Lanthanide complexes combined with chiral salen ligands: application in the enantioselective epoxidation reaction of \(\alpha,\beta\)-unsaturated ketones

Xuexiu Xia,\textsuperscript{a,b} Chengrong Lu,\textsuperscript{a,*} Bei Zhao\textsuperscript{b,*ab} and Yingming Yao\textsuperscript{b,ab}

Readily available lanthanide amides \(\text{Ln}[\text{N(SiMe}\text{3})\text{2}]\text{3} \) (\(\text{Ln} = \text{Nd} \text{ (1)}, \text{Sm} \text{ (2)}, \text{Eu} \text{ (3)}, \text{Yb} \text{ (4)}, \text{La} \text{ (5)})\), combined with chiral salen ligands \(\text{H}_\text{2}\text{L} \text{a} \) \(\text{C}-\text{C}, \text{N},\text{N}\text{'-di-(3,5-disubstituted-salicylidene)-1,2-cyclohexanediamine} \) and \(\text{H}_\text{2}\text{L} \text{b} \) \(\text{C}-\text{N},\text{N}\text{'-di-(3,5-disubstituted-salicylidene)-1,2-diphenyl-1,2-ethanediamine} \) were employed in the enantioselective epoxidation of \(\alpha,\beta\)-unsaturated ketones. It was found that the salen–La complex shows the highest efficiency and enantioselectivity. A relatively broad scope of \(\alpha,\beta\)-unsaturated ketones was investigated, and excellent yields (up to 99\%) and moderate to good enantioselectivities (37–87\%) of the target molecules were achieved.

Introduction

Salen ligands are a particular class of Schiff bases, which are produced by condensation of two salicylaldehydes with a diamine. The use of salen metal complexes for a large variety of catalytic transformations has emerged, mainly because the salen ligands are easily available and highly tunable, and are capable of coordinating to many different metals to form various catalysts.\textsuperscript{1} In recent years, chiral salen ligands have become one of the most popular chiral ligands and a series of salen-transition metal catalysts have found application in enantioselective synthesis. In 2001, Kozlowski developed a set of modular bifunctional salen ligands, which showed enhanced reactivity in the asymmetric addition of diethylzinc to aldehydes and achieved excellent yield (up to 99\%) with high enantioselectivity (up to 91\%).\textsuperscript{2} In 2003, Jiang used salen-Ti complexes to catalyze the enantioselective addition of \(\text{TMSCN} \) to ketones.\textsuperscript{3} Rawal reported that the enantioselective carbonyl–ene reactions were catalyzed by a salen–Co complex, which generated chiral homoallylic alcohols in excellent yields, enantioselectivities and diastereoselectivities.\textsuperscript{4} In 2014, the asymmetric conia-ene-type cyclization of \(\alpha\)-functionalized ketones was catalyzed by a chiral salen–Fe complex.\textsuperscript{5} Salen–Zr complexes catalyzed enantioselective \(\alpha\)-hydroxylation of \(\beta\)-ketones esters using cumene hydroperoxide (CHP) as the oxidant in excellent yields and enantioselectivities.\textsuperscript{6} Epoxidation of non-functionalised alkenes catalyzed by \(\text{Mn}–\text{salen} \) was investigated by Vyas.\textsuperscript{7}

However, to the best of our knowledge, examples of highly active lanthanide complexes bearing chiral salen ligands are limited, and their applications are restricted to ring–opening reaction of epoxides,\textsuperscript{8} aminooalkene hydroamination/cyclisation,\textsuperscript{9} and nitro–mannich reaction.\textsuperscript{10} Shibasaki developed asymmetric epoxidation of the electron-deficient \(\text{C}==\text{C} \) bonds in enones, \(\alpha,\beta\)-unsaturated amides and esters, using the combination of lanthanide–BINOL–\(\text{Ph}_\text{3}\text{As}=\text{O} \) as catalyst.\textsuperscript{11} Some lanthanide–BINOL and its derivatives have also been investigated in such a transformation, which gave rise to high enantioselectivities in many cases.\textsuperscript{12} Feng employed \(\text{Sc(OTf)}\text{3/}N,N',N'-\text{dioxide} \) as catalyst to realize the asymmetric epoxidation of \(\alpha,\beta\)-unsaturated ketones with excellent enantioselectivities.\textsuperscript{13}

Recently, our group reported a series of rare-earth metal complexes together with phenoxy-functionalized chiral prolinol amides which are highly efficient catalysts in the epoxidation of \(\alpha,\beta\)-unsaturated ketones. Both bisubstituted and trisubstituted chalcone produced the corresponding epoxides in excellent yields (up to 99\%) and enantioselectivities (up to 99\%) using tert-butylhydroperoxide (TBHP) as the oxidant.\textsuperscript{14} As a continuation of our research on the lanthanide-mediated asymmetric transformation, we herein report rare-earth metal complexes bearing chiral salen ligands and their catalytic potential in the enantioselective epoxidation of \(\alpha,\beta\)-unsaturated ketones.

Results and discussion

To test the reactivity and selectivity of lanthanide amides in combination with chiral salen ligands, five amides \(\text{Ln} \text{[N(SiMe}\text{3})\text{2}]\text{3} \) (\(\text{Ln} = \text{Nd} \text{ (1)}, \text{Sm} \text{ (2)}, \text{Eu} \text{ (3)}, \text{Yb} \text{ (4)}, \text{La} \text{ (5)})\), two series of phenoxy-functionalized chiral salen ligands \((\text{C},\text{S})\text{-}N,N',\text{N'}\text{-di-(3-R}\text{1}-5\text{-salicylidene})\text{-}1\text{-cyclohexanediamine}, \text{[R}\text{1} = \text{R}\text{2} = \text{CH}_\text{3},\text{H},\text{CH}=\text{CH},\text{CH}_\text{2}==\text{CH}_{\text{2}},\text{CH}_\text{2}==\text{C}_\text{6}\text{H}_\text{4},\text{C}_\text{6}\text{H}_\text{4}-\text{CH}==\text{CH})(\text{C},\text{S})\text{-}N,N',\text{N'}\text{-di-(3-R}\text{1}-5\text{-salicylidene})\text{-}1\text{-cyclohexanediamine}, \text{[R}\text{1} = \text{R}\text{2} = \text{CH}_\text{3},\text{H},\text{CH}=\text{CH},\text{CH}_\text{2}==\text{CH}_{\text{2}},\text{CH}_\text{2}==\text{C}_\text{6}\text{H}_\text{4},\text{C}_\text{6}\text{H}_\text{4}-\text{CH}==\text{CH})\) with excellent yields (up to 99\%) and high enantioselectivities (up to 99\%) using TBHP as the oxidant.
Me (H2L1); R1 = R2 = 'Bu (H2L2); R1 = H, R2 = Cl (H2L3); R1 = H, R2 = 'Bu (H2L3); R1 = 'Bu, R2 = H (H2L4); R1 = Me, R2 = H (H2L5); R1 = 'Bu, R2 = 1-adam (H2L6); (S,S)-N,N'-3-R'-5-R''-salicylidene)-1,2-diphenyl-1,2-ethanedi amine [R1 (H2L8); R1 = H2L9]; R1 = R2 = H (H2L4); R1 = R2 = 'Bu (H2L6)].

With the neodymium amide 1 and the salen ligand H2L1 in hand, the epoxidation reaction of chalcone was carried out in the presence of TBHP in THF. The results are listed in Table 1. The model reaction underwent quantitatively with unsatisfying enantioselectivity (99% yield and 31% ee). On the basis of this finding, the influence of the chiral salen ligands on enantioselectivity was carefully investigated via the modification of the phenol moiety. The yields of the corresponding epoxides remained excellent and the ee values varied from 11–31% (Table 1, entries 1–7). If the chiral linkage was changed to (S,S)-1,2-diphenyl-1,2-ethanedi amine (H2L8 and H2L9), no significant improvement is observed (Table 1, entries 1–9).

Thus, the chiral salen ligand H2L1 was the optimal choice for the model reaction considering both yield and enantioselectivity. Lanthanide amides of different metal centers were studied, and the lanthanum amide 5 gave the best result. The ee value of 7a reached 41% without sacrificing yield (Table 1, entries 1 and 10–13).

To further improve enantioselectivity, different solvents were screened. Fortunately, when acetoni trile was used as the solvent in the model reaction, the ee value increased to 57%, while the yield of 99% was maintained (Table 1, entries 13–17). Some successful cases in the asymmetric epoxidation reactions also achieved high ee values in acetoni trile.14,15 Perhaps the weak coordination of acetoni trile to the central lanthanide metal changes the coordination environment. And it leads to better match for the catalyst and substrate, which may plays an important role in the metal-based catalytic asymmetric reaction. A relatively low temperature is usually helpful to improve the enantioselectivity of the asymmetric reaction. To our delight, attempts to lower the reaction temperature have a positive effect on the enantioselectivity. The ee value significantly increased when the reaction temperature decreased, and the 80% ee of the epoxide 7a was obtained at −20 °C (Table 1, entries 17–20). Finally, the ratio of the lanthanum amide 5 to the chiral salen ligand H2L1 was studied in CH3CN and the results showed that the 1 : 1.2 molar ratio was optimal for the model reaction (Table 1, entries 19, 21–22). Thus, 10 mol% of La amide 5 in the combination of 12 mol% of chiral salen ligand H2L1 was an optimal catalytic system for the asymmetric epoxidation of chalcone with TBHP in CH3CN at −20 °C.

Subsequently, various α,β-unsaturated ketones were synthesized and investigated, and the results are summarized in Chart 1. Most of the disubstituted α,β-unsaturated ketones underwent the transformation to give epoxides in excellent yields (92–99%) and good to high enantioselectivities (57–83%), with the exception of 7h (37% ee) (Chart 1, 7a–7d). Delightedly, much better enantioselectivities, ranging from 80–87%, were observed in reactions of trisubstituted α,β-unsaturated ketones, which are in general bulky and challenging substrates (Chart 1, 7p–7y).

It is noteworthy that these substrates are not only trisubstituted, but also cyclic with restricted mobility, hence more rigid transition states are supposed to generate, which may play a critical role in controlling the enantioselectivity. Relatively high results include the lanthanide–BINOL and its derivatives by Shibasaki,11 Inanaga12 and Ding,13 and Sc(OTf)3/diox ide catalyst by Feng,12 and rare-earth metal complexes together with phenox y-functionalized chiral prolinols reported by us.14

The real active species in the current system was investigated. La amide 5 was treated with 1.2 equiv. chiral salen ligand H2L1 in THF. After workup, complex 8 was isolated as yellow crystals (Scheme 1). Its 1H NMR spectrum shows absence of a peak at 0.1980 ppm, which is ascribed to the coordinated -N(SiMe3)2 group. Signals at 3.87–3.55, 1.60 and 1.02 ppm are assigned to cyclohexyl linkage. The peaks at 8.10, 7.91, 7.63, and 7.57 ppm are ascribed to the CH = N double bond. These observations prove the formation of complex 8 bearing the chiral salen ligand. Finally, the ratio of the lanthanum atom to chiral salen ligand is determined to be 2 : 3, based on results of elemental analysis and complex titration.

To find out whether complex 8 is the active species, it was tested in the model asymmetric epoxidation of chalcone under

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### Table 1  Optimization of the reaction conditions"}

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*The reaction was performed with chalcone (0.3 mmol), TBHP (0.36 mmol) in 1 mL of solvent. bHPLC yield. cDetermined by chiral HPLC analysis.
standard conditions. However, neither the yield nor ee value was comparable with results of \textit{in situ} generated catalyst. The target epoxide was obtained in 91% yield and only 70% ee (Table 2, entry 1). Comparing described catalyst system with complex 8, the difference is HN(SiMe\(_3\))\(_2\) generated \textit{in situ} in the former, which may have the positive effects on the asymmetric transformation. To verify the hypothesis, complex 8 together with 20 mol% HN(SiMe\(_3\))\(_2\) were added to the model reaction. The outcome of 98% yield with 78% ee indicates that the addition of HN(SiMe\(_3\))\(_2\) indeed has a positive effect on the asymmetric catalytic process (Table 2, entry 2).

Screening of basic additives, including 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), Et\(_3\)N, pyridine, and 2,2'-bipyridine, proved that HN(SiMe\(_3\))\(_2\) (20 mol%) is the optimal choice (Table 2, entries 2–9).

Finally, the outcome of the model reaction on a gram scale was satisfactory with an appropriate prolonging of the reaction time and the absolute configuration of the epoxides was determined by single crystal diffraction analysis, chiral HPLC and optical rotation analysis of a representative crystal 7e (Scheme 2).

### Table 2  The effect of additives on the asymmetric epoxidation of chalcone\(^a\)

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\(^a\) Reactions were performed with chalcone (0.3 mmol), TBHP (0.36 mmol), 1 mL CH\(_3\)CN. \(^b\) HPLC yield. \(^c\) Determined by chiral HPLC analysis.
Conclusions

In summary, the asymmetric epoxidation of \( \alpha,\beta \)-unsaturated ketones was catalyzed by a new series of lanthanide amides with chiral salen ligands. After careful screening, 10 mol% of the La amide \( \text{La}[[\text{N(SiMe}_3]_2]_3 \), together with the chiral salen ligand \( (S,S\)-(3,5-dimethylsalicylidene)-1,2-cyclohexanediamine) \) in a 1:1.2 molar ratio were found to be the optimal catalyst in \( \text{CH}_2\text{CN} \) at \(-20^\circ\text{C}\). For the disubstituted chalcone derivatives, the target epoxides were obtained in excellent yields (92–99%) with moderate to good ee values (57–83%), while epoxides from the trisubstituted \( \alpha,\beta \)-unsaturated ketones were generated in high enantioselectivities (80–87%) and relative low yields (32–57%). Complex 8 resulting from reaction of lanthanum amide and salen ligand was isolated and characterized, which, together with \( \text{HN(SiMe}_3]_2 \) additive, gave comparable catalytic result with that of \textit{in situ} generated catalyst. The absolute configuration of the target chiral epoxides was determined by single crystal diffraction analysis.

Experimental

General information

All manipulations and reactions involving air and water sensitive components were performed with the standard Schlenk techniques. Solvents, such as THF, toluene and hexane, were degassed and distilled from sodium benzophenone ketyl under argon before use. Analytical thin layer chromatography (TLC) was performed using F254 pre-coated silica gel plate (0.2 mm thickness). After elution, plates were detected using UV radiation (254 nm) on a UV lamp. Flash chromatography was performed using 200–300 mesh silica gel with freshly distilled solvents. Nuclear magnetic resonance spectra were obtained on a Bruker AV-400 apparatus (CDCl3 as solvent). High Resolution Mass (HRMS) spectra were obtained using Bruker ESI-TOF. Rare-earth metal analysis was performed by EDTA titration techniques. Solvents, such as THF, toluene and hexane, were degassed with a vacuum line and then flushed with argon before use. Analytical thin layer chromatography (TLC) was performed using F254 pre-coated silica gel plate (0.2 mm thickness). A scan of single crystal di-

Synthesis of lanthanum complex 8

Under a standard Schlenk vacuum line, to a THF solution of 4 mmol \( \text{La}[[\text{N(SiMe}_3]_2]_3 \), 6 mmol \( \text{H}_2\text{L}^1 \) in 4 mL THF was added dropwise at room temperature. The mixture was continued to stir overnight. Then, removing the THF solvent \textit{in vacuo}, the crude product was washed with hexane for three times and a faint yellow solid was obtained by centrifugal separation. Finally, complex 8 was purified by recrystallization in the mixed solvent of toluene and hexane.

General procedure for the synthesis of the substituted epoxides 7a–7y

Under argon atmosphere, lanthanum amide \( \text{La}[[\text{N(SiMe}_3]_2]_3 \) (0.03 mmol, 18.65 mg) was added to a solution of \( \text{H}_2\text{L}^2 \) (0.36 mmol, 13.62 mg) in \( \text{CH}_2\text{CN} \) (1 mL). After stirring for 30 min, unsaturated ketones (0.3 mmol) was added and stirred for further 30 min. After that, oxidant TBHP (0.36 mmol) was added to the mixture. The system was stirred for 10 h at \(-20^\circ\text{C}\). Quenched by the saturated solution of \( \text{Na}_2\text{SO}_3 \), the crude product was extracted by ethyl acetate, then purified by column chromatography (ethyl acetate–petroleum ether, 1:10) to obtain the target epoxide. The enantiomeric excess of epoxide was determined by chiral HPLC analysis.

Spectroscopic data for ligands

\((S,S\)-(3,5-dimethylsalicylidene)-1,2-cyclohexanediamine) (HL1). A yellow solid; yield: 80% \( [\alpha]_D^{25} = -265^\circ \) (c 1.0 in CHCl3). \( ^1\text{H} \) NMR (400 MHz, CDCl3): \( \delta 13.39(\text{s, 2H, OH}), 8.20(\text{s, 2H, CH}) \), 7.33 \( (d, J = 2.4 \text{ Hz, 2H, Ar-H}) \), 7.01 \( (d, J = 2.4 \text{ Hz, 2H, Ar-H}) \), 6.94 \( (d, J = 1.5 \text{ Hz, 2H, Ar-H}) \), 3.29 \( (m, 2H, CH) \), 2.20 \( (d, J = 6.7 \text{ Hz, 2H, CH}_2) \), 1.88 \( (m, 4H, CH_2CH_2) \), 1.70 \( (m, 2H, CH_3) \), 3.14 \( (t, J = 9.6 \text{ Hz, 2H, CH}_2) \). \( ^13\text{C} \) NMR (100 MHz, CDCl3): \( \delta 164.3, 156.5, 133.7, 128.6, 126.5, 124.8, 117.1, 72.2, 32.7, 23.7, 19.8, 14.9, \) ppm. HRMS (ESI-MS) calcd for \( \text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_2 \) [M + H]$: 379.2386, found: 379.2391.

\((S,S\)-(3,5-di-butylsalicylidene)-1,2-cyclohexanediamine) (HL2). A yellow solid; yield: 70% \( [\alpha]_D^{25} = -255^\circ \) (c 1.0 in CHCl3). \( ^1\text{H} \) NMR (400 MHz, CDCl3): \( \delta 13.73(\text{s, 2H, OH}), 8.32(\text{s, 2H, CH}) \), 7.33 \( (d, J = 2.4 \text{ Hz, 2H, Ar-H}) \), 7.01 \( (d, J = 2.4 \text{ Hz, 2H, Ar-H}) \), 3.32 \( (m, 2H, CH) \), 2.20 \( (d, J = 6.7 \text{ Hz, 2H, CH}_2) \), 1.88 \( (m, 4H, CH_2CH_2) \), 1.70 \( (m, 2H, CH_3) \) ppm. HRMS (ESI-MS) calcd for \( \text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_2 \) [M + H]$: 547.4264, found: 547.4261.

\((S,S\)-(3,5-chlorosalicylidene)-1,2-cyclohexanediamine) (HL3). A yellow solid; yield: 80% \( [\alpha]_D^{25} = -195^\circ \) (c 1.0 in CHCl3). \( ^1\text{H} \) NMR (400 MHz, CDCl3): \( \delta 13.20(\text{s, 2H, OH}), 18.18(\text{s, 2H, CH}) \), 7.29 \( (d, J = 6.6 \text{ Hz, 2H, Ar-H}) \), 7.12 \( (d, J = 2.6 \text{ Hz, 2H, Ar-H}) \), 6.84 \( (d, J = 8.8 \text{ Hz, 2H, Ar-H}) \), 3.23 \( (m, 2H, CH) \), 1.95 \( (m, 4H, CH_2CH_2) \), 1.72 \( (m, 2H, CH_3) \), 1.48 \( (t, J = 10.0 \text{ Hz, 2H, CH}_2) \). \( ^13\text{C} \) NMR (100 MHz, CDCl3): \( \delta 163.6, 159.5, 132.2, 130.6, 123.3, 119.3, 118.4, 72.7, 32.9, 24.1, \) ppm. HRMS (ESI-MS) calcd for \( \text{C}_{26}\text{H}_{23}\text{Cl}_2\text{O}_2 \) [M + H]$: 547.4264, found: 547.4261.

\((S,S\)-(5-tert-butylsalicylidene)-1,2-cyclohexanediamine) (HL4). A yellow solid; yield: 70% \( [\alpha]_D^{25} = -175^\circ \) (c 1.0 in CHCl3). \( ^1\text{H} \) NMR (400 MHz, CDCl3): \( \delta 13.09(\text{s, 2H, OH}), 8.25(\text{s, 2H, CH}) \), 7.33 \( (d, J = 2.6 \text{ Hz, 2H, Ar-H}) \), 7.12 \( (d, J = 2.5 \text{ Hz, 2H, Ar-H}) \), 6.63 \( (d, J = 6.8 \text{ Hz, 2H, Ar-H}) \), 3.31 \( (m, 2H, CH) \), 2.18 \( (d, J = 18.0, 9.9 \text{ Hz, 4H, CH}_2CH_2) \), 1.72 \( (dd, J = 20.6, 9.8 \text{ Hz, 2H, CH}_2) \), 1.47 \( (t, J = 10.1 \text{ Hz, 2H, CH}_2) \), 1.24 \( (s, 18H, C(CH_3)_2) \). \( ^13\text{C} \) NMR (100 MHz, CDCl3): \( \delta 165.0, 158.5, 141.2, 129.5, 127.9, 118.0, 116.3, 72.8, 33.9, 33.2, \) ppm

\[(S,S)-N\text{,}N\text{-Di(3-tert-butylsalicylidene)}\text{-1,2-cyclohexanediamine} (H_{2}L_{5})\]. A yellow solid; yield: 72\%. \(\delta_{1}^{13}C 159.0\text{ ppm. HRMS (ESI-MS) calcd for } C_{22}H_{27}N_{2}O_{2} [M + H^{+}]: 351.2073, found: 351.2077.\]

Spectroscopic data for symmetric epoxidation products

\((2R,3S)-3\text{-Phenylxiran-2-yl)}\text{-phenylmethanone 7a}^{14e}\) A white powder; yield 99\%, ee 80\%; \(\delta_{1}^{13}C 43.5^{\circ}\text{ in acetone.}\)

H NMR (400 MHz, CDCl$_{3}$) \(\delta 8.40 (s, 2H, CH), 3.13 (s, 18H, C(CH$_{3}$)$_{3}$). \(13C NMR (100 MHz, CDCl$_{3}$): \(\delta 167.1, 159.0, 140.1, 139.9, 136.4, 128.3, 128.1, 127.5, 127.2, 126.4, 117.9, 80.2, 35.1, 34.1, 31.5, 29.5 ppm. HRMS (ESI-MS) calcd for \(C_{44}H_{37}N_{2}O_{2} [M + H^{+}]: 645.4420, found: 645.4426.\)
[3-Methoxylphenyl][2R,3S]-3-phenyloxiran-2-yl-methanone 7h. A white powder; yield 93%, ee 37%; [α]D 25° = 49° (0.3 in acetone). 1H NMR (400 MHz, CDCl3) δ 7.57 (dd, J = 4.9, 3.6 Hz, 1H, Ar–H), 7.52 (m, 1H, Ar–H), 7.38 (m, 6H, Ar–H), 7.16 (m, 1H, Ar–H), 4.29 (d, J = 1.9 Hz, 1H, CH), 4.07 (d, J = 1.8 Hz, 1H, CH), 3.84 (s, 3H, CH3). HPLC: OD-H column, 90% hexanes, 10% 1PrOH, 1.0 mL min–1, t r (minor) = 8.7 min, t r (major) = 11.3 min. HRMS (EI, m/z) cale for C14H15O2Na [M + Na]+: 273.0578, found: 273.0533. MP: 44–47 °C.

[2R,3S]-3-(4-Fluorophenyl)oxiran-2-yl-methanone 7i. A white powder; yield 95%, ee 71%; [α]D 25° = –93° (0.3 in acetone). 1H NMR (400 MHz, CDCl3) δ 7.60 (dd, J = 7.8, 0.9 Hz, 1H, Ar–H), 7.51 (m, 6H, Ar–H), 7.22 (d, J = 7.6 Hz, 1H, Ar–H), 4.35 (s, 1H, CH), 2.82 (dd, J = 8.5, 4.1 Hz, 2H, CH2), 2.43 (m, 1H, CH2), 1.85 (m, 1H, CH2). HPLC: OD-H column, 97% hexanes, 3% 1PrOH, 1.0 mL min–1, t r (minor) = 19.5 min, t r (major) = 21.1 min. HRMS (ESI, m/z) cale for C12H13O2Na [M + Na]+: 273.0891, found: 273.0897. MP: 73.5–75.5 °C.

[2R,3S]-3-(4-Methylphenyl)3,4-dihydro-1H-spiro[naphthalene-2,2′-oxiran]1-one 7j. A white powder; yield 43%, ee 87%; [α]D 25° = –111° (0.3 in acetone). 1H NMR (400 MHz, CDCl3) δ 8.10 (d, J = 7.8 Hz, 1H, Ar–H), 7.51 (m, 1H, Ar–H), 7.35 (t, J = 7.5 Hz, 1H, Ar–H), 7.29 (d, J = 8.6 Hz, 2H, Ar–H), 7.22 (d, J = 7.6 Hz, 1H, Ar–H), 6.93 (d, J = 6.6, 4.8 Hz, 2H, Ar–H), 4.30 (s, 1H, CH), 3.83 (s, 3H, CH3), 2.83 (dd, J = 8.5, 4.0, 2H, CH2), 2.44 (m, 1H, CH2), 1.86 (m, 1H, CH2). HPLC: OD-H column, 97% hexanes, 3% 1PrOH, 1.0 mL min–1, t r (minor) = 30.0 min, t r (major) = 28.7 min. HRMS (ESI, m/z) cale for C14H14O2Na [M + Na]+: 303.0997, found: 303.0999. MP: 76–79 °C.

[2R,3S]-3′-(4-Methylphenyl)-3,4-dihydro-1H-spiro[naphthalene-2,2′-oxiran]-1-one 7k. A white powder; yield 41%, ee 81%; [α]D 25° = –41° (0.3 in acetone). 1H NMR (400 MHz, CDCl3) δ 8.11 (d, J = 7.9, 1.0 Hz, 1H, Ar–H), 7.51 (m, 1H, Ar–H), 7.36 (t, J = 7.5 Hz, 1H, Ar–H), 7.25 (m, 6H, Ar–H), 4.32 (s, 1H, CH2), 2.43 (dd, J = 8.5, 4.1 Hz, 2H, CH2), 2.44 (m, 1H, CH2), 2.38 (s, 3H, CH3), 1.86 (m, 1H, CH2). HPLC: OD-H column, 90% hexanes, 10% 1PrOH, 1.0 mL min–1, t r (minor) = 14.9 min, t r (major) = 20.9 min. HRMS (ESI, m/z) cale for C16H17O2Na [M + Na]+: 287.1048, found: 287.1051. MP: 165–169 °C.

[2R,3S]-3′-(3-Methylphenyl)-3,4-dihydro-1H-spiro[naphthalene-2,2′-oxiran]-1-one 7l. A white powder; yield 99%, ee 80%; [α]D 25° = –78° (0.3 in acetone). 1H NMR (400 MHz, CDCl3) δ 8.11 (d, J = 7.9, 1.0 Hz, 1H, Ar–H), 7.51 (m, 1H, Ar–H), 7.36 (t, J = 7.5 Hz, 1H, Ar–H), 7.25 (m, 6H, Ar–H), 4.32 (s, 1H, CH2), 2.43 (dd, J = 8.5, 4.1 Hz, 2H, CH2), 2.44 (m, 1H, CH2), 2.38 (s, 3H, CH3), 1.86 (m, 1H, CH2). HPLC: OD-H column, 90% hexanes, 10% 1PrOH, 1.0 mL min–1, t r (minor) = 7.8 min, t r (major) = 6.9 min. HRMS (ESI, m/z) cale for C14H15O2Na [M + Na]+: 287.1048, found: 287.1052. MP: 96–98 °C.
(2R,3'S)-3'(2-Methylenyl)-3,4-dihydro-1H-spiro[naphtho-

lène-2,2'-oxiran]-1-one 7. A white powder; yield 99%, ee 87%;

$[\alpha]_{D}^{25}$ −88° (c 0.3 in acetone). 1H NMR (400 MHz, CDCl₃) δ 8.13
(dd, J = 7.9, 1.0 Hz, 1H, Ar–H), 7.53 (m, 1H, Ar–H), 7.36 (dd, J =
12.4, 5.4 Hz, 2H, Ar–H), 7.25 (m, 3H, Ar–H), 7.18 (dd, J = 6.4,
2.2 Hz, 1H, Ar–H), 4.36 (s, 1H, CH₂), 2.83 (m, 2H, CH₂), 2.37 (m,
1H, CH₂), 2.25 (s, 3H, CH₃), 1.74 (m, 1H, CH₂). HPLC: OD-H
column, 90% hexanes, 10% 2ProH, 1.0 mL min⁻¹, tᵣ (minor)
= 6.6 min, tᵣ (major) = 6.9 min. HRMS (ESI, m/z) calcd for
C₁₉H₂₀O₂Na [M + Na⁺]: 287.0502, found: 287.0506. Mp: 132–
134 °C.

Conflicts of interest

The authors declare no competing financial interest.

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Notes and references


2 (a) M. Kitamura, S. Suga, K. Kawai and R. Noyori, J. Am.
Chem. Soc., 1986, 108, 6671–6672; (b) R. Noyori and M.

3 (e) M. Quirmbach, A. Kless, J. Holz, B. Tararov and
A. Böerner, Tetrahedron: Asymmetry, 1999, 10, 1803–1811; (d)
A. Kless, R. Kadyrov, A. Böerner, J. Holz and H. B. Kagan,
Tetrahedron Lett., 1995, 36, 4601–4602; (e) E. F. DiMauro

4 (a) E. F. DiMauro and M. C. Kozlowski, J. Am. Chem.
Soc., 2002, 124, 12668–12670; (b) C. Garcia, L. K. LaRochelle

(c) T. Vojkovsky, Tetrahedron Lett., 1999, 40, 8147–8149; (d)
K. Yabu, S. Masumoto, M. Kanai, D. P. Curran and
S. Masumoto, M. Suzuki, M. Kanai and M. Shibasaki,
H. Deng, M. P. Snapper and A. H. Hoveyda, Angew. Chem.,
Int. Ed., 2002, 41, 1009–1011; (h) F. X. Chen, X. M. Feng,
949–952.

5 (a) D. A. Evans, C. S. Burgey, N. A. Paras, T. Vojkovsky and
S. W. Tregay, J. Am. Chem. Soc., 1998, 120, 5824–5825; (b)
D. A. Evans, S. W. Tregay, C. S. Burgey, N. A. Paras and
Y. Yuan, X. Zhang and K. Ding, Angew. Chem., Int. Ed.,
2003, 42, 5478–5480; (d) D. A. Evans and J. Wu, J. Am.
Chem. Soc., 2005, 127, 8006–8007; (e) G. E. Huston,

6 (a) F. D. Denes, A. Perez-Luna and F. Chemla, Chem.
Rev., 2010, 110, 2366–2368; (b) B. K. Corkey and F. D. Toste,
J. Am. Chem. Soc., 2005, 127, 17168–17169; (c) T. Yang,
Chem. Soc., 2009, 131, 9140–9141; (d) A. Matsuzawa,
T. Mashiko, N. Kumagai and M. Shibasaki, Angew. Chem.,
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