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Phase-transfer catalyzed asymmetric epoxidation of chalcones using chiral crown ethers derived from D-glucose, D-galactose, and D-mannitol

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Abstract—Chiral monoaza-15-crown-5 lariat ethers synthesized from D-glucose, D-galactose, and D-mannitol have been applied as phase-transfer catalysts in the enantioselective epoxidation of chalcones with *tert*-butylhydroperoxide. The type of monosaccharide on the crown ether and the substituents at the nitrogen atom of the crown-ring has a major influence on both the chemical yield and enantioselectivity. Among the catalysts, the crown ether annellated to methyl-4,6-*O*-benzylidene-α-D-glucopyranoside, with 3-hydroxypropyl side arm at the nitrogen atom **1f** proved to be the most effective (92% ee). The enantioselectivity was also affected by the substituents on the aromatic rings of the chalcone. The absolute configurations of epoxyketones **6a**, **6b**, **6d**, **6i**, **6k**, and **6m** were determined by CD spectroscopy; the complete stereostucture of **6b** was determined by single crystal X-ray analysis.

1. Introduction

One of the most attractive approaches in catalytic asymmetric syntheses is the phase-transfer catalytic technique in which the enantioselectivity is generated by a chiral crown ether catalyst.[1] A prominent group of optically active crown ethers contains a carbohydrate moiety as the source of chirality. Although a number of chiral crown ethers have been prepared from monosaccharides,[2] only a few of them have been successfully used as catalysts in asymmetric reactions.[3] Recently, we reported an asymmetric Michael addition and a Darzens condensation, in which the glucose-based chiral lariat ethers of type **1** and **2** generated high enantioselectivity (95% and 72%, respectively).[3,4] Herein we report a new model reaction, in which the monosaccharide-based chiral macrocycles proved to be effective catalysts. This is the epoxidation of chalcones under phase-transfer conditions.

The enantioselective epoxidation of α,β-unsaturated ketones employing chiral catalysts has received considerable attention in recent years.[5] A variety of methods have been developed including the use of polyphasic systems involving hydrogen peroxide in the presence of polyamino acids,[6] alkylperoxides in conjuction with lanthanoid–binaphthol complexes,[7] tartrate-modified metal *tert*-butyl-peroxides,[8] and hydrogen peroxide in the presence of chiral platinium(II) complexes.[9] Good enantioselectivities have also been achieved using non-catalytic systems, such as molecular oxygen in the presence of diethyl zinc/chiral amino alcohols.[10] The use of chiral quaternary ammonium salts as phase-transfer catalyst for this transformation has also been investigated;[11] however, results to date have been disappointing.

Herein, the asymmetric epoxidation of chalcone was investigated in the presence of α-methyl-glucopyranoside-based **1**, β-phenyl-glucopyranoside-based **2**,

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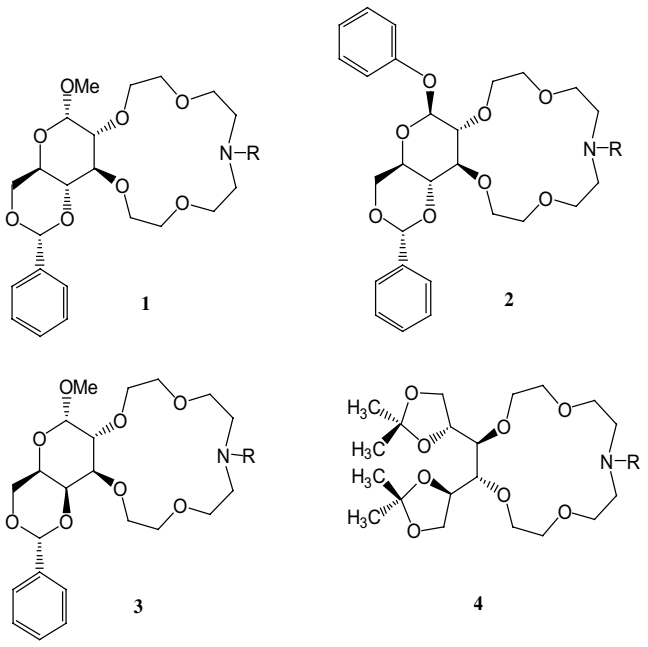


Figure 1. Monosaccharide-based crown ether catalysts for asymmetric epoxidation.

α-methyl-galactopyranoside-based **3**, and 1,2:5,6-di-*O*-isopropylidene-mannitol-based **4** lariat ether catalysts, the structures of which are shown in Figure 1. These compounds have been synthesized by methods reported in our earlier papers.[4c,12]

2. Results and discussion

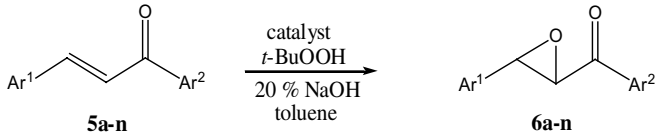
2.1. Asymmetric epoxidation of chalcones in the presence of sugar-based crown ethers

The epoxidation of chalcones **5** with *tert*-butylhydroperoxide (TBHP, 2 equiv) was carried out in a liquid–liquid two-phase system in toluene, employing 20% aq NaOH (3.5 equiv) as the base and 7 mol% of chiral crown catalyst at a temperature of 5 °C (Scheme 1).

After the usual work-up procedure, the product was isolated by preparative TLC. The asymmetric induction, expressed in terms of the enantiomeric excess (ee), was monitored by determining the specific rotation of product **6a** and comparing it with literature values and also by ^{1}H NMR analysis using (+)-Eu(hfc)$_3$ as a chiral shift reagent **6a**–**n**. The *trans*-epoxyketone **6** was obtained in all experiments.

Table 1 summarizes the results obtained in the presence of a series of lariat ethers, such as α-D-glucopyranoside—**1a**–**i**, β-D-glucopyranoside—**2d** and **2f**, the α-D-galactopyranoside—**3d** and **3f**, and D-mannitol-based **4d** and **4f** derivatives, as catalysts. It can be seen that the yield and enantioselectivity are significantly affected by the type of monosaccharide and by the N-substituents of the crown ring.

Concerning the activity of the α-methyl-glucopyranoside-based lariat ethers **1a**–**i** (entries 1–9), the lowest enantiomeric excess values (ca. 8–11%) were recorded in the cases of catalysts **1b**, **1c**, and **1i** containing an *n*-butyl, a benzyl and a diphenylphosphinobutyl N-substituent, respectively. The best results, 92% and 81% ee, were obtained applying catalysts with γ-hydroxypropyl and β-hydroxyethyl substituents **1f** and **1d**, respectively; however 41% ee detected using the δ-hydroxybutyl derivative **1h** was also considerable. It can be concluded that the length of the chain connecting the hydroxy group to the nitrogen atom plays an important role in the asymmetric induction; a chain with three carbon atoms is the optimum, as in **1f** (R = [CH$_2$]$_3$OH). It is also interesting that the methylation of the hydrophilic functions in **1d** and **1f** resulted in a dramatic decrease in the enantioselectivity as demonstrated by the ee of 20% and 23% obtained with **1e** and **1g**, respectively. It is clear that the hydrophilic substituents improve the transport of the catalyst between the two phases (toluene and water), while the lipophilic (CH$_2$)$_n$OMe sub-



5a-n **6a-n**

Compound	Ar^1	Ar^2	Compound	Ar^1	Ar^2
a	Ph	Ph	**h**	4-CH$_3$-Ph	Ph
b	Ph	4-CH$_3$-Ph	**i**	4-NO$_2$-Ph	Ph
c	Ph	4-CH$_3$O-Ph	**j**	4-CH$_3$O-Ph	4-NO$_2$-Ph
d	Ph	4-Cl-Ph	**k**	4-Cl-Ph	4-Cl-Ph
e	Ph	2,4-di-Cl-Ph	**l**	4-F-Ph	2-Cl-Ph
f	Ph	3,4-di-Cl-Ph	**m**	4-CH$_3$-Ph	4-CH$_3$-Ph
g	Ph	4-NO$_2$-Ph	**n**	4-CH$_3$-Ph	2,4-di-Cl-Ph

Scheme 1.

Table 1. Effect of chiral crown catalysts **1**–**4** on the asymmetric epoxidation of chalcone by *t*-BuOOH, at 5 °C

Entry	Catalyst		Time (h)	Yield[a] of **6a** (%)	$[\alpha]_D$[b]	Ee[c] (%)
	Compound	R				
1	**1a**	H	4	47	+59	28
2	**1b**	Butyl	10	59	−24.3	11
3	**1c**	Benzyl	10	33	−16	8
4	**1d**	$(CH_2)_2OH$	1	65	−173	81 (82)[d]
5	**1e**	$(CH_2)_2OCH_3$	3	58	−43	20
6	**1f**	$(CH_2)_3OH$	1	82	−196	92 (94)[d]
7	**1g**	$(CH_2)_3OCH_3$	2	61	−49	23
8	**1h**	$(CH_2)_4OH$	1	65	−88	41
9	**1i**	$(CH_2)_4P(O)Ph_2$	2	64	−23	11
10	**2d**	$(CH_2)_2OH$	5	70	−142	66
11	**2f**	$(CH_2)_3OH$	6	51	−162	76 (75)[d]
12	**3d**	$(CH_2)_2OH$	8	28	−96	45
13	**3f**	$(CH_2)_3OH$	10	35	−113	53
14	**4d**	$(CH_2)_2OH$	10	42	+45	21
15	**4f**	$(CH_2)_3OH$	7	40	+64	30

[a] Based on isolation by preparative TLC.
[b] In CH_2Cl_2 at 22 °C.
[c] Determined by specific rotation.
[d] Determined by ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$ as chiral shift reagent.

stituents have an opposite effect. The discrimination between the prochiral planes of the chalcone is the most efficient, when catalyst **1f** assists the formation of the transient complex.

It is worth mentioning that the use of catalysts **1b**–**i** promoted the formation of the (2*R*,3*S*)-isomer of epoxyketone **6a** (with negative specific rotation).[13,14] In contrast, the unsubstituted catalyst **1a** favored the formation of antipode **6a** (with positive rotation).

Comparing the enantioselectivities obtained in the presence of the different catalysts **1**–**4**, the use of the α-methyl-glucopyranoside-based lariat ethers **1** gave the best results. The experiments applying β-phenyl-glucopyranoside-based lariat ethers **2** gave less satisfactory results. Hence, the presence of the sterically more demanding 1-phenoxy group was unfavorable. Even lower enantioselectivities were obtained using α-methyl-galactopyranoside-based crown catalysts **3**, which seems to be the consequence of the different configuration of C4. In the α-galacto-lariat ether **3**, the 4,6-*O*-benzylidene-acetal ring is axial, while in gluco-compound **1**, the same substituent is equatorial. The lowest enantioselectivities were detected when mannitol-based aza-crowns **4** were tested. The above trend was well demonstrated by the ee values obtained in the presence of the members of the **1f**, **2f**, **3f**, and **4f** series containing a hydroxypropyl substituent on the nitrogen atom. In the above order, ee values of 92%, 76%, 53%, and 30%, respectively, were measured. The shortening of the carbon chain between the nitrogen atom and the hydroxyl group in macrocycles **1d**, **2d**, **3d**, and **4d** resulted in lower ee values, (81%, 66%, 45%, and 21%, respectively), which, however, followed the same trend.

In the experiments carried out with lariat ethers incorporating a mannitol unit **4** as catalyst, the epoxyketone **6** with a positive specific rotation (2*S*,3*R*) was obtained in excess. This is presumably connected to the relative configuration of the monosaccharides in the crown ether, which is (2*R*,3*S*) in D-glucose and D-galactose and (3*S*,4*R*) in D-mannitol. The low asymmetric induction of the crown ether with mannitol unit can be explained with the relatively higher flexibility of **4** in comparison to that of macrocycles **1**–**3**. While the latter crown ethers are rigid due to anellation with the sugar ring, **4** was not blocked by such anellation. In general, rigid molecules are more suitable for enantiomeric discrimination than flexible ones.

The epoxidation of a series of chalcones **5a**–**n** was examined in the presence of catalyst **1f**, which proved to be the most efficient in the enantioselective epoxidation of chalcone **5a** ($Ar^1 = Ar^2 = Ph$) (Table 2). Due to solubility problems, the experiments were carried out at room temperature. The corresponding *trans*-epoxyketones **6a**–**n** were obtained in all cases, with enantiomeric excesses with negative specific rotations. The oxidation of the monosubstituted derivatives **6a**–**d** and **6h**–**i** took place with higher enantioselectivities (77–82%, entries 2–4 and 8–9), when compared to that of the unsubstituted chalcone **6a** (73% ee). Among the disubstituted chalcones, the epoxydation of the derivatives containing 4-chloro or 4-methyl group in both phenyl rings, **6k** and **6m**, led to an ee of ca. 77% (entries 11 and 13). Presumably, the significant differences observed in the enantioselectivities are the consequences of steric and electronic effects. The substitution pattern had an impact on the solubility and lipophility of the substrates.

The efficiency of the chiral crown ether in this oxidation, can be explained by assuming a mechanism, in which the *t*-$BuOO^-$ anion[15] accompanied by the crown-sodium cation attacks the electron-deficient alkene. The efficiency of the crown ether in the asymmetric induction suggests that the substituent on the nitrogen atom assists the complexation of the cation of the salt in the third dimension. The complexing interaction is optimal in case of the hydroxypropyl substituent. To determine the

Table 2. Epoxidation of substituted chalcones by *t*-BuOOH in the presence of catalyst **1f** at room temperature

Entry	Ar^1	Ar^2	Time [h]	Yield[a] [%]	$[\alpha]_D$[b]	Ee[c] [%]
1	Ph	Ph	1	**6a**, 78	−155.1	73
2	Ph	4-Me–Ph	3	**6b**, 62	−169.7	81
3	Ph	4-MeO–Ph	3	**6c**, 53	−167.9	82
4	Ph	4-Cl–Ph	1	**6d**, 57	−156.1	80
5	Ph	2,4-di-Cl–Ph	1	**6e**, 82	−91.1	47
6	Ph	3,4-di-Cl–Ph	0.5	**6f**, 61	−129.3	66
7	Ph	4-NO_2–Ph	7	**6g**, 74	−37.8	16
8	4-Me–Ph	Ph	3	**6h**, 57	−183.4	77
9	4-NO_2–Ph	Ph	2	**6i**, 38	−195.9	79
10	4-MeO–Ph	4-NO_2–Ph	4	**6j**, 29	−45.2	27
11	4-Cl–Ph	4-Cl–Ph	1	**6k**, 66	−154.7	77
12	4-F–Ph	2-Cl–Ph	1	**6l**, 77	−6.6	3
13	4-Me–Ph	4-Me–Ph	3	**6m**, 64	−171.9	76
14	4-Me–Ph	2,4-di-Cl–Ph	0.5	**6n**, 82	−87.8	42

[a] Based on isolation by preparative TLC.
[b] Determined at *c* 1 in CH_2Cl_2 at 22 °C.
[c] Determined by ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$ as the chiral shift reagent.

absolute configurations of the obtained epoxyketones the complete stereostructure of **6b** was determined by single crystal X-ray diffraction, while the CD spectra of several products involving **6b** were analyzed.

2.2. X-ray structure determination and analysis

There were two crystallographically independent molecules in the asymmetric unit around the pseudo twofold axis (Fig. 2). Both molecules are *trans* isomers (C4–C2–C3–C13). The absolute configuration of C2 is *R* and C3 is *S* in both molecules, more likely, since the effect of anomalous dispersion of X-ray intensities is very small.

2.3. CD spectra of chalcone epoxides

The CD spectra of the two enantiomers of the unsubstituted *trans*-chalcone epoxide **6a** are displayed in Figure 3. The spectra of **6b** and **6i** are also given in the figure to illustrate the circular dichroic features of the substituted products obtained in the phase-transfer catalyzed reactions. The positions and intensities of bands observed in the CD spectra of **6a**, **6b**, **6d**, **6i**, **6k**, and **6m** are presented in Table 3 [The data for the (2*R*,3*S*) isomer of **6a** are in good agreement with those published in lit.[13]].

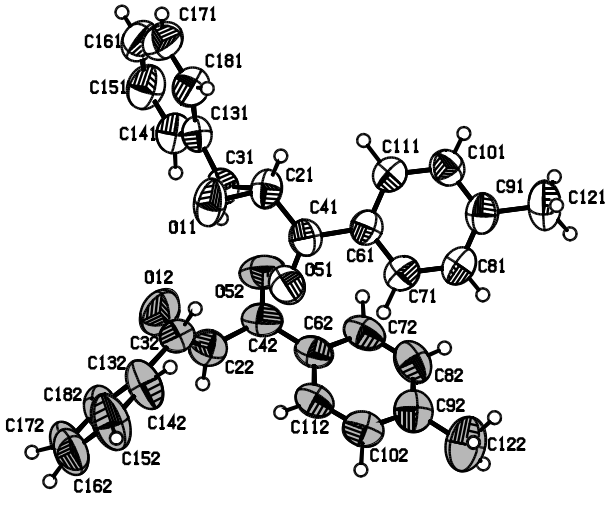


Figure 2. ORTEP diagram at 50% probability level showing the two crystallographically independent molecules in the asymmetric unit (residues are identified by the last number of the label). Residue 1 is presented in white, residue 2 with gray octant shaded heavy atoms.

As can be seen, the pattern of the bands in the CD spectra of all the substituted products shows a close similarity to that in the spectrum of (−)-**6a**. The CD signals around 320 nm belong to the $n \rightarrow \pi^*$ transition of the C=O groups. The absolute configurations of the stereogenic centers in optically active ketones can be determined from the sign of this band with help of the 'octant rule'.[16] Providing that the conformations of our epoxyketones **6a**–**6n** in solution are similar to the conformation of **6b** in its crystalline state, the chemical bonds around the carbonyl units of the (2*R*,3*S*) isomers of **6a**–**n** are arranged as shown schematically in Figure 3b. The octant rule for such an arrangement predicts a negative Cotton-effect, since the majority of the atoms contributing to the chiral disturbance of the carbonyl group lie in the lower left back octant. Thus, the negative sign of the bands in the range of the $n \rightarrow \pi^*$ transitions in the spectra of the substituted chalcone epoxides **6b**–**n** clearly indicate an excess of the (2*R*,3*S*)-isomers in these products. It should be noted that the carbonyl CD bands of some α,β-epoxy ketones, for example, of isoflavone epoxides, do not follow the octant rule.[17] Those molecules are, however, structurally completely different from ours: They are cyclic ketones with a rigid quasi-planar ring system, from which the epoxy oxygen atom sticks out.[18]

The (+)/(−) band at 230 nm and the (−)/(+) band around 250 nm in the spectrum of the (2*R*,3*S*)/(2*S*,3*R*) isomer of **6a** belong to $\pi \rightarrow \pi^*$ transitions. In the spectra of the substituted derivatives these bands are shifted while their signs remain unaltered. A detailed assignment of these $\pi \rightarrow \pi^*$ bands requires further experimental and theoretical work.

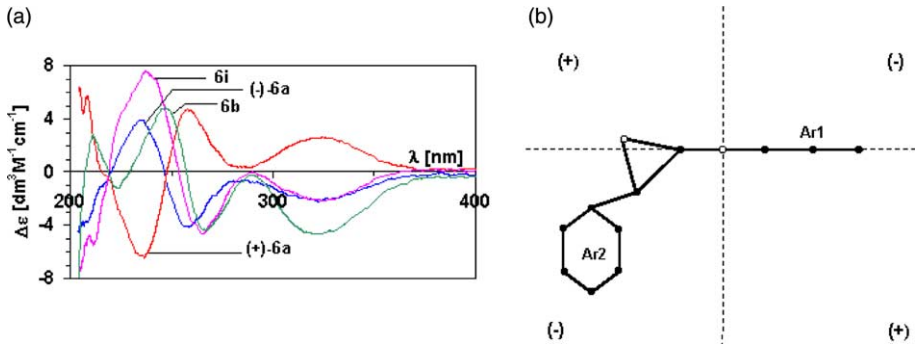


Figure 3. (a) CD spectra of the enantiomers of unsubstituted chalcone epoxides (+)-**6a** and (−)-**6a** and of the substituted derivatives **6b** and **6i** [5×10^{-5} M solutions in ethanol, ee values: (+)-**6a** 90%, (−)-**6a** 80%, **6b** 81%, **6i** 79%]. (b) Octant projection diagram for the (2*R*,3*S*) isomers of chalcone epoxides.

Table 3. CD spectra of chalcone epoxides (EtOH, 25 °C, ee values as given in the Experimental section)

Compound	Spectral bands λ_{max} [nm] ($\Delta\varepsilon$ [dm^3 M^{-1} cm^{-1}])			
(+)-**6a**	208 (+5.60)	236 (−6.46)	259 (+4.70)	324 (+2.61)
(−)-**6a**	206 (−4.05)	235 (+3.94)	258 (−4.19)	323 (−2.23)
6b	211 (−5.47)	237 (+7.61)	265 (−4.69)	325 (−2.21)
6d	209 (−2.50)	244 (+1.92)	273 (−0.42)	320 (−1.11)
6i	222 (−1.16)	248 (+4.77)	267 (−4.38)	324 (−4.66)
6k	214 (−7.63)	242 (+5.97)	265 (−6.25)	322 (−3.05)
6m		237 (+13.0)	265 (−2.32)	330 (−5.24)

3. Experimental

3.1. General procedures

Melting points were determined using a Büchi 510 apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 °C, while the IR spectra were recorded on a Perkin–Elmer 237 spectrophotometer. NMR spectra were obtained on a Bruker DRX-500 instrument in $CDCl_3$. Mass spectra were obtained on a Varian MAT 312 instrument. Chemical ionization was applied as the ionization technique. Elemental analysis was determined on a Perkin–Elmer 240 automatic analyzer. Analytical and preparative thin layer chromatography was performed on silica gel plates (60 GF-254, Merck), while column chromatography was carried out using 70–230 mesh silica gel (Merck). CD spectra were recorded on a Jasco 810 spectropolarimeter.

3.2. General procedure for the epoxidation of chalcones

A solution of enone (1.44 mmol) and the appropriate catalyst (0.1 mmol) in toluene (3 mL) containing sodium hydroxide (1 mL 20% aq) was treated with 50% *tert*-butylhydroperoxide in decane (0.5 mL, 2.88 mmol) and the mixture stirred at 6 °C. After a reaction time of 1–10 h, a new portion of toluene (7 mL) was added and the mixture stirred with water (10 mL). The organic phase was washed with 10% aq hydrochloric acid (10 mL) twice and then with (10 mL) water. The organic phase was dried over Na_2CO_3. The crude product obtained after evaporating the solvent was purified by preparative TLC (silica gel, hexane–ethyl acetate, 10:1, eluent) to give adduct **6** in its pure form.

3.2.1. (2*R*,3*S*)-2,3-Epoxy-1-(4-tolyl)-3-phenylpropan-1-one, 6b. Yield: 62% (white crystals); mp 59–60 °C (lit.[19] 59–60 °C); $[\alpha]_D^{20} = -169.7$ (*c* 1, CH_2Cl_2); 81% ee; ^{1}H NMR ($CDCl_3$) δ ppm: 2.42 (s, 3H, CH_3), 4.07 (d, $J = 1.2$ Hz, 1H), 4.27 (d, $J = 1.7$ Hz, 1H), 7.28 (d, 2H, COPhH-*m*), 7.39 (m, 5H, CHPhH), 7.91 (d, 2H, COPhH-*o*); HRMS calcd for $C_{16}H_{14}O_2$ 238.0998, found 238.0995.

3.2.2. (2*R*,3*S*)-2,3-Epoxy-1-(4-methoxyphenyl)-3-phenylpropan-1-one, 6c. Yield: 53% (white crystals); mp 69–70 °C; $[\alpha]_D^{20} = -167.9$ (*c* 1, CH_2Cl_2); 82% ee; ^{1}H NMR ($CDCl_3$) δ ppm: 3.87 (s, 3H, CH_3), 4.07 (d, $J = 1.3$ Hz, 1H), 4.25 (d, $J = 1.7$ Hz, 1H), 6.95 (d, 2H, COPhH-*m*), 7.39 (m, 5H, CHPhH), 8.01 (d, 2H, COPhH-*o*); HRMS calcd for $C_{16}H_{14}O_3$ 254.0950, found 254.0948.

3.2.3. (2*R*,3*S*)-2,3-Epoxy-1-(4-chlorophenyl)-3-phenylpropan-1-one, 6d. Yield: 57% (white crystals); mp 116 °C (lit.[20] 114–116 °C); $[\alpha]_D^{20} = -156.1$ (*c* 1, CH_2Cl_2); 80% ee {lit.[20] $[\alpha]_D^{20} = -202$ (*c* 1, CH_2Cl_2), 99% ee}; ^{1}H NMR ($CDCl_3$) δ ppm: 4.07 (d, $J = 1.3$ Hz, 1H), 4.23 (d, $J = 1.6$ Hz, 1H), 7.36 (d, 2H, CHPhH-*o*), 7.40 (t, 3H, CHPhH-*m.p*), 7.46 (d, 2H, COPhH-*m*), 7.96 (d, 2H, COPhH-*o*); HRMS calcd for $C_{15}H_{11}O_2Cl$ 258.0450, found 258.0447.

3.2.4. (2*R*,3*S*)-2,3-Epoxy-1-(2,4-dichlorophenyl)-3-phenylpropan-1-one, 6e. Yield: 82% (white crystals); mp 128–129 °C; $[\alpha]_D^{20} = -91.1$ (*c* 1, CH_2Cl_2); 47% ee; ^1H NMR ($CDCl_3$) δ ppm: 4.09 (d, $J = 1.3$ Hz, 1H), 4.23 (d, $J = 1.6$ Hz, 1H), 7.36 (d, 2H, CHPhH-*o*), 7.42 (t, 2H, CHPhH-*m*), 7.45 (t, 1H, CHPhH-*p*), 7.48 (d, 1H, COPhH-*o*), 7.96 (d, 1H, COPhH-*m*), 8.01 (s, 1H, COPhH-*m*); HRMS calcd for $C_{15}H_{10}O_2Cl_2$ 292.0060, found 292.0058.

3.2.5. (2*R*,3*S*)-2,3-Epoxy-1-(3,4-dichlorophenyl)-3-phenylpropan-1-one, 6f. Yield: 61% (white crystals); mp 133–141 °C; $[\alpha]_D^{20} = -129.3$ (*c* 1, CH_2Cl_2); 66% ee; ^1H NMR ($CDCl_3$) δ ppm: 4.09 (d, $J = 1.3$ Hz, 1H), 4.23 (d, $J = 1.6$ Hz, 1H), 7.36 (d, 2H, CHPhH-*o*), 7.42 (t, 2H, CHPhH-*m*), 7.45 (t, 1H, CHPhH-*p*), 7.47 (d, 1H, COPhH-*o*), 7.96 (d, 1H, COPhH-*m*), 8.02 (s, 1H, COPhH-*o*); HRMS calcd for $C_{15}H_{10}O_2Cl_2$ 292.0060, found 292.0056.

3.2.6. (2*R*,3*S*)-2,3-Epoxy-1-(4-nitrophenyl)-3-phenylpropan-1-one, 6g. Yield: 74% (white crystals); mp 142–144 °C; $[\alpha]_D^{20} = -37.8$ (*c* 1, CH_2Cl_2); 16% ee; ^1H NMR ($CDCl_3$) δ ppm: 4.21 (d, $J = 1.1$ Hz, 1H), 4.29 (d, $J = 1.6$ Hz, 1H), 7.38 (t, 2H, CHPhH-*m*), 7.40 (t, 1H, CHPhH-*p*), 7.54 (d, 2H, CHPhH-*o*), 8.04 (d, 2H, COPhH-*o*), 8.32 (d, 2H, COPhH-*m*); HRMS calcd for $C_{15}H_{11}NO_4$ 269.0690, found 269.0686.

3.2.7. (2*R*,3*S*)-2,3-Epoxy-1-phenyl-3-(4-tolyl)-propan-1-one, 6h. Yield: 57% (white crystals); mp 78 °C (lit.[21] 77–78 °C); $[\alpha]_D^{20} = -183.4$ (*c* 1, CH_2Cl_2); 77% ee; ^1H NMR ($CDCl_3$) δ ppm: 2.37 (s, 3H, CH_3), 4.04 (d, $J = 1.3$ Hz, 1H), 4.28 (d, $J = 1.6$ Hz, 1H), 7.21 (d, 2H, CHPhH-*o*), 7.26 (d, 2H, CHPhH-*m*), 7.48 (t, 2H, COPhH-*m*), 7.61 (t, 1H, COPhH-*p*), 8.00 (d, 2H, COPhH-*o*); HRMS calcd for $C_{16}H_{14}O_2$ 238.0998, found 238.0994.

3.2.8. (2*R*,3*S*)-2,3-Epoxy-1-phenyl-3-(4-nitrophenyl)-propan-1-one, 6i. Yield: 38% (yellow crystals); mp 139–141 °C (lit.[20] 138–140 °C); $[\alpha]_D^{20} = -195.9$ (*c* 1, CH_2Cl_2); 79% ee {lit.[20] $[\alpha]_D^{20} = -272$ (*c* 1, CH_2Cl_2) for pure enantiomer}; ^1H NMR ($CDCl_3$) δ ppm: 4.21 (d, $J = 1.1$ Hz, 1H), 4.27 (d, $J = 1.7$ Hz, 1H), 7.52 (t, 2H, COPhH-*m*), 7.54 (d, 2H, CHPhH-*m*), 7.66 (t, 1H, COPhH-*p*), 8.01 (d, 2H, CHPhH-*o*), 8.27 (d, 2H, COPhH-*o*); HRMS calcd for $C_{15}H_{11}NO_4$ 269.0690, found 269.0688.

3.2.9. (2*R*,3*S*)-2,3-Epoxy-1-(4-nitrophenyl)-3-(4-methoxyphenyl)-propan-1-one, 6j. Yield: 29% (yellow crystals); mp 135–136 °C; $[\alpha]_D^{20} = -45.2$ (*c* 1, CH_2Cl_2); 27% ee; ^1H NMR ($CDCl_3$) δ ppm: 3.74 (s, 3H, CH_3), 4.24 (d, $J = 1.3$ Hz, 1H), 4.30 (d, $J = 1.8$ Hz, 1H), 7.22 (d, 2H, CHPhH-*o*), 7.28 (d, 2H, CHPhH-*m*), 8.16 (d, 2H, COPhH-*o*), 8.24 (d, 2H, COPhH-*m*); HRMS calcd for $C_{16}H_{13}NO_5$ 299.0800, found 299.0798.

3.2.10. (2*R*,3*S*)-2,3-Epoxy-1-(4-chlorophenyl)-3-(4-chlorophenyl)-propan-1-one, 6k . Yield: 66% (yellow crystals); mp 116–118 °C; $[\alpha]_D^{20} = -154.7$ (*c* 1, CH_2Cl_2); 77% ee; ^1H NMR ($CDCl_3$) δ ppm: 4.09 (d, $J = 1.3$ Hz, 1H), 4.24 (d, $J = 1.6$ Hz, 1H), 7.40 (d, 2H, CHPhH-*o*), 7.44 (d, 2H, CHPhH-*m*), 7.47 (d, 2H, COPhH-*o*), 7.98 (d, 2H, COPhH-*m*); HRMS calcd for $C_{15}H_{10}O_2Cl_2$ 292.0060, found 292.0057.

3.2.11. (2*R*,3*S*)-2,3-Epoxy-1-(2-chlorophenyl)-3-(4-fluorophenyl)-propan-1-one, 6l. Yield: 77% (yellow crystals); mp 99–101 °C $[\alpha]_D^{20} = -6.6$ (*c* 1, CH_2Cl_2); 3% ee; ^1H NMR ($CDCl_3$) δ ppm: 4.11 (d, $J = 1.3$ Hz, 1H), 4.25 (d, $J = 1.6$ Hz, 1H), 7.43 (d, 2H, CHPhH-*o*), 7.47 (d, 2H, CHPhH-*m*), 7.49 (t, 1H, COPhH-*m*), 7.51 (t, 1H, COPhH-*p*), 7.54 (d, 1H, COPhH-*o*), 8.01 (d, 1H, COPhH-*m*); HRMS calcd for $C_{15}H_{10}O_2ClF$ 276.0357, found 276.0355.

3.2.12. (2*R*,3*S*)-2,3-Epoxy-1-(4-tolyl)-3-(4-tolyl)-propan-1-one, 6m. Yield: 64% (white crystals); mp 99–100 °C; $[\alpha]_D^{20} = -171.9$ (*c* 1, CH_2Cl_2); 76% ee; ^1H NMR ($CDCl_3$) δ ppm: 2.37 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.03 (d, $J = 1.4$ Hz, 1H), 4.27 (d, $J = 1.8$ Hz, 1H), 7.20 (d, 2H, CHPhH-*o*), 7.26 (m, 4H, PhCH), 7.91 (d, 2H, COPhH-*o*); HRMS calcd for $C_{17}H_{16}O_2$ 252.1148, found 252.1145.

3.2.13. (2*R*,3*S*)-2,3-Epoxy-1-(2,4-dichlorophenyl)-3-(4-tolyl)-propan-1-one, 6n. Yield: 82% (white crystals); mp 111–112 °C; $[\alpha]_D^{20} = -87.8$ (*c* 1, CH_2Cl_2); 42% ee; ^1H NMR ($CDCl_3$) δ ppm 2.37 (s, 3H, CH_3), 4.08 (d, $J = 1.3$ Hz, 1H), 4.23 (d, $J = 1.6$ Hz, 1H), 7.36 (d, 2H, CHPhH-*m*), 7.40 (d, 2H, CHPhH-*o*), 7.46 (d, 1H, COPhH-*o*), 7.96 (d, 1H, COPhH-*m*), 8.01 (s, 1H, COPhH-*m*); HRMS calcd for $C_{16}H_{12}O_2Cl_2$ 306.0218, found 306.0214.

3.3. X-Ray structure analysis of compound 6b

Single crystals were grown from methanol solution by controlled solvent evaporation rate technique at room temperature. Crystal data: $C_{16}H_{14}O_2$, formula wt: 238.27, colorless, block, size: $0.60 \times 0.40 \times 0.30$ mm, orthorhombic, space group $P2_12_12_1$, $a = 8.807(1)$, $b = 10.911(2)$, $c = 27.532(3)$ Å, $V = 2645.6(6)$ Å^3, $T = 293(2)$ K, $Z = 8$, $F(000) = 1008$, $D_x = 1.196$ Mg/m^3, $\mu = 0.622$ mm^{-1}. A single crystal of **6b** was mounted on a glass fiber. Cell parameters were determined by least-squares of the setting angles of 25 ($35.25° \leqslant \theta \leqslant 38.67°$) reflections. Intensity data were collected on an Enraf-Nonius CAD4 diffractometer (graphite monochromator; Cu-Kα radiation, $\lambda = 1.54184$ Å) at 293(2) K in the range $3.21° \leqslant \theta \leqslant 75.65°$ using ω–2θ scans. Backgrounds were measured half the total time of the peak scans. The intensities of three standard reflections were monitored regularly in every 60 min. The intensities of the standard reflections indicated a crystal decay of 4%, the data were corrected for decay. A total of 6321 reflections were

collected of which 5385 were unique [$R_{int} = 0.0113$, $R\sigma = 0.0140$]; intensities of 4494 reflections were greater than $2\sigma(I)$,[22] completeness to $2\theta = 1.000$. A semi-empirical (ψ-scan) absorption correction[23] was applied to the data (the minimum and maximum transmission factors were 0.930 and 0.991). The structure was solved by direct methods.[24] Anisotropic full-matrix least-squares refinement[25] on F^2 for all nonhydrogen atoms yielded $R_1 = 0.0383$ and $wR_2 = 0.1171$ for 4494 [$I > 2\sigma(I)$] and $R_1 = 0.0468$ and $wR_2 = 0.1227$ for all (5385) intensity data. Number of parameters = 438, goodness-of-fit = 1.083; the maximum and mean shift/esd 0.561 and 0.068; extinction coefficient = 0.0074(6). The maximum and minimum residual electron density in the final difference map was 0.129 and -0.137 e/Å^3. Absolute structure parameter[26] $x = 0.1(2)$. Hydrogen atom positions were located in difference maps and were refined. (ORTEP diagram[27]) CCDC number 233942.

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