Chapter I

A Green Route Synthesis of Imines and Diimines from β- amino Alcohols as Promising Enantiopure Ligands
1. General introduction

1.1 Asymmetric synthesis

Asymmetric synthesis is about making single enantiomers. To make single enantiomers we have to borrow chirality from nature. General methods used to achieve this goal are: (a) Resolution, which requires resolving agents. (b) Chiral pool synthesis, in this method optically pure starting materials such as α-amino acids (AAs), carbohydrates, hydroxyl acids, terpenes etc. are desirable. (c) Asymmetric synthesis, this comprises use of chiral auxiliaries which is disposable part of the starting material by which chiral reagents and catalysts are prepared. First two methods are not suitable, since these methods are either cumbersome or not economical. Asymmetric synthesis has gained much attention in recent years due to its simplicity and carried out by using chiral catalyst.

Conditions for good asymmetric synthesis

(a) The synthesis should have a high chemical yield with high enantiomeric excess (ee).

(b) The chiral reagent/auxiliary/catalyst should be available cheaply, abundantly and easily with high enantiomeric purity. It should have very good chemical and optical stability.

(c) The chiral reagent/auxiliary/catalyst should be easily recoverable from the reaction mixture in high yield and purity – both chemical and optical.

Enantiomeric excess is the formation of one enantiomer in excess over other. Enantiomeric excess (ee) usually quoted as % ee and is calculated by using following formula:

$$\%\text{ee} = \left(\frac{\text{Amount of one enantiomer} - \text{Amount of other enantiomer}}{\text{Total amount obtained}}\right) \times 100$$

Asymmetric catalysis is rapidly turning an important tool for both small scale laboratory synthesis and bulk industrial production of enantiomerically enriched compounds. Among many chiral catalysis, metal complexes feature prominently [1].
1.2 Common chiral ligands
Some of the commercially available chiral diamines and β-amino alcohols used in asymmetric synthesis are represented in Fig.1.1

![Fig 1.1: Commercial chiral ligands for asymmetric synthesis](image-url)

Diamines are the most common chiral moieties employed in asymmetric synthesis. In addition to diamines enantiopure chiral molecules such as (S)-BINAP, (R, R)-DIPAMP, L-(+)-DET, DHQD/DHQ, and most often chiral imines/diimines are also operational with equal ease. After successful chiral catalysis by Jacobson and Bernardo [2, 3] continuous efforts are being made to develop most effective chiral catalyst.

1.3 Importance of chirality
In addition to chiral catalysis, metal complexes of Co, Ni, Cu, Zn, Pd and Pt are extensively studied for their broad spectrum biological activities. High selectivity of chiral molecules is paramount in entire biological features. Chirality determines the precise role in the fields of pharmaceutical, flavors, agrochemicals and fragrances [4]. Important enantiomers in the biological and pharmaceutical fields are represented the Fig. 1.2.
To prepare enantiopure compounds from reactions of prochiral substrates with reagents, large amounts of homogeneous chiral metal catalysts are required. To make available such chiral catalysts, large quantities of enantiomerically pure ligands are required. To begin with the task, α-amino acids are selected as a primary source of chirality in present work. These α-amino acids are effectively reduced to their corresponding β-amino alcohols and condensed with aromatic aldehydes to obtain chiral Schiff base ligands (CSBLs), which are good mixed donor atom (N,O) chelating agents to get chiral metal complexes.

1.4 Chiral Schiff Base Ligands (CSBLs)
Schiff bases (SBs) were first reported by Schiff [5] in 1864. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R1. These compounds are also known as imines or azomethines. Presence of a lone pair of electrons in an sp² hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance. SBs are excellent chelating agents [6-8] especially when a functional group like –OH or –SH is present close to the azomethine group.
1.5 Importance of CSBLs

CSBLs are mainly investigational in the field of experimental coordination chemistry. Metal complexes of these CSBLs are generally used as catalyst in many asymmetric organic transformations [9] which include:

<table>
<thead>
<tr>
<th>Polymerization</th>
<th>Carbyonlation</th>
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</thead>
<tbody>
<tr>
<td>Ring opening polymerization</td>
<td>Heck reaction</td>
</tr>
<tr>
<td>Oxidation</td>
<td>Benzylolation of alanine</td>
</tr>
<tr>
<td>Epoxidation</td>
<td>Amidation of hydrocarbon</td>
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<tr>
<td>Ring opening reactions of epoxides</td>
<td>Cyclopropanation</td>
</tr>
<tr>
<td>Reduction of ketones</td>
<td>Isomerisation of norbornation to quadricyclane</td>
</tr>
<tr>
<td>Allylic alkylation</td>
<td>Aldol condensations</td>
</tr>
<tr>
<td>Hydrosilation of acetophenone</td>
<td>Diels Alder reactions</td>
</tr>
<tr>
<td><strong>Michael addition</strong></td>
<td>Desymmetrization of meso compounds and Annulation</td>
</tr>
</tbody>
</table>

In addition to catalyst in asymmetric synthesis, many chiral schiff base ligands (CSBLs) find applications in the medicine [10], chiral pool synthesis of homo allylic amines [11], simple amines [12], 2-aryl/2, 5-bis(aryl)pyrrolidines [13], N-nitroso-1, 3-oxazolidines [14], novel cyclodextrin derivatives of benzimido-β-cyclodextrin [15], chiral auxiliary by Strecker reaction [16], five or six membered ring [4. 3. 0] heterobicyclic system of monomeric boronates [17] and pinnacol coupling [18]. Some of the CSBLs also find applications in the preparation of dyes, rubber accelerators and liquid crystals for electronics as an important intermediates [19].

1.6 Objective of the research work

Our main aim is to synthesize the chiral metal complexes of imines, which could be used for the several asymmetric transformations in organic chemistry and also to evaluate their antimicrobial activity. To synthesize these complexes chiral imines are required in bulk quantities. Thus on scrutinizing the chemical literature we found that few aromatic Schiff bases were synthesized in saturated aqueous solutions and in the presence of various
catalysts at different pH values [20]. A recent report [21] where imines, diimines and macrocyclic diimines are synthesized in aqueous solutions has prompted us to report our results in this field. Our final target was to prepare variety of chiral imines and diimines from optically active β-amino alcohols and coordinate them with Ni(II)/Pd(II) ions to synthesize novel chiral metal complexes.

1. 7 Reduction of α-AAs
Optically active α-amino acids viz. R-2-phenylglycine, (S)-2-phenylglycine, (R)-2-amino-3-phenylpropanoic acid and (S)-valine are conveniently reduced to their corresponding β-amino alcohols by using NaBH₄/I₂ in dry THF according to minor modification in the known procedure [22] as a primary source of optically active compounds. Reduction of α-AAs itself is difficult task due to their less solubility in water. Although various regents are available [23-25]; NaBH₄/I₂ in dry THF is found to be most suitable for the reduction of AAs to their corresponding β-amino alcohols. These amino alcohols are very important in the field of biochemistry. Also they are directly used in asymmetric synthesis of peptide, pharmaceutical, insecticidal compounds and in resolution of racemic mixtures.

1. 8 Green approach
In recent years water has emerged as a versatile solvent for organic synthesis. Water as a solvent in chemical manufacturing is not only inexpensive and environmentally benign, but also provides safety in operational processes and social benefits [26]. In early decades it was believed that, water is a contaminant in organic synthesis [27] but now a days, extraordinary attention has been paid to organic reactions in water. Research and development in this area is still increasing exponentially [28].

Due to environmental concern it has become inevitable to develop a “Green” process of synthesis for bulk materials that avoids the use of potentially harmful or nonrenewable organic solvents [29]. Organic chemistry in water is not limited to classical organic transformations such as hydrolysis, esterification and substitutions but almost all organic reactions are explored in aqueous medium with more or less successful results [27, 28]. Asymmetric catalysis is growing rapidly, the industrial production of enantiomerically enriched compounds requires use of expensive chiral catalysts. The synthesis and
purification of these chiral catalysts is tedious and laborious. Chiral imines or Chiral Schiff’s base ligands (CSBLs) are extensively used as chiral ligands in the synthesis of transition metal complexes as successful catalysts [30]. Generally such imines are synthesized by simple condensation of aldehydes / carbonyl compounds with primary amines in anhydrous organic solvents [31]. The difficult task of elimination of water from reaction mixture is often achieved by addition of drying agents such as Na$_2$SO$_4$ [32-35], MgSO$_4$ [36], or by refluxing the reaction mixture in Dean-Stark apparatus [37, 38], for several hours and this method is still in practice to synthesize the diimines [39]. More recently CSBLs are synthesized by refluxing aldehydes or carbonyl compounds with primary amines in EtOH or MeOH [40-43]. This method consumes most of the time to obtain final product, since reaction mixture is refluxed for prolonged time and then kept for slow evaporation of solvent to get required imine, the chances of epimerization cannot be ruled out in such cases. CSBLs can form variety of transition metal complexes by participating in binding with metal ions via nitrogen lone pair electrons. The chiral metal complexes of imine showed high enantioselectivity in organic transformation such as nitroaldol (Henry) reaction [40] and hydro phosphorylation of aldehydes [44]. Hence it has become primarily important to explore, simple, inexpensive, racemization free and environment friendly route to synthesize the CSBLs. The β-amino alcohols on simple condensation with aromatic aldehydes in water under mild condition offered the imines and diimines in quantitative yields. All the reactions were carried out in the simplest manner, by mixing directly the β-amino alcohols and aromatic aldehydes in water, without adding any other organic solvent, catalyst or buffer solution at room temperature. When the imines did not separate directly from the aqueous solution, extraction was used. However, these unusual, but simple, economically practical reaction conditions are of wide application and of preparative value in the field of CSBLs synthesis. To the best of our knowledge there is only one report so far disclosed by László Lázár and coworkers [45] where in condensation of (S)-2-amino-2-phenylethanol or (S)-2-amino-3-phenylpropanol with substituted benzaldehydes is carried out in methanol and water. The method is successful only for imines of aromatic aldehyde and aryl amines. Other reports for reactions in water [46, 47] are devoted to synthesis of non-chiral Schiff bases. The
synthesis of chiral imines in aqueous solutions for present work is reported in six sections: first four, deals with general experiments which show the scope and limitations of the chiral imine synthesis in water and two with the synthesis of open chain diimines that are promising chelating agent for metallic cations.

2. Present work and results

2.1 synthesis of β-amino alcohols from optically pure AAs
Four optically pure α-AAs (1-4) are selected as primary source of chirality. These α-AAs can also be directly used to coordinate with metal ions to produce the chiral metal complexes but this method is very crude and many byproducts are formed which becomes very difficult to separate them and coordination compound never crystallizes as a fine solids. Due to this, we decided to reduce these α-AAs to their corresponding β-amino alcohols (1a-4a) (Scheme 1) and then condensed with suitable aldehyde to furnish chiral imines.

Optically active α-amino acids viz. (R-2-phenylglycine, (S)-2-phenylglycine, (R)-2-amino-3-phenylproanoic acid and (S)-valine are conveniently reduced to their corresponding β-amino alcohols by using NaBH₄/ I₂ in dry THF. Some of these β-amino alcohols are commercially available but are costly and moreover optical and chemical purity could not be ascertained.

![Scheme 1: Racemization free reduction of α-AAs](image)

1a, R = (R)-(+) = Ph
2a, R = (S)-(+) = Ph
3a, R = (R)-(+) = CH₂Ph
4a, R = (R)-(+) = CH(CH₃)₂
Synthesized β-amino alcohols are characterized by FT-IR and $^1$HNMR spectroscopic methods before reacting with the aromatic aldehydes. Physical constant and specific rotation measured at room temperature are in good agreement with the reported values in the literature (Table 1).

**Table 1**: Racemization free reduction of α-AAs

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Compound</th>
<th>Temp °C</th>
<th>Yield %</th>
<th>MP/BP °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>0-5/65-70</td>
<td>76</td>
<td>74-76 (77-78) [47a]</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>0-5/65-70</td>
<td>70</td>
<td>73-75 (76-78) [47b]</td>
</tr>
<tr>
<td>3</td>
<td>3a</td>
<td>0-5/65-70</td>
<td>95</td>
<td>92 (93-94) [47c]</td>
</tr>
<tr>
<td>4</td>
<td>4a</td>
<td>0/ 65-70</td>
<td>50</td>
<td>187 (80, 0.2 torr) [47d]</td>
</tr>
</tbody>
</table>

Note: Figures in the round bracket indicates the lit. values

2.2 Synthesis of type-1 CSBLs form 4-methoxy benzaldehyde (monoimines)

Schiff bases of aromatic aldehydes are usually easy to obtain under mild conditions at relatively low temperature, by condensation reaction with amines [48]. General chemistry of this process showed a two-step reaction, with intermediate formation of amino alcohol and final elimination of water [49]. Thus, in order to obtain desired product excess of suitable organic solvent is generally used for azeotropic removal of water from the system [37, 38]. In a completely different approach, we attempted the synthesis of variety of chiral imine derivatives in water and in the absence of any catalyst or buffering mixture. As a starting material in the first series, $p$-methoxy benzaldehyde (5) together with chiral β-amino alcohols (1a-3a) were used to get chiral monoimines 1b-3b (Scheme-2).

β-Amino alcohols are readily soluble in water, on the other hand aromatic aldehydes form emulsion droplets in water at room temperature. These droplets generally contain hydrophobic interiors which would concentrate the β-amino alcohols onto the surface of droplets and enhance the reaction rate towards the side of dehydrated product. Water molecules generated during the reaction are expelled out from the droplets due to hydrophobic nature of their interiors which shifts the equilibrium towards the products.
Mono imines of this series are isolated by extraction of aqueous reaction mixture with diethyl ether. The crude products, after characterization by FT IR, $^1$H NMR and GC showed a trace amount of unreacted aldehydes. Recrystallization of the crude product from hot pet ether eliminated the aldehyde impurity and yielded solid monoimines of high purity.

2.3 Synthesis of type-2 CSBLs from 4-methyl benzaldehyde (monoimines)

Similar process is being used for the synthesis of monoamines of this series. The $p$-methyl benzaldehyde (6) in water stirred at room temperature and equimolar (slightly excess) water solution of $\beta$-amino alcohols (1a-3a) added to above solution with constant stirring. CSBLs are not precipitated out as solid even after stirring for longer time. Extraction of reaction mixture with organic solvent yielded crude products which recrystallizes as a fine prisms (Scheme 3).

Both CSBLs of type 1 and 2 requires more time if stirred at room temperature. The condensed products consists trace amount of unreacted aldehydes, which is completely removed after purification by recrystallization from organic solvents. The purity of the products checked by spectroscopic techniques and by physical constants. The yield of both types CSBLs (Table 2) is moderate but synthesis of the CSBLs can be made feasible in purely aqueous medium without any catalyst or drying agents.
The bi dentate CSBLs (Type 1 and 2) can coordinate to metal ion through N atom to form one type of metal complexes or through mixed donor atoms (N, O) to form another mononuclear complexes.

**Table 2**: Condensation of p-substituted benzaldehydes with β-amino alcohols to obtain bi dentate CSBLs.

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Compound</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>M P (°C)</th>
<th>$[\alpha]_{D}^{0}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>12</td>
<td>66</td>
<td>85</td>
<td>98.72</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>12</td>
<td>63</td>
<td>94-95</td>
<td>-103.2</td>
</tr>
<tr>
<td>3</td>
<td>3b</td>
<td>8</td>
<td>72</td>
<td>76-77</td>
<td>423.56</td>
</tr>
<tr>
<td>4</td>
<td>4b</td>
<td>12</td>
<td>69</td>
<td>82-82</td>
<td>84.54</td>
</tr>
<tr>
<td>5</td>
<td>5b</td>
<td>12</td>
<td>58</td>
<td>80-81</td>
<td>-107.84</td>
</tr>
<tr>
<td>6</td>
<td>6b</td>
<td>8</td>
<td>86</td>
<td>91</td>
<td>319.2</td>
</tr>
</tbody>
</table>

**Scheme 3**: Synthesis of CSBLs type 2
2.4 Synthesis of type-3 CSBLs from 2-hydroxy benzaldehyde (monoimines)

After getting satisfactory results in the synthesis of CSBLs of type 1 and 2, third type of CSBLs which may act as mixed donor (N, O) tri dentate chelating agent in the formation of chiral coordination compound are synthesized. In this category of CSBLs o-hydroxy benzaldehydes (7) is stirred in water and aqueous solution of β-amino alcohol (1a-4a) is added slowly to it. The CSBLs of this type separated as a solid immediately after complete addition of β-amino alcohol solution (Scheme 4). The rate of reaction is fast as compared to the first two type of CSBLs. Aqueous reaction mixture is continuously stirred at room temperature and after completion of the reaction, the products (1c-4c) are isolated merely by filtration. Purification by recrystallization afforded extremely fine crystals. The yield of this category of CSBLs is high as compared to other types of CSBLs (Table 3). All four β-amino alcohols can be effectively condensed with o-hydroxy benzaldehyde. Anisaldehyde exists in a strong intramolecular H-bonding due to which the electrophilic character of carbonyl group is more and the nucleophile attack by NH$_2$ group is more rapid than other aldehydes without hydroxyl substituent. This may be the reason to have quantitative yields and comparatively less time to get the final CSBLs. Characterization techniques showed highest purity of this type of CSBLs.

**Scheme 4**: Synthesis of CSBLs type 3
2. 5 Synthesis of type-4 CSBLs from 2-hydroxynaphthaldehyde (monoimines)

In this attempt additional aromatic character ring for aldehyde is selected for the synthesis of CSBLs. The o-hydroxy naphthaldehyde (8) does not form droplets in water like other aldehydes 5, 6 and 7 but remained suspended in water. To this suspension when water solution of β-amino alcohols (1a-4a) is added aldehyde dissolved slowly and CSBLs separated out as a solid from aqueous reaction medium (Scheme 5).

![Scheme 5: Synthesis of CSBL type 4](image)

All four β-amino alcohols reacts with o-hydroxy naphthaldehyde with equal ease and high yields (Table 3) but reaction product (8c) with β-amino alcohol 4a indicated poor yields and also requires isolation by column chromatograph. These CSBLs prepared from o-hydroxy naphthaldehyde are also characterized by FT IR and $^1$H NMR spectroscopic techniques and other characterization methods.
Table 3: Condensation of o-substituted aromatic aldehydes with β-amino alcohols to obtain tri dentate CSBLs.

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Compound</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>M P (°C)</th>
<th>$[\alpha]_D^{oC}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1c</td>
<td>2</td>
<td>89</td>
<td>86-88(87-88) [40]</td>
<td>160.5(99.3) [40]</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td>2</td>
<td>81</td>
<td>88-90(91-93) [18]</td>
<td>-123.70(-122) [50]</td>
</tr>
<tr>
<td>3</td>
<td>3c</td>
<td>2</td>
<td>93</td>
<td>65(62-64) [58]</td>
<td>395.04</td>
</tr>
<tr>
<td>4</td>
<td>4c</td>
<td>4</td>
<td>92</td>
<td>100(104-106) [37]</td>
<td>-29.85(-25) [37]</td>
</tr>
<tr>
<td>5</td>
<td>5c</td>
<td>6</td>
<td>68</td>
<td>168-170</td>
<td>514.76</td>
</tr>
<tr>
<td>6</td>
<td>6c</td>
<td>6</td>
<td>67</td>
<td>165-166</td>
<td>-202.08</td>
</tr>
<tr>
<td>7</td>
<td>7c</td>
<td>6</td>
<td>70</td>
<td>170-171</td>
<td>467.80</td>
</tr>
<tr>
<td>8</td>
<td>8c</td>
<td>6</td>
<td>70</td>
<td>92-95</td>
<td>-60</td>
</tr>
</tbody>
</table>

Note: Figures in round bracket indicates lit. values.

2. 6 Synthesis of type-5 CSBLs (Open chain dimines)
Demonstrability in the synthesis of four types of CSBLs directed the findings in this field towards the synthesis of more complex CSBLs. In this category of CSBLs, β-amino alcohols are condensed with dialdehydes (9, 10) prepared by coupling two o-hydroxy benzaldehydes through oxygen.

Most of this type of diimines are synthesized from alkyl diamines and suitable aldehydes / ketones to constitute Schiff bases which could be transformed into metal ion salen complexes as successful chiral catalysts [2, 51]. The synthesis of such salen complexes in the present report is restricted, since we used optically pure β-amino alcohols (1a-4a) as a primary source of chirality. In salen type of complexes, diamine is optically active source but in the present study non chiral dialdehyde is condensed with optically pure β-amino alcohols.

Both types of aromatic dialdehydes (9, 10 and 11-12) were obtained by bridging o-hydroxy and p-hydroxy benzaldehydes with dibromoalkanes viz. 1, 2-dibromoethane and 1, 4-
dibromobutane \((n = 2, 4)\) in 2\% NaOH by known procedure [52]. Crude products are purified by recrystallized from hot ethanol (Scheme 6).

Scheme 6: Coupling of dibromoalkanes with \(o/p\)-hydroxy benzaldehydes

Dimines synthesized are well characterized before reacting with \(\beta\)-amino alcohol. The synthesis of diimine was designed by similar condensation of dialdehydes with chiral \(\beta\)-amino alcohols in water at room temperature (Scheme – 7). The diimines formed may be used as possible chelating agents to coordinate with metal ion through N and O mixed donor atoms.
Initially, stoichiometric quantities of dialdehydes and \( \beta \)-amino alcohols (little excess) were stirred in water at room temperature. The progress of reaction was monitored by extracting aqueous reaction mixture after every two hours by TLC, GC, FT IR and \( ^1H \) NMR techniques. The analysis of reaction mixture revealed partial diimine formation. Therefore, stirring was continued for prolonged time at the same temperature. Even after prolonged time, reaction could not go to completion. The GC analysis of crude product indicated monomine formation instead of diimine which was further confirmed by IR and \( ^1H \) NMR spectroscopic analysis. Aldehyde carbonyl (\( >C=O \)) and imine (\( >C=N^- \)) group frequencies appear very close to each other in the FT IR spectrum (1710-1785 and 1689-1471 cm\(^{-1} \) respectively).

Two distinct peaks at 1688 cm\(^{-1} \) (\( >C=O \)) and 1638 cm\(^{-1} \) (\( >C=N^- \)) respectively in the IR spectra of crude product confirmed the monomine formation since the latter frequency for imine is not present in the starting dialdehyde. Similar observations were made by examining the \( ^1H \) NMR spectra, where both peaks for aldehyde proton singlet at 9.9\( \delta \) and for imine proton at 8.34\( \delta \) were appeared simultaneously in the \( ^1H \) NMR spectra.

**Scheme 7**: Condensation of 2, 2’- and 4, 4’-(alkane-1, 2-diylbis(oxy))dibenzaldehyde with \( \beta \)-amino alcohols in water.
In the initial stage of diimine synthesis, we presumed that solvent might be playing an important role; therefore the diimine synthesis was also carried out by changing the solvent such as absolute EtOH, MeOH, DMF and CH$_3$CN at room temperature as well as at elevated temperature. In these conditions also similar results were obtained. Finally the reaction mixture along with excess of β-amino alcohols was refluxed in distilled water for few hours in oil bath. As mentioned previously, β-amino alcohols are readily soluble in water, but dialdehydes remained insoluble at room temperature. These dialdehydes formed oil droplets at elevated temperature and reaction proceeded towards the product which was separated as a white precipitate from aqueous solution (Scheme 7). The refluxing continued for 3-6 hrs. The product was separated by filtration, was purified by recrystallization from hot pet ether and ethyl acetate. $^1$H NMR and IR spectroscopy confirmed diimine formation except for compound 2d and 4d where minor peak appeared in NMR spectroscopy at 9.9δ indicating aldehyde proton. The purity of all other compounds was confirmed by GC, IR, $^1$H NMR and elemental analysis. The aldehyde proton peak in $^1$H NMR completely disappeared and a new peak for imine proton appeared at lower chemical shift (8.34δ) as compared to aldehydic proton chemical shift. The IR spectrum also confirmed the absence of aldehyde carbonyl frequency and new frequency for imine (–HC=N–) bond appeared at 1633cm$^{-1}$. Thus a series of diimines 1d-4d are synthesized by refluxing stoichiometric quantities of the suitable β-amino alcohols (slightly excess) and dialdehydes in aqueous solution in good yields (Table - 4).

2. 7 Synthesis of type-6 CSBLs (Open chain diimines)

The synthesis of this type of dimines is attempted in the similar manner as in case of type 5. These dimines are relatively easy to synthesize as compared to other ortho substituted dimines. The product purity obtained in this type of dimines (1e-6e) is also high as compared to type 5.
**Scheme 8**: Condensation of 2, 2’- and 4, 4’-(alkane-1, 2-diylbis(oxy))dibenzaldehyde with β-amino alcohols in water.

This observed trend in the synthesis of dimines may be due to less steric hindrance at para substitution which is generally more when substituents are at ortho position (Scheme 8). The specific rotation for all the CSBLs synthesized is measured in MeOH/CH₂Cl₂ at room temperature (Table 4).
Table 4: Condensation of \( o \)-and \( p \)-substituted dialdehydes with \( \beta \)-amino alcohols to obtain tetra dentate CSBLs.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Compound</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>MP (°C)</th>
<th>([\alpha]_D^{oC})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1d</td>
<td>6</td>
<td>62</td>
<td>88-90</td>
<td>102.72</td>
</tr>
<tr>
<td>2</td>
<td>2d</td>
<td>5</td>
<td>54</td>
<td>65</td>
<td>-248</td>
</tr>
<tr>
<td>3</td>
<td>3d</td>
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<td>4d</td>
<td>8</td>
<td>68</td>
<td>168-170</td>
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<td>142-144</td>
<td>184.40</td>
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<td>2e</td>
<td>6</td>
<td>57</td>
<td>142-144</td>
<td>-120</td>
</tr>
<tr>
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<td>3e</td>
<td>6</td>
<td>67</td>
<td>116-118</td>
<td>166.40</td>
</tr>
<tr>
<td>8</td>
<td>4e</td>
<td>6</td>
<td>63</td>
<td>100</td>
<td>381.80</td>
</tr>
<tr>
<td>9</td>
<td>5e</td>
<td>6</td>
<td>70</td>
<td>98</td>
<td>-71.60</td>
</tr>
<tr>
<td>10</td>
<td>6e</td>
<td>5</td>
<td>72</td>
<td>86</td>
<td>189.40</td>
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3. Characterization of CSBLs

All the CSBLs synthesized in aqueous medium without the help of any catalyst or drying agent are fine crystalline compounds and are well characterized by various spectroscopic techniques.
3. 1 UV-Visible spectroscopy

UV-visible spectra of all the CSBLs synthesized were studied for their structural differences and hydrogen bonding between OH/-N=CH- groups. Dilute solutions (1.0 - 1.5 X 10^{-5} M) in MeOH / CH_2Cl_2, depending upon the solubility of CSBLs were prepared for electronic absorption spectra. Electronic spectra of Schiff bases, generally feature a strong band below 300nm and a medium band due to intra-ligand n-\pi* and \pi-\pi* transitions respectively [52-54]. Electronic absorption of CSBLs (1b-6b) in MeOH show absorption maxima between 254-269nm (\varepsilon = 11930-26090 dm^3 m^{-1} cm^{-1}) below 300nm for azomethane (Fig. 1.3). In case of CSBLs 1b-3b this band shifts towards longer wavelength (269nm) as expected due to p-methoxy in aromatic aldehyde of parent chromophore but this effect is not prominent in 4b-6b since in these CSBLs aromatic aldehyde moiety is substituted with p-methyl group.

![UV-Visible spectra of 1.0-1.5 x 10^{-5} M solutions of CSBLs 1b-6b in MeOH](image)

**Fig 1.3:** UV – Visible spectra of 1.0-1.5 x 10^{-5} M solutions of CSBLs 1b-6b in MeOH (Values in the bracket indicate absorbance of individual \lambda_{max}.)

CSBLs synthesized by condensation of salicyldehyde and 2-hydroxy naphthaldehyde with \beta-amino alcohols (1c-7c) shows further enhancement in the absorption maxima in addition to the band below 300nm. Additional bands (307-316nm, \varepsilon = 3100-4990 dm^3 m^{-1} cm^{-1}) for 1c-4c and two bands at longer wavelength (400-420nm) for 5c-7c (Fig. 1.4) are observed.
The additional band at 307-316nm is attributed to the strong intra-molecular H-bonding between \( \alpha \)-hydroxyl of the aromatic aldehyde moiety and N of azomethane [55, 56] H-bonding helps to maintain the co-planarity of the overall chromophore to extend the conjugation. Well resolved two bands with appreciable intensity at 400 - 420nm appeared for \( 5c-7c \) which are due to naphthalene ring of the aldehyde moiety [57].

**Fig 1.4:** UV – visible spectra of \( 1.0 \times 10^{-5} \text{M} \) solutions of CSBLs \( 1c-7c \) in MeOH (Values in the bracket indicate absorbance of individual \( \lambda_{\text{max}} \)).

C2 symmetric diimines \( 1e-6e \) in CH\(_2\)Cl\(_2\) exhibit a strong single band at 271-272 nm (\( \varepsilon = 45240-113100 \text{ dm}^3 \text{ m}^{-1} \text{ cm}^{-1} \)). The effect of double identical chromophore (azomethane) is not observed in the electronic spectra of these CSBLs (**Fig.5**). A small rise in the wavelength as compared to first type of CSBLs \( 1b-6b \) may be due to solvent effect.
Fig 1.5: UV – visible spectra of 1.0 – 1.5 x 10^{-5}M solutions of CSBLs 1e-6e in CH_2Cl_2
(Values in the bracket indicate absorbance of individual λ_{max}.)

3. 2 FT IR Spectroscopy
FT IR spectra are recorded for all the CSBLs in KBr pallets and compared to the IR spectra of their respective aromatic aldehydes. The most prominent vibrational frequency for carbonyl group in mono aldehydes generally appears in the range of 1710-1785 cm\(^{-1}\). This band completely disappeared and new band to lower value in the range of 1630-1640 cm\(^{-1}\) for imine group (>C=N) of CSBLs of types 1-4 is observed in the IR spectra of this types of imines. Similar trend is observed for the dimines synthesized from dialdehydes. The carbonyl vibrational frequency for dialdehyde is noticed somewhat at lower value (1681-1687 cm\(^{-1}\)), this value further reduced in the range of 1633-1637 cm\(^{-1}\)for the synthesized
dimines which confirms the condensation of aldehyde group to form dimines. The representative FT IR spectra are depicted in Figs 1.6a-1.12a.

3.3 $^1$H NMR Spectroscopy
$^1$H NMR spectra of CSBLs is distinct for the imine proton signal in the range of 7.8-8.35δ. The aldehyde proton generally resonates at 9-10δ value this signal is completely disappeared in case of all monoimines and there are minor shifts in the proton signals of aromatic and aliphatic protons. Small amount of unreacted aldehyde proton peak was seen in the $^1$H NMR in case of dimines which is also removed after refined product by recrystallization. $^1$H NMR spectrums of some representative CSBLs is shown in Figs. 1.6b-1.12b.
Fig 1.6: (a) FT IR and (b) $^1$H NMR type I CSBLs
Fig. 1.7: (a) FT IR and (b) $^1$H NMR CSBLs of type 2
Fig 1.8: (a) FT IR and (b) $^1$H NMR type 3 CSBLs
Fig 1.9: (a) FT IR and (b) $^1$H NMR type 4 CSBLs
Fig 1.10: (a) FT IR and (b) $^1$H NMR type 5 CSBLs
Fig 1.11: (a) FT IR and (b) $^1$H NMR type 6 CSBLs
Fig 1.12: (a) FT IR and (b) $^1$H NMR type 6 CSBLs
4. Experimental

4.1 General details

Distilled water was used in all experiments. The optically active β-amino alcohols (1-4) were prepared by reduction of optically pure α-amino acids. Monoaldehydes (5-8) were purchased from local chemical companies and were purified before use. Dialdehydes (9-12) were synthesized by known procedure and purified by recrystallization before use. Some of these β-amino alcohols are commercially available.

All melting points recorded are uncorrected. NMR spectra were recorded on Varian Mercury Y. H., 300MHz spectrometer in CDCl₃ with (Me)₄Si as internal standard and chemical shifts recorded in δ units. Coupling constants are given in Hz. Identification of monoimines were made by GC and comparing of mps with literature values were done where ever applicable. Infrared spectra were recorded on FT-IR 8400 Shimadzu model as KBr discs. The characteristics absorption is reported as broad (br), strong (s), medium (m) or weak (w) bands. Optical rotations were recorded on Perkin-Elmer polarimeter in a quartz cell of 1 dm at room temperature using sodium D-line and suitable solvent that is reported along with concentration in g/100ml. Elemental analysis was performed on Thermoflash microanalyzer with K factors calibration method.

4.2 General procedure for the synthesis of β-amino alcohols

4.2.1 (R)-2-Amino-3-phenylpropan-1-ol

In a 100ml round bottom flask, D-phenyl alanine (2.0g, 12.12mmol) and sodium borohydride (1.1g, 28.95mmol) was taken in 25ml dry THF. The flask was cooled to 0 °C and a solution of iodine (3.1g, 12.12mmol) in THF was added drop wise and flask was heated to reflux for 18h and cooled to room temperature. The methanol added till the mixture becomes clear. After stirring for 30 minutes solvent was removed under reduced pressure leaving white paste which was dissolved by addition of 20% KOH. Solution was stirred for another 4h extracted with CH₂Cl₂ (3x30ml). Organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure affording a white semisolid compound. The crude product was then recrystallized from ethyl acetate to get pure β-
amino alcohols. 1.75g, 95%, MP 92°C. Other three β-amino alcohols are prepared by the same procedure. (S)-2-amino-3-methylbutan-1-ol was used without purification. Unreacted alcohol is easily removed during the product isolation because final product is solid and this alcohol is liquid at room temperature.

4.2.2 (R)-2-amino-2-phenylethanol, 1.26gm, 76%, MP 74-760C.
4.2.3 (S)-2-amino-2-phenylethanol, 1.16gm, 70%, MP 73-750C.
4.2.4 (S)-2-amino-3-methylbutan-1-ol 0.62gm, 50%, BP 186-1880C (Decomposes).

4.3 General procedures for synthesis of monoimines: 1b-6b and 1c-8c.

In a standard procedure, in a round bottom flask equipped with Teflon coated magnetic bar with a magnetic stirrer and optionally with a reflux condenser were introduced 10 mmol of aldehydes and 25 ml distilled water. The β-amino alcohol (10mmol) was added in one portion and the flask was kept at room temperature under vigorous mechanical stirring for overnight in the case of monoimines 1b-6b and 6-10 hours for 1c-8c. Monoamines (1c-8c) were separated from aqueous medium within mixing time but stirring at room temperature was continued till all starting aldehyde is converted into imine (TLC). When no precipitation occurred, the aqueous reaction mixture was extracted thrice with diethyl ether. The combined organic layers were dried over Na₂SO₄. The organic solvent was evaporated off and the residues were analyzed by GC and NMR. All the synthesized monoimines are fine solids and are purified by recrystallization from hot pet ether except for compounds (5c and 8c) which were purified by column chromatography (Hexane: ethyl acetate, 80:20).

The experimental data for 1b-6b and 1c-8c

4.3.1 (R)-(+)-(4-methoxybenzylideneamino)-2-phenylethanol(1b)
Colourless floppy mass, mp 85°C (Pet ether: ethyl acetate, 80:20), Yield (1.68g, 68%), 
\[\alpha\]^{27}_{D} = 98.72° (c 1, MeOH), IR (KBr), \(\nu_{\text{max}}/\text{cm}^{-1}\) 3198, 1639, 1602, 1508, 1454, 1383, 1305, 1263, 1172, 1880, 1030, ^1H NMR (CDCl₃,300 MHz) \(\delta = 8.32 (s,1H)\), 7.83 (d, 2H, J
= 8.54Hz), 7.2-7.5 (m, 5H), 6.95 (d, 2H, J = 8.54Hz), 4.91 (t, 1H, J = 4.27Hz), 3.87 (s, 3H), 2.45 (brs, 1H). [Anal. Calcd for C_{16}H_{17}NO_{2}: C, 75.27; H, 6.71; N, 5.49; O, 12.53. Found: C, 74.97, H, 6.71, N, 5.61].

4.3.2 (S)-(−)-2-(4-methoxybenzylideneamino)-2-phenylethanol (2b)
Fine needles, mp 94-95°C (Pet ether: ethyl acetate, 80:20), Yield (1.6g, 63%), [α]_{D}^{27} = -103.2^0 (c 1, MeOH), IR(KBr), v_{max}/cm\(^{-1}\) 1028,1076,1172,1259,1301,1383,1450, 1506, 1602, 3198. \(^1\)H NMR (CDCl\(_3\) 300MHz) δ = 8.35 (s, 1H), 7.77 (d, 2H, J = 8.84Hz), 7.28-7.47 (m, 5H), 6.94 (d, 2H, J = 8.8 Hz), 4.48 (dd, 1H, J = 4.6Hz), 3.94 (ddd, 2H, J = 4.67 and 3.5Hz), 3.87 (s, 3H), 2.05 (brs, 1H). [Anal. Calcd for C_{16}H_{17}NO_{2}: C, 75.27; H, 6.71; N, 5.49; O, 12.53. Found: C, 74.97, H, 6.71, N, 5.61].

4.3.3 (R)-(−)-2-(4-methoxybenzylideneamino)-3-phenylpropan-1-ol (3b)
Fine needles, mp 76-77°C (Pet ether: ethyl acetate, 80:20). Yield (2g, 72%), [α]_{D}^{27} = 423.56^0 (c1,MeOH), IR(KBr), v_{max}/cm\(^{-1}\) 1043,1085,1080,1225,1307,1450,1512,1604,1641, 3211. \(^1\)H NMR (CDCl\(_3\) 300MHz) δ = 7.86 (s,1H), 7.63(d, 2H, J = 8.54Hz), 7.14-7.26(m 5H), 6.90 (d, 2H, J = 8.54Hz), 3.84 (s, 3H), 3.79-3.89(m, 2H), 3.50 (m, 1H), 2.91 (dd, 2H, J = 8.25 and 5.5Hz), 2.07(brs, 1H). [Anal. Calcd for C_{17}H_{19}NO_{2}: C, 75.81; H, 7.11; N, 5.20; O, 11.88. Found: C, 75.55, H, 7.12, N, 5.26].

4.3.4 (R)-(−)-2-(4-methylbenzylideneamino)-2-phenylethanol (4b)
Pale yellow prisms, mp 80-82°C (Pet ether: ethyl acetate, 80:20). Yield (1.64g, 69%), [α]_{D}^{27} = 84.54^0(c 1, MeOH), IR(KBr), v_{max}/cm\(^{-1}\) 1062, 1207, 1325, 1375, 1421, 1471, 1620(b), 3280. \(^1\)HNMR (CDCl\(_3\), 300MHz) δ = 8.34(s, 1H), 7.66(d, 2H J = 7.97Hz), 7.21(d, 2H J = 7.97Hz), 7.25-7.41(m, 5H), 4.47(dd, 1H J = 4.40Hz), 3.96(m, 2H), 2.36(s, 3H), 2.25(brs, 1H). [Anal. Calcd for C_{16}H_{17}NO: C, 80.30; H, 7.16; N, 5.85; O, 6.69; Found: C, 80.27, H, 7.18, N, 6.04].
4.3.5 (S)-(−)-2-(4-methylbenzylideneamino)-2-phenylethanol (5b)
Yellow brown prisms, mp 80-81°C (Pet ether: ethyl acetate, 80:20). Yield (1.38g, 58%).
\([\alpha]_{D}^{27} = -107.84^\circ\) (c 1, MeOH), IR (KBr), \(v_{\text{max}}/\text{cm}^{-1}\) 1049, 1178, 1222, 1307, 1342, 1450, 1498, 1610, 1641, 3279. 1H NMR (CDCl₃, 300MHz) \(\delta = 8.35(s, 1H), 7.68(d, 2H, J = 7.93Hz), 7.21(d, 2H, J = 7.93Hz), 7.26-7.44(m, 5H), 4.48 (dd, 1H, J = 4.27Hz), 3.85-3.95(m, 2H), 2.39(s, 3H), 2.36 (brs, 1H). [Anal. Calcd for C₁₆H₁₇NO: C, 80.30; H, 7.16; N, 5.85; O, 6.69; Found: C, 80.16, H, 7.17, N, 5.99].

4.3.6 (R)-(−)-2-(4-methylbenzylideneamino)-3-phenylpropan-1-ol (6b)
Colourless needles, mp 91°C (Pet ether: ethyl acetate, 80:20). Yield (2.17g, 86%), \([\alpha]_{D}^{27} = 319.20^\circ\) (c 1, MeOH), IR (KBr), \(v_{\text{max}}/\text{cm}^{-1}\) 11057(s), 1205, 1271, 1402, 1475, 1602, 3227 (br). 1H NMR (CDCl₃, 300MHz) \(\delta = 7.95(s, 1H), 7.53(d, 2H, J = 7.93Hz), 7.12-7.35(m, 7H), 3.5(dd, 2H, J = 6.71Hz), 3.48(dd, 1H J = 6.71Hz), 2.95(ddd, 2H, J = 7.90 and 5.40Hz), 2.37(s, 3H), 2.35(brs, 1H). [Anal. Calcd for C₁₇H₁₉NO: C, 80.60; H, 7.56; N, 5.53; O, 6.32. Found: C, 79.86, H, 7.41, N, 5.55].

4.3.7 (R)-(−)-2-((2-hydroxy-1-phenylethylimino)methyl)phenol (1c)
Pale yellow floppy mass, mp 86-88°C (Pet ether: ethyl acetate, 80:20), (87-88) [58]. Yield (2.15g, 89%) \([\alpha]_{D}^{27} = 160.50^\circ\) (c 1, MeOH), (99.3) [58]. IR(KBr), \(v_{\text{max}}/\text{cm}^{-1}\) 1057(s), 1205, 1248, 1512, 1604, 1637(s), 3198 (br). 1H NMR (CDCl₃, 300MHz) \(\delta = 8.47(s, 1H), 7.25-7.41(m, 7H), 6.99(d, 1H, J = 6.52Hz), 6.89(t, 1H, J = 7.25Hz), 4.47(t, 1H, J = 8.25Hz), 3.91(d, 2H, J = 6.25Hz), 1.88(brs, 2H). [Anal. Calcd for C₁₅H₁₅NO₂: C, 74.67; H, 6.27; N, 5.81, O, 13.26. Found: C, 74.57, H, 6.26. N, 5.72].

4.3.8 (S)-(−)-2-((2-hydroxy-1-phenylethylimino)methyl)phenol (2c)
Pale yellow spongy mass, mp 88-90°C (Pet ether: ethyl acetate, 80:20), (91-93) [18], Yield (1.95g, 81%), \([\alpha]_{D}^{27} = -123.70^\circ\) (c 1, MeOH), (−22) [50]. IR(KBr), \(v_{\text{max}}/\text{cm}^{-1}\) 1024, 1045, 1087, 1174, 1261, 1305, 1448, 1512, 1604, 1637(s), 3198 (br). 1H NMR (CDCl₃, 300MHz) 8.49(s, 1H), 7.25-7.41(m, 7H), 6.98(d, 1H, J = 8.25Hz), 6.89(t, 1H, J = 7.2Hz), 4.47(t, 1H, J

4.3.9 (S)-(+-)-2-((1-hydroxy-3-phenylpropan-2-limino)methyl)phenol (3c)
Lemon yellow coloured crystals, mp 65^\circ C. (Pet ether: ethyl acetate, 80:20), (62-64) [58] Yield (2.37g 93%), [\alpha]_D^{27} = 395.04^0 (c 1, MeOH). IR (KBr), \nu_{max}/cm^{-1} 1047, 1062, 1207, 1292, 1406, 1483, 1627, 3173, 3352 (br). \^1H NMR (CDCl_3) \delta = 13.19(brs, 1H), 8.09(s, 1H), 7.13-7.33(m, 7H), 6.96(d, 1H, J = 8.54Hz), 6.84(t, 1H J = 7.32Hz), 3.80-3.86(m, 2H), 3.48-3.36(m, 1H), 3.92,(dd, J = 8.54 and 4.88Hz). [Anal. Calcd for C_{16}H_{17}NO_2: C, 75.27; H, 6.71; N, 5.51, O, 12.53. Found: C, 74.83, H, 6.69. N, 5.54].

4.3.10 (S)-(-)-2-((1-hydroxy-3-methylbutan-2-ylimino)methyl)phenol (4c)
Lemon yellow spongy mass, mp 100^\circ C (Pet ether: ethyl acetate, 80:20), (104-106) [54]. Yield (1.92g, 92%), [\alpha]_D^{27} = -29.85^0 (c 0.5, MeOH) (-25) [54]. IR (KBr) 1047, 1062, 1207, 292, 1406, 1483, 1627, 3173, 3352 (br)cm^{-1}. \^1H NMR (CDCl_3) \delta = 8.35 (s, 1H), 7.2(dd, 2H, J = 1.65Hz), 6.90(dd, 2H, J = 7.7 and 8.25Hz), 3.79(d, 2H, J = 8.25 and 7.7Hz), 3.06(q, 1H, J = 3.5Hz), 1.94(s, 1H, J = 6.8Hz), 0.93(q, 6H, J = 6.8 and 4.1Hz). [Anal. Calcd for C_{12}H_{17}NO_2: C, 69.54; H, 8.27; N, 6.76; O, 15.44. Found: C, 69.57, H, 8.29. N, 6.90].

4.3.11 (R)-(+-)-3-((2-hydroxy-1-phenylethylimino)methyl)naphthalen-2-ol (5c)
Greenish yellow prisms, mp 168-170^\circ C (Pet ether: ethyl acetate, 80:40). Yield (1.97g, 68%), [\alpha]_D^{27} = 198.76^0 (c 0.5, MeOH), IR(KBr), \nu_{max/cm^{-1}} 1078,1174,1276,1406(w), 1489, 1541,1630(s),3230(brs). \^1H NMR (CDCl_3, 300MHz) \delta = 14.96(brs, 1H), 8.9(s, 1H), 7.81(d, 1H, J = 8.54Hz),7.16-7.53(m, 9H), 6.88(d, 1H, J = 9.76Hz), 4.68(dd, 1H, J = 4.67Hz), 3.99-4.06(m, 2H), 3.5(brs, 1H). [Anal. Calcd for C_{19}H_{17}NO_2: C, 78.33; H, 5.88; N, 4.81; O, 10.98. Found: C, 77.84, H, 5.67: N, 4.63].
4.3.12 (S)-(-)-3-((2-hydroxy-1-phenylethylimino)methyl)naphthalen-2-ol (6c)

Yellow floppy mass, mp 165-166°C (Pet ether: ethyl acetate, 80:40), Yield (1.94g, 67%), $\alpha^2_D = -202.08^\circ$ (c 0.5, MeOH), IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1078,1174,1276,1406(w),1489, 541,1630(s), 3230. $^1$H NMR (CDCl$_3$, 300MHz) $\delta = 14.96$(brs, 1H), 902(s, 1H), 7.88(d, 1H, $J =8.43$Hz), 7.63(d,1H, $J = 9.28$Hz), 7.57(d, 1H, $J = 8.15$Hz), 7.23-7.46(m, 7H), 6.96(d, 1H, $J = 8.99$Hz), 4.68(dd, 1H, $J = 5.3$Hz), 4.0 (t, 2H, $J = 4.5$Hz), 2.93(brs, 1H). Anal. Calcd for C$_{19}$H$_{17}$NO$_2$: C, 78.33; H, 5.88; N, 4.81; O, 10.98. Found: C, 77.79, H, 5.87; N, 4.92.

4.3.13 (S)-(+)3-((1-hydroxy-3-phenylpropan-2-ylimino)methyl)naphthalen-2-ol (7c)

Brown yellow floppy mass, mp 170-171°C (Pet ether: ethyl acetate, 80:40), Yield (2.13g, 70%), $\alpha^2_D = 467.80^\circ$(c 1, MeOH), IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1047, 1062, 1207, 1292, 1406, 1483, 1627, 3173, 3352 (br). $^1$H NMR (CDCl$_3$, 300MHz) $\delta = 14.95$(brs, 1H), 8.49(s, 1H), 7.58(d, 1H, $J = 8.53$Hz), 7.12-7.48(m, 9H), 7.80(d, 1H, $J = 9.35$Hz), 3.91(dd, 1H, $J = 8.52$Hz), 3.50(brs 1H), 3.01(ddd, 2H, $J = 7.79$ and 4.95Hz). Anal. Calcd for C$_{20}$H$_{19}$NO$_2$: C, 78.66; H, 6.27; N, 4.59; O, 10.48. Found: C, 78.50, H, 6.26; N, 4.59.

4.3.14 (S)-(-)-3-((1-hydroxy-3-methylbutan-2-ylimino)methyl)naphthalen-2-ol (8c)

Yellow floppy mass, mp 92-95°C (Pet ether: ethyl acetate, 80:40), Yield (1.79g, 70%), $\alpha^2_D = -60.26^\circ$(c 0.6, MeOH), IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1047, 1062, 1207, 1292, 1406, 1483, 1632, 3173, 3342 (br). $^1$H NMR (CDCl$_3$, 300MHz) $\delta = 14.29$(brs, 1H), 8.65(s, 1H), 7.57(d, 1H, $J = 8.54$Hz), 7.11-7.46(m, 4H), 6.77(d, 1H, $J = 8.54$Hz), 4.50(brs, 1H), 3.79(ddd, 2H, $J = 8.8$ and 3.9Hz), 3.29(d, 1H, $J = 3.8$Hz), 0.83(dd, 6H, $J = 7.7$Hz). Anal. Calcd for C$_{16}$H$_{19}$NO$_2$: C, 74.68; H, 7.44; N, 5.44; O, 12.44. Found: C, 74.50, H, 7.36; N, 5.42.
4. 4 General procedure for synthesis of dialdehydes 9-12

Dialdehydes 9-12 were synthesized according to known procedure [52]

4.4.1 2, 2’-(ethane-1, 2-diylibis(oxy))dibenzaldehyde 9

Colourless, mp 127°C (Ethanol), Yield (5.13g, 38%), IR(KBr), ν max/cm⁻¹ 1064, 1107, 1247, 1294, 1400, 1452, 1485, 1597, 1685, 2771(s), 3338. ¹H NMR (CDCl₃, 300MHz) δ = 10.44 (s, 2H), 7.05-7.86(m, 8H), 4.53δ (s, 4H).

4.4.2 4,4’-(ethane-1,2-diylibis(oxy))dibenzaldehyde 10

Colourless, mp 115°C (Ethanol), Yield (6.35g, 47 %,), IR (KBr), ν max/cm⁻¹ 1072, 1112, 1226, 1259, 1427, 1460, 1508, 1599, 1687, 2758(s), 2850, 2945, 3064, 3350. ¹H NMR (CDCl₃, 300MHz) δ = 9.89(s, 2H), 7.85(d, 4H, J = 8.8Hz), 7.05 (d, 4H, J=8.5Hz), 4.44δ (s, 4H).

4.4.3 2, 2’-(butane-1, 4-diylibis(oxy))dibenzaldehyde 11

Colourless, mp 110°C (Ethanol), Yield (6.5g, 44%), IR (KBr), ν max/cm⁻¹ 1045, 1109, 1244, 1305, 1510, 1600, 1681(s), 2843, 2953, 3039(w). ¹H NMR δ = 10.95(s, 2H), 7.83, (dd, 2H, J = 1.65Hz), 7.51-7.57(m, 2H), 6.97-7.06(m, 8H), 4.19δ, (s, 4H), 2.10(s, 4H).

IV.4.4 4, 4’-(butane-1, 4-diylibis(oxy))dibenzaldehyde 12

Brown flakes, mp 100°C(Ethanol), Yield (6.94g, 47%), IR (KBr), ν max/cm⁻¹ 1045, 1109, 1244, 1305, 1510, 1600, 1681(s), 2843, 2953, 3039(w). ¹H NMR(CDCl₃, 300MHz) δ = 9.89, (s, 2H), 7.84(d, 4H, J = 8.5Hz), 7.14, (d, 4H, J = 8.5Hz), 4.14(s, 4H), 2.05δ, (s, 4H).

4. 5 General procedure for synthesis of diimines 1d-4d and 1e-6e

In a round bottom flask equipped with Teflon coated magnetic bar with a magnetic stirrer and a reflux condenser were introduced 1mmol of dialdehydes and 25 ml distilled water. The β-amino alcohol (2 mmol) was added in one portion and the flask was kept at room temperature under vigorous mechanical stirring for 30 minutes. The flask was transferred to oil bath and stirring continued for 16-24h with oil bath temperature 110°C. Reaction
progress was checked by TLC. The flask was allowed to cool, after completion of the reaction, when no precipitation occurred, the aqueous reaction mixture was extracted thrice with diethyl ether. The combined organic layers were dried over Na$_2$SO$_4$. The organic solvent was evaporated off and the residue was analyzed by GC and NMR. All the synthesized diimines are solid substances and are purified by recrystallization from hot pet ether and ethyl acetate (1:1).

The data for diimines

4.5.1 (2R,2'R)-(+-)(2,2'-(ethane-1,2-diylbis(oxy))bis(2,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(2-phenylethanol) (1d)

Colourless amorphous solid, mp 88-90 °C (Pet ether: ethyl acetate, 1:1), Yield (0.24g, 47%), $[\alpha]_D^{27} = 102^\circ$ (c 0.05, CHCl$_3$). IR (KBr), $\nu_{max}/cm^{-1}$: 1055, 1114, 1161, 1238, 1290, 1384, 1452, 1485, 1597, 1633(s), 2874, 2922, 3066, 3171(br), 3441. $^1$H NMR (CDCl$_3$, 300MHz) $\delta =$ 8.72(s, 2H), 8.10(d, 2H, J = 1.79Hz), 7.20-7.43(m, 12H), 7.04(t, 2H, J = 7.6Hz), 6.96(d, 2H, J = 8.50Hz), 4.39(s, 4H), 4.32(dd, 2H, J = 4.5Hz), 3.74-3.91(m, 4H), 2.45(brs, 2H). [Anal. Calcd for C$_{32}$H$_{32}$N$_2$O$_4$: C, 75.57; H, 6.34; N, 5.51; O, 12.58. Found: C, 75.34, H, 6.54, N, 5.23].

4.5.2 (2S,2'S)-(+-)(2,2'-(ethane-1,2-diylbis(oxy))bis(2,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(2-phenylethanol) (2d)

Colourless amorphous solid, mp 65 °C (Pet ether: ethyl acetate, 1:1), Yield (0.27g, 54%), $[\alpha]_D^{27} = -248^\circ$ (c 0.05, CH$_2$Cl$_2$). IR (KBr): 1055, 1114, 1161, 1238, 1290, 1384, 1452, 1485, 1597, 1633(s), 2874, 2922, 3066, 3171(br), 3441cm$^{-1}$. $^1$H NMR (CDCl$_3$, 300MHz) $\delta =$ 8.74(s, 2H), 8.10(d, 2H, J = 1.8Hz), 6.89-7.55(m, 14H), 4.40(s, 4H), 4.32(dd, 2H, J = 4.5Hz), 3.74-3.91(m, 4H), 2.45(brs, 2H). [Anal. Calcd for C$_{32}$H$_{32}$N$_2$O$_4$: C, 75.57; H, 6.34; N, 5.51; O, 12.58. Found: C, 75.10, H, 6.19, N, 5.40].

4.5.3 (2R,2'R)-(+-)(2,2'-(ethane-1,2-diylbis(oxy))bis(2,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(3-phenylpropan-1-ol) (3d)
CHAPTER I

Colourless solid, mp 100 °C (Pet ether: ethyl acetate, 1:1), Yield (0.34g, 64%), $[\alpha]_D^{27} = 400^o$ (c 0.05, CH$_2$Cl$_2$). IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1055,1114,1161,1238,1290,1384,1452,1485, 1597,1633(s), 2874, 2922,3066,3171(br), 3441. $^1$H NMR (CDCl$_3$, 300MHz) $\delta =$ 7.89(s, 2H), 7.58(d, 4H, J = 8.30Hz), 7.12-7.37(m, 10H), 6.93(d, 4H, J = 7.79Hz), 4.35(s, 4H), 3.78(ddd, 4H, J = 2.5, 3,4 and 6.8Hz), 3.35(brs, 2H), 2.92(dddd,4H, J = 4.9, 5.3,83Hz), 2.3(brs, 2H). [Anal. Calcd for C$_{34}$H$_{36}$N$_2$O$_4$: C, 76.09; H, 6.76; N, 5.22; O, 11.93.  Found: C, 75.86, H, 6.92. N, 5.09].

4.5.4 (2R,2'R)-(++)-(2,2'-(butane-1,4-diylbis(oxy))bis(2,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(3-phenylpropan-1-ol) (4d)

Colourless, mp 168-170 °C (Pet ether: ethyl acetate, 1:1), Yield (0.36g, 68%), $[\alpha]_D^{27} = 315.08^o$ (c 0.5, CH$_2$Cl$_2$). IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1058,1116,1161,1228,1290,1384, 1452,1485,1597,1633(s), 2874, 2922,3066,3171(br), 3445. $^1$H NMR (CDCl$_3$, 300MHz) $\delta =$ 8.42(s, 2H), 7.88(dd, 2H, J = 1.7Hz ), 6.94-7.32(m, 14H), 6.84(dd, 4H, J = 1.7Hz), 4.12(s, 4H), 3.7(brs, 2H), 3.37(s. 4H), 2.92(dddd,4H, J = 5.3, 6.8Hz), 2.45(brs, 2H), 2.04(s, 4H). [Anal. Calcd for C$_{34}$H$_{36}$N$_2$O$_4$: C, 76.09; H, 6.76; N, 5.22; O, 11.93.  Found: C, 75.66, H, 6.62. N, 5.14].

4.5.5 (2R,2'R)-(++)2,2'-(((ethane-1,2-diylbis(oxy))bis(4,1-phenylene))bis(methanylylidene)) bis(azanylylidene))bis(2-phenylethanol) (1e)

Colourless, mp 142-144 °C (Pet ether: ethyl acetate, 1:1), Yield (0.29g, 57%), $[\alpha]_D^{29.6} = 184.4^o$ (c 0.1 CH$_2$Cl$_2$). IR(KBr), $\nu_{\text{max}}$/cm$^{-1}$ 1035,1070, 1174,1247,1506,1600, 1633(s), 2868, 2928, 3242(br)cm$^{-1}$ $^1$H NMR (CDCl$_3$,300MHz) $\delta =$ 8.35(s, 2H), 7.77(d, 4H, J = 8,6Hz), 7.28-7.46 (m, 10H), 6.99(d, 4H, J = 8,6Hz), 4.48(dd, 2H J = 4.8Hz), 4.40(s, 4H), 3.94(dd, 4H, J = 4.8Hz), 2.06(brs, 2H). [Anal. Calcd for C$_{32}$H$_{32}$N$_2$O$_4$: C, 75.57; H, 6.34; N, 5.51; O, 12.58; Found: C, 74.76; H, 6.36; N, 5.43].
4.5.6 (2S,2’S)-(-)-2,2’-(((ethane-1,2-diylbis(oxy))bis(4,1-phenylene))bis(methanlylidene))bis(azanylylidene))bis(2-phenylethanol) (2e)

Colourless, mp 144-146 °C (Pet ether: ethyl acetate, 1:1), Yield (0.3g, 57%), \([\alpha]^{29.3}_D = -120^o(c\ 0.1\ CH_2Cl_2)\). IR (KBr), \(\nu_{max}/cm^{-1}\) 1035, 1070, 1174, 1247, 1506, 1600, 1633(s), 2866, 2928, 3242(br). \(^1\)H NMR (CDCl\(_3\), 300MHz) \(\delta = 8.36(s, 2H), 7.78(d, 4H, J = 9Hz), 7.28-7.47 (m, 10H), 6.99(d, 4H, J = 9Hz), 4.47(dd, 2H J = 4.8Hz), 4.40(s, 4H), 3.94(dd, 4H, J = 4.8Hz), 2.06(brs, 2H). [Anal. Calcd for C\(_{32}\)H\(_{32}\)N\( _2\)O\(_4\): C, 75.57; H, 6.34; N, 5.51; O, 12.58; Found: C, 74.70; H, 6.33; N, 5.38].

4.5.7 (2R, 2’R)-(+)-2,2’-(((ethane-1,2-diylbis(oxy))bis(4,1-phenylene))bis(methanlylidene))bis(azanylylidene))bis(3-phenylpropan-1-ol) (3e)

Colourless, mp 116-118 °C (Pet ether: ethyl acetate, 1:1), Yield (0.35g, 67%), \([\alpha]^{29.5}_D = 166.4^o(c\ 0.1\ CH_2Cl_2)\). IR (KBr), \(\nu_{max}/cm^{-1}\) 1043, 1074, 1170, 1244, 1575, 1604, 1635(s), 2858, 2928, 3433(br). \(^1\)H NMR (CDCl\(_3\), 300MHz) \(\delta = 7.92(s, 2H), 7.61(d, 4H, J = 9Hz), 7.24-7.27 (m, 10H), 6.95(d, 4H, J = 9Hz), 4.36(s, 4H), 4.40(s, 4H), 3.89(dd, 4H, J = 3.4Hz), 3.40(m, 2H), 2.90(dd, 4H, J = 8.1 and 5.8Hz), 2.0(brs, 2H). [Anal. Calcd for C\(_{34}\)H\(_{36}\)N\( _2\)O\(_4\): C, 76.09; H, 6.76; N, 5.22; O, 11.93; Found: C, 75.96; H, 6.60; N, 5.13].

4.5.8 (2R,2’R)-(+)-(4,4’-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene))bis(2-phenylethanol) (4e)

Colourless, mp 100 °C (Pet ether: ethyl acetate, 1:1), Yield (0.33g, 63%), \([\alpha]^{29.7}_D = 331.80^o(c\ 0.1\ CH_2Cl_2)\). IR(KBr), \(\nu_{max}/cm^{-1}\) 1041, 1064, 1172, 1251, 1508, 1602, 1635(s), 2868, 2924, 3234(brs)cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\),300MHz) \(\delta = 8.33(s, 2H), 7.74(d, 4H, J = 8.5Hz), 7.27-7.45 (m, 10H), 6.92(d, 4H, J = 8.5Hz), 4.46(dd, 2H J = 4.3Hz), 4.08(s, 4H), 3.92(dd, 4H, J = 4.3Hz), 2.0(s, 4H), 1.79(brs, 2H). [Anal. Calcd for C\(_{34}\)H\(_{36}\)N\(_2\)O\(_4\): C, 76.09; H, 6.76; N, 5.22; O, 11.93; Found: C, 74.79; H, 6.80; N, 5.50].
4.5.9 (2S,2'S)-2,2'(-)(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(2-phenylethanol) (5e)

Colourless, mp 98 °C (Pet ether: ethyl acetate, 1:1), Yield (0.37g, 70%), \([\alpha]^{29.3}_D = -71.6^\circ\) (c 0.1 CH2Cl2). IR (KBr), \(\nu_{\text{max}}/\text{cm}^{-1}\) 1049, 1170,1247,1508,1602, 1637(s), 2872, 2943, 3377(br). \(^1\)H NMR (CDCl3,300MHz) \(\delta = 8.32(\text{s, 2H}), 7.72(\text{d, 4H, } J = 8.5\text{Hz}), 7.26-7.48(\text{m, 10H}), 6.92(\text{d, 4H, } J = 8.5\text{Hz}), 4.46(\text{dd, 2H, } J = 4.8\text{Hz}), 4.06(\text{s, 4H}), 3.91(\text{dd, 4H, } J = 4.8\text{Hz}), 2.06(\text{brs, 2H}), 2.0(\text{s, 4H}). \) [Anal. Calcd for C34H36N2O4: C, 76.09; H, 6.76; N, 5.22; O, 11.93; Found: C, 75.17; H, 6.50; N, 5.30].

4.5.10 (2R,2'R)-(++)-(4,4'-(butane-1,4-diylbis(oxy))bis(4,1-phenylene))bis(methan-1-yl-1-ylidene)bis(azan-1-yl-1-ylidene)bis(3-phenylpropan-1-ol) (6e)

Colourless, mp 86 °C (Pet ether: ethyl acetate, 1:1), Yield (0.40g, 72%), \([\alpha]^{29.5}_D = 189.4^\circ\) (c 0.1 CH2Cl2). IR (KBr), \(\nu_{\text{max}}/\text{cm}^{-1}\) 1047, 1082, 1172,1251,1510,1602, 1637(s), 2862, 2920, 3227(br). \(^1\)H NMR (CDCl3,300MHz) \(\delta = 7.91(\text{s, 2H}), 7.58(\text{d, 4H, } J = 9\text{Hz}), 7.13-7.31(\text{m, 10H}), 6.88(\text{d, 4H, } J = 9\text{Hz}), 4.06(\text{s, 4H}), 3.77(\text{dd, 4H, } J = 3.8\text{Hz}), 3.48(\text{brs, 2H}), 2.91(\text{dddd, 4H, } J = 8.1 \text{ and } 5.3\text{Hz}), 2.03(\text{brs, 2H}), 1.98(\text{s, 4H}). \) [Anal. Calcd for C36H40N2O4: C, 76.57; H, 7.14; N, 4.96; O, 11.33; Found: C, 75.28; H, 7.24; N, 5.05].
5. Conclusions

From the above studies it has been found that, organic solvents proved to be less effective than water to obtain the chiral imines and diimines in quantitative yield. A simple and convenient route is developed to synthesize CSBLs by condensation of aldehydes and dialdehydes with optically active β-amino alcohols in water without using any catalyst or buffer. Condensation of o-hydroxy aldehydes with β-amino alcohols is rapid and provide excellent yield at room temperature. The synthesis of monoimines and diimines can be achieved completely in aqueous medium in excellent yield except for monoimines of p-methoxy/methyl substituted aldehydes where organic solvent is used for extraction of aqueous reaction mixture to isolate the CSBLs. All other monoimines and diimines are separated from aqueous medium after completion of reactions as a precipitate. Diimine synthesis requires boiling of aqueous reaction mixture. Co planarity of aromatic ring and azomethane is maintained due to strong intramolecular H-bonding in o-hydroxy imines which is responsible for longer wavelength of absorption in UV-vis. spectroscopy.

The synthesized CSBLs may be explored as bidentate or tridentate chiral ligands while diimines as a chelating agent for synthesis of chiral transition metal complexes which are generally excellent chiral catalyst for many organic transformations in organic synthesis.
6. References


