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Enantioselective syntheses of β-amino alcohols catalyzed by recyclable chiral Fe(III) metal complex

Rajkumar Tak[a,b], Manish Kumar[a,c], Rukhsana I. Kureshy*[a,b], Manoj Kumar Choudhary[a,b], Noor-ul H. Khan[a,b], Sayed H. R. Abdi[a,b] and Hari C. Bajaj[a,b]

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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An efficient asymmetric desymmetrization of *meso*-epoxides with anilines catalysed by a series of simple and environmentally benign *in situ* generated Fe(III) complexes based on chiral tridentate ligands **L_1-L_7** having achiral and chiral linkers (methylene, piperazine, *R*/*S* Binol and diethyl tartrate) was carried out at rt. The *in situ* generated iron metal complex based on ligand **L_5a** emerged as improved (low catalyst loading) catalyst for asymmetric desymmetrization of *meso*-epoxides with anilines giving high enantioselectivity (up to 99%) and high yield (95%) of enantiopure β-amino alcohols in 14 h. While excellent results for ARO of cyclic as well as aliphatic epoxides with anilines was achieved with *in situ* generated complex from the ligand **L_4h** and Fe(III) chloride, the catalyst was recoverable and recyclable (five times) with retention of its performance.

Introduction

The desymmetrization of *meso*-epoxides by the anilines is a simple, precise and straight forward strategy for the synthesis of chiral β-amino alcohols.[1,2] The enantiopure β-amino alcohols are important key structural units found in many biologically active compounds and are also used for the preparation of fine chemicals, synthetic drugs and amino acids.[3] In recent years, chiral amino alcohols alone[4] or in the presence of a metal ion[5] have been used efficiently to catalyse various asymmetric organic transformations. On the principle of electrophilic activation of epoxide ring, various efficient catalytic methods have been reported for the asymmetric ring opening (ARO) of *meso*-epoxides with alkyl/aryl amines/indoles, using various transition metal ions[6-13] and rare earth metal ions[14] with fair success in term of yield and enantioselectivity of β-amino alcohols. Among them, recyclable Ti(IV)-catalyzed ARO reaction of *meso*-epoxides with anilines using (*S*)-BINOL[5a], (*1R,2S*)-(-)-2-aminodiphenyl ethanol derived Schiff bases[6a], chiral polymeric salen[6b] and dinuclear aminoindanol[5b] derived ligands with chiral linker have shown better performance over organo-catalytic systems[15] in terms of low temperature, high catalyst loading, long reaction time, and use of inorganic and organic bases as co-catalyst. Hence it is utmost importance that the metal ion should be environmental friendly, non-toxic and the resulting complex should also be recyclable. Ollevier *et al.* demonstrated for the first time the use of a very simple experimental procedure for the synthesis of chiral *syn*-β-amino alcohols by ARO of aromatic *meso*-epoxides with anilines/indoles using Fe(II) Bolm's bipyridine complexes as catalysts.[10] Excellent yields and enantioselectivities of β-amino alcohols were achieved with these complexes at higher catalyst loading (5 mol %) with no recyclability data. In the present study we have developed a new and efficient dinuclear Fe(III) based catalytic systems for ARO of aromatic *meso* as well as aliphatic/cyclic epoxides with anilines. The synthesized chiral tridentate Schiff base ligands (**L_1-L_7**) having diverse stereogenic centres due to the different chiral/achiral linkers (*R*)/(*S*)-BINOL, diethyl D-(-)-tartrate, methylene and piperazine with various iron metal source have been used to comprehend their catalytic efficiency (low catalyst loading) in the asymmetric ARO reaction of *meso*-stilbene oxide **5**, *cis*-butene oxide **7** and cyclohexene oxide **8** with amines **6a-l**. Among all the ligands screened, we are pleased to find out that the ligand **L_5a** derived from (*R*)-BINOL with (1*S*,2*R*)-2-amino-1,2-diphenylethanol worked synergistically with $Fe(acac)_3$ giving very high enantioselectivity (>99%) and very good yield (95%) in the ARO reaction of *meso*-stilbene oxide **5** with aniline **6a** at low catalyst loading (2.5 mol %) while ligand **L_4h** in combination with Fe(III) chloride gave β-amino alcohols of aliphatic and cyclic epoxide with anilines yield (up to 96%) with excellent ee (up to 99%). The *in situ* generated catalysts were found to be stable and were easily separated from the catalytic reaction mixture and reused several times.

Results and Discussion

Inclusion of an extra element of chirality and catalytic sites while designing a chiral catalyst often helps in improving the catalyst performance.[5b,6c] Keeping this fact in mind achiral/chiral linker with diverse diastereomeric combinations of amino alcohols based ligands **L_1-L_7** were synthesised in two steps. In the first step achiral linker (methylene **a**, piperazine **b**) and chiral linker (diethyltartrate **c**, (*S*)/(*R*)-BINOL **d**) were

[a]*Discipline of Inorganic Materials and Catalysis, CSIR-Central Salt and Marine Chemicals Research Institute.*
[b]*Academy of Scientific and Innovative Research, Central Salt and Marine Chemicals Research Institute (CSMCRI), Council of Scientific & Industrial Research (CSIR), G. B. Marg, Bhavnagar- 364 002, Gujarat, India.*
[c]*Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia.*
E-mail: rukhsana93@yahoo.co.in†
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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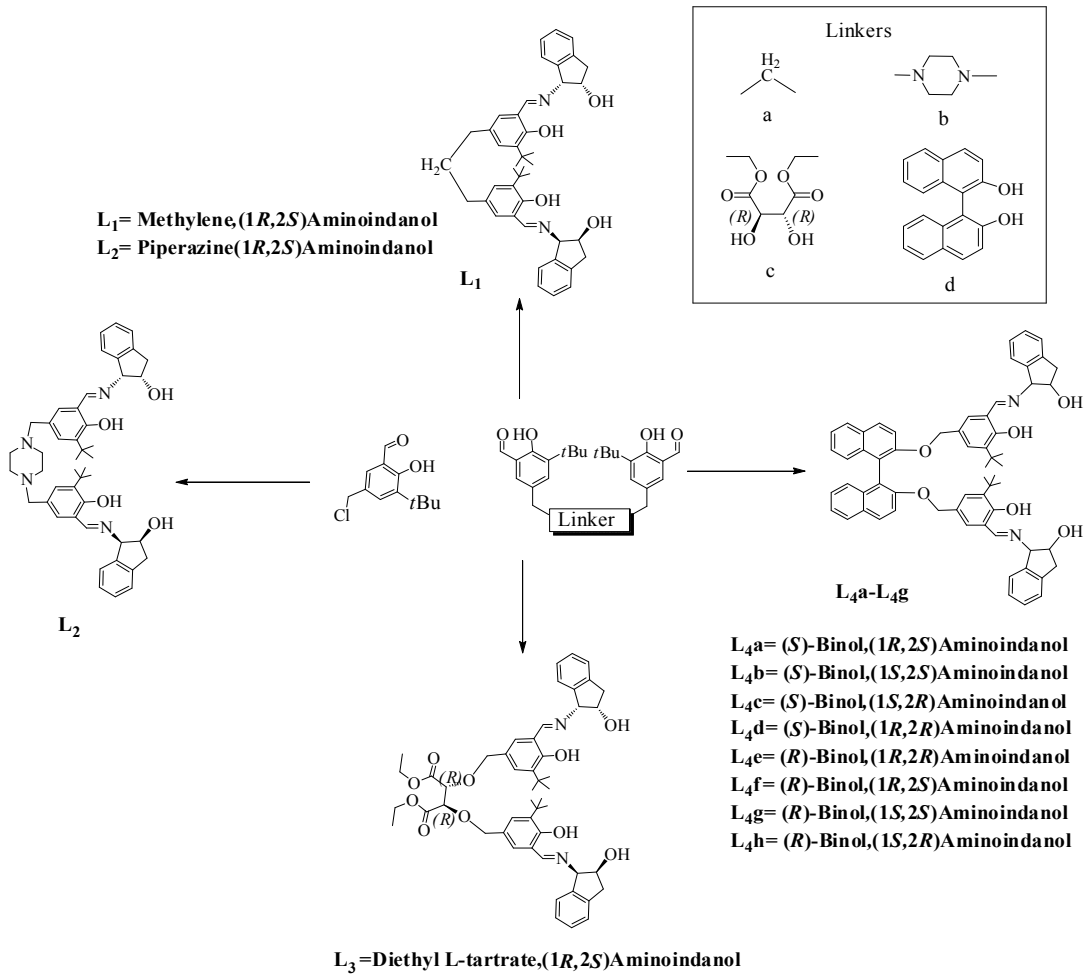
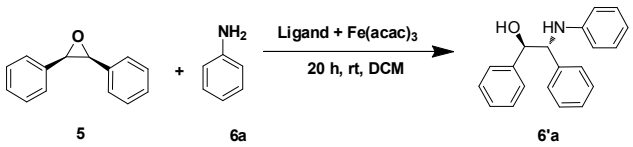


Scheme 1. Structure of the ligands L_1- L_7

reacted with 3-*t*-Bu-5-(chloromethyl)-2-hydroxybenzaldehyde to get dialdehydes which on condensation with (1*R*,2*S*), (1*S*,2*S*), (1*S*,2*R*), (1*R*,2*R*) amino alcohols gave tridentate ligands **L_1-L_7** (Scheme 1).[5b] At the very beginning, to determine the effect of various linkers on the activity of catalysts formed by the reaction of chiral tridentate ligands **L_1-L_4a** (5 mol %) with $Fe(acac)_3$ (1:1) were examined for ARO reaction of *meso*-stilbene oxide **5** as a model substrate and aniline **6a** as a nucleophile in DCM at rt for 20 h (Table 1, entries 1-4). The outcome of these reactions were encouraging particularly with the ligand **L_4a** where we got the ring opened product *syn*-β amino alcohol in good yield (68%) and enantioselectivity (ee, 51%; entry 4) which reflects that inclusion of (*S*)-BINOL as an additional element of chirality has distinct advantage. These observations are in consonance with our earlier results on different organic transformations.[16] To further ascertain this finding we used ligand **L_7**, which is a simpler version of **L_4a** (having no BINOL linker) and the results were inferior to **L_4a**.Moreover, the complex derived from **L_7** was not recyclable due to its high solubility in most organic solvents.

Table 1 Optimization of linkers for ARO reaction of *meso*-stilbene oxide **5** with aniline **6a** using the *in situ* generated catalyst from ligand **L_1-L_4a** and $Fe(acac)_3$[a]



Entry	Ligand	Yield [b] [%]	ee[c] [%]
1	L_1	40	18
2	L_2	45	22
3	L_3	50	28
4	L_4a	68	51

[a] Conditions: *Meso*-stilbene oxide **5** (0.2 mmol), Aniline **6a** (0.22 mmol), Chiral ligand **L_1- L_4a** (0.01 mmol), $Fe(acac)_3$ (0.01 mmol). [b] Isolated yield after flash chromatography. [c] ee determined on Chiralcel AD column.

Encouraged by the preliminary results with the optimized catalyst generated in situ and to ascertain the role of effective metal complex for the catalytic reaction, we carried out systematic screening of various iron salts (both divalent and trivalent) with the chiral ligand **L_4a** (most active and enantioselective). The rationale behind this is based on the concept that iron sources with different counter ions are known to form structurally different complexes with a given ligand, hence strongly affect the catalytic activity. Therefore, we screened different metal salts viz., iron(III) chloride, iron(III) bromide, iron(III) triflate, iron(III) perchlorate, iron(II) triflate, iron(II) perchlorate and iron(II) acetylacetonate (5 mol %) (1:1) to see the performance of ligand **L_4a** as catalyst precursor in the ARO of *meso*-stilbene oxide **5** as a model substrate with aniline **6a** as a nucleophile under the above mentioned reaction condition. Among the different iron salts screened iron(III) acetylacetonate worked well to give good yield (68%) and enantioselectivity (ee, 51%; Table 2, entry 3) of *syn*-β amino alcohol. We have also observed that trivalent iron salts give better results than divalent iron possibly due to higher Lewis acidity of the trivalent iron.

Table 2 Optimization of iron metal salts for ARO reaction of *meso*-stilbene oxide **5** with aniline **6a** using the *in situ* generated catalyst from ligand **L_4a**[a]

Entry	Metal source	Yield[b] [%]	ee[c] [%]
1	$FeCl_3$	60	45
2	$FeBr_3$	65	40
3	$Fe(acac)_3$	68	51
4	$Fe(acac)_2$	40	48
5	$Fe(ClO_4)_3$	70	30
6	$Fe(ClO_4)_2$	72	25
7	$Fe(CF_3SO_3)_3$	68	33
8	$Fe(CF_3SO_3)_2$	69	23

[a] Conditions: *Meso*-stilbene oxide **5** (0.2 mmol), Aniline **6a** (0.22 mmol), Chiral ligand **L_4a** (0.01 mmol), iron salts (0.01 mmol) in CH_2Cl_2 at rt for 20 h. [b] Isolated yield after flash chromatograph. [c] ee determined on Chiralcel AD column.

It is well known in literature that a catalytically active metal complex when generated *in situ* from a ligand and a metal source, their molar ratios of the two distinctly influence the yield and enantioselectivity of the product.[5a,5b,5c,5g] This may be due to the varying degree of complexation occurring in the solution during catalysis. Therefore, we gradually increased the

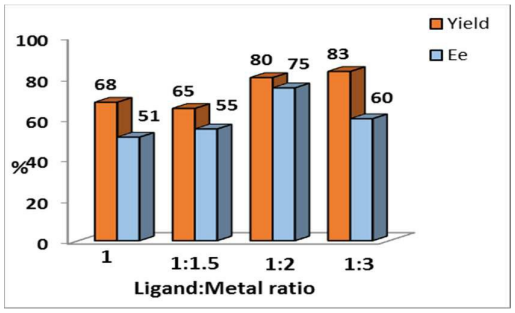


Figure 1 Variation of ligand metal ratio for the synthesis of syn β-amino alcohols

ligand to metal ratio from 1:1 to 1:3 for carrying out the ARO reaction of **5** with **6a** in presence of **L_4a** and $Fe(acac)_3$ and data is given as Figure 1. It is evident from the data (Figure 1) that the ditopic ligand **L_4a** and $Fe(acac)_3$ (1:2) gave best results in term of the product yield 80% with ee 75% of *syn*-β amino alcohol due to the presence of two catalytically active centres. An increase in the metal content (M:L,3:1) caused some enhancement in the product yield with a reduction in the ee, possibly due to the presence of excess free metal working as a catalyst to produce racemic product thereby bringing down the overall enantioselectivity.

To ascertain the in situ formation of active complex with M:L (2:1) we have performed UV-Vis titration using Job's method, where we varied the concentration of [Fe(acac)$_3$] against the ligand **L$_4$a** using 1x10^{-3}M concentration in CH_2Cl_2.(Figure S-1) The absorbance maximum at 551 nm was measured and plotted against the concentration of molar equivalent of Fe(acac)$_3$ to get parabolic curve (Figure 2). It is evident from the plot that absorbance maxima obtained at M:L molar ratio of 2:1 suggesting the formation of dinuclear complex.

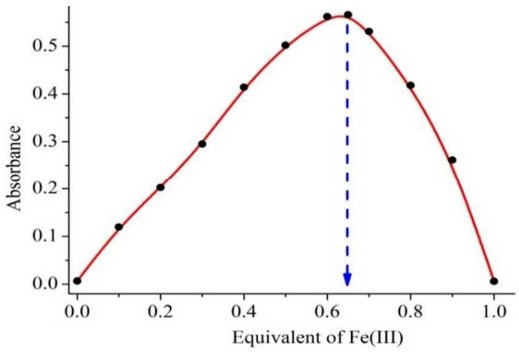


Figure 2. Job's plot drawn between ligand **L$_4$a** and Fe(acac)$_3$ (1x10^{-3}) from UV-visible spectral data based on the absorbance obtained from λmax = 551 nm.

In order to further improve the results we optimized other reaction parameters like catalyst loading, solvent variation and temperature. First we assessed the catalyst (derived from **L$_4$a** with L:M ratio 1:2) loading from 1-10 mol % with respect to the substrate *meso*-stilbene oxide **5** with aniline **6a** (Table 3, entries 1-5). It was found that 2.5 mol % of catalyst loading is sufficient to give 79% yield of β-amino alcohol with 75% ee (entry 2). Next we screened different solvents viz., toluene, THF, ACN, $CHCl_3$ and DCE (Table 3, entries 6-10) for asymmetric ARO reaction keeping other optimized reaction parameters constant (as per entry 2). Among the various solvents DCM showed promishing result (entry 2) and choosen as the solvent of choice in our subsequent studies.The reaction was further subjected to temperature variation (entries 10-12). The data suggest that rt is the optimum temperature to carry out ARO reaction (entry 2) because on lowering the reaction temperature below rt the results were adversely effected, particularly the product yield while enantioselectivity remained unchanged. This protocol has shown similar performance for the formation of *syn*-β-amino alcohol even at relatively higher scale (10 mmol) in 12 h (Table 3, entry 13). To further improve the results, the optimal reaction conditions as established above (Table 3, entry 2) was then extended to all the 8 diastereomers of ligand **L$_4$** as well as to ligands **L$_5$a**, **L$_5$b**, **L$_6$** and **L$_7$** derived from (*R*/*S*)-BINOL backbone in combination with various diastereomeric forms of amino alcohols such as 1-amino-2,3-dihydro-1*H*-inden-2-ol, 2-amino-1,2-diphenylethanol and (*S*)-valinol to generate active complex with Fe(acac)$_3$ for the enantioselective epoxide ring opening reaction of *meso*-stilbene oxide **5** with aniline **6a** as a nucleophile. In the entire matrix of results, the complex generated from ligand **L$_5$a** (Figure 3) was found to be the best for the ring opening reactions of *meso*-stilbene oxide **5** with aniline **6a** to give the product amino alcohols in high yield (95%) and ee (>99%). These results are superior in terms of yield of *syn*-β-amino alcohol and enantioselectivity using lower catalyst loading (2.5 mol %) than the previously reported chiral Ti(IV) systems, which needed higher catalyst loading (15 mol %) at rt with the same ligand[5b] and Fe(II) Bolm's bipyridine complex (5 mol %).[10] Interestingly the configuration of the product *syn*-β-amino alcohol is directly dependent on the configuration of indanol collar irrespective of the configuration of BINOL. Hence it is possible to get the desired configuration in the product by selecting appropriate configuration of the catalyst itself. In the present case, the iron complex based on the ligand **L$_5$a** provided (1*S*,2*S*)-configuration and on changing the iron catalyst to the **L$_5$b** we observed (1*R*,2*R*)-configuration of the product. It is important to note that in ligand system having diverse asymmetric centre, each chirality element contributes significantly towards enantioselectivity of the product and in the catalyst **L$_5$a** only specific combination of chirality of BINOL (*R*) with diphenyl aminoalcohol (1*S*,2*R*) was found to be more suitable. This observation is in agreement with our earlier reports in other organic transformations.[16b,16c] Further, in order to understand the structure of the *in situ* formed complex, **[Fe$_2$L$_5$a(acac)$_2$]**, incorporating the ligand **L$_5$a** and Fe(acac)$_3$ was prepared and characterized by different techniques, such as IR, UV-visible, ESI-MS and MALDI-TOF. A molecular peak at m/z = 1362.89 attributable to **[Fe$_2$L$_5$a(acac)$_2$]** and 1361 assigned to **[Fe$_2$L$_5$a(acac)$_2$-H]** in ESI-MS and Matrix-assisted Laser deposition/ionization (MALDI) spectra confirm the formation **[Fe$_2$L$_5$a(acac)$_2$]**, which is in consonance with other analytical data (data is given in supporting information). Our repeated attempts to get single crystal of the complex, suitable for the X-ray analysis failed. To find out the general applicability of the catalyst, **[Fe$_2$L$_5$a(acac)$_2$]** the above optimized reaction condition was further used for the asymmetric ARO reaction *meso*-stilbene oxide **5** with a variety of different amines **6a-l**.

Table 3 Optimization of reaction conditions for ARO reaction of *meso*-stilbene oxide 5 with aniline 6a using the in situ generated catalyst from ligand L$_4$a with Fe(acac)$_3$[a]

Entry	Catal. mol %	Solvent	Temperature °C	Time [h]	Yield[b] [%]	ee[c] [%]
1	1.0	DCM	rt	14	68	70
2	2.5	DCM	rt	14	79	75
3	5	DCM	rt	14	80	75
4	7.5	DCM	rt	14	85	74
5	10	DCM	rt	12	89	70
6	2.5	Toluene	rt	16	90	72
7	2.5	THF	rt	10	78	74
8	2.5	ACN	rt	18	70	60
9	2.5	$CHCl_3$	rt	14	91	68
10	2.5	DCE	rt	15	87	66
11	2.5	DCM	10	20	70	75
12	2.5	DCM	0	25	65	77
13[d]	2.5	DCM	rt	12	79	75

[a] Conditions: *Meso*-stilbene oxide **5** (0.2 mmol), Aniline **6a** (0.22 mmol). [b] Isolated yield after flash chromatography. [c] ee determined on Chiralcel AD column. [d] Reaction performed at 10 mmol scale keeping other conditions as per entry 2

In most of the cases, the active dinuclear **[Fe$_2$L$_5$a(acac)$_2$]** catalyst smoothly catalyzed the reaction with good to excellent yield (up to 95 %) with high enantioinduction (up to 99%) (Table 4). 4-Substituted anilines viz., 4-Me, 4-Et, 4-OMe, 4-Cl

except 4-NO_2 aniline were found to be more reactive with better enantioselectivity in the product than with 2-substituted anilines (entries 1-8), possibly due to the steric interaction arising from *ortho* substitution on the nucleophile which disfavours higher enantioselectivity (entries 5,7).

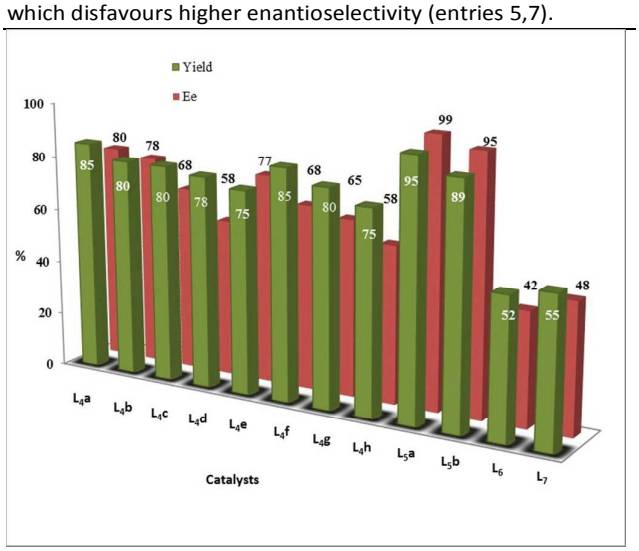
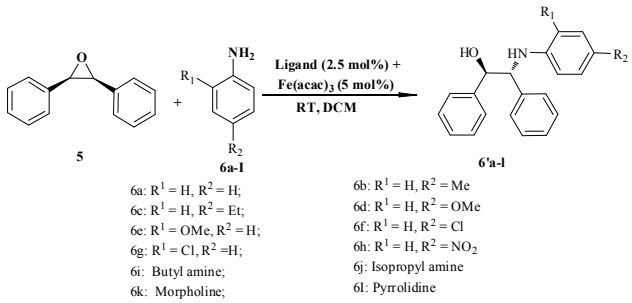


Figure 3. Optimization of ligands **L_4-L_7** for ARO reaction of *meso*-stilbene oxide **5** with aniline **6a**

Table 4 Product yield and ee values of ARO of *meso*-stilbene oxide **5** with different amines **6a-l** as nucleophile catalyzed by *in-situ* generated Fe-complex based on **L_5a** ligand under the optimized reaction conditions[a]



Entry	Amines	Time [h]	Yield[b] [%]	ee[c] [%]
1	Aniline **6a**	14	95	99
2	4-Me aniline **6b**	14	90	98
3	4-Et aniline **6c**	18	94	90
4	4-MeO aniline **6d**	14	90	95
5	2-OMe-aniline **6e**	18	30	28
6	4-Cl aniline **6f**	24	89	90
7	2-Cl-aniline **6g**	24	20	38
8	4-NO_2 aniline **6h**	30	trace	Nd
9	Butyl amine **6i**	30	-	Nd
10	Isopropyl amine **6j**	30	-	Nd
11	Morpholine **6k**	30	-	Nd
12	Pyrrolidine **6l**	30	-	Nd

[a] Conditions: *Meso*-stilbene oxide **5** (0.2 mmol), amines **6a-l** (0.22 mmol), chiral ligand L_5a (0.005 mmol), $Fe(acac)_3$ (0.01 mmol), in CH_2Cl_2 at rt. [b] Isolated yield after flash chromatography. [c] ee determined on Chiralcel AD, OD, OJ HPLC columns.

Further, due to the less reactivity of 4-NO_2-aniline we got the product in trace amount (entry 8). Moreover, the use of aliphatic amines such as butyl amine **6i**, isopropyl amine **6j**, morpholine **6k** and pyrrolidine **6l** (Table 4, entries 9-12) were unable to open the ring of *meso*-stilbene oxide **5** even after prolonged reaction time possibly due to higher basicity of these amines causing blockage of acidic sites of the metal catalyst leaving behind the epoxide un-activated.[15]

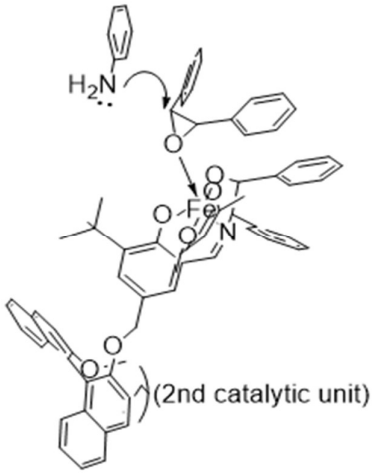
After successful optimization of iron catalyst derived from the ligand **L_5a** for aromatic ring opening reaction, we also explored the same protocol for ARO reaction of aliphatic epoxide (*cis*-butene oxide **7**) and cyclic epoxide (cyclohexene oxide **8**) with various anilines but unfortunately we got unsatisfactory results. So we thought of screening our previously used ligands (Figure 3) for the ARO of *cis*-butene oxide **7** and cyclic epoxide **8** with different anilines (Table 5, entries 1-10). Fortunately, fair success in terms of yield (89-96%) and ee (62-99%) was achieved with ligand **L_4h** using $FeCl_3$ as a source of metal as catalyst and substituted anilines (entries 2-4). Noticeably, with aniline as a nucleophile only moderate enantioselectivity (entry 1) was obtained. Here again, 4-NO_2-aniline was unable to open the epoxide ring of aliphatic substrates due to its poor nucleophilicity (entries 5 and 10). These observations are in agreement with the earlier metal based and organocatalyzed ARO reaction of epoxides with amines.[5b,15]

Table 5 Product yield and ee values of ARO of different *meso*-epoxides **7-8** with different anilines as nucleophile by *in-situ* generated Fe-complex based on **L_4h** ligand[a]

Entry	Epoxide	Amines	Time [h]	Yield[b] [%]	ee[c] [%]
1	*Cis*-butene oxide **7**	Aniline **6a**	14	96	62
2		4-Me aniline **6b**	14	90	99
3		4-Et aniline **6c**	14	89	90
4		2-Cl aniline **6g**	18	80	85
5		4-NO_2 aniline **6h**	24	trace	nd
6	Cyclohexene oxide **8**	Aniline **6a**	15	97	63
7		4-Me aniline **6b**	15	90	85
8		4-Et aniline **6c**	15	87	95
9		2-Cl aniline **6g**	24	78	80
10		4-NO_2 aniline **6h**	30	trace	nd

[a] Conditions: epoxide **7-8** (0.2 mmol), anilines **6a-c,g,h** (0.22 mmol), chiral ligand **L_4a**(0.005 mmol), $FeCl_3$ (0.01 mmol), in CH_2Cl_2 at rt. [b] Isolated yield after flash chromatography. [c] ee determined on Chiralcel AD, OD, OJ columns.

Based on experimental results a working model can be proposed for the possible transition state (Scheme 2). In the catalytic cycle, epoxide is activated through weak interaction of its oxygen atom to Lewis acid centre (iron). The attack of aniline to thus activated epoxide (by iron center) gives the product *syn* β-amino alcohol. To further strengthen the probable mechanism a stepwise UV-visible spectral study was carried out with *meso*-stilbene oxide **5** (0.2 mmol) as substrate and aniline **6a** (0.22 mmol) as nucleophile in DCM (0.8 ml) as solvent at rt (Figure 4). The UV-Vis spectrum of ligand **L_5a** (0.005 mmol) has n–π* transition at 334 nm which showed red-shift (bathochromic) to higher wavelength (354 nm as LMCT band) after addition of $Fe(acac)_3$ (0.01 mmol), confirming the formation of *in situ* generated **[Fe_2L_5a(acac)$_2$]** complex with a new band at 539 nm assigned to d–d transition.[17] After addition of substrate to the solution of the complex **[Fe_2L_5a(acac)$_2$]** both the LMCT and d-d bands showed isosbestic points at ~393 nm & ~588 nm. These observations confirm the direct co-ordination of the substrate to Fe(III) complex through the lone pair of the oxygen atom of the epoxide **5**. The generation of the isosbestic points may be due to the changes in the geometry of the iron complex on interaction of substrate to the iron. On further addition of the aniline to the reaction mixture we did not observe considerable change in an isosbestic points confirming no further change in the geometry of the iron complex. The interesting feature of these Fe(III) complexes is in their inherent tendency to precipitate out in non-polar solvents like hexane due to their higher molecular weight and lower solubility. Hence, the recyclability of the catalyst was checked for the *in situ* generated complex with ligand **L_4h** in combination with



Scheme 2. Plausible transition state of complex

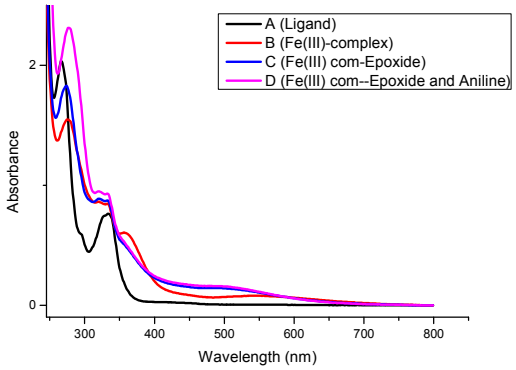


Figure 4. Stepwise UV-Vis spectra recorded in DCM (**A**) Ligand (0.005 mmol), (**B**) Complex (L:M 0.005:0.01), (**C**) Complex & Epoxide (0.2 mmol), (**D**) Complex, Epoxide & aniline (0.22 mmol), (after 1h).

$FeCl_3$ for the ring opening of *cis*-butene oxide **7** with 4-methyl aniline **6b** at 1 mmol level under the optimized reaction conditions (Table 5, entry 2). After completion of the catalytic reaction, the catalyst was precipitated with *n*-hexane and retrieved quantitatively. The product β-amino alcohol was recovered from the organic layer and separated by column chromatography. The recovered complex was dried in vacuum and was used as such for the subsequent catalytic runs, which worked well up to 4 catalytic runs with retention of reactivity and enantioselectivity. From the recycling experiments it is evident that the *in situ* formed catalyst is fairly stable and do not deteriorate during the course of ARO reaction (Figure 5). In order to confirm the stability of the recovered catalyst during

the ARO reaction, the IR spectra (Figure 6) were recorded both for fresh catalyst and recovered catalyst which matched well suggesting that no major structural changes had taken place during the course of post-catalytic workup. To further check the Leaching of the metal from the isolated complex after first use, the filtrate obtained at the time of isolating the complex was subjected to ICP which does not show the trace of metal.

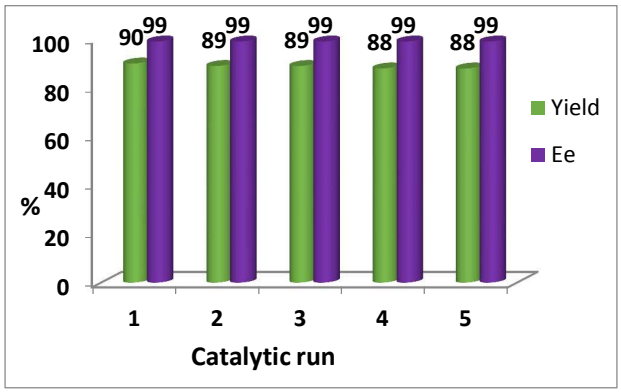


Figure 5. Recyclability study of the catalytic system using *cis*-butene oxide **7** and 4-methyl aniline **6b** as model substrate.

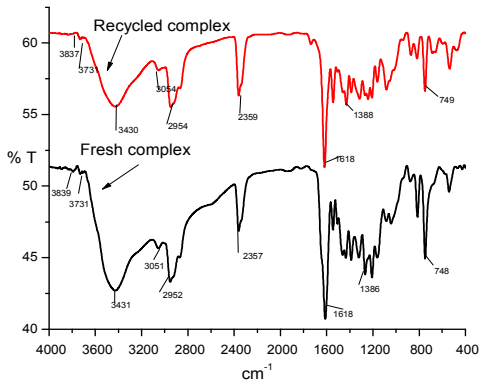


Figure 6. IR spectra of fresh and recycled catalyst

Experimental Section

(*S*)-BINOL) / (*R)*-BINOL), iron metal salts viz., iron(III) chloride, iron(III) bromide, iron(III) triflate, iron (III) perchlorate, iron(II) triflate, iron(II) perchlorate and iron(II) acetylacetonate, anilines like 4-methyl, 4-ethyl-, 4-methoxy, 4-chloro, 4-NO_2 aniline, butyl amine, isopropyl amine, morpholine, pyrrolidine **6a-l**, and *meso*-epoxides namely *meso*-stilbene oxide **5**, *cis*-butene oxide **7**, cyclohexene oxide **8** were purchased from Aldrich Chemicals and were used as received. All the solvents used in the present study were dried by known purification technique. NMR spectra were obtained with 500 MHz /200 MHz and are referenced internally with TMS. Enantiomeric excess (ee) were determined by HPLC using Daicel Chiralpak OD, OJ and AD chiral columns with 2-propanol/hexane as eluent. FTIR spectra were carried out using KBr. Optical rotations were determined by automatic polarimeter (Digipol 781). Leaching of the metal was determined by inductively coupled plasma (ICP) spectrometer (Perkin- Elmer, Optima 2000 DV) and by using TGA (Mettler Toledo) with detection limit. For the product purification flash chromatography was performed using silica gel 100-200 mesh. Thus, in a stepwise manner, 3-*tert*-butyl salicylaldehyde was chloromethylated to give 3-*tert*-butyl-5-(chloromethyl)-2-hydroxybenzaldehyde which on reaction with (*R*)/(*S*)-BINOL, diethyl D-(-)-tartrate, methylene and piperazine gave dialdehydes.[5b]

Preparation of Ligands

The dialdehydes of different linkers **a-d** were dissolved in dry THF to which two equimolar quantity of (1*R*,2*S*)-1-amino-2,3-dihydro-1*H*-inden-2-ol/(1*R*,2*R*)-1-amino-2,3-dihydro-1*H*-inden-2-ol/(1*S*,2*R*)-1-amino-2,3-dihydro-1*H*-inden-2-ol/(1*S*,2*S*)-1-amino-2,3-dihydro-1*H*-inden-2-ol (*S*)-2-amino-3-methylbutan-1-ol/ (1*R*,2*S*)-(-)-2-amino1,2-diphenylamino alcohols and L-valinol was added slowly under nitrogen atmosphere. The resulting solution was stirred for 4 h at rt (TLC checked) and the solvent was partially removed from the reaction mixture on a rotary evaporator that gave yellow precipitate. The solid obtained after filtration was washed with hexane: DCM (50:1) to get the yellow colour desired ligands **L_1-L_7.**

Typical experimental procedure for ring opening of epoxides

To a 5 ml round bottom flask fitted with rubber septum and equipped with a magnetic stirring bar, a solution of chiral ligands **L_1-L_7** (0.005 mmol) in DCM, 0.8 ml and iron salts (0.01 mmol) were charged and the resulting solution was allowed to stir at room temperature (27±2 °C) for 1 h. Subsequently, an appropriate epoxide viz., *meso*-stilbene oxide **5**/ *cis*-butene oxide **7**/cyclohexene oxide **8** (0.2 mmol) was added to the above stirring solution and after a gap of 10 min., appropriate amines **6a-l** (0.22 mmol) was added and the reaction mixture was allowed to stir for the specified time. The progress of the reaction was checked on TLC using hexane/ethyl acetate (8:2) as mobile phase. After the completion of reaction, solvent was removed under vacuum and the product was purified by column chromatography using silica gel 100-200 mesh as stationary phase and hexane/ethyl acetate (8:2) as mobile phase. All the products were characterized by appropriate spectroscopic techniques, microanalysis, LCMS and optical rotation which were found to be in consonance with the reported values.[5b]

Conclusion

In the present manuscript we have revealed the use of Fe(III) chiral metal complexes derived from tridentate ligands possessing achiral and chiral linkers in ARO of *meso*-, aliphatic and cyclic epoxides with anilines to give corresponding enantioenriched β-amino alcohols (ee up to >99%) with high

yield (up to 95%) at low catalyst loading. The ligand $\mathbf{L_5a}$ with iron(III) acetylacetonate and $\mathbf{L_4h}$ with iron(III) chloride were found to be the best combination for ARO reaction of aromatic/ aliphatic and cyclic epoxides with anilines respectively. The products from the ARO of *cis*-butene oxide with 4-Me-aniline viz. *syn*-β-amino alcohols (ee, 99 %) were efficiently separated from the catalyst by precipitation with hexane and the recovered catalyst worked very well up to five cycles.

Acknowledgements

(CSMCRI Communication No.106 /2015). Rajkumar Tak and RIK are thankful to DST, UGC and CSIR-Indus Magic Project CSC0123 for financial assistance. Rajkumar Tak is thankful to AcSIR for Ph. D. Registration. Authors are also thankful to Analytical Science and centralized instrument facilities for providing instruments facilities.

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Enantioselective syntheses of β-amino alcohols catalyzed by recyclable chiral Fe(III) metal complex

Rajkumar Tak[a,b,] Manish Kumar[a,c], Rukhsana I. Kureshy*[a,b], Manoj Kumar Choudhary[a,b], Noor-ul H. Khan[a,b], Sayed H. R. Abdi[a,b] and Hari C. Bajaj[a,b]

[a]*Discipline of Inorganic Materials and Catalysis, CSIR-Central Salt and Marine Chemicals Research Institute.*

[b]*Academy of Scientific and Innovative Research, Central Salt and Marine Chemicals Research Institute (CSMCRI), Council of Scientific & Industrial Research (CSIR), G. B. Marg, Bhavnagar- 364 002, Gujarat, India.*

[c]*Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia.*

E-mail: rukhsana93@yahoo.co.in