.6, 128.3, 130.5, 137.0 ppm. HRMS: calcd. for $C_{10}H_{14}O_2$ 166.0994; found 166.0997.

Supporting Information (see also the footnote on the first page of this article): NMR spectra for the catalysts and epoxide products, and HPLC traces for the epoxide products.

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