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Article

Asymmetric Aminolytic Kinetic Resolution of Racemic Epoxides Using Recyclable Chiral Polymeric Co(III)-Salen Complexes: A Protocol for Total Utilization of Racemic Epoxide in the Synthesis of (R)-Naftopidil and (S)-Propranolol

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Asymmetric Aminolytic Kinetic Resolution of Racemic Epoxides Using Recyclable Chiral Polymeric Co(III)-Salen Complexes: A Protocol for Total Utilization of Racemic Epoxide in the Synthesis of (*R*)-Naftopidil and (*S*)-Propranolol

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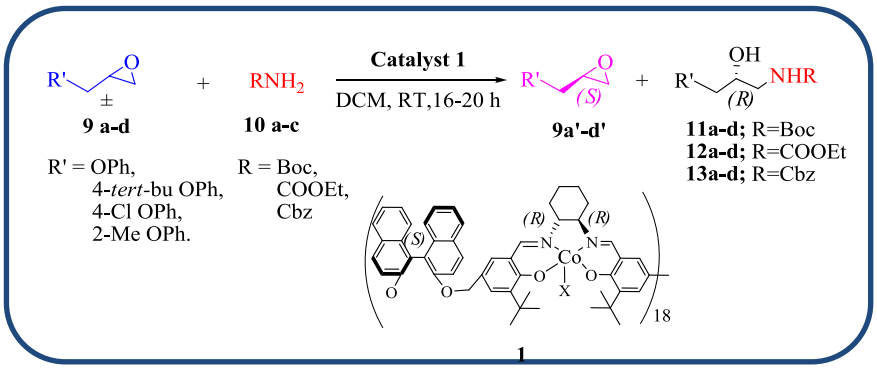
ABSTRACT:



Chiral polymeric Co(III) salen complexes with chiral ((*R*)/(*S*)-BINOL, diethyl tartrate) and achiral (piperazine and trigol) linkers with varying stereogenic centres were synthesised for the first time and used as catalysts for aminolytic kinetic resolution (AKR) of a variety of terminal epoxides and glycidyl ethers to get enantio-pure epoxides (ee, 99%) and *N*-protected *β*-amino alcohols (ee, 99%) with quantitative yield in 16 h at RT under optimized reaction conditions. This protocol is also used for the synthesis of two enantiomerically pure drug molecules (*R*)-Naftopidil (α_1-blocker) and (*S*)-Propranolol (β-blocker) as a key step via AKR of single racemic naphthylglycidylether with Boc-protected isoproylamine with 100%

epoxide utilization at 1 gram level. The catalyst **1** was successfully recycled for a number of times.

INTRODUCTION

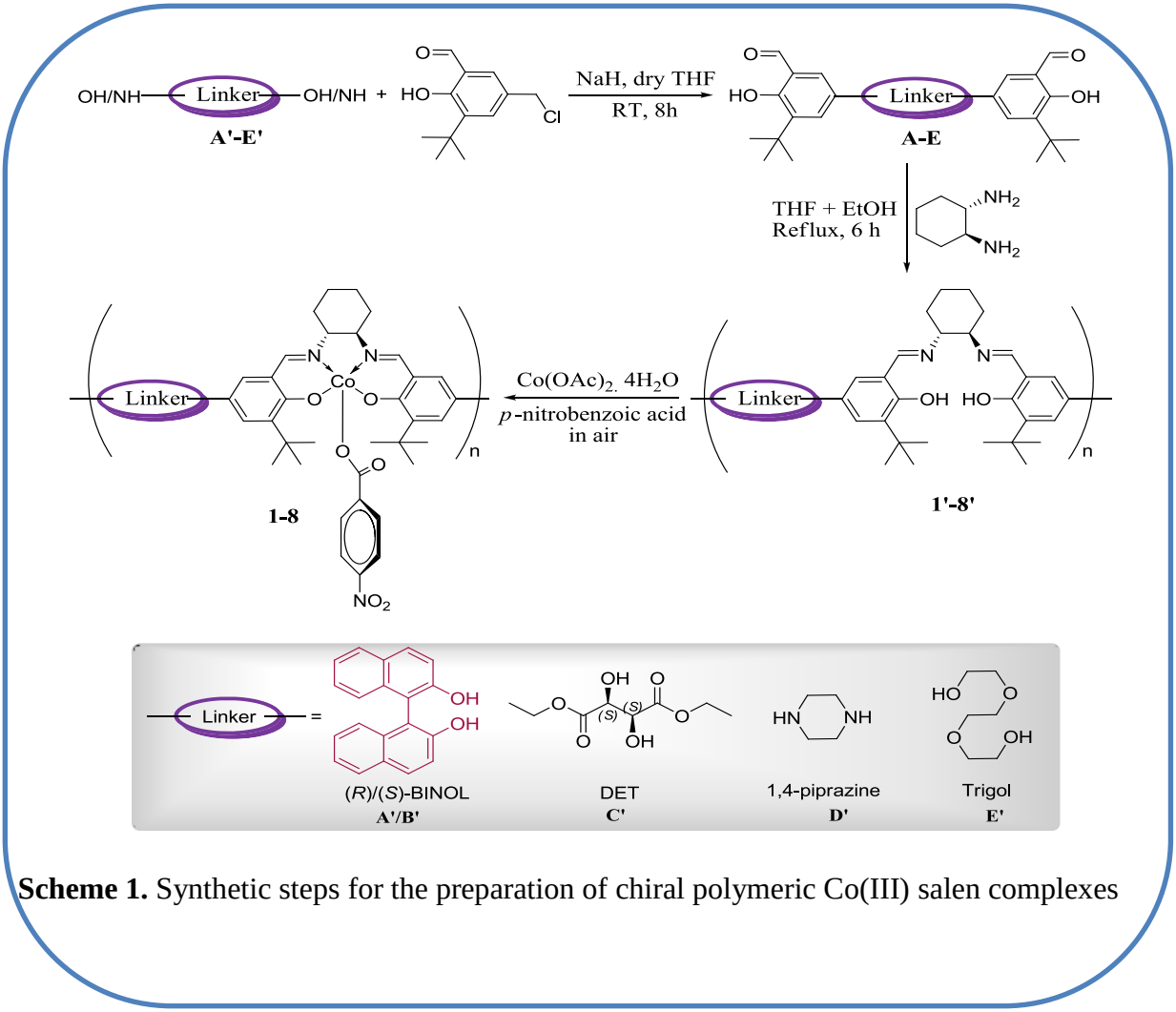
Aminolytic kinetic resolution (AKR) of racemic epoxides is a simple, convenient and highly efficient method to prepare highly valuable enantio-pure *β*-amino alcohols[1] and corresponding chiral epoxides[2] in one go. Driven by the potential application of chiral *β*-amino alcohols[1] and epoxides,[2] the last couple of decades have seen spurt of excellent reports on use of chiral salen complexes of various metal ions for the synthesis of these molecules.[2,3] Subsequently, Bartoli et al.[4] effectively used chiral non-recyclable monomeric Cr(III) and Co(III) salen complexes (2-5 mol%) for the AKR of aryloxy/trans epoxides with aniline/carbamates. While recently, L. Vares et al.[5] have made use of monomeric chiral Co(III) salen complexes for the resolution of bis-epoxides through hydrolytic and aminolytic kinetic resolution with water and *N*-protected amine derivatives as nucleophile giving excellent results in term of yield and ee of the products. Consequently, we reported a couple of modifications in the catalyst design[6a-c] and use of ionic liquids[6d-e] in order to improve the efficiency of AKR reaction and to make the catalyst recyclable. In asymmetric catalysis often an extra element of chirality and multiple catalytic sites embedded in the catalyst, play an important role in enhancing the catalyst performance.[7] However, in such cases multi-step catalyst synthesis is detrimental for their practical application. Therefore, to keep catalyst synthesis simple we visualized self-assembled polymer where chiral salen units are suitably linked through chiral ((*R*)/(*S*)-BINOL, diethyltartrate as extra element of chirality) and non-chiral (trigol and piperazine) groups. Such a self-assembled polymer can be easily synthesised in two steps from substituted chloromethyl salicylaldehyde[8] with readily

available chiral cyclohexanediamine and then treated with suitable metal source cobalt acetate to obtain the corresponding catalyst. To demonstrate their application in the AKR of racemic epoxides, we chose *N*-protected amines as nucleophiles, as at the end of the reaction the protecting group can easily be removed to get the desired amino alcohol in high regioselectivity with practically no side-products. Among the catalysts **1-8** synthesized for the AKR of racemic epoxides, the catalyst **1** with (*S*)-BINOL linker was found to be the best that worked well with a catalyst loading of 1 mol% at which both *N*-protected amino alcohol and epoxide were obtained in very high optical purity (ee, >99%). The catalyst **1** was recycled six times without any loss of its performance. We further extended this protocol in the synthesis of two important chiral drugs viz., (*R*)-Naftopidil[9] and (*S*)-Propranolol[10] at a gram scale from single racemic epoxide in most atom economic way reported so far.

RESULTS AND DISCUSSION

Chiral polymeric salen ligands **1'-8'** with chiral/achiral linker were synthesised in two steps. In 1st step (*R*)/(*S*)-BINOL and diethyltartrate **A'-C'** as chiral linker and piperazine, trigol **D', E'** as achiral linker were reacted with 3-*t*-Bu-5-(chloromethyl)-2-hydroxybenzaldehyde to get a dialdehydes **A-E**[7a,11-13] which on condensation with (1*R*,2*R*)/(1*S*,2*S*) cyclohexanediamine gave polymeric salen ligands **1'-8'**. All the chiral polymeric salen ligands were characterised by NMR, IR, MASS spectrometry, elemental analysis, GPC and optical rotation (data are given in experimental section). GPC analysis of representative polymeric ligand **1'** has shown an average molecular weight (Mn,13999) with polymer distribution index (PDI) 1.08. Cobalt complexes of these ligands **1'-8'** were obtained in quantitative yield by their reaction with Cobalt(II) acetate in Methanol:Toluene (1:1) first under inert atmosphere followed by the addition of *p*-nitrobenzoic acid (PNBA) while

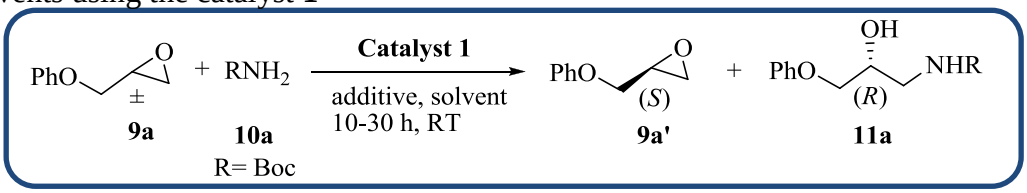
exposing the reaction mixture to air for auto-oxidation to get active Co(III) catalysts **(Scheme-1)** (data for all the polymeric salen complexes is given in experimental section).



Scheme 1. Synthetic steps for the preparation of chiral polymeric Co(III) salen complexes

The role of additives as counter ion/axial ligand and choice of solvent[14] is crucial in Co(III) catalysed AKR of racemic epoxides. Therefore, ligand **1'** was initially picked to optimize these parameters in combination with Co(II) acetate to catalyse AKR of racemic 1,2-epoxy-3-phenoxypropane **9a** as a model substrate with *tert*-butylcarbamate **10a** as nucleophile in DCM at RT. The polymeric Co(III) salen complexes of this ligand (2.5 mol%) was prepared in situ by its reaction with Co(II) acetate first in inert atmosphere and then in air in the presence of acetic

Table 1. Optimization of reaction conditions for enantioselective AKR of **9a** with **10a** in different solvents using the catalyst **1**[a]



Entry	Catalyst loading	Solvent	Additive	Time (h)	Unreacted Epoxide ee(%)[b]	*N*-protected 1,2-amino alcohol	
						Conv.(%)[c]	ee(%)[d]
1	2.5	DCM	Acetic acid	25	76	68	82
2	2.5	DCM	Trichloro acetic acid	25	65	75	74
3	2.5	DCM	PNBA	14	99.4	99.3	99.2
4	2.5	DCM	LPTS	48	-	-	-
5	2.5	DCM	PF6	30	75	72	81
6	5	DCM	PNBA	12	99.2	99.5	99.7
7	1.5	DCM	PNBA	14	99.4	99.4	99.6
8	1	DCM	PNBA	16	99.3	99.5	99.8
9	0.5	DCM	PNBA	20	76	86	75
10	1	ACN	PNBA	25	45	65	58
11	1	THF	PNBA	24	76	70	84
12	1	Toluene	PNBA	24	85	88	91
13	1	DCE	PNBA	26	90	95	92
14	1	Chloroform	PNBA	16	86	90	90
15	1	Propylene carbonate	PNBA	40	90	68	93

[a] Reaction was conducted with epoxide **9a**: $BocNH_2$ **10a** :: 0.2 mmol: 0.1 mmol: in 0.5 mL solvent with **1**.

[b] Determined by HPLC (chiral pack OD column)

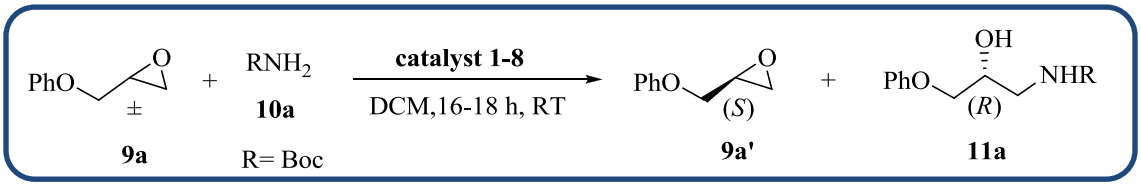
[c] Based on HPLC (Chiral pack AD-H Column) using the calibration curve of racemic *N*-protected amino alcohol.

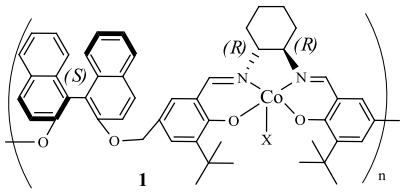
[d] Determined by HPLC (chiral pack AD-H column)

acid, trichloroacetic acid, *p*-nitrobenzoic acid, lutidine 2,6-dimethyl pyridiniumtosylate (LPTS) and ferrocenium hexafluorophosphate as counter ion/axial ligand and their AKR performance is given in Table 1 as entries 1-5 respectively. Among these the Co(III) complex obtained with PNBA hence forth designated as **1** was found to be the best to give the product *R*-amino alcohol (**11a**) in excellent yield and ee (>99%) with concomitant recovery of *S*-enantioenriched epoxides (**9a'**) (ee, >99%) in quantitative yield (entry 3). Although it is unclear at this point, why PNBA as additive fared better with salen complex **1** for the AKR of 1,2 epoxy-3-phenoxypropane **9a**, a similar trend has been reported earlier by Bartoli et al.[4b] and us.[6d] The effect of loading of the catalyst **1** (0.5-5 mol%) in the AKR of model reaction was then evaluated in DCM at RT (Table 1, entries 6-9). The data revealed that 1 mol% of complex **1** (entry 8) matched the performance, albeit with marginally higher reaction time (16 h) of initially used 2.5 mol% catalyst loading (entry 3, reaction time is 14 h). The nature of the solvent is known to influence the reactivity and enantioselectivity of AKR of racemic epoxides with amines. Therefore, 1 mol% of complex **1** (entry 8) at RT was used to screen various solvents that include non-polar (toluene) and polar aprotic (CH_3CN, $CHCl_3$, DCM, DCE, THF, propylene carbonate) solvent data is shown in Table 1 (entries 8,10-15). However, no other solvent could match the performance of DCM.

The above optimized conditions with catalyst **1** (Table 1, entry 8) was then used to evaluate other chiral polymeric salen complexes viz., **2-8** (1 mol%) for AKR reaction of 1,2 epoxy-3-phenoxypropane **9a** as model substrate with *tert*. butyl carbamates **10a** as nucleophile (Table 2). Among these, the performance of BINOL based catalysts **1-4** (entries 1-4) were better than the rest **6-8** (entry 6-8) both in terms of product yield and ees except in the case of **5** (entry 5), where the ligand was derived from racemic BINOL and (*R*,*R*)-1,2-diaminocyclohexane gave significantly lower ee (36%) of epoxide as well as in amino alcohol ee (63%). A possible explanation for this behaviour could be the distortions (random twists) in

TABLE 2. Screening of chiral polymeric Co(III) salen complexes **1-8** for AKR of **9a** with **10a**[a]

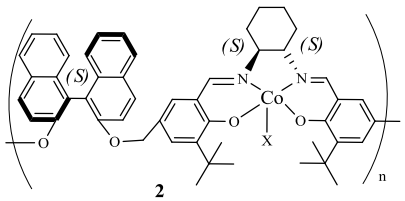




1

Entry 1

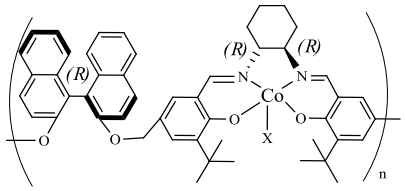
Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
16	99	99	99



2

Entry 2

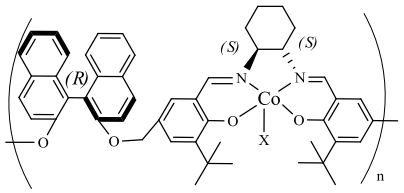
Time (h)	ee of **9a'** (%)[d]	Conv. (%)[c]	ee of **11a** (%)[b]
16	98	99	99



3

Entry 3

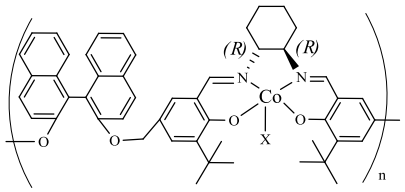
Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
16	99	99	99



4

Entry 4

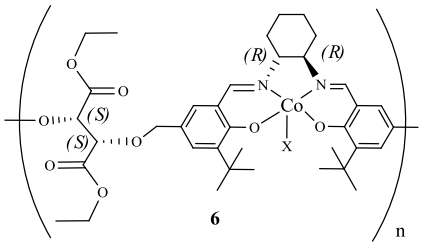
Time (h)	ee of **9a'** (%)[d]	Conv. (%)[c]	ee of **11a** (%)[b]
16	99	99	99



5

Entry 5

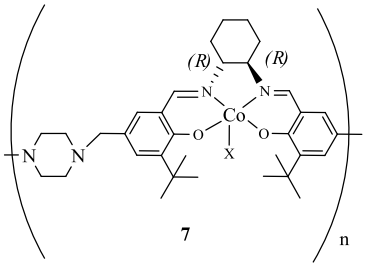
Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
16	36	99	63



6

Entry 6

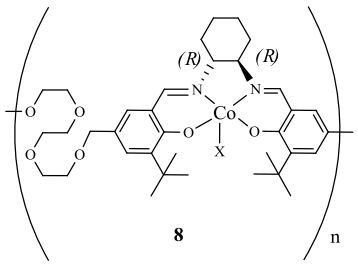
Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
15	55	78	62



7

Entry 7

Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
16	48	91	51



8

Entry 8

Time (h)	ee of **9a'** (%)[b]	Conv. (%)[c]	ee of **11a** (%)[d]
18	54	85	65

x = *p*-nitrobenzoicacid

[a] Reaction was conducted with epoxide **9a**: $BocNH_2$ 10a: catalyst 1-8 :: 0.2 mmol: 0.1 mol:0.002 in 0.5 mL DCM

[b] Product configuration is (*S*) determined by HPLC.

[c] Based on HPLC (Chiral pack AD-H Column) using the calibration curve of racemic *N*-protected amino alcohol .

[d] Product configuration is (*R*) determined by HPLC.

the structure of the polymeric salen ligand in the case of ligand **5'** prepared from racemic BINOL where both (*R*) and (*S*)-BINOL motifs may possibly present randomly in a single polymeric chain. This possibility does not exist in the case of catalysts **1-4** prepared with pure (*S*) and (*R*)-BINOLs. In fact when we took physical 1:1 mixture of catalyst **1** and **3** and used these for the AKR of the model reaction, we got the *R*-amino alcohol and *S*-enantiopure epoxides in >99% ee. The configuration of the product amino alcohol is directly dependent on the diamine collar of salen irrespective of the configuration of BINOL. That is, catalysts derived from (*1R,2R*)-1,2-diaminocyclohexane yielded *R* form of amino alcohol in excess leaving behind *S* form of the epoxides. Similarly catalysts originating from (*1S,2S*)-1,2-diaminocyclohexane favours the formation of *S* form of amino alcohol and *R* form of the epoxide in excess. It can also be concluded from these results that, though salen motif is mainly responsible for the enantioselectivity, distance and/or orientation between the salen motifs also play an important role as it is evident from the results obtained with other chiral and non-chiral linkers of variable lengths, which were inferior (relatively lower product yield and ee, entries 6-8) than BINOL based catalysts. To further strengthen this finding and to understand the probable chirality element significantly contributing towards product enantioselectivity we have recorded CD spectra of complexes **1-3** in DCM **(Figure 1).** The complexes **1** and **2** having (*S*)- BINOL as linker with (1*R*,2*R*)/(1*S*,2*S*) cyclohexanediamine

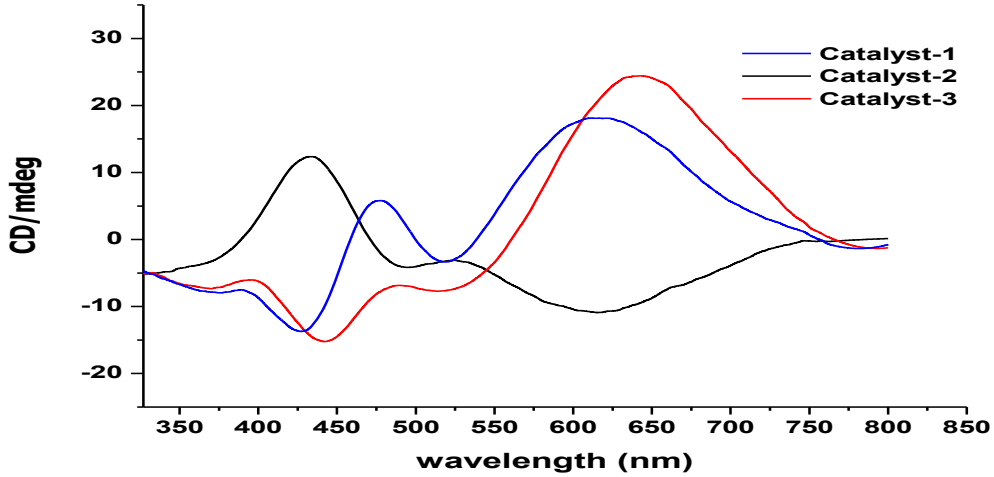
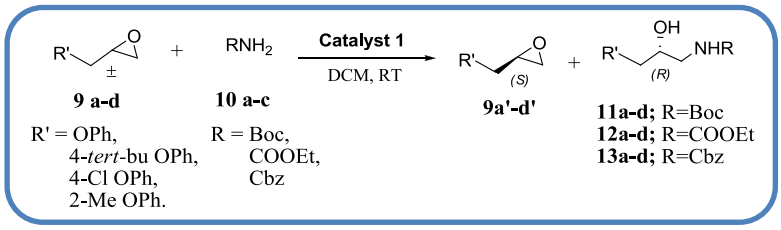


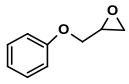
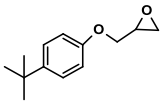
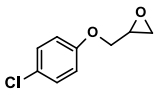
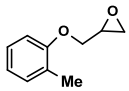
Figure 1. CD Spectra of complexes **1-3** recorded in DCM.

collar gave the d-d bands near 620 nm and d $\rightarrow\pi^*$ bands at 430 nm of opposite cotton effect while the complex **3** derived from ((*R*)-BINOL with (1*R*,2*R*) cyclohexanediamine collar and complex **1** derived from (**(***S*-BINOL with (1*R*,2*R*) cyclohexanediamine) gave the similar trend in CD spectra for d-d and d $\rightarrow \pi^*$ bands confirming that the configuration of the product is controlled by the chirality of the diamine used and independent of the chiral linker (*S*)/(*R*)-BINOL.

Having achieved very good results with the catalyst **1** under the optimised reaction conditions, the scope of **1** (Table 1, entry 8) was further extended for AKR of variety of aryloxy epoxides like 1,2-epoxy-3-phenoxy propane **9a**, 4-*tert*-butyl phenyl glycidyl ether **9b**, 4-chloro phenyl glycidyl ether **9c**, glycidyl 2-methyl phenyl ether **9d** with different nucleophiles viz., *tert*-butyl carbamate **10a** ($BocNH_2$), urethane **10b** and benzyl carbamate **10c**. In general, substrates irrespective of electron donating or withdrawing group on phenyl ring gave the products with excellent conversion (94-99 %) of *N*-protected amino alcohol (Table 3, entries 1-12) with high enantioselectivity (97-99 %) in 16-20 h. Pleasantly corresponding epoxides were also obtained in high quantitative yield and enantioselectivity (Table 3, entries 1-12). The reactivity and selectivity of the catalyst **1** was further investigated with other terminal epoxides viz., epichlorohydrin **9e**, 1,2-epoxyhexane **9f**, benzyl glycidyl ether **9g** and naphthylglycidylether **9h** with $BocNH_2$ **10a** as nucleophile where excellent results in term of yield (99%) and enantioselectivity (ee, 99%) of both *N*-protected amino alcohols and epoxides were achieved in 20 h (Table 4).

Table 3. Enantioselective AKR of **9a-d** with **10a-c** in DCM using the polymeric catalyst **1**[a]



Entry	Epoxides	*N*-protected amines	Time (h)	Unreacted Epoxide[b] ee(%)	*N*-protected 1,2-amino alcohol		(k_{rel})[e]
					Conv.(%)[c]	ee(%)[d]	
1		**10a**	16	99	99.5	99.8	4990
2		**10b**	18	99	99	99.0	857
3	**9a**	**10c**	16	99	99	99.9	9111
4		**10a**	18	99	99	99.9	9111
5		**10b**	20	99	99	98.5	543
6	**9b**	**10c**	16	99	96	99.4	1093
7		**10a**	16	99	94	99.7	1978
8		**10b**	18	99	98	98.3	426
9	**9c**	**10c**	20	99	98	97.4	266
10		**10a**	21	99	99	98.8	695
11		**10b**	20	99	99	99.9	9111
12	**9d**	**10c**	20	99	97	99.8	3580

[a] Reaction was conducted with epoxides **9a-d** : RNH_2 **10 a-c: 1** :: 0.2 mmol: 0.1:0.002 mmol. in 0.5 mL DCM.

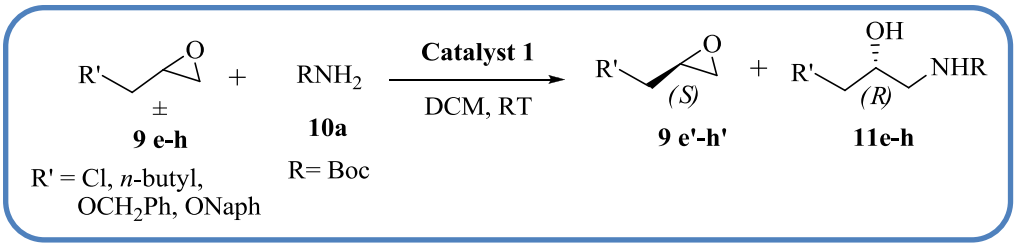
[b] Product configuration is (*S*) determined by HPLC.

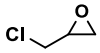
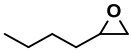
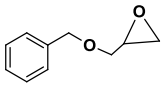
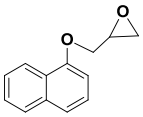
[c] Based on HPLC (Chiral pack AD-H Column) using the calibration curve of racemic *N*-protected amino alcohol.

[d] Product configuration is (*R*) determined by HPLC.

[e] k_{rel} = ln[1 - *c*(1 + ee)]/ln[1 - *c*(1 - ee)], where *c* is the conversion and ee is the enantiomeric excess of the resulting product *N*-protected 1,2-amino alcohol

Table 4. Enantioselective AKR of **9e-h** with **10a** in DCM using the polymeric catalyst **1**[a]



Entry	Epoxides	Time (h)	Unreacted Epoxide[b] ee(%)	*N*-protected 1,2-amino alcohols		(k_{rel})[e]
				Conv. (%)[c]	ee(%)[d]	
1	 **9e**	20	99	99.4	99.9	10131
2	 **9f**	20	99	99	99.9	9111
3	 **9g**	20	99	98	98.5	488
4	 **9h**	16	98	99	99.9	9111

[a] Reaction was conducted with epoxides 9e-h,: $BocNH_2$ 10a: **1** :: 0.2 mmol: 0.1:0.002 mmol in 0.5 mL DCM.

[b] Product configuration is (*S*) determined by HPLC and GC.

[c] Based on HPLC (Chiral pack AD-H Column) using the calibration curve of racemic *N*-protected amino alcohol.

[d] Product configuration is (*R*) determined by HPLC.

[e] k_{rel} = ln[1 - *c*(1 + ee)]/ln[1 - *c*(1 - ee)], where *c* is the conversion and ee is the enantiomeric excess of the resulting product *N*-protected 1,2-amino alcohol

In addition, the chiral polymeric catalyst **1** was precipitated out quantitatively from the reaction mixture by the addition of hexane. The precipitated catalyst was washed with hexane and directly used for next catalytic run without further purification. The products *N*-protected amino alcohol **11a** and chirally enriched epoxide **9a'** were recovered from the organic layer

by column chromatography. In this way the same catalyst was successfully reused six times with complete retention of enantioselectivity (Figure 2). As there were no changes in the *ee* of the product in the 6 recycled experiments conducted. This was further substantiated by the microanalysis and FT-IR of the recovered catalyst which matched well with the fresh catalyst. In order to ascertain the stability of the complex **1**, kinetic experiments for the AKR of epichlorohydrin **9e** (20 mmol) as a representative substrate with *tert*-butyl carbamate

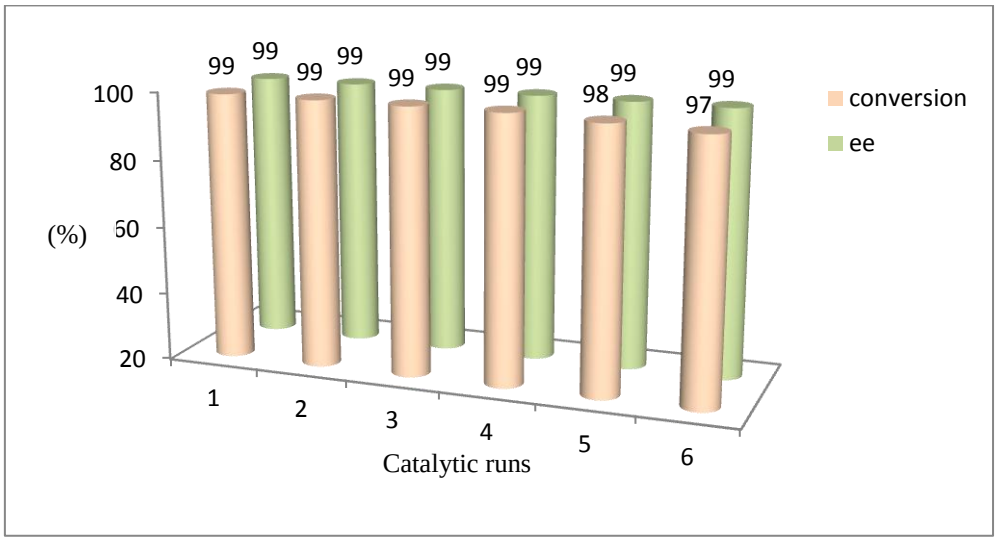


Figure 2. Catalyst performance in enantioselective AKR of **9a** with **10a** in DCM using recovered catalyst **1**

($BocNH_2$) **10a** (10 mmol) was performed with fresh and recovered catalyst which gave quantitative yield with high optical purity (98-99%) of *N*-protected amino alcohol (**Figure 3**). The kinetic data thus obtained clearly showed that the complex **1** is stable under the AKR condition used in the present study. Encouraged by the overall results in term of yield and enantioselectivity of *N*-protected amino alcohol and chiral epoxide obtained with the catalyst **1** we extended this protocol in the synthesis of chiral drugs viz., (*R*)-Naftopidil[9] and (*S*)-Propranolol,[10] with 100% utilization of the racemic naphthylglycidylether[15] (**Scheme 2**)

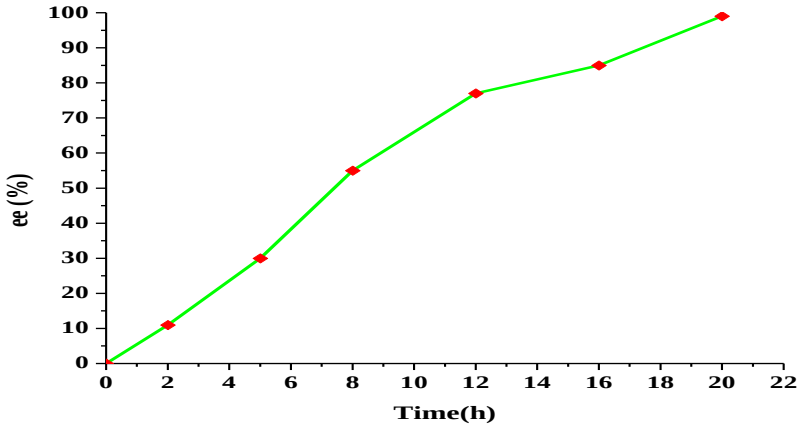
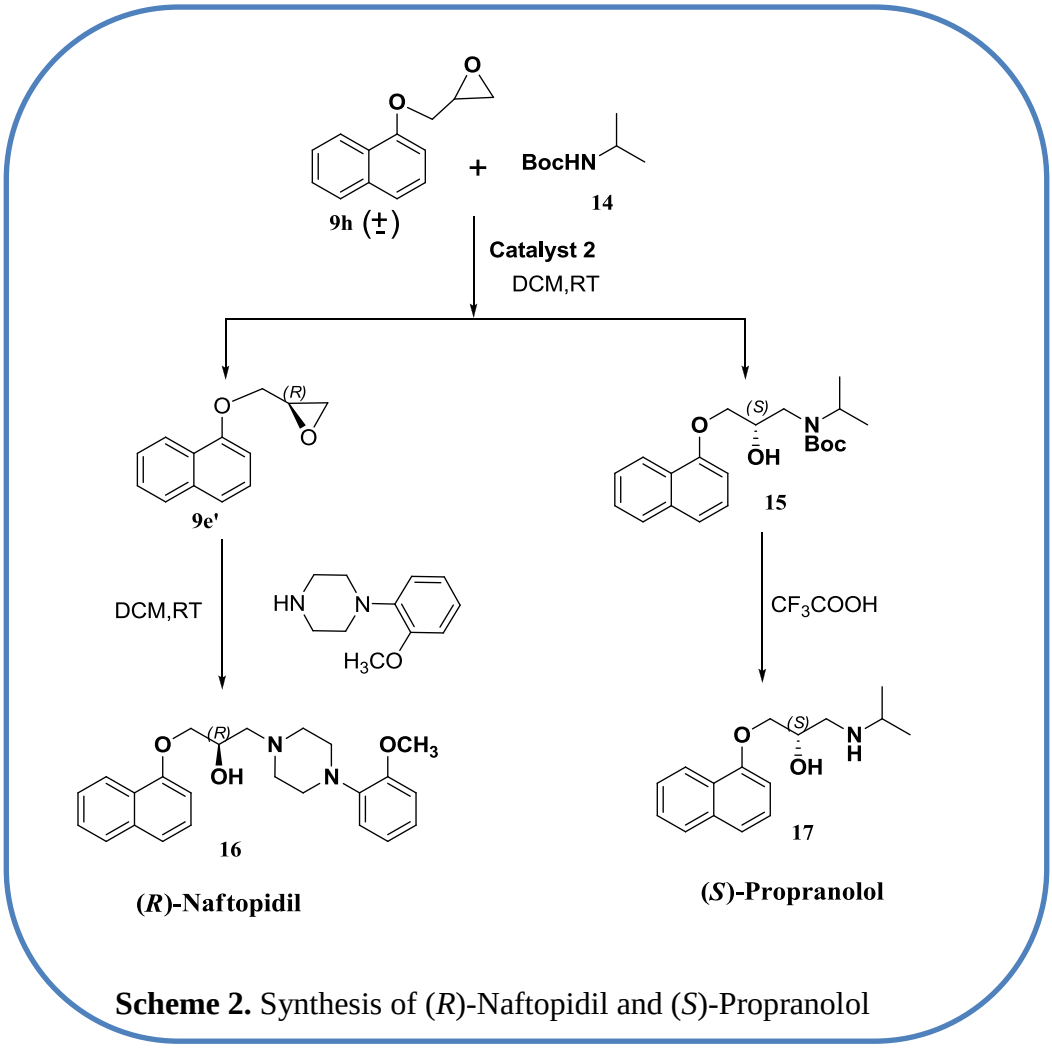


Figure 3. Enantioselective AKR of **9e** with **10a** in DCM using catalyst **1** at different time intervals.

by the catalyst **2**. The reported synthesis of (*S*)-Propranolol through AKR involved the use of $BocNH_2$ as nucleophile in 3 steps[4b]. However, we prepared Boc-protected isoproylamine[16] and used as nucleophile in the AKR of racemic naphthylglycidylether. Thus we got the Boc-protected amino alcohol in 99% ee, which on deprotection directly gave (*S*)-Propranolol. The remaining chirally pure (*R*)-epoxide on reaction with 1-(2-methoxyphenyl)piperazine gave (*R*)-Naftopidil in DCM in one step. This process was also scaled up to one gram level with complete retention of the results obtained at 1 mmol scale. This is to the best of our knowledge and a rare example where both the products of AKR were utilized in making valuable products making the entire process very high at atom economic way. (Details of the experimental procedure are given in the experimental section).



Scheme 2. Synthesis of (*R*)-Naftopidil and (*S*)-Propranolol

Conclusion

In conclusion we have designed efficient chiral Co(III) polymeric salen ligands with chiral and achiral linkers for AKR of aryloxy and terminal epoxides with *N*-protected amine derivatives. The catalyst **1** gave synthetically valuable enantio-pure epoxides (ee, 99%) and *N*-protected 1,2-amino alcohol (ee, 99%) with quantitative yield in 16-20 h and the reaction was scaled to one gram scale for the synthesis of chiral drugs viz., (*R*)-Naftopidil and (*S*)-Propranolol, α_1-adrenergic receptor antagonist or α-blocker and (β-blocker) respectively with 100% utilization of the racemic naphthylglycidylether in atom economic way. The catalyst was recycled six times successfully.

Experimental Section

Synthesis of Polymeric Salen Ligands 1'-8'. Di-aldehydes **A-E** *viz.,* (*R*)-5,5'-(1,1'-binaphthyl-2,2'-diylbis(oxy))-bis(methylene)bis(3-tert-butyl-2-hydroxybenzaldehyde) **A** / (*S*)-5,5'-(1,1'-binaphthyl-2,2'-diylbis(oxy))-bis(methylene)-bis(3-tert-butyl-2-hydroxybenzaldehyde)[7a] **B**, (2*S*,3*S*)-diethyl2,3-bis(3-tert-butyl-5-formyl-4-hydroxybenzyloxy) succinate[11] **C**, 5,5'-(piperazine-1,4-diylbis(methylene))bis(3-tert-butyl-2-hydroxy benzaldehyde)[12] **D** and 5,5'-(2,5,8,11-tetraoxadodecane-1,12-diyl) bis (3-tert-butyl-2- hydroxybenzaldehyde)[13] **E** (1 mmol) were dissolved in dry THF: EtOH mixture (2:1) at 65 ^{o}C to which (1*R*,2*R*)/(1*S*,2*S*)-diaminocyclohexane (0.14 g, 1.2 mmol) in EtOH were added slowly under nitrogen atmosphere. The resulting solutions were stirred for 4 h under refluxing condition (TLC checked) and the solvent was partially removed from the each reaction mixture on a rotary evaporator that gave yellow precipitate. The solid obtained after filtration were washed with hexane:DCM (50:1) to get the yellow colored desired polymeric ligands **1'-8'** (Scheme 1).

Preparation of Polymeric Salen Catalysts 1-8. In 50 ml three neck RBF (equipped with a magnetic bar) under nitrogen atmosphere, the polymeric salen ligands **1'-8'** (1 mmol) were dissolved in deoxygenated toluene (10 ml). In another 25 ml vial $Co(OAc)_2.4H_2O$ (0.37 g, 1.5 mmnol) was dissolved in methanol (10 ml) and deoxygenated by N_2 for 10 min to ensure complete deoxygenation. The solution of $Co(OAc)_2.4H_2O$ in MeOH (purple) was transferred under N_2 via cannula to the solution of polymeric salen ligand (yellow), affording a dark red precipitate. The mixture was stirred for 2 h at RT and then the solvent was removed under vacuum, dissolved the residue in DCM (50 ml) and passed through celite-545 pad to remove the excess of $Co(OAc)_2.4H_2O$. The filtrate was evaporated by vacuum afforded a dark red powder. To get the desired active catalyst, Co(II) chiral polymeric salen complexes were

dissolved in DCM (2 ml) under dry oxygen atmosphere and PNBA (1.2 mmol) was added to them and the resulting solutions were stirred for 5 h to convert Co(II) chiral polymeric salen complexes to Co(III) chiral polymeric salen complexes **1-8** (Scheme 1).

Typical procedure for the AKR of racemic terminal epoxides. In a 5 ml RBF equipped with a magnetic stirring bar, chiral Co(III) polymeric salen complexes **1-8** (0.002 mmol) were dissolved in DCM and to these solutions appropriate carbamate **10a**–**c** (0.1 mmol) was added. The resulting mixture was stirred for 10 min, and then the desired epoxides **9a–h** (0.2 mmol) was added slowly. The reaction mixture was stirred until the HPLC/GC analysis showed disappearance of the peak of the (*R*) enantiomer of the epoxide (for HPLC/GC profiles of the products please see the supporting information). At the end of the reaction, the crude mixture was repeatedly extracted with *n*-hexane/diethyl ether (90:10). The product, *N*-protected 1,2-amino alcohols **11a**–**h**, and the unreacted chiral epoxides **9a'–h'** were recovered by flash chromatography. The remaining mass was dried under vacuum and stored in a desiccator for use in subsequent catalytic runs. The enantiomeric excess (*ee*) of the products **9a'**–**h'** and **11a**–**h** were determined by HPLC analysis using OD, AD-H, OJ, IC chiral columns with *i*PrOH/n-hexane as eluent and GC analysis by chiral BTA column (see the Supporting Information). HPLC traces of the products were compared with the corresponding racemic samples prepared with racemic salen Co (III) complexes as catalyst.

Polymeric salen ligand 1': yield 0.56 g, 98%; yellow crystalline solid; m. p. 220 ^{o}C; $[\alpha]_D^{27}$ -151.27 (c 0.25, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.22 (s, 18H), 1.61-1.65 (m, 3H), 1.76-1.88 (m, 5H), 4.71-4.91 (m, 6H), 6.24-6.51(m, 2H), 6.84-6.95 (m, 2H), 7.15-7.42 (m, 10H), 7.68-7.76 (m, 2H), 7.84-7.92 (m, 6H), 13.72 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 25.6, 26.1, 30.6, 33.3, 71.8, 73.9, 116.1, 117.9, 124.7, 125.2, 126.9, 127.6, 127.8, 129.2, 129.6, 130.5, 135.5, 138.31, 138.4, 138.5, 155.5, 166.5. IR (KBr) ν= 3431, 3055, 2930, 2860,

1627, 1592, 1155, 1082, 869 cm^{-1}; GPC: Average molecular weight (Mn) 13999, polymer molecular weight distribution (PDI) 1.08; Anal. Calcd. for $C_{51}H_{56}N_2O_4$. C, 80.49; H, 7.42; N, 3.68; Found: C, 80.04; H, 7.16; N, 3.45; UV-Vis. (MeOH) λ_{max} 330 nm.

Polymeric salen ligand 2': yield 0.21 g, 96%; yellow crystalline solid; m. p. 210 ^oC; $[\alpha]_D^{27}$ +165.25 (c 0.25, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ = 1.18 (s, 18H), 1.60-1.65 (m, 3H), 1.78-1.92 (m, 5H), 4.43-4.92 (m, 6H), 5.90-5.94 (m, 2H), 6.61-6.83 (m, 3H), 6.89-7.04 (m, 3H), 7.08-7.19 (m, 6H), 7.46-7.49 (m, 2H), 7.64-7.68 (m, 2H), 7.72-7.85 (m, 4H), 13.91 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 24.2, 24.9, 29.2, 34.5, 70.4, 72.5, 114.7, 116.5, 118.0, 121.0, 123.3, 123.8, 125.5, 126.4, 127.8, 128.2, 129.1, 129.2, 129.4, 129.5, 129.6, 134.0, 134.2, 154.1, 165.1; IR (KBr) ν = 3432, 3057, 2930, 2859, 1812, 1711, 1626, 1593, 1156, 1086, 869 cm^{-1}; GPC: Average molecular weight (Mn) 13448, polymer molecular weight distribution (PDI) 1.07; Anal. Calcd. for $C_{51}H_{56}N_2O_4$. C, 80.49; H, 7.42; N, 3.68; Found: C, 80.41; H, 7.26; N, 3.55; UV-Vis. (MeOH) λ_{max} 330 nm.

Polymeric salen ligand 3': yield 0.20 g, 95%; yellow crystalline solid; m. p. 215 ^oC; $[\alpha]_D^{27}$ +136.54 (c 0.01, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ = 1.22 (s, 18H), 1.57-1.69 (m, 3H), 1.78-1.91 (m, 5H), 4.70-4.92 (m, 6H), 6.23-6.31 (m, 2H), 6.44-6.66 (m, 2H), 6.84-6.98 (m, 2H), 7.11-7.16 (m, 3H), 7.21-7.23 (m, 2H), 7.30-7.45 (m, 4H), 7.68-7.71 (m, 2H), 7.76-7.92 (m, 5H), 13.72 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ= 23.8, 24.3, 28.6, 34.0, 35.97, 69.8, 72.0, 114.1, 115.9, 117.5, 120.6, 122.8, 123.3, 125.0, 125.6, 125.8, 126.1, 127.3, 127.8, 127.9, 128.7, 128.9, 128.9, 133.5, 133.6, 153.6, 164.7; IR (KBr) ν = 3430, 3055, 2931, 2860, 1811, 1736, 1627, 1592, 1155, 1082, 870 cm^{-1}; GPC: Average molecular weight (Mn) 13435, polymer molecular weight distribution (PDI) 1.09; Anal. Calcd. for $C_{51}H_{56}N_2O_4$. C, 80.49; H, 7.42; N, 3.68; Found: C, 80.23; H, 7.32; N, 3.48; UV-Vis (MeOH) λ_{max} 330 nm.

Polymeric salen ligand 4': yield 0.22 g, 96%; yellow crystalline solid; m. p. 218 ^oC; $[\alpha]_D^{27}$ +158.34 (c 0.125, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ = 1.22 (s, 18H), 1.56-1.69 (m, 3H),

1.80-1.90 (m, 5H), 4.70-4.92 (m, 6H), 6.23-6.51(m, 2H), 6.61-6.95 (m, 3H), 7.21-7.26 (m, 3H), 7.30-7.46 (m, 5H), 7.68-7.70 (m, 2H), 7.77-8.03 (m, 6H), 13.75 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 23.8, 24.3, 28.6, 34.0, 69.8, 72.00, 114.1, 115.9, 117.5, 122.8, 123.3, 125.0, 125.6, 126.1, 127.9, 128.7, 129.1, 133.5, 133.7, 153.5, 164.63; IR (KBr) ν = 3432, 3056, 2931, 2860, 1808, 1722, 1626, 1591, 1326, 1156, 1086, 869, 696 cm^{-1}; GPC: Average molecular weight (Mn) 13658, polymer molecular weight distribution (PDI) 1.06; Anal. Calcd. for $C_{51}H_{56}N_2O_4$. C, 80.49; H, 7.42; N, 3.68; Found: C, 80.09; H, 7.18; N, 3.35; UV-Vis (MeOH) λ_{max} 330 nm.

Polymeric salen ligand 5': yield 0.225 g, 98%; yellow crystalline solid; m. p. 225 ^oC; $[\alpha]_D^{27}$ -142.91(c 0.25, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.18 (s, 18H), 1.62-1.68 (m, 3H), 1.78-1.83 (m, 5H), 4.41-4.72 (m, 6H), 5.90-5.96 (m, 2H), 6.61-6.84 (m, 3H), 7.00-7.06 (m, 3H), 7.10-7.19 (m, 5H), 7.46-7.49 (m, 2H), 7.64-7.70 (m, 2H), 7.76-7.94 (m, 6H), 13.91 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 25.6, 26.3, 30.0, 35.9, 71.8, 73.9, 116.1, 117.9, 124.7, 125.2, 126.9, 127.6, 127.8, 129.2, 129.6, 129.9, 130.5, 135.5, 155.59, 165.5; IR (KBr) ν = 3431, 3055, 2931, 2860, 1736, 1627, 1592, 1505, 1155, 1082, 869, 744 cm^{-1}; GPC: Average molecular weight (Mn) 13208, polymer molecular weight distribution (PDI) 1.04, Anal. Calcd. for $C_{51}H_{56}N_2O_4$. C, 80.49; H, 7.42; N, 3.68; Found: C, 80.38; H, 7.38; N, 3.55; UV-Vis (MeOH) λ_{max} 330 nm.

Catalyst 1: yield 0.64 g, 99%; dark brown solid; m. p. 190 ^oC; $[\alpha]_D^{27}$ -921.54 (c 0.025, $CHCl_3$); IR (KBr) ν= 3431, 3057, 2937, 2861, 1695, 1621, 1592, 1523, 1015, 872, 721 cm^{-1}; Anal. Calcd. for $C_{58}H_{58}CoN_3O_8$. C, 70.79; H, 5.94; N, 4.27; Found: C, 70.70; H, 6.06; N, 4.17; UV-Vis (MeOH) λ_{max} 330, 400 nm.

Polymeric salen ligand 6': yield 0.55 g, 95%; yellow crystalline solid; m. p. 110 ^oC; $[\alpha]_D^{27}$ +187.09 (c 0.01, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.97 (t, *J*=7 Hz, 6H), 1.34 (s,

18H), 1.74-1.90 (m, 8H), 3.32-3.36 (m, 2H), 3.87-4.14 (m, 5H), 4.23-4.28 (m, 6H), 4.59-4.74 (m, 3H), 6.95 (s, 2H), 7.11 (s, 2H), 8.24 (s, 2H), 13.86 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 13.9, 14.1, 24.2, 24.6, 29.3, 33.1, 33.6, 34.6, 54.6, 61.1, 72.3, 73.3, 76.4, 78.3, 118.1, 125.9, 130.1, 137.3, 160.4, 165.1, 169.2; IR (KBr) ν = 3437, 2932, 2862, 1755, 1629, 1158, 1100, 1027, 863, 704 cm^{-1}; GPC: Average molecular weight (Mn) 3466, polymer molecular weight distribution (PDI) 1.21; Anal. Calcd. for $C_{39}H_{56}N_2O_8$. C, 68.80; H, 8.29; N, 4.11; Found: C, 68.76; H, 7.98; N, 4.05; UV-Vis. (MeOH) λ_{max} 260, 330 nm.

Catalyst 6: yield 0.65 g, 97%; dark brown solid; m. p. 130 ^{o}C; $[\alpha]_D^{27}$ -724.72 (c 0.025, $CHCl_3$); IR (KBr) ν = 3429, 3113, 2929, 2861, 1950, 1749, 1638, 1162, 1098, 1022, 875, 721 cm^{-1}.; Anal. Calcd. for $C_{47}H_{60}CoN_3O_{12}$. C, 61.50; H, 6.59; N, 4.58; Found: C, 61.45; H, 6.34; N, 4.48; UV-Vis (MeOH) λ_{max} 400 nm.

Polymeric salen ligand 7': yield 0.58 g, 96%; yellow crystalline solid; m. p. 215 ^{o}C; $[\alpha]_D^{27}$ +93.35 (c 0.25, $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$) δ = 1.29 (s, 18H), 1.47-1.66 (m, 3H), 1.7-1.81 (m, 5H), 2.07(s, 2H), 2.29 (m, 8H), 2.79 (bs, 1H), 3.25-3.35 (m, 6H), 6.86 (m, 2H), 7.00-7.17 (m, 2H), 8.17 (s, 2H), 13.69 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 24.3, 29.4, 30.9, 34.7, 52.8, 62.5, 72.3, 118.2, 126.6, 130.3, 136.7, 151.7, 159.3, 165.4; IR (KBr) ν = 3421, 2934, 2863, 2807, 1629, 1159, 1095, 1013, 878 cm^{-1}; GPC: Average molecular weight (Mn) 4529, polymer molecular weight distribution (PDI) 1.42; Anal. Calcd. for $C_{35}H_{52}N_4O_2$. C, 74.96; H, 9.35; N, 9.99; Found: C, 74.86; H, 9.08; N, 9.69; UV-Vis (MeOH) λ_{max} 262, 330 nm.

Catalyst 7: yield 0.70g, 98%; dark brown solid; m. p. 220 ^{o}C; $[\alpha]_D^{27}$ +245.75 (c 0.025, $CHCl_3$); IR (KBr) ν = 3425, 2925, 2856, 1629, 1524, 1162, 1096, 1025, 876, 724 cm^{-1}; Anal. Calcd. for $C_{47}H_{60}CoN_3O_{12}$. C, 61.50; H, 6.59; N, 4.58; Found: C = 61.35; H = 6.44; N, 4.48; UV-Vis (MeOH) λ_{max} 262, 400 nm.

Polymeric salen ligand 8': yield 0.54g, 96%; yellow crystalline solid; m. p. 100 ^{o}C; $[\alpha]_D^{27}$ -160.01 (c 0.25, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.38 (s, 18H), 1.69-1.75 (m, 3H), 1.85-2.06 (m, 5H), 3.30-3.32 (m, 3H), 3.56-3.63 (m, 14H), 4.38 (m, 5H), 6.98 (m, 2H), 7.20 (m, 2H), 8.26 (s, 2H), 13.55 (bs, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 23.7, 28.8, 32.5, 34.2, 68.5, 70.0, 71.8, 72.6, 117.6, 126.5, 129.0, 136.6, 159.4, 164.8; IR (KBr) ν = 3432, 2927, 2862, 1629, 1444, 1265, 1098, 1026, 870, 706 cm^{-1}; GPC: Average molecular weight (Mn) 4543, polymer molecular weight distribution (PDI) 1.66; Anal. Calcd. for $C_{37}H_{56}N_2O_6$. C, 71.12; H, 9.03; N, 4.48; Found: C, 70.98; H, 9.08; N, 4.20; UV-Vis. (MeOH) λ_{max} 260, 330 nm.

Catalyst 8: yield 0.25 g, 95%; dark brown solid; m. p. 110 ^{o}C; $[\alpha]_D^{27}$ -638.69 (c 0.025, $CHCl_3$); IR (KBr) ν= 3432, 2925, 2856, 2364, 1722, 1638, 1526, 1262, 1094, 1026, 873, 790 cm^{-1}; Anal. Calcd. for $C_{44}H_{58}CoN_3O_{10}$. C, 62.33; H, 6.89; N, 4.96; Found: C, 61.95; H, 6.84; N, 4.78; UV-Vis (MeOH) λ_{max} 262, 400 nm.

14: In a two neck 10 ml RBF, isopropyl amine (11 mmol, 0.94 ml) was added gradually to the molten di-tert-butyl dicarbonate (Boc_2O) (2.18 g, 10 mmol,) at room temperature. The resulting solution was stirred for 45 minutes which result in the formation of precipitate. The excess isopropyl amine was removed under vacuum until only product remained..

Characterization data of products

14: yield 1.5 g, 95%; white crystalline solid; m. p. 68 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.11 (d, *J*=6 Hz, 6H), 1.44 (s, 9H), 3.70-3.79 (m, 1H), 4.35 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 23.0, 28.4, 42.5, 78.9, 155.1; IR (KBr) ν = 3350, 2979, 2934, 1684, 1536, 1458, 1367, 1358, 1252, 1174, 1079 cm^{-1}; ESI-MS *m/z* 160 $[M+H]^+$; Anal. Calcd. for $C_8H_{17}NO_2$: C, 60.35; H, 10.76; N, 8.80; found C, 60.33; H, 10.72; N, 8.71.

15: yield 0.81 g, 90%; isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 98 ^{o}C; $[\alpha]_D^{27}$ +48.83 (*c* 0.1, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 12.63 min (*R*, major) and 17.94 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.10 (d, *J*=6 Hz, 6H), 1.44 (s, 9H), 3.64-3.89 (m, 3H), 4.00-4.49 (m, 4H), 6.82 (bs, 1H), 7.36-7.47 (m, 4H), 7.79 (bs, 1H), 8.22 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 23.0, 28.3, 42.4, 63.8, 69.2, 70.5, 79.0, 104.9, 120.8, 121.5, 125.3, 125.7, 126.4, 127.5, 134.4, 154.0; IR (KBr) ν = 3415, 2957, 2830, 1645, 1458, 1254, 1069 cm^{-1}; ESI-MS *m/z* 360 $[M+H]^+$; Anal. Calcd. for $C_{21}H_{29}NO_4$ C, 70.17; H, 8.13; N, 3.90; found C, 70.11; H, 8.05; N, 3.82.

(*R*)-Naftopidil 16: yield 0.87 g, 89%; isolated by column chromatography (hexane/AcOEt 90/20) as a white solid; m. p. 128 ^{o}C; $[\alpha]_D^{27}$ -3.00 (*c* 1.50, MeOH); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.51-2.55 (m, 4H), 2.69-2.74 (m, 2H), 2.90-3.02 (m, 4H), 3.67 (s, 3H), 3.96-4.20 (m, 3H), 6.63 (t, *J*=8 Hz, 2H), 6.75-6.85 (m, 3H), 7.15-7.34 (m, 5H), 7.61-7.65 (m, 1H), 8.14-8.19 (m, 1H); ^{13}C NMR(50 MHz, $CDCl_3$) 50.7, 53.7, 55.4, 61.1, 65.8, 70.6, 105.0, 111.3, 118.3, 120.6, 120.8, 121.1, 122.0, 123.1, 125.3, 125.7, 125.9, 126.5, 127.6, 134.5, 141.1, 152.3, 154.5; ESI-MS *m/z* 393 $[M+H]^+$; Anal. Calcd. For $C_{24}H_{28}N_2O_3$ C, 73.44; H, 7.19; N, 7.14; found: C, 73.40; H, 7.04; N, 7.10.

(*S*)-Propranolol 17: yield 0.61 g, 94%; isolated by column chromatography (hexane/AcOEt 90/20) as a white solid; m. p. 72-73 ^{o}C; $[\alpha]_D^{27}$ -10.05 (*c* 0.5, EtOH); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.90 (d, *J*= 6 Hz, 6H), 2.55-2.77 (m, 3H), 3.40 (bs, 1H), 3.89-4.19 (m, 3H), 6.54-6.64 (m, 1H), 7.11-7.27 (m, 5H), 7.60 (d, *J*= 4 Hz, 1H), 8.12 (m, 1H); ^{13}C NMR(50 MHz, $CDCl_3$) δ = 22.8, 49.0, 49.8, 68.4, 70.9, 104.9, 120.6, 121.9, 125.3, 125.6, 125.9, 126.5, 127.6, 134.5, 154.4; ESI-MS *m/z* 260 $[M+H]^+$, 283$[M+Na]^+$; Anal. Calcd. for $C_{16}H_{21}NO_2$. C, 74.10; H, 8.16; N, 5.40; found C, 74.02; H, 8.12; N, 5.36.

(*R*)-*tert*-butyl-2-hydroxy-3-phenoxypropylcarbamate (11a): The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 82-85 ^{o}C; $[\alpha]_D^{27}$ +10.5 (*c* 2, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 12.63 min (*R*, major) and 17.94 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$)**:** δ = 1.42 (s, 9H), 3.21 (bs, 1H), 3.25-3.35 (m, 1H), 3.42-3.55 (m, 1H), 3.91-4.03 (m, 2H), 4.08-4.19 (m, 1H), 5.02 (bs, 1H, NH), 6.90-7.00 (m, 3H), 7.26-7.33 (m, 2H); ESI-MS *m/z* 268 $[M+H]^+$.

***(R)*-ethyl-2-hydroxy-3-phenoxypropylcarbamate (12a):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +8.6 (*c* 1.04, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 21.12 min (*R*, major) and 32.02 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.25 (t, *J* = 7.2, 3H), 3.14 (bs, 1H), 3.30-3.39 (m, 1H), 3.47-3.56 (m, 1H), 3.94 (dd, *J* = 6.4 Hz, 9.6 Hz, 1H), 3.98 (dd, *J* = 4.8 Hz, 9.6, 1H), 4.06-4.13 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 5.15 (br. s, 1H), 6.87-7.02 (m, 3H), 7.26-7.34 (m, 2H); ESI-MS *m/z* 240 $[M+H]^+$.

***(R)*-benzyl-2-hydroxy-3-phenoxypropylcarbamate (13a):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 79-82 ^{o}C; $[\alpha]_D^{27}$ +6.8° (*c* 1.04, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 34.44 min (*R*, major); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.94 (d, *J* =4.0 Hz, 1H), 3.34-3.45 (m, 1H), 3.51-3.59 (m, 1H), 3.90-4.04 (m, 2H), 4.10-4.19 (m, 1H), 5.14 (s, 2H), 5.20 (bs, 1 H), 6.82-7.02 (m, 3H), 7.26-7.48 (m, 7H); ESI-MS *m/z* 302 $[M+H]^+$.

***(R)-tert*-butyl-3-(4-tert-butylphenoxy)-2-hydroxypropylcarbamate (11b):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m.

p.115-120 ^{o}C ; $[\alpha]_D^{27}$ +588.17 (*c* 0.012, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 15.28 min (*R*, major) and 21.22 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.33 (s, 9H), 1.44 (s, 9H), 2.78 (bs, 1H), 3.76-3.88 (bs, 2H), 3.90 (bs, 1H), 4.03-4.10 (m, 1H), 4.32-4.46 (bs, 2H), 6.84-6.90 (dd, *J* = 4 Hz, 4.5, 2H), 7.30-7.34 (t, *J* = 7.5 Hz, 2H); ESI-MS *m/z* 324 $[M+H]^+$.

***(R)*-ethyl-3-(4-tert-butylphenoxy)-2-hydroxy propylcarbamate (12b):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +24.96 (*c* 0.16, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 17.78 min (*R*, major) and 20.19 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) 1.26 (t, *J*=7.2 Hz, 3H), 1.44 (s, 9H), 3.40-3.45 (m, 1H), 3.49-3.64 (m, 1H), 3.96 (dd, 1H, *J*=6.4 Hz, 9.6 Hz, 4.08-4.12 (m,1H), 4.18 (q, *J*=7.2 Hz, 2H), 4.60-4.64 (m, 2H), 5.11 (s, 1H), 6.89 (d, *J* = 5.5 Hz, 2H), 7.34 (d, *J* = 10 Hz, 2H); ESI-MS *m/z* 295 $[M+1]^+$.

***(R)*-benzyl-3-(4-tert-butylphenoxy)-2-hydroxy propylcarbamate (13b):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 110-115 ^{o}C ; $[\alpha]_D^{27}$ +245.91 (*c* 0.02, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 n-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 27.95 min (*R*, major) and 32.26 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.46 (s, 9H), 3.01-3.08 (m, 1H), 3.20-3.26 (m, 1H), 3.42-3.45 (m, 2H), 3.62-3.63 (d, *J* = 5 Hz, 1H), 3.68-3.69 (d, *J* = 3.5 Hz, 1H), 3.78-3.80 (t, *J* = 4.5 Hz, 1H), 5.08 (s, 2H), 7.32-7.65 (m, 9H); ESI-MS *m/z* 357 $[M+H]^+$.

***(R)*-tert-butyl-3-(4-chlorophenoxy)-2-hydroxy propylcarbamate (11c):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 92-95 ^{o}C ; $[\alpha]_D^{27}$ +25.0 (*c* 0.16, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H

column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 68.17 min (*R*, major) and 73.69 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.42 (s, 9H), 3.20=3.28 (m, 1H), 3.37 (bs, 1H), 3.66-3.98 (m, 2H), 4.07-4.08 (m, 2H), 4.85-5.02 (m, 1H), 6.90-7.12 (d, *J* = 6 Hz, 2H), 7.26-7.47 (d, *J* = 6, 2H); ESI-MS *m/z* 302 $[M+H]^+$.

***(R)*-ethyl-3-(4-chlorophenoxy)-2-hydroxy propylcarbamate (12c):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +25.0 (*c* 0.16, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 75.00 min (*R*, major) and 82.49 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.24 (t, *J* = 7 Hz, 3H), 1.80 (bs, 1H), 3.77-3.99 (m, 3H), 4.09, (bs, 1H), 4.14 (q, *J* = 7 Hz, 2H), 4.68-4.69 (m, 2H), 6.85-7.22 (m, 4H); ESI-MS *m/z* 274 $[M+H]^+$.

***(R)*-benzyl-3-(4-chlorophenoxy)-2-hydroxy propylcarbamate (13c):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a White solid; m. p. 86-90 ^oC ; $[\alpha]_D^{27}$ +16.5 (*c* 0.2, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 13.94 min (*R*, major) and 17.79 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$δ 3.49 (bs, 1H), 3.70-3.75 (m, 1H), 3.82-3.87 (m, 1H), 4.03-4.08 (m, 2H), 4.15-4.17 (m, 1H), 4.70 (s, 1H), 5.10 (s, 2H), 6.82-6.90 (d, *J* = 8.5 Hz, 2H), 7.25-7.35 (m, 5H), 7.37 (d, *J* = 4 Hz, 2H); ESI-MS *m/z* 336 $[M+H]^+$.

***(R)*-*tert*-butyl-2-hydroxy-3-(O-tolyloxy)propylcarbamate (11d):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid. m. p. 98-102 ^oC; $[\alpha]_D^{27}$ +17.0 (*c* 2, $CHCl_3$). The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 38.20 min (*R*, major) and 45.81 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.45 (s, 9H), 2.27 (s, 3H), 2.72 (bs,

1H),3.72-3.90 (m, 2H), 4.05-4.10 (m, 2H), 4.14-4.17 (m, 1H), 6.82 (d, *J*= 8 Hz, 1H), 6.89 (t, *J* = 7 Hz, 1H), 7.12-7.15 (m, 2H); ESI-MS *m/z* 282 $[M+H]^+$.

***(R)*-ethyl-2-hydroxy-3-(O-tolyloxy)propylcarbamate (12d):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +19.24 (*c* 0.15, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 36.69 min (*R*, major); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.27 (t, *J* = 7 Hz, 3H), 2.24 (s, 3H), 2.70 (bs, 1H), 3.81-3.97 (m, 2H), 4.02-4.12(m, 2H), 4.16 (q, *J* = 7 Hz, 2H), 4.20-4.33 (m, 2H), 6.84 (d, *J* = 8 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 7.14-7.26 (m, 2H); ESI-MS *m/z* 254 $[M+H]^+$.

***(R)*-benzyl-2-hydroxy-3-(o-tolyloxy)propylcarbamate (13d):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a white solid; m. p. 98-105 ^oC ; $[\alpha]_D^{27}$ +12.8 (*c* 0.25, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 n-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 22.91 min (*R*, major) and 25.13 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.23 (s, 3H), 2.94 (bs, 1H), 3.75-3.86 (m, 2H), 3.90-4.13 (m, 2H), 4.21-4.33 (m, 2H), 5.09 (s, 2H), 6.84-6.87 (d, *J* = 8 Hz, 1H), 6.94 (bs, 1H), 7.10-7.18 (m, 2H), 7.21-7.36 (m, 5H); ESI-MS *m/z* 316 $[M+H]^+$.

***(R)*-3-chloro-2-hydroxy-propyl)-carbamicacidtert-butylester (11e):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +37.82 (*c* 0.25, $CHCl_3$); The *ee* was determined by HPLC on the corresponding *O*-benzyl derivative (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 21.88 min (*R*, major) and 24.21 min (*S*, minor); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.98 (bs, 1H), 3.23-3.34 (m, 1H), 3.41-3.51 (m, 1H), 3.54-3.60 (m, 2H), 3.92-4.04 (m, 1H), 5.10 (s, 2H), 7.21-7.36 (m, 5H); ESI-MS *m/z* 244 $[M+H]^+$.

***(R)*-benzyl 2-hydroxyheptylcarbamate (11f):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a colorless oil; $[\alpha]_D^{27}$ +48.32 (*c* 0.25, $CHCl_3$); The *ee* was determined by HPLC the corresponding *O*-benzyl derivative (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 18.58 min (*R*, major); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 0.87 (t, *J* = 7.2 Hz, 3H), 1.26-1.41 (m, 4H), 1.43-1.52 (m, 2H), 2.98 (bs, 1H), 3.23-3.34 (m, 1H), 3.41-3.51 (m, 1H), 3.92-4.04(m, 1H), 5.03 (bs, 1H); 5.10 (s, 2H), 7.21-7.36 (m, 5H); ESI-MS *m/z* 266 $[M+H]^+$.

***(R)-tert*-butyl-3-(benzyloxy)-2-hydroxypropylcarbamate (11g):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a White solid; m. p. 102-107 ^oC; $[\alpha]_D^{27}$ +116.6 (*c* 0.02, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 30.71 min (*R*, major) and 35.63 min (*S*, minor); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.45 (s, 9H), 2.61 (bs, 1H), 2.98 (bs, 1H), 3.49-3.50 (bs, 2H), 3.52 (bs, 1H), 3.62-3.65 (m, 1H), 3.88 (bs, 1H), 4.54, (s, 2H), 7.25-7.34 (m, 5H); ESI-MS *m/z* 282 $[M+H]^+$.

***(R)*-2-hydroxy-3-(naphthalen-1-yloxy)-propyl-carbamic acid tert-butyl ester (11h):** The title compound was isolated by column chromatography (hexane/AcOEt 90/10) as a White solid; m. p. 102-107 ^oC; $[\alpha]_D^{27}$ +54.8 (*c* = 0.25, $CHCl_3$); The *ee* was determined by HPLC (Chiralpak AD-H column) mobile phase, 90/10 *n*-hexane/*i*-PrOH; flow rate 0.7 mL/min; t_R = 22.91 min (*R*, major) and 25.13 min (*S*, minor); ^{1}H NMR ($CDCl_3$): δ = 1.46 (s, 9H), 3.36 (bs, 1H), 3.39-3.48 (m, 1H), 3.52-3.65 (m, 1H), 4.16 (d, *J* = 5.6 Hz, 2H), 4.20-4.31 (m, 1H), 5.08 (bs, 1H), 6.82-6.87 (m, 1H), 7.37-7.54 (m, 4H), 7.79-7.84 (m, 1H), 8.16-8.22 (m, 1H); ESI-MS *m/z* 318 $[M+H]^+$.

(*S*)-Naphthylglycidylether(9h'): The title compound was isolated by column chromatography (hexane/AcOEt 90/20) as a yellow color viscous liquid; $[\alpha]_D^{27}$ -34.2 (*c* 1.50, MeOH); The *ee* was determined by HPLC (Chiralpak OD column) mobile phase, 80/20 *n*-hexane/*i*-PrOH; flow rate 0.8 mL/min; t_R = 10.11 min (*R*, minor) and 11.35 min (*S*, major); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.75 (m, 1H), 2.86 (t, *J*=4 Hz, 1H), 2.72 (bs, 1H),3.38-3.43 (m, 1H), 3.99-4.07 (dd, *J*=12 Hz, *J*=10 Hz, 1H), 4.27-4.34 (dd, *J*=12 Hz, *J*=12 Hz, 1H), 6.71 (d, *J*= 6 Hz, 1H), 7.39-7.47 (m, 3H), 7.74-7.78 (m, 1H), 8.26-8.31 (m, 1H); ^{13}C NMR(50 MHz, $CDCl_3$) δ = 44.1, 49.8, 68.4, 104.5, 120.4, 121.6, 124.9, 125.1, 125.4, 126.1, 127.1, 134.1, 153.7; ESI-MS *m/z* 201 $[M+H]^+$.

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Supporting Information

^{1}H, ^{13}C NMR spectra, HPLC, GC and GPC profiles are given for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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