Chapter - 5

Application of 1-(α-Aminobenzyl)-2-naphthol as Chiral Solvating Agent
INTRODUCTION

As discussed in chapter-1, the synthesis and applications of Aminonaphthol derivatives have been widely studied. The developments in this field are adequately summarized by Szatmari and Fulop in the recently published review. The pioneering work on similar molecules started in the early 20th century when Italian chemist Mario Betti first reported on the synthesis of aminobenzyl naphthol or Betti base. Since then, several derivatives have been prepared with achiral amines and then resolved to access chiral aminonaphthols or chiral derivatives prepared directly utilizing non-racemic amines for Mannich reactions. The reaction of β-naphthol with a chiral primary amine and an aldehyde follows an aromatic Mannich reaction via an initially formed chiral imine. The reaction usually proceeds with considerable stereocontrol due to the chiral amine, and produces the second stereogenic center with high selectivity.

Due to this simple synthesis of chiral analogues of Betti base or 1-(α-Aminobenzyl)-2-naphthols much attention has been focused on exploring their applications. Some of the significant applications of these ligands in asymmetric transformations include enantioselective alkyations of aldehydes, asymmetric reductions of acetophenone, resolution of important chiral molecules such as BINOL and ibuprofen, as chiral auxiliaries for the synthesis of enantiomerically pure products such as 2,5-disubstituted pyrrolidines, piperidines, and α-aminophosphonic acids, and the synthesis of chiral phosphine ligands and chiral calix[4]arenes. In addition to the chiral analogues, many derivatives of achiral aminonaphthols have been studied for several applications, including our own attempt to use them as phosphine free ligands in palladium catalyzed coupling reactions.

The significance of chiral molecules is not restricted to bioactive molecules such as pharmaceuticals, flavoring agents and fragrances, but has covered many other areas of molecular recognition and material science. Many properties of such molecules are clearly linked to the chirality of the system and hence it is vital to know the composition of the isomers present in a test sample. This has necessitated a need for quick, accurate and reliable technique to establish the ratio of enantiomers in
chiral samples. More routinely used contemporary techniques for such determinations are based on chromatographic separations such as GC and HPLC but their success mainly depends on the efficiency and compatibility of the chiral stationary phases of the columns. Among other available methods, NMR spectroscopy has found to be particularly effective in detail investigation of chiral purity of many molecules particularly recording spectra is a simple, fast and accurate process; it is non-destructive and suited to study the dynamic interactions. With the advent of NMR spectrometers most of the laboratories dealing with chiral chemistry have access to high resolution machines for this kind of analysis.

Two enantiomers of a chiral sample cannot be recognized in an achiral environment by NMR spectroscopy; hence the technique require some modifications. Enantiomers which show identical NMR need to be converted, temporarily or otherwise, in to diastereomers which are expected to show different spectroscopic patterns. Converting the chiral test sample to diastereomers can be carried out in two ways, by forming covalent bonds with chiral derivatizing agents (CDA) or alternatively by forming temporary supramolecular interactions with chiral solvating (or complexing) agents (CSA). The first option is cumbersome and time consuming while the second one is simple, practical and hence has been investigated considerably in recent years. In the case of CSA, the temporary formation of diastereomers with enantiomerically pure reagents results in non-equivalence of the chemical shifts of the protons of the two enantiomers of the analyte. This technique has the distinct advantages of simplicity, more accurate analysis compared to the derivatization process with CDA and is non-destructive due to weak non-covalent interactions with the CSA.

In the earlier decades more focus was on the use of chiral lanthanide shift reagents for diastereomer formation for determination of enantiomer ratio. However, due to high cost, some operational difficulties such as low solubility in some NMR solvents, poor resolution of signals, occasionally limited availability of such lanthanide reagents etc., there was a need to explore organic molecules capable of forming non-covalent supramolecular interactions with chiral analytes. Such intermolecular interactions including dipole-dipole, charge transfer, Van der Waals,
π-π stacking and the formation of H-bonding etc., were then exploited by many researchers in the design and testing of a series of CSAs.

A variety of compounds such as amines, amides, lactams, carboxylic acids, cyclodextrins, etc. with suitable coordination cite and orientation have been developed to be effective in recognizing the analytes and function as CSAs.\textsuperscript{14} Few of them will be discussed here.

A new macrocyclic compound has been synthesized from a derivative of a bis-aminonaphthyl system and its application as a chiral solvating agent has been investigated by Zhang et al.\textsuperscript{15} The authors have prepared a novel chiral macrocyclic compound 3 from a $C_2$-asymmetric aminonaphthol in a high yield (Scheme 1). This macrocyclic compound 3 showed excellent ability to discriminate the enantiomers of a broad variety of carboxylic acids (Figure 1) by $^1$H NMR spectroscopy.

\begin{center}
\textbf{Scheme 1: Synthesis of chiral macrocyclic compound 3}
\end{center}
In the presence of 3, chiral acids have large nonequivalent chemical shifts in \(^1\)H-NMR spectra. From the quantitative analysis of a series of mandelic acids with different enantiomeric purities showed that host 3 is an excellent chemical shift reagent for chiral carboxylic acids.

Several chiral crown ethers have also been designed as effective CSAs where the interactions could be of a different nature.\textsuperscript{16} Anderson et. al. prepared a series of new chiral macrocycles containing the trans-1,2-diaminocyclohexane (DACH) subunit and arene and oligoethylene glycol-derived spacers in enantiomerically pure form.\textsuperscript{16e} Four of the macrocycles have been characterized by X-ray crystallography which reveals a consistent mode of intramolecular N-H---N hydrogen bonding and conformational variants about the N-benzylic bonds. Most of the macrocycles were found to differentiate the enantiomers of mandelic acid (MA) by \(^1\)H-NMR spectroscopy in CDCl\(_3\); within the series of macrocycles tested, enantiodiscrimination was promoted by (i) a meta-linkage geometry about the arene spacer, (ii) the presence of naphthalene - rather than phenylene - derived arene spacers, and (iii) increasing length of the oligoethylene glycol bridge.
$^1$H-NMR titrations were performed with optically pure MA samples, and the data indicated towards a simultaneous 1:1 and 2:1 binding model, yielding estimates of 2:1 binding constants between some of the macrocycles and MA enantiomers. In several cases, NOESY spectra of the MA:macrocyclc complexes show differential intramolecular correlations between protons adjacent to the amine and carboxylic acid groups of the macrocycles and MA enantiomers respectively, thus demonstrating geometric differences between the diastereomeric intermolecular complexes.

Guo et al. reported the synthesis of chiral macrocycles\textsuperscript{14j} with multiple binding sites from D-phenylalanine as chiral solvating agents (CSAs) for the enantiomeric discrimination and determination of the enantiomeric excess of carboxylic acids and $\alpha$-amino acid derivatives by the $^1$H-NMR spectroscopy.
Scheme 2: Synthesis of Chiral compounds 9 and 10. Reagents and conditions: (i) NaOH (1 M), isopropanol, (Boc)_2O; (ii) EtOAc, o-phenylenediamine, ice-salt bath to rt, N_2; (iii) TFA, CH_2Cl_2, N_2; (iv) CH_3OH, salicylaldehyde, reflux, N_2; (v) DMF, Zn powder, MsOH, -35°C to 0°C; (vi) K_2CO_3, DMF, 2,6-dibromomethylpyridine, N_2.

The results showed that chiral macrocycles 9 and 10 are effective CSAs towards the carboxylic acids and α-amino acids derivatives.

Figure 3: Structures of the guests studied

(-)-Epigallocatechin gallate (EGCG), a polyphenolic bioflavonoid abundantly present in the green tea,^{14k} is well-known for its biological activities, including anticancer, antidiabetic, antibacterial, and anti-inflammatory, and also as an antioxidant that inhibits cellular oxidation of low density lipoprotein in the body. Because of its numerous health benefits and it is a natural product, EGCG has drawn
the attention of many researchers. In this regard, Suryaprakash and Bandyopadhyay\textsuperscript{14k} reported a special, hitherto-unexplored property of (-)-epigallocatechin gallate (EGCG) as a chiral solvating agent for enantiodiscrimination of $\alpha$-amino acids in the polar solvent DMSO. This phenomenon has been investigated by $^1$H-NMR spectroscopy. The mechanism of the interaction property of EGCG with $\alpha$-amino acids has been understood as arising out of hydrogen-bonded non covalent interactions, where the -OH groups of two phenyl rings of EGCG play dominant roles.

![Figure 4: Structure of (-)-EGCG and the guests studied](image)

The conversion of the enantiomeric mixture in to diastereomers yielded well-resolved peaks for D and L amino acids permitting the precise measurement of enantiomeric composition. Often one encounters complex situations when the spectra are severely overlapped or partially resolved hampering the testing of enantiopurity and the precise measurement of enantiomeric excess ($ee$). Though higher concentration of EGCG yielded better discrimination, the use of lower concentration being economical, they have exploited an appropriate 2D NMR experiment in overcoming such problems. Thus, they have successfully demonstrated the utility of the bioflavonoid (-)-EGCG, a natural product as a chiral solvating agent for the discrimination of large number of $\alpha$-amino acids in a polar solvent DMSO. Another
significant advantage of this new chiral sensing agent is that it is a natural product and does not require tedious multistep synthesis.

The success of this technique depends on the proper combination of supramolecular interactions between the two partners of the complex. Hence, even though a large number of CSAs are available, there is a need to design more molecules which can be readily prepared in enantiomerically pure form while they may be easily modified to suit a particular requirement. In this chapter we present simple synthesis of a series of chiral derivatives of aminonaphthol and their assessment as CSAs for the test case of mandelic acid.
Result and Discussion

In this part, synthesis of a series of optically active aminonaphthol derivatives will be discussed. Their applications as chiral solvating agents will also be presented.

The basic unit 1-(α-Aminobenzyl)-2-naphthol 4 was prepared by a three component aromatic Mannich reaction of β-naphthol 1 with the imine formed in situ from (S)-1-phenylethylamine 2 and benzaldehyde 3 (Scheme 3). We have chosen this system due to the simplicity of its preparation from readily available materials and the juxtaposition of two vital functional groups of a weakly acidic phenolic hydroxyl group and the secondary amine closely situated to the stereogenic centre. The two heteroatoms are also separated by three carbons, two being aromatic sp² centre and the third being a stereogenic sp³ centre.

Scheme 3: Synthesis of enantiopure aminoalkynaphthol by solvent free asymmetric Mannich reaction

Herein we planned to make different derivatives of this enantiomerically pure 1-(α-aminobenzyl)-2-naphthol 4 where the two functional groups could be modified and the molecules generated would be screened as CSAs for chiral discrimination of DL-mandelic acid as the standard test substrate in ¹H-NMR spectroscopy.

Compound (S,S)-4 was subjected to alkylation with excess methyl iodide and sodium hydroxide as the base; as expected both the NH and OH were converted into N-Me and O-Me groups to afford dialkylated aminonaphthol (S,S)-5 in good yield (Scheme 4). This compound 5 lacks the hydrogens attached to heteroatoms, which may prevent it forming H-bonds with the hydrogen acceptor atoms of the test substrate in the proposed CSA interaction. We have also studied its single crystal X-ray diffraction pattern and the ORTEP plot is presented in Figure 5.17
In the next proposed modification we plan to block the N-H functionality while exposing the acidic OH group of the aminonaphthol to interactions with the analyte. With this aim a sample of (S,S)-4 was converted into a 1,3-oxazine system 6 by condensing with formaldehyde, which was then selectively reduced with lithium aluminium hydride to give the N-Me, OH derivative (S,S)-7 with excellent conversion (Scheme 5).  

The fourth combination was prepared whereby the acidic phenolic group was protected by selectively converting it into a methyl ester using dimethyl sulfate in an alkaline medium (Scheme 6) in a one-step reaction. In this variant of the methoxy derivative (S,S)-8, the NH is free to form H-bonds with the test substrate and may possibly offer a good binding site.
After preparation of the four derivatives, they were then screened to see their efficacy in binding with a test sample of DL-mandelic acid in \(^1\)H-NMR analysis. The NMR experiments were run with stoichiometric amounts of mandelic acid and CSA (1:1) (22 mM, CDCl\(_3\), 400 MHz). The upfield change in the position of the signal of \(\text{C}^\text{a}\text{H}\) proton of mandelic acid upon treatment with CSA was measured as chemical shift change (\(\Delta\delta\)) while the degree of splitting was measured by the differences in the separated peaks in terms of chemical shift non-equivalences (\(\Delta\Delta\delta\)).

The first four entries of Table 1 indicate that the basic unit \((S,S)-4\) with free NH and OH groups showed very poor recognition (entry 1), while the \(N\)-Me, OH derivative \((S,S)-7\) remained totally ineffective (entry 3). The derivative \((S,S)-5\) with \(N\)-Me and \(O\)-Me showed poor selectivity (entry 2) while the one with free NH and OMe \((S,S)-8\) showed promising results (entry 4).
Encouraged by this, we decided to vary the substituents on this molecule. Under a slightly alkaline medium, the basic unit of (S,S)-4 was treated with several alkyl bromides to perform a selective O-alkylation reaction. A few representative molecules with different types of the O-alkyl group were prepared (Scheme 7) and then screened for CSA activity. The single crystal X-ray diffraction analysis of (S,S)-10 was also performed (Figure 6).17

![Scheme 7: Synthesis of O-alkyl/ O-aryl derivative of aminonaphthol](image)

The aliphatic derivatives (S,S)-9 with an isopropyl group and (S,S)-10 with an n-butyl group did not show much improvement (entries 5 & 6), whereas O-benzyl derivative (S,S)-11 showed much enhancement in the interaction (Figure 7). In order to further explore the scope of the present derivative and to study the effect of substituents on the aromatic ring of the O-benzyl, a series of molecules (S,S)-12 to (S,S)-15 were similarly prepared. These benzyl derivatives with different substitutions

![Figure 6: List of O-alkyl/ O-aryl derivative of aminonaphthol, ORTEP plot of (S,S)-10](image)
on the aromatic ring were scanned for the CSA interactions, which showed selectivity in the similar range (entries 8-11). This observation perhaps indicates that the presence of the aromatic system is sufficient to offer a $\pi-\pi$ interaction between the aromatic rings of CSA and that of mandelic acid.

Figure 7: Effect of CSA on the $^1$H-NMR spectra (400 MHz, CDCl$_3$): C$^\alpha$H proton of DL-mandelic acid (a), C$^\alpha$H proton of DL-mandelic acid + (S,S)-11 (1:1 at 22 mM) (b).

This possibility was further evaluated by introducing $p$-toluene-sulfonyl ester on the aminonaphthyl system, with a free NH in (S,S)-16 and by blocking it as an N-Me derivative of (S,S)-17 (Scheme 8). Both of these molecules were tested for their interactions in the $^1$H-NMR and the results were as expected; the molecule with the free NH showed good activity 16, while N-Me 17 did not recognize mandelic acid (entries 12 & 13, Table 1).

Scheme 8: Synthesis of OTs derivatives of aminonaphthyl system
This hypothesis was further investigated by introducing a carbonyl system in place of the aromatic ring in the ester of aminonaphthol. Accordingly α-aryloxy acetate (S,S)-18 was prepared from (S,S)-4 and ethyl bromoacetate (Scheme 9). This molecule showed comparable activity as a CSA for resolution of the signals of mandelic acid (entry 14, Table 1) as that of the O-Bn derivative (S,S)-11.

![Scheme 9: Synthesis of α-aryloxy acetate derivative](image)

This particular case is significant since the presence of a carbonyl of the ester in place of the aromatic ring was also probably providing sufficient binding to the mandelic acid unit for stability of the electrostatic ion pair with the analyte.

Two more derivatives of the chiral aminonaphthol were prepared by changing the 1º amine to (S)-1-(1-naphthyl)ethylamine 19 and L-methyl valinate 21, while keeping the other two components the same (Scheme 10). Both of these molecules, 20 and 22, were screened as CSAs and the results showed that the former displays a similar range of resolution (entry 15, Table 1) while the latter one is not effective (entry 16, Table 1).

![Scheme 10: Synthesis of aminonaphthols with other chiral sources](image)
Table 1: Effect of the aminonaphthyl derivatives as CSA on the $\alpha$-proton of the racemic mandelic acid. [$\Delta\delta =$ induced chemical shift$^a$; $\Delta\Delta\delta =$ chemical shift non-equalities.]

<table>
<thead>
<tr>
<th>No</th>
<th>Aminonaphthyl derivative</th>
<th>Spectra</th>
<th>Probe Signal</th>
<th>$\Delta\delta$ (ppm)</th>
<th>$\Delta\Delta\delta$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(S,S)-4</td>
<td>![Spectrum Image]</td>
<td>PhC/H(OH)COOH</td>
<td>-0.22</td>
<td>0.005</td>
</tr>
<tr>
<td>2</td>
<td>(S,S)-5</td>
<td>![Spectrum Image]</td>
<td>PhC/H(OH)COOH</td>
<td>-0.24</td>
<td>0.012</td>
</tr>
<tr>
<td>3</td>
<td>(S,S)-7</td>
<td>![Spectrum Image]</td>
<td>PhC/H(OH)COOH</td>
<td>-0.09</td>
<td>--$^b$</td>
</tr>
<tr>
<td>4</td>
<td>(S,S)-8</td>
<td>![Spectrum Image]</td>
<td>PhC/H(OH)COOH</td>
<td>-0.33</td>
<td>0.021</td>
</tr>
<tr>
<td>5</td>
<td>(S,S)-9</td>
<td>![Spectrum Image]</td>
<td>PhC/H(OH)COOH</td>
<td>-0.28</td>
<td>0.009</td>
</tr>
</tbody>
</table>
(S,S)-10

(S,S)-11

(S,S)-12

(S,S)-13

(S,S)-14

(S,S)-15
The difference between the signals of DL-mandelic acid in CDCl₃ solution and the average of the signals of the two enantiomers after the addition of the CSA. *Not resolved.*
Having concluded that the compound \((S,S)-11\) showed reasonably good CSA activity, we prepared a set of samples of different enantiomeric purity of mandelic acid and evaluated with the same amine. The ratio of the two isomers was experimentally established by CSA analysis with \((S,S)-11\) and compared with the actual values and found to be in good agreement (Figure 8).

![Figure 8: Select region of $^1$H-NMR spectra of (±)-mandelic acid of various ratios of optical purity in presence of \((S,S)-11\). Values in parenthesis are observed purity. [Left] Correlation of observed and actual values of $ee$ of test sample of DL-mandelic acid. $R^2 = 0.999$

The probable mode of recognition of the isomers of mandelic acid is by complex formation between the carboxylate ion of the acid and the protonated nitrogen of the aminonaphthyl unit. The formation of the carboxylate anion was confirmed when the position of the carbonyl stretch \(1716 \text{ cm}^{-1}\) for mandelic acid decreased in the FT-IR spectra of a 1:1 mixture of \((S,S)-11\) and DL-mandelic acid, and strong peaks appeared at 1623 and 1596 \text{ cm}^{-1} \text{ (the COO}^\text{-} \text{ stretch)}. Similar observations have previously been noted for different CSA systems.\textsuperscript{11, 15b} This may support the suggestion that the binding of the carboxylate ion of a racemic acid with a
chiral CSA provides a diastereomeric complex structure where the aromatic ring of the acid may favor a \(\pi-\pi\) interaction with the \(O\)-benzyl ring.

This will also corroborate the other experimental observations of the requirement of the N-H and a \(\pi\)-system attached to the hydroxyl group of the naphthyloxy function of this type of solvating agent for effective electrostatic interactions and suitable \(\pi-\pi\) interactions between the two aromatic rings of the analyte and guest molecules. A schematic representation of the structure - CSA activity may be made to summarize the conclusion (Scheme 11).

![Scheme 11: Summary of the structural features of chiral aminonaphthol on the efficiency as CSA](image)

All the chiral ligands were purified by column chromatography and characterized by \(^1\text{H}\)-NMR, \(^{13}\text{C}\)-NMR, IR and Mass analysis. In the \(^1\text{H}\)-NMR spectra of all ligands, -OH proton of 2-naphthyl ring gives the most downfield singlet around 13 \(\delta\), Ph-\(\text{CH}^2\)-NH proton appears as singlet at \(\delta = 5-6\) ppm, the methine -CH proton in chiral amine group shows quartet at \(\delta = 3-4\) ppm and the -Me protons in chiral amine group gives doublet at \(\delta = 1-1.5\) ppm. The benzylic protons in ligand 11 show two doublets at \(\delta = 5.13 - 4.93\) (\(J = 12\) Hz), whereas the -O-\(\text{CH}_2\)-CO-protons in ligand 18, give two doublet at \(\delta = 4.59 - 4.23\) (\(J = 16\) Hz), one of the doublets get merged with quartet given by -O-\(\text{CH}_2\)-\(\text{CH}_3\) protons. In the \(^1\text{H}\)-NMR spectra of ligand 22, -NH proton gives doublet at 2.7 \(\delta\).
**Experimental Section**

Thin Layer Chromatography was performed on silica gel plates quoted on aluminium sheets. The spots were visualized under UV light or with iodine vapor. All the compounds were purified by column chromatography on silica gel (60-120 mesh). All reactions were carried out under an inert atmosphere (nitrogen) unless other conditions are specified. NMR Spectra were recorded on 400 MHz Spectrometer (400 MHz for \(^1\)H-NMR & 100 MHz for \(^{13}\)C-NMR) with CDCl\(_3\) as solvent and TMS as internal standard. Single crystal X-ray diffraction data was collected Xcalibur, Eos, Gemini diffractometer. Mass spectra were recorded on GCMS instrument in the direct injection EI-mode. IR Spectra were recorded as KBr pallets. Melting points were recorded in Thiele’s tube using paraffin oil and are uncorrected.

1-[Phenyl(1-phenylethlamino)methyl]naphthalen-2-ol ([S,S]-4):

**Procedure:** A mixture of 2-naphthol (1.0 g, 6.94 mmol), benzaldehyde (0.88 g, 8.32 mmol) and (S)-(−)-1-phenylethylamine (0.88 g, 7.28 mmol) was stirred at 60°C for 8 h under nitrogen atmosphere. Then the reaction mixture was dispersed at room temperature with EtOH (5 mL). The white crystalline solid separated were collected and washed with EtOH (3 x 3 mL).

**Yield:** 90% (2.21 g), White crystalline solid.

**M.P.** 152 - 154°C (Lit.\(^4\)b 155 - 156°C), \([\alpha]^{25}_D = +266.7\) (C 2.12, CHCl\(_3\)).

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): \(\delta\) 13.76 (br s, 1H), 7.77 - 7.73 (m, 2H), 7.45 - 7.34 (m, 4H), 7.27 - 7.2 (m, 10H), 5.47 (s, 1H), 3.92 (q, \(J = 6.8\) Hz, 1H), 2.31 (br s, 1H), 1.54 - 1.52 (d, \(J = 6.8\) Hz, 3H).

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): \(\delta\) 157.3, 143.1, 141.5, 132.6, 129.8, 129.1, 129.0, 128.8, 128.7, 128.0, 127.9, 127.7, 126.7, 126.4, 122.4, 121.1, 120.1, 113.1, 60.3, 56.7, 23.0.

**IR (KBr):** \(\nu\) 3448, 3276, 3059, 3025, 2963, 1950, 1894, 1752, 1622, 1601, 1581, 1515, 1493, 1414, 1379, 1317, 1270, 1130, 1077, 946, 874, 841, 766, 744, 699 cm\(^{-1}\).
**MS (EI):** $(m/z)$ 354 (M$^+$, 28), 353 (M$^+$, 24), 261 (12), 234 (26), 233 (100), 157 (22), 106 (20), 105 (88), 91 (8).

[(2-Methoxynaphthalen-1-yl)phenylmethyl]methyl(1-phenylethyl)amine  [(S,S)-5]:

**Procedure:** Powdered NaOH (0.28 g, 7.08 mmol) was added to a solution of (S,S)-4 (0.5 g, 1.42 mmol) in THF (10 mL). After 10 minutes CH$_3$I (0.9 mL, 14.15 mmol) was dropped into the slurry. The mixture was stirred for 6 h and then a solution of saturated NH$_4$Cl was added. After extraction with ethyl acetate, the organic extracts were dried with anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel with hexane/EtOAc (10:1) as eluent to give a white solid (0.785 g, 97 % Y).

**Yield:** 97% (0.785 g), White solid.

**M.P.** 120 - 122$^\circ$C, $[\alpha]_D^{25} = +61.63$ (c 0.753, CHCl$_3$).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.65-9.63 (d, $J = 8.8$ Hz, 1H), 7.78-7.1 (m, 15H), 5.88 (s, 1H), 4.32-4.26 (q, $J = 6.8$ Hz, 1H), 4.04 (s, 3H), 2.09 (s, 3H), 1.5-1.48 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 154.7, 143.5, 142.1, 133.2, 129.6, 129.3, 128.4, 128.2, 128.0, 127.8, 126.6, 126.5, 126.2, 125.9, 123.9, 123.4, 113.6, 64.0, 56.7, 56.6, 33.6, 13.9.

**IR (KBr):** $\nu$ 3056, 2847, 1684, 1599, 1509, 1488, 1464, 1419, 1371, 1313, 1260, 1248, 1184, 1148, 1080, 1069, 1048, 1024, 808, 752, 704 cm$^{-1}$.

**MS (EI):** $(m/z)$ 380.95 (M$^+$, 42%), 365.91 (12%), 303.81 (8%), 275.87 (12%), 246.75 (100%), 214.76 (13%), 104.88 (6%), 90.87 (11%).

**HRMS:** 382.5242 (calculated, M+H) Found: 382.2165.

1-Phenyl-2-(1-phenyl-ethyl)-2, 3-dihydro-1H-naphtho[1,2-e][1,3]oxazine  [(S,S)-6]:

**Procedure:** To a solution of (S,S)-4 (1.0 g, 2.82 mmol) in THF (10 mL), were added 40% aqueous formaldehyde (0.25 mL). The reaction mixture was stirred at room temperature for 4 h and then diluted and extracted with ethyl acetate (2 x 50 mL). The
extracts were washed with water and brine, dried over Na$_2$SO$_4$ and then concentrated under reduced pressure. The residue was submitted to chromatographic separation on silica gel with petroleum ether/EtOAC (20:1) as eluent to give a white solid.

**Yield:** 90% (1.09 g), White solid.

**M.P.** 124 - 126°C (Lit.$^4b$ 125 - 128°C).

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 7.91 - 7.89 (m, 2H), 7.47 - 7.23 (m, 11H), 7.0 - 6.94 (m, 3H), 5.23 - 5.2 (dd, $J_1$ = 10 Hz, $J_2$ = 1.2 Hz, 1H), 5.18 (s, 1H), 4.84 - 4.82 (d, $J$ = 8 Hz, 1H), 3.99 - 3.95 (q, $J$ = 5.2 Hz, 1H), 1.53 - 1.51 (d, $J$ = 8 Hz, 3H).

**IR (KBr):** $\nu$ 3025, 2924, 1945, 1903, 1804, 1762, 1686, 1654, 1598, 1516, 1492, 1434, 1371, 1318, 1306, 1279, 1193, 1117, 1050, 985, 858, 847, 798, 668 cm$^{-1}$.

**MS (EI):** (m/z) 365 (M$^+$, 5), 232 (47), 231 (100), 202 (25), 105 (84), 91 (15).

1-[[Methyl(1-phenylethyl)amino]phenylmethyl]naphthalen-2-ol [(S,S)-7]:

**Procedure:** In a 25 mL round bottom flask containing LiAlH$_4$ (75 mg, 1.97 mmol) and dried THF (3 mL), was added (S,S)-6 (0.6 g, 1.64 mmol) in THF (5 mL) at 0°C. After the mixture was stirred for 5 h, the reaction was quenched with water. Then the reaction mixture was extracted with ethyl acetate (2 x 25 mL), the combined organic layer was washed with water, brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was recrystallized from petroleum ether/EtOAc, furnishing white crystals.

**Yield:** 99% (0.6 g), White crystals.

**M.P.** 126 - 128°C (Lit.$^4c$ 128 - 129°C).

$^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 14.05 (s, 1H), 7.86 - 7.7 (m, 4H), 7.42 - 7.21 (m, 12H), 5.36 (s, 1H), 4.23 (q, $J$ = 6.4 Hz, 1H), 2.12 (s, 3H), 1.6 - 1.54 (d, $J$ = 6.4 Hz, 3H).

**IR (KBr):** $\nu$ 3062, 3025, 2996, 2969, 1943, 1622, 1598, 1453, 1268, 1234, 1152, 1124, 1045, 1021, 825, 756, 705 cm$^{-1}$.
[(2-Methoxynaphthalen-1-yl)phenylmethyl](1-phenylethyl)amine [(S,S)-8]:

**Procedure:** Powdered NaOH (0.16 g, 3.95 mmol) was added to a solution of (S,S)-4 (0.2 g, 0.56 mmol) in THF-H₂O (1:1, 6 mL). After 10 minutes Me₂SO₄ (0.27 mL, 2.82 mmol) was dropped into the slurry. The reaction mixture was heated at 70°C for 2 days. Then the reaction mixture was quenched with water and extracted with ethylacetate (2 x 25 mL). The combined organic layer was washed with water, the combined organic extracts were dried with anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel with hexane/EtOAc (10:1) as eluent to give a pale yellow solid (0.125 g, 60% Y).

**Yield:** 60% (0.125g), Pale yellow solid.

**M.P.** 102 - 104°C (Lit. 10b 104 - 106°C), [α]D = -59.2 (C 1.2, CHCl₃).  

**1H-NMR (CDCl₃, 400 MHz):** δ 7.85 - 7.8 (m, 2H), 7.65 - 7.63 (d, J = 8 Hz, 1H), 7.4 - 7.1 (m, 13H), 5.59 (s, 1H), 3.68 (s, 3H), 3.62 - 3.57 (q, J = 6.4 Hz 1H), 1.26 - 1.24 (d, J = 8 Hz, 3H).

**13C-NMR (CDCl₃, 100 MHz):** δ 155.6, 146.3, 145.0, 133.5, 129.4, 129.2, 128.7, 128.2, 127.8, 127.3, 126.8, 126.4, 125.8, 125.0, 123.5, 114.2, 56.4, 55.8, 55.1, 25.9.

**IR (KBr):** ν 3442, 3056, 2969, 1954, 1753, 1625, 1585, 1492, 1386, 1315, 1272, 1131, 1074, 948, 873, 840, 765, 740, 686 cm⁻¹.

**MS (EI):** (m/z) 367 (M⁺, 71), 352 (19), 336 (11), 290 (78), 262 (94), 248 (13), 247 (100), 214 (11), 186 (19), 105 (20), 91 (11).

[(2-Benzzyloxynaphthalen-1-yl)phenylmethyl](1-phenylethyl)amine [(S,S)-11]:

**Procedure:** To a solution of (S,S)-4 (0.1 g, 0.28 mmol), K₂CO₃ (0.06 g, 0.42 mmol) and 18-crown-6 (0.015 g, 0.056 mmol) acetonitrile were added Benzyl chloride (0.072 g, 0.42 mmol). The reaction mixture was heated at 75°C for 24 h. Then the reaction mixture was quenched with water and extracted with ethylacetate (2 x 25 mL). The combined organic layer was washed with water, dried over Na₂SO₄ and then concentrated under reduced pressure. The residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (20:1) as eluent to give a white solid (0.107 g, 86% Y).
Yield: 86% (0.107g), White solid.

M.P. 116 - 118°C, [α]_D^{25} = -68.56 (c 1.0, CHCl₃).

^1H NMR (400 MHz, CDCl₃): δ 7.87 - 7.71 (m, 3H), 7.47 - 7.18 (m, 16H), 7.06 - 7.05 (m, 2H), 5.71 (s, 1H), 5.13 - 5.12 (d, J = 11.6 Hz, 1H), 4.90 - 4.93 (d, J = 12 Hz, 1H), 3.70 - 3.65 (q, J = 6.4 Hz, 1H), 1.26 - 1.25 (d, J = 6.8 Hz, 3H).

^13C NMR (100 MHz, CDCl₃): δ 154.6, 146.4, 145.1, 143.8, 129.1, 128.6, 128.5, 128.3, 127.8, 127.3, 127.2, 126.8, 126.5, 125.9, 123.6, 114.9, 71.0, 55.7, 55.1, 25.9.

IR (KBr): ν 3348, 3056, 3028, 2968, 2871, 1684, 1623, 1595, 1593, 1492, 1455, 1368, 1352, 1236, 1168, 1123, 1067, 1027, 964, 880, 804, 768, 745, 697 cm⁻¹.

MS (EI): (m/z) 442.83 (M⁺, 9%), 440.89 (100%), 338.15 (16%).

HRMS: 444.5950 (calculated, M+H) Found: 444.2332.

[(2-Isopropoxynaphthalen-1-yl)phenylmethyl](1-phenylethyl)amine [(S,S)-9]:

Procedure was same as (S,S)-11.

Yield: 70% (0.195g), White solid.

M.P. 128 - 130°C, [α]_D^{25} = -71.1 (c 1.0, CHCl₃).

^1H NMR (400 MHz, CDCl₃): δ 7.81 - 7.84 (m, 2H), 7.63 - 7.61 (d, J = 8 Hz, 1H), 7.44 - 7.16 (m, 13H), 5.60 (s, 1H), 4.70 - 4.60 (h, 1H), 3.70 - 3.64 (q, J = 6.4 Hz, 1H), 3.06 (br s, 1H), 1.30 - 1.28 (d, J = 6.8 Hz, 6H), 0.82 (br s, 3H).

^13C NMR (100 MHz, CDCl₃): δ 153.4, 146.4, 145.5, 128.8, 128.5, 128.2, 127.6, 127.3, 126.8, 126.4, 125.8, 125.6, 123.2, 115.1, 69.9, 55.7, 55.0, 26.0, 22.5, 21.3.

IR (KBr): ν 3343, 3056, 3028, 2984, 2952, 1620, 1596, 1512, 1493, 1463, 1448, 1332, 1249, 1234, 1111, 1060, 1031, 981, 880, 827, 810, 771, 746, 716, 704 cm⁻¹.

MS (EI): (m/z) 395.23 (M⁺, 11%), 318.31 (27%), 317.43 (24%), 290.65 (96%), 289.4 (100%), 247.44 (24%).

HRMS: 396.5510 (calculated, M+H) Found: 396.2328.
[(2-Butoxynaphthalen-1-yl)phenylmethyl](1-phenylethyl)amine [(S,S)-10]:

Procedure was same as (S,S)-11.

Yield: 78% (0.09g), White solid.

M.P. 126 - 128°C, $[\alpha]_{D}^{25} = -45.6$ (c 1.0, CHCl₃).

$^1$H NMR (400 MHz, CDCl₃): $\delta$ 7.85 - 7.64 (m, 3H), 7.44 - 7.12 (m, 13H), 5.62 (s, 1H), 4.09 - 4.04 (q, $J = 6.8$ Hz, 1H), 3.78 - 3.72 (q, $J = 6.4$ Hz, 1H), 3.65 - 3.60 (q, $J = 6.4$ Hz, 1H), 2.30 (br s, 1H), 1.5 - 1.43 (m, 2H), 1.28 - 1.18 (m, 5H), 0.88 - 0.84 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl₃): $\delta$ 155.0, 146.3, 145.3, 129.0, 128.6, 128.2, 127.7, 127.2, 126.7, 126.3, 125.0, 123.3, 114.6, 68.7, 55.6, 55.1, 31.4, 25.9, 19.1, 13.8.

IR (KBr): $\nu$ 3339, 3056, 3026, 2961, 2874, 1622, 1596, 1515, 1492, 1460, 1447, 1368, 1351, 1252, 1240, 1171, 1148, 1119, 1083, 1068, 1025, 960, 880, 805, 768, 748, 715, 704 cm⁻¹.

MS (El): (m/z) 409.59 (M⁺, 16%), 331.37 (24%), 303.53 (100%), 288.22 (11%), 105.15 (9%).

HRMS: 410.5778 (calculated, M+H) Found: 410.2478.

{(2-(4-Bromobenzyloxy)naphthalen-1-yl)phenylmethyl}(1-phenylethyl)amine [(S,S)-12]:

Procedure was same as (S,S)-11.

Yield: 77% (0.17g).

Pale yellow oil, $[\alpha]_{D}^{25} = +44.2$ (c 1.38, CHCl₃).

$^1$H NMR (400 MHz, CDCl₃): $\delta$ 7.85 - 7.68 (m, 3H), 7.43 - 7.29 (m, 10H), 7.26 - 7.16 (m, 5H), 6.82 - 6.8 (d, $J = 8$ Hz, 2H), 5.64 (s, 1H), 5.05 - 5.02 (d, $J = 12$ Hz, 1H), 4.82 - 4.79 (d, $J = 11.6$ Hz, 1H), 3.65 - 3.6 (q, $J = 6.4$ Hz, 1H), 1.23 - 1.22 (d, $J = 6.8$ Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl₃): $\delta$ 154.2, 135.7, 131.5, 129.2, 129.0, 128.6, 128.3, 127.9, 127.2, 126.8, 126.6, 125.91, 123.7, 121.7, 114.7, 70.2, 55.7, 55.0, 26.0.
IR (neat): v 3349, 3059, 3025, 2959, 1652, 1622, 1596, 1514, 1489, 1456, 1433, 1368, 1351, 1217, 1170, 1147, 1121, 1069, 1012, 960, 880, 841, 805, 760, 701 cm⁻¹.

MS (EI): (m/z) 523.48 ([M+1]⁺, 16%), 522 ([M]⁺, 18%), 521 (22%), 446.07 (46%), 418.36 (100%), 414.93 (92%), 402.71 (85%), 351.97 (66%), 104.84 (70%).

HRMS: 523.4911 (calculated, M+H) Found: 523.1464.

{(2-(3,5-Dibromobenzyloxy)naphthalen-1-yl)phenylmethyl}(1-phenylethyl)amine [(S,S)-13]:
Procedure was same as (S,S)-11.

Yield: 72% (0.61g), White solid.

M.P. 104 - 106°C, [α]D²⁵ = +66.12 (c 1.0, CHCl₃).

¹H NMR (400 MHz, CDCl₃): δ 7.87 - 7.84 (m, 2H), 7.71 (br s, 1H), 7.6 - 7.59 (t, 1H), 7.43 - 7.11 (m, 15H), 5.66 (s, 1H), 5.01 - 4.98 (d, J = 12.4 Hz, 1H), 4.71 - 4.68 (d, J = 12 Hz, 1H), 3.64 - 3.6 (q, J = 6.4 Hz, 1H), 2.77 (br s, 1H), 1.26 - 1.24 (d, J = 6.4 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 154.0, 146.1, 144.9, 140.7, 133.6, 129.6, 129.3, 128.9, 128.7, 128.3, 128.0, 127.2, 126.9, 126.7, 126.6, 126.4, 126.1, 124.0, 123.7, 123.0, 114.9, 69.7, 55.7, 54.9, 26.0.

IR (KBr): v 3344, 3080, 3060, 3022, 2956, 1622, 1556, 1513, 1491, 1456, 1425, 1367, 1349, 1282, 1245, 1218, 1200, 1168, 1107, 1088, 1068, 1027, 957, 880, 848, 795, 742, 720, 698, 676, 548, 511 cm⁻¹.

HRMS: 602.3872 (calculated, M+H) Found: 602.0509.

{(2-(4-Fluorobenzyloxy)naphthalen-1-yl)phenylmethyl}(1-phenylethyl)amine [(S,S)-14]:
Procedure was same as (S,S)-11.

Yield: 75% (0.49g), White solid.

M.P. 78 - 80°C, [α]D²⁵ = +61.33 (c 1.0, CHCl₃).
\( ^1 \text{H NMR (400 MHz, CDCl}_3 \): } \delta 7.86 - 7.84 (d, \ J = 9.2 \text{ Hz, 2H}), 7.43 - 7.18 (m, 13H), 6.97 - 6.9 (m, 4H), 5.67 (s, 1H), 5.07 - 5.04 (d, \ J = 11.2 \text{ Hz, 1H}), 4.84 - 4.81 (d, \ J = 11.6 \text{ Hz, 1H}), 3.66 - 3.61 (q, \ J = 6.4 \text{ Hz, 1H}), 1.23 - 1.22 (d, \ J = 6.4 \text{ Hz, 3H}).

\( ^{13} \text{C NMR (100 MHz, CDCl}_3 \): } \delta 163.6, 161.2, 154.4, 146.2, 145.1, 132.5, 132.5, 129.3, 129.2, 128.7, 128.3, 127.9, 127.2, 126.8, 126.5, 125.9, 125.7, 123.7, 115.4, 115.2, 114.9, 70.4, 55.7, 55.0, 25.9.

\( \text{IR (KBr): } \nu 3344, 3056, 2960, 1623, 1596, 1513, 1492, 1461, 1445, 1368, 1352, 1228, 1156, 1119, 1078, 1067, 1019, 960, 880, 861, 828, 804, 763, 705, 704 \text{ cm}^{-1}.

\( \text{MS (EI): } (m/z) 460.27 (6\%), 441.55 (7\%), 356.15 (32\%), 355.15 (17\%), 339.62 (18\%), 232.34 (18\%), 230.9 (100\%), 104.89 (6\%).

\( \text{HRMS: } 462.5851 \text{ (calculated, M+H) Found: } 462.2229.\)

\[\text{[(2-(4-Methoxybenzyloxy)naphthalen-1-yl)phenylmethyl](1-phenylethyl)amine} \]

\([\text{(S,S)-15}]: \]

Procedure was same as (S,S)-11.

Yield: 84\% (0.563g), White solid.

M.P. 116 - 118\textdegree C, \([\alpha]_{D}^{25} = +58.97 \text{ (c 1.01, CHCl}_3\).

\( ^1 \text{H NMR (400 MHz, CDCl}_3 \): } \delta 7.86 - 7.84 (d, \ J = 8.8 \text{ Hz, 2H}), 7.68 (br s, 1H), 7.43 - 7.17 (m, 13H), 6.96 - 6.94 (d, \ J = 8 \text{ Hz, 2H}), 6.83 - 6.81 (m, 2H), 5.67 (s, 1H), 5.06 - 5.04 (d, \ J = 11.2 \text{ Hz, 1H}), 4.84 - 4.81 (d, \ J = 11.2 \text{ Hz, 1H}), 3.84 (s, 3H), 3.68 - 3.63 (q, \ J = 6.4 \text{ Hz, 1H}), 1.25 - 1.23 (d, \ J = 6.4 \text{ Hz, 3H}).

\( ^{13} \text{C NMR (100 MHz, CDCl}_3 \): } \delta 159.3, 154.6, 129.1, 128.8, 128.6, 128.3, 127.8, 127.3, 126.9, 126.8, 126.5, 125.9, 123.5, 115.0, 113.8, 70.8, 55.8, 55.3, 25.8.

\( \text{IR (KBr): } \nu 3341, 3053, 2962, 2836, 1616, 1593, 1515, 1491, 1461, 1388, 1370, 1352, 1304, 1248, 1178, 1119, 1076, 1066, 1029, 1014, 960, 880, 859, 805, 761, 745, 701 \text{ cm}^{-1}.

\( \text{MS (EI): } (m/z) 473.57(M^+, 10\%), 472.43 (19\%), 367.46 (27\%), 352.43 (84\%), 351.23 (81\%), 245.86 (64\%), 239.88 (70\%), 230.42 (50\%), 121.29 (99\%), 120.54 (100\%), 104.84 (22\%).

\( \text{HRMS: } 474.6208 \text{ (calculated, M+H) Found: } 474.2431.\)
Toluene-4-sulfonic acid-1-[phenyl(1-phenylethylamino)methyl]naphthalen-2-yl ester [(S,S)-16]:

Procedure: \( p \)-Toluenesulfonyl chloride (0.324 g, 1.7 mmol) was slowly added to a solution of (S,S)-4 (0.3 g, 0.85 mmol) and Et\(_3\)N (0.24 mL, 1.7 mmol) in CH\(_2\)Cl\(_2\) (7 mL) at 0°C. The reaction mixture was warmed to room temperature and stirred for 2 days. After removal of the solvent under reduced pressure, the resulting residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (20:1) as eluent to give (S,S)-16 as a light yellow oil.

Yield: 86% (0.37 g).

Light yellow oil, \([\alpha]_D^{25} = +11.15\) (c 1.01, CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.9 - 7.86 (m, 2H), 7.67 - 7.61 (m, 2H), 7.47 - 7.1 (m, 14H), 6.91 - 6.89 (m, 2H), 5.23 (s, 1H), 3.62 - 3.6 (q, \( J = 6.4 \) Hz, 1H), 2.24 (s, 3H), 1.19 - 1.18 (d, \( J = 6.4 \) Hz, 3H).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 146.9, 145.7, 144.9, 143.4, 132.7, 130.0, 129.6, 129.2, 128.3, 127.9, 127.7, 127.4, 126.9, 126.9, 126.5, 126.0, 125.7, 121.2, 56.0, 55.1, 25.7, 21.6.

IR (neat): \( \nu \) 3358, 3057, 3026, 2960, 1684, 1597, 1511, 1492, 1374, 1306, 1202, 1173, 1093, 1044, 1029, 963, 936, 885, 819, 757, 701, 679 cm\(^{-1}\).

HRMS: 508.6590 (calculated, M+H) Found: 508.1941.

Toluene-4-sulfonic acid-1-[methyl(1-phenylethyl)amino]phenylmethyl)naphthalen-2-yl ester [(S,S)-17]:

Procedure was same as (S,S)-16.

Yield: 67% (0.095 g), White solid.

M.P. 84 - 86°C, \([\alpha]_D^{25} = +296.81\) (c 0.44, CHCl\(_3\)).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 9.71 - 9.69 (d, \( J = 8.8 \) Hz, 1H), 7.94 - 7.92 (m, 2H), 7.8 - 7.12 (m, 17H), 5.87 (s, 1H), 4.28 - 4.23 (q, \( J = 6.8 \) Hz, 1H), 2.50 (s, 3H), 1.94 (s, 3H), 1.36 - 1.34 (d, \( J = 6.8 \) Hz, 3H).
\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\text{): }\delta 146.2, 145.6, 144.1, 142.1, 133.9, 132.7, 132.6, 130.1, 130.1, 129.4, 128.4, 128.4, 128.1, 128.1, 127.7, 127.7, 126.8, 126.4, 126.4, 125.9, 120.3, 65.2, 56.3, 32.7, 21.8, 10.1.\]

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\text{): }\delta 146.2, 145.6, 144.1, 142.1, 133.9, 132.7, 132.6, 130.1, 130.1, 129.4, 128.4, 128.4, 128.1, 128.1, 127.7, 127.7, 126.8, 126.4, 126.4, 125.9, 120.3, 65.2, 56.3, 32.7, 21.8, 10.1.\]

\[^{1}\text{H}\text{ NMR (400 MHz, CDCl}_3\text{): }\delta 7.85 - 7.82 (m, 2H), 7.67 - 7.14 (m, 14H), 5.64 (s, 1H), 4.59 - 4.55 (d, J = 16 Hz, 1H), 4.3 - 4.23 (m, 3H), 3.7 - 3.65 (q, J = 6.4 Hz, 1H), 1.33 - 1.3 (m, 6H).\]

\[^{13}\text{C}\text{ NMR (100 MHz, CDCl}_3\text{): }\delta 169.0, 153.6, 146.2, 144.8, 129.7, 129.3, 128.6, 128.3, 128.0, 127.9, 127.7, 127.3, 126.9, 126.8, 126.7, 126.2, 125.9, 124.0, 123.6, 114.4, 66.2, 61.4, 55.8, 55.1, 25.7, 14.1.\]

**IR (neat):** $\nu$ 3337, 2971, 2921, 1751, 1684, 1623, 1598, 1512, 1492, 1464, 1448, 1381, 1356, 1280, 1203, 1164, 1096, 1044, 1028, 964, 880, 861, 812, 770, 746, 704 cm$^{-1}$.

**HRMS:** 440.5600 (calculated, M+H) Found: 440.2220.
**1-[(1-Naphthalen-1-yl-ethylamino)-phenyl-methyl]-naphthalen-2-ol [(S,S)-20]:**

Procedure was same as (S,S)-4.

**Yield:** 20% (0.22 g), White solid.

**M.P.** 192 - 194°C (Lit.4b 195 - 197°C).

\[ [\alpha]_{D}^{25} = 381.7 \text{ (C 1.01, CHCl}_3) \].

**1H-NMR (CDCl\textsubscript{3}, 400 MHz):** \( \delta \) 13.72 (br s, 1H), 7.88 - 7.86 (d, \( J = 8 \text{ Hz}, 2\text{H} \)), 7.77 - 7.75 (d, \( J = 8 \text{ Hz}, 1\text{H} \)), 7.7 - 7.68 (d, \( J = 8 \text{ Hz}, 1\text{H} \)), 7.67 - 7.6 (m, 2H), 7.41 - 6.99 (m, 12H), 5.49 (s, 1H), 4.89 (q, 1H), 1.64 - 1.62 (d, \( J = 8 \text{ Hz}, 3\text{H} \)).

**2-[[2-Hydroxynaphthalen-1-yl]phenylmethyl]amino]-3-methylbutyric acid methyl ester [(S,S)-22]:**

**Procedure:** A mixture of β-naphthol (0.44 g, 3.05 mmol), benzaldehyde (0.32 g, 3.05 mmol) and L-valine methyl ester (0.4 g, 3.05 mmol) was stirred at 80°C for 72 h under nitrogen atmosphere. The reaction mixture was dispersed at room temperature with Ethanol and purified by column chromatography on silica gel with hexane/EtOAc (10:1) as eluent to give white solid.

**Yield:** 26% (0.285 g), White solid.

**M.P.** 146 - 148°C

\[ [\alpha]_{D}^{25} = +427.97 \text{ (c 0.36, CHCl}_3) \].

**1H NMR (400 MHz, CDCl\textsubscript{3}):** \( \delta \) 12.58 (s, 1H), 7.78 - 7.76 (d, \( J = 8.4 \text{ Hz}, 2\text{H} \)), 7.63 - 7.61 (d, \( J = 8.4 \text{ Hz}, 1\text{H} \)), 7.47 - 7.25 (m, 7H), 7.21 - 7.18 (d, \( J = 8.8 \text{ Hz}, 1\text{H} \)), 5.60 (s, 1H), 3. 81 (s, 3H), 3.39 - 3.34 (q, \( J = 5.2 \text{ Hz}, 1\text{H} \)), 2.73 - 2.7 (d, \( J = 12.8 \text{ Hz}, 1\text{H} \)), 2.15 - 2.07 (m, 1H), 1.02 - 0.98 (m, 6H).

**13C NMR (100 MHz, CDCl\textsubscript{3}):** \( \delta \) 174.5, 156.5, 140.5, 132.9, 130.0, 129.1, 128.9, 128.7, 128.2, 128.0, 126.6, 122.6, 121.0, 120.0, 112.6, 65.4, 61.6, 51.9, 31.7, 19.0.

**IR (KBr):** \( \nu \) 3330, 2953, 1730, 1624, 1601, 1520, 1456, 1428, 1369, 1316, 1202, 1071, 1031, 991, 956, 907, 876, 852, 811, 715 cm\textsuperscript{-1}.

**MS (EI):** \( m/z \) 362.83 (M\textsuperscript{+}, 20%), 233.33 (15%), 232.24 (19%), 230.79 (100%), 202.17 (10%).

**HRMS:** 364.4624 (calculated, M+H) Found: 364.1907.
Spectral Data

$^1$H-NMR Spectra of Compound 4 (400 MHz, CDCl$_3$)

$^{13}$C-NMR Spectra of Compound 4 (100 MHz, CDCl$_3$)
$^{1}$H-NMR Spectra of Compound 5 (400 MHz, CDCl$_3$)

$^{13}$C-NMR Spectra of Compound 5 (100 MHz, CDCl$_3$)
EI-Mass Spectra of Compound 5

$^{1}$H-NMR Spectra of Compound 6 (400 MHz, CDCl$_3$)
$^1$H-NMR Spectra of Compound 7 (400 MHz, CDCl$_3$)

$^1$H-NMR Spectra of Compound 8 (400 MHz, CDCl$_3$)
$^{13}$C-NMR Spectra of Compound 8 (100 MHz, CDCl$_3$)

EI-Mass Spectra of Compound 8

Exact Mass: 367

EI-Mass Spectra of Compound 8
$^1$H-NMR Spectra of Compound 9 (400 MHz, CDCl$_3$)

$^{13}$C-NMR Spectra of Compound 9 (100 MHz, CDCl$_3$)
EI-Mass Spectra of Compound 9

1H-NMR Spectra of Compound 10 (400 MHz, CDCl₃)

Exact Mass: 395
C-NMR Spectra of Compound 10 (100 MHz, CDCl₃)

EI-Mass Spectra of Compound 10

Exact Mass: 409

13C-NMR Spectra of Compound 10 (100 MHz, CDCl₃)

EI-Mass Spectra of Compound 10

Exact Mass: 409

El-Mass Spectra of Compound 10
H-NMR Spectra of Compound 11 (400 MHz, CDCl₃)

C-NMR Spectra of Compound 11 (100 MHz, CDCl₃)

$^1$H-NMR Spectra of Compound 11 (400 MHz, CDCl₃)

$^{13}$C-NMR Spectra of Compound 11 (100 MHz, CDCl₃)
EI-Mass Spectra of Compound 11

1H-NMR Spectra of Compound 12 (400 MHz, CDCl₃)

Exact Mass: 443
$^{13}$C-NMR Spectra of Compound 12 (100 MHz, CDCl$_3$)

EI-Mass Spectra of Compound 12

Exact Mass: 522

EI-Mass Spectra of Compound 12

Exact Mass: 522
$^1$H-NMR Spectra of Compound 13 (400 MHz, CDCl$_3$)

$^{13}$C-NMR Spectra of Compound 13 (100 MHz, CDCl$_3$)
$^1$H-NMR Spectra of Compound 14 (400 MHz, CDCl₃)

$^{13}$C-NMR Spectra of Compound 14 (100 MHz, CDCl₃)
EI-Mass Spectra of Compound 14

$\text{Exact Mass: 461}$

$1^\text{H-NMR Spectra of Compound 15 (400 MHz, CDCl}_3\text{)}$

$\text{Exact Mass: 461}$
$^{13}$C-NMR Spectra of Compound 15 (100 MHz, CDCl$_3$)

EI-Mass Spectra of Compound 15

Exact Mass: 473
1H-NMR Spectra of Compound 16 (400 MHz, CDCl₃)

13C-NMR Spectra of Compound 16 (100 MHz, CDCl₃)
**1H-NMR Spectra of Compound 17 (400 MHz, CDCl₃)**

**13C-NMR Spectra of Compound 17 (100 MHz, CDCl₃)**
$^1$H-NMR Spectra of Compound 18 (400 MHz, CDCl$_3$)

$^{13}$C-NMR Spectra of Compound 18 (100 MHz, CDCl$_3$)
$^1$H-NMR Spectra of Compound 20 (400 MHz, CDCl$_3$)

$^1$H-NMR Spectra of Compound 22 (400 MHz, CDCl$_3$)
C-NMR Spectra of Compound 22 (100 MHz, CDCl₃)

EI-Mass Spectra of Compound 22

Exact Mass: 363
**Single Crystal X-ray Data**

Crystallographic data for the structures of compound \((S,S)-5\) and \((S,S)-10\) have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 960671 and CCDC 977361, respectively). Copies of the data can be obtained from http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CD21EZ, UK (fax: +441223 336 033; e-mail: eposat@ccdc.cam.ac.uk).

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ORTEP plot of Compound \((S,S)-5\)

ORTEP plot of Compound \((S,S)-10\)
<table>
<thead>
<tr>
<th>Source</th>
<th>(S,S)- 5</th>
<th>(S,S)- 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavelength (Å)</td>
<td>1.5418</td>
<td>1.5418</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>(\text{C}<em>{27}\text{H}</em>{27}\text{N}_1\text{O}_1)</td>
<td>(\text{C}<em>{29}\text{H}</em>{31}\text{N}_1\text{O}_1)</td>
</tr>
<tr>
<td>Formula Weight</td>
<td>381.52</td>
<td>409.58</td>
</tr>
<tr>
<td>Crystal size (mm(^3))</td>
<td>0.18×0.08×0.04</td>
<td>0.52×0.34×0.24</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>(P\ 2_1\ 2_1\ 2_1)</td>
<td>(P\ 2_1\ 2_1\ 2_1)</td>
</tr>
<tr>
<td>(a/A)</td>
<td>6.88285(9)</td>
<td>20.4197(5)</td>
</tr>
<tr>
<td>(b/A)</td>
<td>16.20813(19)</td>
<td>14.2081(4)</td>
</tr>
<tr>
<td>(c/A)</td>
<td>19.1995(2)</td>
<td>8.16535(19)</td>
</tr>
<tr>
<td>(α/\text{deg})</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>(β/\text{deg})</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>(γ/\text{deg})</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Volume (Å(^3))</td>
<td>2141.86(4)</td>
<td>2368.98(11)</td>
</tr>
<tr>
<td>(Z)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>(D_{\text{calc.}})</td>
<td>1.1830</td>
<td>0.2661</td>
</tr>
<tr>
<td>(F(000))</td>
<td>818.2993</td>
<td>882.4458</td>
</tr>
<tr>
<td>(\mu(\text{MoKα})) (mm(^{-1}))</td>
<td>0.546</td>
<td>0.524</td>
</tr>
<tr>
<td>Temperature(K)</td>
<td>298</td>
<td>293</td>
</tr>
<tr>
<td>Observed reflns ([I &gt; 2σ(I)])</td>
<td>4020</td>
<td>3787</td>
</tr>
<tr>
<td>params refined</td>
<td>264</td>
<td>285</td>
</tr>
<tr>
<td>goodness of fit</td>
<td>1.0030</td>
<td>0.9855</td>
</tr>
<tr>
<td>Final R1 on observed data</td>
<td>0.0405</td>
<td>0.0637</td>
</tr>
<tr>
<td>Final wR2 on observed data</td>
<td>0.1092</td>
<td>0.2334</td>
</tr>
</tbody>
</table>
CONCLUSION

A series of derivatives of chiral 1-(α-Aminobenzyl)-2-naphthol were synthesized and tested their efficacy as chiral solvating agents or chiral complexing agents in $^1$H-NMR spectroscopy to discriminate the C$\alpha$H of DL-mandelic acid. A linear relationship has been observed between the experimental and observed values of ee indicating the possible use of these compounds for quick and reliable analysis of enantiomerically enriched samples of mandelic acid.

From the experiments performed a preliminary conclusion indicated that the CSA with a free NH group and the O-benzyl derivative of the phenol of 1-(α-aminobenzyl)-2-naphthols are most effective in chiral discrimination of the mandelic acid in $^1$H-NMR analysis. This class of CSAs are easy to make and quite effective in chiral discrimination in NMR spectroscopy.
References


17. Crystallographic data for the structures of compound (S,S)-5 and (S,S)-10 have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 960671 and CCDC 977361 respectively). Copies of the data can be obtained from http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CD21EZ, UK (fax: +44-1223-336-033; e-mail: eposit@ccdc.cam.ac.uk).