CHAPTER II
Conformationally Rigid Chiral Pyridine N-Oxides as Organocatalyst: Asymmetric Allylation of Aldehydes
2.1. INTRODUCTION

The chiral homoallylic alcohols are very important building blocks for the construction of biologically active compounds and natural products. The homoallylic alcohols are generally obtained from carbonyl compounds using alkylation reaction. The first carbonyl group alkylation using allylboron reagents was introduced by Mikhailov and Bubnov (1964). Later, Hosomi and Sakurai (1976) have devised the methodology for the alkylation of carbonyl compounds using allylsilane reagents to synthesize racemic homoallylic alcohols. In the year 1978, the first chirally modified allyl metal reagent was introduced by Hoffmann et al. for the synthesis of chiral homoallylic alcohols. Following this report, number of chirally modified allyl metal reagents have been developed by several research group in the world: Kumada (1982), Brown (1983), Roush (1985), Seebach (1987), Reetz (1988), Masamune (1989), Duthaler (1989), Corey (1989), Panek (1991), Leighton (2002), and Soderquist (2005). The prominent results are tabulated in Figure 1.

Figure 1. Chirally modified allyl metal reagents for enantioselective alkylation reaction.
Though, excellent enantioselectivity was achieved using chiral allyl metal reagents,\textsuperscript{5-15} the requirement of stoichiometric quantity as well as the involvement of multiple steps to prepare them demands the need for the development of new methodology for generating chiral homoallylic alcohols.

To circumvent these difficulties, the catalytic enantioselective protocols have been introduced for the allylation of prochiral carbonyl compounds such as aldehydes to generate chiral homoallylic alcohols. Yamamoto and coworkers have reported the first successful introduction of allyl group on to carbonyl group using allylstannane reagent in presence of catalytic quantity of chiral inducer generated from (R)-BINOL and titanium (IV)isopropoxide in 1991. Following this methodology, the allylation of benzaldehyde produced the homoallylic alcohol in 88\% yield with 90\% ee (Scheme 1).\textsuperscript{16} Later, independently, by Umani-Ronchi (1993)\textsuperscript{17} and by Keck (1993)\textsuperscript{18} generated the chiral homoallylic alcohol from prochiral aldehydes upon reaction with allyltri-\textit{n}-butylstannane in presence of (S)-BINOL-titanium complex.

\begin{center}
\begin{tikzpicture}
\node (1a) at (0,0) {\includegraphics[width=0.3\textwidth]{Scheme1}};
\end{tikzpicture}
\end{center}

\textbf{Scheme 1.} Catalytic enantioslective allylation of aldehydes

Though these methods are very effective for the synthesis of chiral homoallylic alcohols (Scheme 1),\textsuperscript{16-18} the reaction also produces the stoichiometric amount of highly poisonous tin byproduct. To overcome this drawback alternative methods have been developed using metallo-\textpi-allyls such as palladium,\textsuperscript{19} rhodium,\textsuperscript{20} iridium\textsuperscript{21} and ruthenium\textsuperscript{22} complexes derived from allylic alcohols. Metal complexes such as chiral indium(III)--PYBOX complexes,\textsuperscript{23} chromium-salan complexes,\textsuperscript{24} have also been developed and shown to catalyze the enantioselective allylation reaction to produce the homoallylic alcohols with good enantiomeric purity.\textsuperscript{25} However, the metal catalyzed reactions are generally associated with the intrinsic drawbacks, such as they are toxic and very expensive; they also require inert atmosphere.

The above said drawbacks are slowly been alleviated with the advent of “organocatalytic” transformations. Chiral homoallylic alcohols have also been successfully prepared through the allyl group transfer from hypervalent silicon reagent to
prochiral aldehydes employing organocatalytic principle and hence avoiding the use of metal reagents.

Denmark et al. have reported first time that the use of chiral Lewis base, phosphoramides as promoters for the asymmetric allylation and crotylation of aldehydes to furnish the chiral homoallylic alcohols (Scheme 2).

**Scheme 2.** Asymmetric allylation of aldehydes with chiral phosphoramides

Following this report, the homoallylic alcohols have been obtained through the activation of allylsilanes using a catalytic quantity of various class of Lewis bases such as chiral phosphoramides, amines, N-oxides, phosphine oxides, sulfoxides and formamides with various aldehydes (Figure 2).

**Figure 2.** Lewis base catalysts for the enantioselective allylation of benzaldehyde
Due to the toxicity associated with the phosphoramides; synthetic difficulty associated with the chiral sulfoxides; the stability and efficiency problem associated with the formamides, the pyridine N-oxides received greater attention to effect the allyl group transfer from hypervalent silicon species.

Since, the N-oxides are known to exhibit a significant nucleophilicity towards the silicon atom, Nakajima et al. have developed the methodology of activation of allylsilanes by chiral N-oxides. Based on this principle, the organocatalytic enantioselective allylation of prochiral aldehydes has been successfully developed using allyltrichlorosilane in presence of axially chiral 3,3’-dimethyl-2,2’-biquinoline N,N’-dioxide 6. The aromatic aldehydes furnished the homoallylic alcohols in 70-91% yield with 71-92% ee and the aliphatic aldehydes generated the homoallylic alcohols in low yield, 27% with poor enantioselectivity, 28% ee (Scheme 3).

Scheme 3. The first N-oxide catalyzed enantioselective allylation of aldehydes

Subsequently, Hayashi et al. (2002) have reported the use of bipyridine analogue 7 and its derivatives as catalyst for allylation of aldehydes. The homoallylic alcohols were obtained with 56-98% ee in presence of 0.1 mol% catalyst at –45 ºC (Scheme 4).

Scheme 4. Bipyridine N,N’-dioxide catalyzed allylation of aldehydes

Malkov, Kočovský and coworkers have synthesized the new class of pyridine N-oxides, such as PINDOX 8, Me₂PINDOX 9 and iso-PINDOX 10 from terpenes and
successfully utilized them as catalyst for the enantioselective allylation of aldehydes. The chiral homoallylic alcohols were produced in 10-85% yield with 4-98% ee (Scheme 5).\(^3\)

**Scheme 5.** Terpene derivatives used in the asymmetric allylation of aldehydes

Particularly, the mono N-oxide 9 produced the homoallylic alcohols in good enantiomeric purity. This may be due to the existence of the combined effect of both axial and central chirality in the catalyst (the free rotation around the bond connecting the two pyridine moieties is restricted by the two methyl groups and the N–O group).

The same research group further analyzed the role of second pyridine ring in the catalysts PINDOX 8, Me\(_2\)PINDOX 9 and iso-PINDOX 10 by replacing it with the trimethoxy phenyl group on pyridine ring. This aryl substituted molecule, METHOX 11, produced the homoallylic alcohols in excellent enantioselectivity with catalyst loading of 1-5 mol\% at \(-40\) °C in acetonitrile.\(^3\) This observation rules out the requirement of the coordination of nitrogen lone pair with silicon as speculated in the case of catalysts 8-10 for the better enantioselectivity. Instead, the arene-arene interaction between the substrate and catalyst is reasoned for the high reactivity and selectivity (Scheme 6).

**Scheme 6.** METHOX catalyzed allylation of aldehydes

Malkov et al. have reported the new quinoline type N-oxide namely QUINOX 12 as catalyst for allylation of aldehydes. The catalyst QUINOX produced the homoallylic alcohols in 25-85% yield with 5-96% ee (Scheme 7).\(^3\)
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Scheme 7. QUINOX catalyzed allylation of aldehydes

Kwong et al. have developed the first series of chiral 2,2′:6,2″-terpyridine tri-N-oxide 13 for the allylation of aldehydes. The catalyst 13 produced the homoallylic alcohols in good yield and moderate enantioselectivity. The aliphatic aldehydes furnished the homoallylic alcohols in good yield with low enantioselectivity (Scheme 8).

Scheme 8. Chiral 2,2′:6,2″-terpyridine tri-N-oxide 13 catalyzed allylation of aldehydes

Snapper et al. have developed the proline based N-oxide 14 as an effective catalyst for asymmetric allylation reaction. The reactions were conducted at room temperature to generate the homoallylic alcohols with good enantioselectivity, 71-92% ee (Scheme 9).

Scheme 9. Proline based N-oxide 14 catalyzed allylation of aldehydes

Benaglia et al. imprinted the chiral unit (proline derivatives) with the pyridine N-oxide and utilized as a catalyst in the enantioselective allylation of aldehydes. For
example, the allylation of benzaldehyde in presence of 15 furnished the homoallylic alcohol in 45% yield with 68% ee at 0 °C. Whereas the electron deficient 4-nitrobenzaldehyde produced the corresponding homoallylic alcohol in 38% yield with 76% ee (Scheme 10).³⁵

![Scheme 10. Proline containing pyridine N-oxide 15 catalyzed allylation of aldehydes](image)

The unsymmetrical axially chiral bipyridine N,N'-dioxide 16 showed the efficient catalytic activity and enantioselectivity in the asymmetric allylation of aldehydes with allyltrichlorosilane. The homoallylic alcohols were produced in 54-87% ee with 1 mol% catalyst loading (Scheme 11).³⁶

![Scheme 11. Chiral bipyridine N,N'-dioxides 16 catalyzed allylation of aldehydes](image)

Nakajima et al. exposed first time that the dinitrones can be used as an effective Lewis base catalyst to exert the chiral induction in allylation of aldehydes using allyltrichlorosilane at room temperature in chloroform. The reaction produced the homoallylic alcohols in good yield and moderate enantioselectivity. For example, the reaction of benzaldehyde with allyltrichlorosilane in presence of dinitrone 17 produced the corresponding homoallylic alcohol in 78% yield with 74% ee, and the electron rich 4-methoxybenzaldehyde, produced the homoallylic alcohol in 68% yield with 63% ee. Electron deficient aldehyde, 4-nitrobenzaldehyde produced the corresponding homoallylic alcohol in 93% yield with 64% ee (Scheme 12).³⁷
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Rowlands et al. have utilized the catalyst containing planar chiral [2.2]paracyclophane-derived pyridine N-oxides for the enantioselective allylation reaction. For example, the reaction of benzaldehyde with allyltrichlorosilane in presence of catalyst 18 furnished the homoallylic alcohol in 72% with 38% ee (Scheme 13).  

Zhu et al. have developed the biscarboline N,N'-dioxide 19 and used for the enantioselective allylation reaction of aldehydes. For example, the reaction of benzaldehyde with allyltrichlorosilane in presence of biscarboline N,N'-dioxide 19 produced the corresponding homoallylic alcohol in 88% yield with 95% ee and the electron rich 4-methoxybenzaldehyde generated the homoallylic alcohol in 99% ee. The aliphatic aldehyde, cyclohexanecarboxaldehyde produced the corresponding homoallylic alcohol in 53% yield with 97% ee (Scheme 13a).
These examples explicitly explain the efficiency and versatility of the pyridine N-oxides in enantioselective allylation reactions. However, most of these chiral pyridine N-oxides are synthesized through difficult synthetic processes and some of the N-oxides were synthesized from natural sources in one particular isomer. These molecules generate homoallylic alcohols in a particular stereoisomeric form.\textsuperscript{33-35} Hence, we have initiated our effort to develop a conformationally rigid novel chiral pyridine N-oxide in both stereoisomeric form to catalyze the enantioselective allylation reaction so as to produce both isomers of chiral homoallylic alcohols.
Catalytic enantio / diastereoselective synthetic protocols are valuable tool for the preparation of enantiomerically pure chiral molecules. The enantioselective allylation of carbonyl functionality to furnish chiral homoallylic alcohols is one of the highly useful tool in modern organic synthesis. Although, there have been a significant success made towards the use of chiral Lewis base catalysts such as chiral phosphoramides, N-oxides, phosphine oxides, amines, sulfoxides and formamides in stereoselective allylation reactions, the need always arises to develop new catalyst system which may be free from the following drawbacks.

1. Many of the organocatalysts used in the stereoselective allylation reactions are derived from natural product such as terpenes or proline. Generally, the naturally occurring isomers are cheaper whereas the unnatural isomers are very expensive.
2. Some of the man made chiral pyridine N-oxides are labile in nature.
3. Most of the allylation reactions were conducted at very low temperature.

Since, we have already designed and synthesized both the isomers of conformationally rigid chiral molecule possessing pyridine sub unit in its structure through classical resolution protocol, we became interested to examine their efficiency in the stereoselective allylation of aldehydes. Further, this molecule renders several opportunities to modify the structures based on steric as well as electronic factors (Figure 3).

Figure 3. Designing of conformationally rigid chiral pyridine N-oxide
2.3. RESULTS AND DISCUSSION

2.3.1. Synthesis of chiral pyridine N-oxide, 21

The conceptually designed and synthesized chiral molecule 20 possess the pyridine unit with conformationally rigid chiral backbone. The presence of pyridine unit in this chiral molecule lead us to examine the feasibility of using the corresponding N-oxide as an organocatalyst in enantioselective allylation of aldehydes with allyltrichlorosilane. It is evident from the literature reports that the enantioselectivity of the allylation reaction often depends on the electronic property of the carbonyl compounds as well as the catalyst used. Hence, the molecule 20 provides an opportunity to regulate both the electronic and steric factor to get the chiral homoallylic alcohols in good yield with good enantioselectivity (Figure 4).

![Figure 4](image_url)

Using the well established procedure, the required enantiomerically pure N-oxide, (11S,12S)-(+)\textsuperscript{-}21, was easily generated in 95% yield by treating (11S,12S)-(+)\textsuperscript{-}20 with \textit{meta}-chloroperbenzoic acid (\textit{m}-CPBA) in dichloromethane at room temperature for 6 h (Scheme 14).

![Scheme 14](image_url)

**Scheme 14.** Synthesis of chiral pyridine N-oxide (+)\textsuperscript{-}21

2.3.2. Enantioselective allylation of 4-methoxybenzaldehyde catalyzed by (+)\textsuperscript{-}21

As a preliminary study, the catalyst (11S,12S)-(+)\textsuperscript{-}21 was examined for the enantioselective allylation reaction of 4-methoxybenzaldehyde with allyltrichlorosilane. For example, the reaction of 4-methoxybenzaldehyde with allyltrichlorosilane,
diisopropylethylamine (DIPEA) and tetrabutylammonium iodide (TBAI) in presence of 20 mol% of catalyst (11S,12S)-(+)−21 at −40 °C in commonly used solvent acetonitrile, delivered the homoallylic alcohol 3a in 60% yield with 33% ee. This result motivated us to screen the catalyst (+)−21 in various solvents such as dichloromethane, chloroform, 1,2-dichloroethane and 1,1,2,2-tetrachloroethane. The homoallylic alcohol 3a was obtained in 60–89% yield with 33–54% ee, when the reactions were performed in these solvents. The results are summarised in Table 1.

Table 1. Effect of catalyst (+)−21 / solvent on efficiency and enantioselectivity

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<th>ee (%)</th>
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<td>5</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>85</td>
<td>47</td>
</tr>
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</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)−21 (20 mol%), (i-Pr)₂NEt (5 equiv.) and TBAI (1 equiv.) in solvents (0.76 mL) at −40 °C for 24 h.

b. Yields are of isolated product.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, t_R = 18.3 min [(S)-3a]], t_R = 21.3 min [(R)-3a]]). The product 3a produced in all experiments are of (S)-(−)-configuration, as revealed by the comparison of HPLC retention times, with the literature values.40a

2.3.3. Tuning the structure of 21 through steric and electronic factors

The catalyst (+)−21 produced the homoallylic alcohol in good yield but the enantiomeric excess of alcohol produced in this reaction was not encouraging. This may be due to the absence of appropriate steric crowd in the catalyst (+)−21. Hence, to increase the enantioselectivity of the allylation reaction, the steric groups such as phenyl, 1-naphthyl and 9-anthracenyl groups have been introduced at 6th position of pyridine ring of the catalyst 21 via chlorination of pyridine N-oxide 21 followed by Suzuki coupling with corresponding boronic acids. The chlorination of pyridine N-oxide 21 was carried out
with phosphorous oxychloride in chloroform at 90 °C for 24 h. The required 6-chloropyridine derivative 22 was obtained in 59% yield along with 27% of 4-chloropyridine derivative 23 (Scheme 15). The formations of 6-chloropyridine and 4-chloropyridine derivatives were confirmed by spectral analysis as well as single crystal X-ray crystallographic analysis (Figure 5 and see the Table A2 in appendix).

Scheme 15. Synthesis of 4- & 6-chloro pyridine derivative

Figure 5. ORTEP representation of the X-ray crystal structure of (+)-22\textsuperscript{41a} and (+)-23\textsuperscript{41b} with 40% probability level

The Suzuki coupling of 6-chloropyridine derivative 22 with aryl boronic acids 24(a-c) was successfully performed in presence of Pd(PPh\textsubscript{3})\textsubscript{4} and NaHCO\textsubscript{3} in a mixture of solvents toluene, methanol and water at 90 °C for 24 h, the corresponding biaryl products 25(a-c) were obtained in 72-96% yields. The biaryls 25(a-c) on treatment with \textit{m}-CPBA in dichloromethane at room temperature for 6 h generated the corresponding pyridine N-oxides 26(a-c) in 40-96% yields (Scheme 16).

Scheme 16. Synthesis of pyridine N-oxides 26(a-c)
The single crystal X-ray crystallographic analysis exposed the presence of cavity like structure once the introduction of aryl moiety at 6th position of the pyridine ring in 20 (Figure 6 and see the Table A3 &A4 in appendix).

Figure 6. ORTEP representation of the X-ray crystal structure of (+)-25a,\(^{41c}\) (-)-25c\(^{41d}\) and (-)-26b\(^{41e}\) with 40% probability level

The efficiency of chiral molecules 26(a-c) as catalysts for the enantioselective allylation of 4-methoxybenzaldehyde with allylchlorosilane in presence of 20 mol% of catalyst loading along with diisopropylethylamine (DIPEA) and tetrabutylammonium iodide (TBAI) at -40 °C in various solvents was evaluated. The homoallylic alcohol was produced in 2-5% yield with 20-56% ee (Table 2, entries 1-5). The enantioselectivity of the homoallylic alcohol 3a was increased as expected, but disappointingly generated the alcohol in very low yield. The enhancement of enantioselectivity may be due to the involvement of an arene-arene interaction as claimed by earlier reports.\(^{31}\) The catalyst (+)-26a successfully produced the homoallylic alcohol with 56% ee in acetonitrile. The other solvents exhibited inferior results. The catalysts (-)-26b and (-)-26c, were failed to catalyze the allylation reaction, which may be due to the combined electronic and steric
effects influencing negatively on the allylation reaction. Further these observations have been supported by the fact that the introduction of either alkyl or aryl groups at 2\textsuperscript{nd} and/or 6\textsuperscript{th} position of the pyridine ring reduces the nucleophilicity / basicity of the pyridine and consequently reduces the nucleophilicity of the corresponding N-oxide.\textsuperscript{42}

**Table 2.** Effect of the catalysts 26(a-c) / solvent on efficiency and selectivity\textsuperscript{a}

<table>
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<th>ee\textsuperscript{d} (%)</th>
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\textsuperscript{a} All the reactions were performed with 4-methoxy-benzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst 26(a-c) (20 mol%), (i-Pr\textsubscript{2})NEt (5 equiv.) and TBAI (1 equiv.) in solvents (0.76 mL) at 40 °C for 24 h.

\textsuperscript{b} The catalyst (+)-26a was synthesized from (+)-22 and the catalysts (–)-26(b & c) were synthesized from (–)-22.

\textsuperscript{c} Yields are of isolated product.

\textsuperscript{d} Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, t\textsubscript{R} = 18.3 min [(S)-3a], t\textsubscript{R} = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (S)-(–)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.\textsuperscript{40a} nr = no reaction, nd = not determined.
Hence, the presence of electron rich aryl rings such as methoxy substituted benzene rings at 6th position of the pyridine moiety in (−)-21 may serve both as electronic regulator to enhance the Lewis base strength of pyridine and nucleophilicity of the N-oxide as well as to serve as a stereodifferenciating group. These molecules may therefore enhances both the reactivity and selectivity. Hence, the Suzuki coupling of 6-chloropyridine derivative (−)-22 with methoxy phenyl boronic acids such as 2-methoxyphenyl boronic acid 27a, 3-methoxyphenyl boronic acid 27b and 4-methoxyphenyl boronic acid 27c was carried out in presence of Pd(PPh₃)₄ and NaHCO₃ in a mixture of solvents toluene, methanol and water at 90 °C for 24 h, the corresponding biaryls (−)-28a, (−)-28b and (−)-28c were obtained in 90-99% yield. The reaction of pyridine molecules (−)-28a, (−)-28b and (−)-28c with m-CPBA in dichloromethane at room temperature for 6 h generated the corresponding N-oxides (−)-29a, (−)-29b and (−)-29c in 90%, 97% and 81% yields respectively (Scheme 17).

![Scheme 17. Synthesis of (−)-29(a-c)](image)

The N-oxides (−)-29a, (−)-29b and (−)-29c were scrutinized for enantioselective allylation of 4-methoxybenzaldehyde with allyltrichlorosilane and 20 mol% of catalyst loading at −40 °C for 24 h. The homoallylic alcohols were obtained in moderate yield with improved enantioselectivity. The results are summarized in Table 3. Promisingly, the catalysts (−)-29a, (−)-29b and (−)-29c furnished the homoallylic alcohol in increased enantiomeric excess, 28-67%, unfortunately with poor yield, 2-22%, while the reactions were carried out in various solvents (Table 3, entries 1-15). The low yield may probably be due to the insufficient nucleophilicity of the chiral Lewis bases 29(a-c). To further increase the nucleophilicity of N-oxide, the additional methoxy groups containing phenyl groups such as 2,6-dimethoxy phenyl and 2,4,6-trimethoxyphenyl were introduced at the 6th position of pyridine moiety in (+)-21.
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Table 3. Efficiency and selectivity of the catalysts (−)-29(a-c)\textsuperscript{a}

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<tr>
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<td>dichloromethane</td>
<td>(−)-29c</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>13</td>
<td>chloroform</td>
<td>(−)-29c</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>14</td>
<td>1,2-dichloroethane</td>
<td>(−)-29c</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>15</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>(−)-29c</td>
<td>nr</td>
<td>nd</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (−)-29(a-c) (20 mol%), (i-Pr)\textsubscript{2}NEt (5 equiv.) and TBAI (1 equiv.) in solvents (0.76 mL) at −40 °C for 24 h.

\textsuperscript{b} Yields are of isolated product.

\textsuperscript{c} Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, \( t_k = 18.3\) min [(S)-3a], \( t_R = 21.3\) min [(R)-3a]). The product 3a produced in all experiments are of (R)-(−)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.\textsuperscript{30a} nr = no reaction, nd = not determined

These aryl groups were introduced successfully utilizing the Suzuki coupling of arylboronic acids 30 or 31 with 6-chloropyridine derivative (−)-22 in presence of Pd(PPh\textsubscript{3})\textsubscript{4} and NaHCO\textsubscript{3} in a mixture of solvents such as toluene, methanol and water at 90 °C for 24 h. The corresponding biaryls (+)-32 and (+)-33 were obtained in 94% and 79% yields respectively. The treatment of chiral pyridine molecules (+)-32 and (+)-33 with m-CPBA in dichloromethane at room temperature for 6 h generated the corresponding N-oxides (+)-34 and (+)-35 in 93% and 70% yields respectively (Scheme 18, Figure 7 see the Table A5 in appendix).
Conformationally Rigid Chiral Pyridine N-Oxides

Enantioselective Allylation of

Scheme 18. Synthesis of (+)-34 and (+)-35

Figure 7. ORTEP representation of the X-ray crystal structure of (--)-28 and (+)-33 with 40% probability level

The pyridine N-oxides (+)-34 and (+)-35 were examined for the enantioselective allylation of 4-methoxybenzaldehyde under the established conditions using allyltrichlorosilane, DIPEA and TBAI in various electrophilic, nucleophilic and neutral solvents (Table 4). Among these two catalysts, (+)-34 and (+)-35, the catalyst (+)-35 enhanced the enantioselectivity as well as the yield of homoallylic alcohol in this reaction (Table 4, entries 6–10). Reactions in solvents such as chloroform and 1,1,2,2-tetrachloroethane furnished the homoallylic alcohol in good yield with higher enantiomeric purity. On the other hand, 1,2-dichloroethane produced the homoallylic alcohol only in 15% yield with 83% ee (Table 4, entry 9). In solvents such as toluene and THF, the catalyst (+)-35 even failed to catalyze the reaction (Table 4, entries 11&12). Thus, the solvents chloroform and 1,1,2,2-tetrachloroethane were selected for further optimization of the reaction condition to enhance the enantioselectivity without diminishing the yield. Lowering the reaction temperature generally enhances the enantioselectivity of the reaction vide infra. But, the freezing point of chloroform and 1,1,2,2-tetrachloroethane respectively are −63.5 °C and −44 °C and that hindered the use of these solvents at −78 °C. Mixing of two solvents is known to reduce the freezing point of the mixture thus enabling the experiment to be conducted at −78 °C. Therefore, the preliminary experiments were carried out in 1:1 mixture of chloroform and 1,1,2,2-
tetrachloroethane at −40 ºC, −55 ºC and −78 ºC with 20 mol% of (+)-35 (Table 5, entries 1–3).

**Table 4.** Efficiency and selectivity of the catalysts (+)-34 and (+)-35a

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>catalyst</th>
<th>yieldb (%)</th>
<th>eec (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>acetonitrile</td>
<td>(+)-34</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>dichloromethane</td>
<td>(+)-34</td>
<td>17</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>chloroform</td>
<td>(+)-34</td>
<td>16</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>1,2-dichloroethane</td>
<td>(+)-34</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>(+)-34</td>
<td>48</td>
<td>78</td>
</tr>
<tr>
<td>6</td>
<td>acetonitrile</td>
<td>(+)-35</td>
<td>64</td>
<td>72</td>
</tr>
<tr>
<td>7</td>
<td>dichloromethane</td>
<td>(+)-35</td>
<td>63</td>
<td>74</td>
</tr>
<tr>
<td>8</td>
<td>chloroform</td>
<td>(+)-35</td>
<td>84</td>
<td>76</td>
</tr>
<tr>
<td>9</td>
<td>1,2-dichloroethane</td>
<td>(+)-35</td>
<td>15</td>
<td>83</td>
</tr>
<tr>
<td>10</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>(+)-35</td>
<td>88</td>
<td>77</td>
</tr>
<tr>
<td>11</td>
<td>Toluene</td>
<td>(+)-35</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>12</td>
<td>THF</td>
<td>(+)-35</td>
<td>nr</td>
<td>nd</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)-34 or (+)-35 (20 mol%), (i-Pr)2NEt (5 equiv.) and TBAI (1 equiv.) in solvents (0.76 mL) at −40 ºC for 24 h.

b. Yields are of isolated product.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tf = 18.3 min [((S)-3a)], tr = 21.3 min [((R)-3a)]. The product 3a produced in all experiments are of (S)-(−)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.10a nr = no reaction, nd = not determined.

The homoallylic alcohol was produced in 84% yield with 87% ee when the experiment was carried out at −78 ºC (Table 5, entry 3). Increasing the concentration of 1,1,2,2-tetrachloroethane reduces the yield of the product (Table 5, entries 4 & 5), while retaining the enantiomeric purity of the homoallylic alcohol. Increasing the percentage of chloroform marginally increases the yield, but reduces the enantiomeric purity of homoallylic alcohol (Table 5, entries 6 & 7). This study, without compromising the yield,
showed better enantioselectivity in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane (Table 5, entry 3).

**Table 5.** Effect of mixture of solvents on efficiency and selectivity of the catalyst (+)-35

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>temp. (°C)</th>
<th>catalyst</th>
<th>yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (1:1)</td>
<td>–40</td>
<td>(+)-35</td>
<td>96</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (1:1)</td>
<td>–55</td>
<td>(+)-35</td>
<td>91</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (1:1)</td>
<td>–78</td>
<td>(+)-35</td>
<td><strong>84</strong></td>
<td><strong>87</strong></td>
</tr>
<tr>
<td>4</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (1:2)</td>
<td>–78</td>
<td>(+)-35</td>
<td>76</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (1:3)</td>
<td>–78</td>
<td>(+)-35</td>
<td>39</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (2:1)</td>
<td>–78</td>
<td>(+)-35</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>CHCl₃: Cl₂(CH₂)Cl₂ (3:1)</td>
<td>–78</td>
<td>(+)-35</td>
<td>86</td>
<td>84</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)-35 (20 mol%), (i-Pr)₂NEt (5 equiv.) and TBAI (1 equiv.) in mixture solvents (0.76 mL) at various temperature for 24 h.

b. Yields are of isolated product.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tᵣ₉ = 18.3 min [(S)-3a]), tᵣₛ = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (S)-(−)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.⁵⁰a

Having identified the appropriate catalyst, temperature and solvent combination, we were intended to identify the appropriate base and additives to get better yield of homoallylic alcohols with good enantioselectivity.

Thus, the experiments were carried out by treating the substrates 4-methoxybenzaldehyde with allyltrichlorosilane, diisopropylethylamine and various additives (TBAF, TBACl, TBABr and TBAI) in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane at −78 °C for 24 h. When the reaction was carried out in the absence of additive, the homoallylic alcohol was obtained in 61% yield with 77% ee (Table 6, entry 1). Considerably better results were obtained while performing the reaction in presence of additives (Table 6, entries 3-5). For example, the homoallylic alcohol 3a was produced in 84% yield with 87% ee in presence of TBAI (Table 6, entry 5).
Table 6. Effect of additives on efficiency and enantioselectivity in presence of (+)-35.

```
+----------+-------+--------+
<table>
<thead>
<tr>
<th>entry</th>
<th>Additive (1 equiv.)</th>
<th>yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nil</td>
<td>61</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>TBAF</td>
<td>4</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>TBACl</td>
<td>66</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>TBABr</td>
<td>80</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>TBAI</td>
<td>84</td>
<td>87</td>
</tr>
</tbody>
</table>
```

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)-35 (20 mol%), (i-Pr)2NEt (5 equiv.) and 1 equiv. of various additives in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane (0.76 mL) at −78 °C for 24 h.

b. Yields are of isolated product.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tR = 18.3 min ([S]-3a)), tR = 21.3 min ([R]-3a)). The product 3a produced in all experiments are of (S)-(−)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.

Next, we turned our attention to identify the appropriate base for the enantioselective allylation reaction catalysed by (+)-35. Therefore, the experiments were performed using 4-methoxybenzaldehyde, allyltrichlorosilane, TBAI, (+)-35 (20 mol%) and in presence of various bases such as DABCO, DIPEA, Et3N, DMPU in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane at −78 °C for 24 h. When the allylation reaction was carried out in the absence of base the reaction failed to furnish the product (Table 7, entry 1). Among various bases examined, the base, diisopropylethylamine (DIPEA) exhibited the promising results as reported earlier vide infra. The use of DIPEA (5 equiv.) produced the homoallylic alcohol in 84% yield with 87% ee (Table 7, entry 3). Other bases such as DABCO, DMAP and DMPU produced the racemic homoallylic alcohol (Table 7, entries 2, 4 & 5). This may be due to the competing catalytic activity of DABCO, DMAP or DMPU instead of catalyst (+)-35.

After identifying the appropriate base, the reactions were conducted with different equivalents of DIPEA (Table 7, entries 3 & 7-11). Because, the base equivalent also important parameter required to get better results. Increasing the base equivalent from 1 equiv. to 20 equiv., decresed the yield of homoallylic alcohol, whereas the enantiomeric excess increased from 72% to 89% (Table 7, entries 7-11). Though 20 equivalent of base
produced the homoallylic alcohol in 89% ee, the yield of homoallylic alcohol was substantially low, 53%. Hence, to obtain good yield and better enantioselectivity of homoallylic alcohol, the allylation reaction requires 5 equivalents of DIPEA (Table 7, entry 3).

**Table 7. Effect of base on efficiency and enantioselectivity in presence of (+)-35\(^a\)**

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>base (equiv.)</th>
<th>yield(^b) (%)</th>
<th>ee(^c) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nil</td>
<td>-</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>2</td>
<td>DABCO</td>
<td>5</td>
<td>10</td>
<td>rac</td>
</tr>
<tr>
<td>3</td>
<td>DIPEA</td>
<td>5</td>
<td>84</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>DMAP</td>
<td>5</td>
<td>26</td>
<td>rac</td>
</tr>
<tr>
<td>5</td>
<td>DMPU</td>
<td>5</td>
<td>70</td>
<td>rac</td>
</tr>
<tr>
<td>6</td>
<td>Et(_3)N</td>
<td>5</td>
<td>10</td>
<td>67</td>
</tr>
<tr>
<td>7</td>
<td>DIPEA</td>
<td>1</td>
<td>92</td>
<td>72</td>
</tr>
<tr>
<td>8</td>
<td>DIPEA</td>
<td>3</td>
<td>85</td>
<td>77</td>
</tr>
<tr>
<td>9</td>
<td>DIPEA</td>
<td>10</td>
<td>71</td>
<td>87</td>
</tr>
<tr>
<td>10</td>
<td>DIPEA</td>
<td>15</td>
<td>62</td>
<td>88</td>
</tr>
<tr>
<td>11</td>
<td>DIPEA</td>
<td>20</td>
<td>53</td>
<td>89</td>
</tr>
</tbody>
</table>

\(^a\) All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)-35 (20 mol%), 1 equiv. TBAI and various bases and equivalents in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane (0.76 mL) at –78 °C for 24 h.

\(^b\) Yields are of isolated product.

\(^c\) Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, \(t_s = 18.3\) min \([\text{S-3a}])\), \(t_R = 21.3\) min \([\text{R-3a}])\). The product 3a produced in all experiments are of (S)-(−)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.\(^{30a}\)

To optimize the amount of catalyst, the allylation reactions were carried in presence of different mol% of the catalyst (+)-35 with 4-methoxybenzaldehyde under the established condition using allyltrichlorosilane, 1 equiv. of TBAI and 5 equiv. of DIPEA in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane at –78 °C for 24 h. Increasing the catalyst loading from 1 mol% to 25 mol%, increased the yield of homoallylic alcohol from 19% to 87% (Table 8, entries 1-5). Enantioselectivity of homoallylic alcohol also increased gradually from 70% to 87%, while increasing the catalyst loading from 1 mol% to 20 mol% (Table 8, entries 1-5). Further increase of catalyst loading to 25 mol% resulted in lower enantioselectivity, 82% ee (Table 8, entry 6).
Table 8. Effect of catalyst (+)-35 loading on efficiency and enantioselectivity

<table>
<thead>
<tr>
<th>entry</th>
<th>cat. (mol %)</th>
<th>yieldb (%)</th>
<th>ee² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>19</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>55</td>
<td>81</td>
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<tr>
<td>3</td>
<td>10</td>
<td>72</td>
<td>81</td>
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<tr>
<td>4</td>
<td>15</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>84</td>
<td>87</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>87</td>
<td>82</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), (i-Pr₂)₂NEt (5 equiv.), 1 equiv of TBAI and different mol% of (+)-35 in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane (0.76 mL) at −78 °C for 24 h.
b. Yields are of isolated product.
c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tₘ = 18.3 min [((S)-3a)], tᵣ = 21.3 min [((R)-3a)]). The product 3a produced in all experiments are of (S)-(-)-configuration (unless otherwise stated), as revealed by the comparison of HPLC retention times, with the literature value.⁶

After extensive experimentation based on the above variables, the best condition was found to be 20 mol% of the catalyst (+)-35 loading with TBAI (1 equiv.) as additive and DIPEA (5 equiv.) as base in 1:1 mixture of chloroform and 1,1,2,2-tetrachloroethane as solvent mixture at −78 °C to produce chiral homoallylic alcohol 3a in 84% yield with 87% ee (Scheme 19).

Scheme 19. Optimized condition for the allylation reaction in presence of (+)-35

Based on this condition, the versatility of catalyst (+)-35 was examined for the enantioselective allylation reaction with various aromatic, heterocyclic and aliphatic aldehydes (Table 9). Interestingly, the aromatic aldehydes with electron releasing functional group or benzaldehyde produced better yield and higher level of asymmetric induction (Table 9, entries 1–4, 6 & 7), even though the aldehydes and catalysts are not
electronically complimentary to each other. To further exemplify this observation, the reaction was carried out with electron withdrawing group containing benzaldehyde such as 4-nitrobenzaldehyde, which generated the corresponding homoallylic alcohol in poor yield with low optical purity (Table 9, entry 7).

Table 9. Asymmetric allylation of aldehydes with allyltrichlorosilane catalyzed by (+)-35a

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehyde</th>
<th>R</th>
<th>yield (%)</th>
<th>ee (%)</th>
<th>configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>4-MeO-C₆H₄</td>
<td>84</td>
<td>87</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>2-MeO-C₆H₄</td>
<td>95</td>
<td>80</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>C₆H₅</td>
<td>87</td>
<td>83</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>9-anthryl</td>
<td>62</td>
<td>92</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>piperonyl</td>
<td>58</td>
<td>81</td>
<td>S</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>3,4-dimethoxy</td>
<td>81</td>
<td>94</td>
<td>S</td>
</tr>
<tr>
<td>7</td>
<td>1g</td>
<td>4-NO₂-C₆H₄</td>
<td>47</td>
<td>25</td>
<td>S</td>
</tr>
<tr>
<td>8</td>
<td>1h</td>
<td>4-Cl-C₆H₄</td>
<td>98</td>
<td>76</td>
<td>S</td>
</tr>
<tr>
<td>9</td>
<td>1i</td>
<td>2-thienyl</td>
<td>71</td>
<td>92</td>
<td>R</td>
</tr>
<tr>
<td>10</td>
<td>1j</td>
<td>3-thienyl</td>
<td>67</td>
<td>89</td>
<td>S</td>
</tr>
<tr>
<td>11</td>
<td>1k</td>
<td>2-furyl</td>
<td>52</td>
<td>93</td>
<td>R</td>
</tr>
<tr>
<td>12</td>
<td>1l</td>
<td>(E)-C₆H₅CH=CH</td>
<td>37</td>
<td>71</td>
<td>S</td>
</tr>
<tr>
<td>13</td>
<td>1m</td>
<td>cyclohexyl</td>
<td>64</td>
<td>33</td>
<td>S</td>
</tr>
</tbody>
</table>

a. All reactions were performed with aldehydes (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (+)-35 (20 mol%), (i-Pr)₂NEt (5 equiv.) and TBAI (1 equiv.) in 1:1 mixture of chloroform: 1,1,2,2-tetrachloroethane (0.76 ml) at –78 °C for 24 h.
b. Yields are of isolated product.
c. ee was determined by chiral HPLC analysis.
d. Absolute configurations were assigned by comparing the HPLC retention time with the literature data.  

Condensed polycyclic aromatic aldehyde, for example, anthracene-9-carboxaldehyde, generated the corresponding homoallylic alcohol in 62% yield with good enantioselectivity (92% ee), which strongly suggest the involvement of sterical factor in enantioselectivity (Table 9, entry 4). The high enantioselectivity (94% ee) was observed for the electron rich 3,4-dimethoxybenzaldehyde (Table 9, entry 6). Aliphatic aldehyde for example cyclohexanecarboxaldehyde also produced the homoallylic alcohol in moderate yield, 64% with low enantioselectivity, 33% ee (Table 9, entry 13).
All the aldehydes, except 2-thiophencarboxaldehyde 1i and 2-furancarboxaldehyde 1k, produced homoallylic alcohols with S configuration in presence of (+)-35. This showed the involvement of six membered chair-like cyclic transition state (Figure 8a), which in turn facilitated the transfer of allyl nucleophile to si-face of the prochiral aldehydes (Table 9, entries 1-8, 10, 12, & 13). The involvement of six membered chair-like transition state was corroborated based on the stereochemical outcome of the reaction between 4-methoxybenzaldehyde and crotyltrichlorosilane (E/Z = 82:18) in presence of catalyst (−)-35. The reaction produced the anti/syn homoallylic alcohols in 81:19 ratio (Scheme 20).

**Scheme 20.** Crotylation of 4-methoxybenzaldehyde

Electron rich heterocyclic carboxaldehyde such as furan and thiophene carboxaldehydes 1i-1k successfully furnished the homoallylic alcohols 3i-3k in excellent enantioselectivity (Table 9, entries 9-11). Surprisingly, the 2-thiophencarboxaldehyde and 2-furfural produced the corresponding homoallylic alcohols in opposite configuration on contrary to the reported stereochemical outcome (Table 9, entries 9 & 11).30b, 46d

![Figure 8.](image)

**Figure 8.** The plausible transition state models to explain the stereochemical outcome.

This stereochemical outcome may be explained by the involvement of an axial orientation of the heterocycles in such a way that the lone pair of electrons on either O/S is stabilizing the positive charge of the β-carbon of allyl reagent as well as ensuring exposure of the re-face of the aldehyde to the γ-carbon of allyl reagent, which then facilitates the transfer of the allyl group from a hypervalent silicon complex to the re-face of the
Conformationally Rigid Chiral Pyridine N-Oxides...... Enantioselective Allylation of......

carbonyl group (Figure 8c). Also we can not rule out the involvement of axial disposition of heterocycles in such a way that the lone pair of electrons on O/S coordinates with silicon atom of allylsilane and exposes the re-face of the aldehyde to γ-carbon of allyl reagent and hence the generation of chiral homoallylic alcohol with “R” configuration (Figure 8b). 

The new chiral pyridine N-oxide (+)-35 produced the homoallylic alcohols in good yield and good enantioselectivity from electron rich aldehydes, benzaldehyde and heterocyclic aldehydes. But, in the case of electron deficient aldehyde, such as 4-nitrobenzaldehyde, the homoallylic alcohol was produced in low yield with poor enantioselectivity. Hence, to improve the yield and enantioselectivity of the homoallylic alcohols from electron deficient aldehydes, further structural modification was undertaken on the chiral catalyst (+)-21.

2.3.4. Designing of C_2-symmetric chiral bipyridine N,N'-dioxide

The C_2-symmetric chiral molecules generally exerts good enantioselectivity in most of the asymmetric transformations. Since, the introduction of DIOP ligand 37 by Dang and Kagan in 1971, the C_2-symmetry has become one among other conceptual factors / guiding force while designing catalyst systems for improved efficiency and selectivity. The C_2-symmetric ligand with two equivalent donor atoms generally reduces the number of possible isomeric metal complexes, as well as the number of different substrate–catalyst arrangements and different reaction pathways, when compared to C_1-symmetric ligands. The C_2-symmetry has the beneficial effect on enantioselectivity as the competing less-selective pathways are possibly eliminated. Hence, we have designed a C_2-symmetric chiral molecule 38 which can be readily derived from our basic chiral molecule 21 through halogenation and homocoupling (Figure 9).

![Figure 9. C_2-symmetric chiral molecule DIOP 37 and designed chiral molecule 38](image-url)
2.3.5. Synthesis of chiral bipyridine $N,N'$-dioxide (−)-38

$C_2$-symmetric chiral bipyridine $N,N'$-dioxides have already been utilized as catalysts for the enantioselective allylation of aldehydes. Following are some of the selected bipyridine $N,N'$-dioxides used in the organocatalytic allylation reaction (Figure 10).\textsuperscript{27f, 46}

![Chemical structures of selected bipyridine $N,N'$-dioxides](image)

Figure 10. $N,N'$-dioxides as organocatalysts (the maximum enantiomeric excess attained for homoallylic alcohol is given here)

These reports (Figure 10) encouraged us to synthesise the $C_2$-symmetric chiral catalyst (−)-38 and examine its efficiency towards the enantioselective allylation reaction. Hence, the required $C_2$-symmetric chiral molecule 38 was synthesized conveniently from the 6-chloropyridine derivative (−)-22 through homo coupling in presence of NiCl$_2$, PPh$_3$
and ZnCl₂ at 70 °C for 12 h. The bipyridine (−)-39 was produced, in 79% yield. The reaction of (−)-39 with m-CPBA produced both mono N-oxide (−)-40 and bipyridine N,N'-dioxide (−)-38 in 10% and 81% yields respectively (Scheme 21).

![Chemical structure diagram]

Scheme 21. Synthesis of chiral bipyridine derivatives

2.3.6. Catalytic efficiency of (−)-38 and (−)-40 in allylation reaction

Both catalysts, (−)-40 and (−)-38 were examined for the enantioselective allylation reaction under standard condition in various solvents. The catalytic efficiency as well as the enantioselectivity exerted by the catalyst (−)-40 was not encouraging (Table 10, entries 1-5). Interestingly, the catalyst (−)-38 delivered the homoallylic alcohols efficiently. The use of catalyst (−)-38, exhibited the 100% conversion and that required only 10 min in all five solvents (Table 10, entries 6-10) as determined from 1H NMR analysis. Hence, the catalyst (−)-38 was chosen for further optimization studies. Having identified the appropriate catalyst (−)-38 and solvent, we tried to optimize the appropriate catalyst loading, temperature, mixture of solvents and base to get good yield and enantioselectivity in the enantioselective allylation of prochiral aldehydes with 20 mol% of the catalyst (−)-38, the homoallylic alcohol was successfully generated from corresponding aldehyde in 10 minutes.
Table 10. Effect of catalyst (–)-38 & (–)-40 / solvent on efficiency and enantioselectivity a

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>catalyst</th>
<th>time</th>
<th>conversion b (%)</th>
<th>ee c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>acetonitrile</td>
<td>(–)-40</td>
<td>24 h</td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>dichloromethane</td>
<td>(–)-40</td>
<td>24 h</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>3</td>
<td>chloroform</td>
<td>(–)-40</td>
<td>24 h</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>4</td>
<td>1,2-dichloroethane</td>
<td>(–)-40</td>
<td>24 h</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>5</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>(–)-40</td>
<td>24 h</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>6</td>
<td>Acetonitrile</td>
<td>(–)-38</td>
<td>10 min</td>
<td>100</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>dichloromethane</td>
<td>(–)-38</td>
<td>10 min</td>
<td>100</td>
<td>54</td>
</tr>
<tr>
<td>8</td>
<td>chloroform</td>
<td>(–)-38</td>
<td>10 min</td>
<td>100</td>
<td>33</td>
</tr>
<tr>
<td>9</td>
<td>1,2-dichloroethane</td>
<td>(–)-38</td>
<td>10 min</td>
<td>100</td>
<td>26</td>
</tr>
<tr>
<td>10</td>
<td>1,1,2,2-tetrachloroethane</td>
<td>(–)-38</td>
<td>10 min</td>
<td>100</td>
<td>25</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (–)-40 or (–)-38 (20 mol%), (i-Pr)₂NEt (5 equiv.) and TBAI (1 equiv.) in solvents (0.8 mL) at –40 °C.

b. Determined from 1H NMR.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, t_R = 18.3 min [(S)-3a], t_R = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (R)-(+) configuration, as revealed by the comparison of HPLC retention times, with the literature value. 44a nr = no reaction, nd = not determined.

Since the catalyst very efficient, hence catalyst loading was decreased to improve the enantioselectivity of the allylation reactions. Accordingly, the allylation reactions were carried out in different mol% of the catalyst (–)-38 with 4-methoxybenzaldehyde using allyltrichlorosilane, 1 equiv. of TBAI and 5 equiv. of DIPEA in dichloromethane at –40 °C.

Decreasing the catalyst loading from 20 mol% to 0.1 mol% also showed 100% conversion, but the reaction time increased from 10 min to 10.5 h (Table 11). Enantioselectivity of homoallylic alcohol also increased marginally from 54% to 58%, while decreasing the catalyst loading from 20 mol% to 0.5 mol% (Table 11, entries 1-6).
Further reduction of catalyst loading from 0.5 mol% to 0.25 mol% and to 0.1 mol% did not improve the enantioselectivity but the time required for the complete conversion of starting material drastically increased from 1 h to 10.5 h (Table 11, entries 6-8). Based on these studies, the optimized catalyst (–)-38 loading was found to be 0.5 mol% to get the homoallylic alcohol in reasonably short reaction time with better enantioselectivity, 58% ee (Table 11, entry 6).

**Table 11. Effect of catalyst (–)-38 loading on efficiency and enantioselectivity**

<table>
<thead>
<tr>
<th>entry</th>
<th>cat. mol %</th>
<th>time</th>
<th>conversion (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>10 min</td>
<td>100</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>10 min</td>
<td>100</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>10 min</td>
<td>100</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>10 min</td>
<td>100</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>30 min</td>
<td>100</td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>1 h</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>7</td>
<td>0.25</td>
<td>3.5 h</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>8</td>
<td>0.1</td>
<td>10.5 h</td>
<td>100</td>
<td>58</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), (i-Pr)₂NEt (5 equiv.), TBAI (1 equiv.) and different equivalents of (–)-38 in dichloromethane (0.8 mL) at –40 °C.

b. Determined from ¹H NMR.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tᵣ = 18.3 min [(S)- 3a], tᵣ = 21.3 min [(R)- 3a]). The product 3a produced in all experiments are of (R)-(+) configuration, as revealed by the comparison of HPLC retention times, with the literature value.⁴⁶

The catalytic activity and selectivity of the catalyst (+)-35 in allylation reaction was found to be better in mixture of solvents than in single solvent system.⁴⁷ Therefore, the experiments were carried out with 1:1 mixture of various solvents at –40 °C in presence of the catalyst (–)-38 (Table 12). Unfortunately, the mixture of solvents system in presence of (–)-38 furnished the homoallylic alcohol in poor enantiomeric purity compared to single solvent system. Consequently, the further studies were performed using single solvent system such as dichloromethane (Table 10, Entry 7).
Table 12. Effect of mixture of solvents on efficiency and selectivity in presence of (−)-38a

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>time</th>
<th>conversion b (%)</th>
<th>ee c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ACN: DCM</td>
<td>30 min</td>
<td>100</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>ACN: CHCl₃</td>
<td>12 h</td>
<td>100</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>ACN: TCE</td>
<td>1.5 h</td>
<td>100</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td>ACN: DCE</td>
<td>6 h</td>
<td>100</td>
<td>47</td>
</tr>
<tr>
<td>5</td>
<td>DCM: DCE</td>
<td>1.5 h</td>
<td>100</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>DCM: TCE</td>
<td>12 h</td>
<td>100</td>
<td>56</td>
</tr>
<tr>
<td>7</td>
<td>DCM: CHCl₃</td>
<td>12 h</td>
<td>100</td>
<td>44</td>
</tr>
<tr>
<td>8</td>
<td>CHCl₃: DCE</td>
<td>12 h</td>
<td>100</td>
<td>42</td>
</tr>
<tr>
<td>9</td>
<td>CHCl₃: TCE</td>
<td>12 h</td>
<td>100</td>
<td>28</td>
</tr>
<tr>
<td>10</td>
<td>TCE: DCE</td>
<td>6 h</td>
<td>100</td>
<td>42</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (−)-38 (0.5 mol), (i-Pr)₂NEt (5 equiv.) and TBAI (1 equiv.) in 1:1 mixture of solvents (0.8 mL) at −40 °C.

b. Determined from ¹H NMR.

c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tᵣ = 18.3 min [(S)-3a], tᵣ = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (R)-(+)-configuration, as revealed by the comparison of HPLC retention times, with the literature value.⁴⁰a

To optimize the reaction temperature, the reactions were carried out in different temperatures (0 °C to −50 °C). While decreasing the temperature from 0 °C to −40 °C, the enantioselectivity was found to show the increasing trend (Table 13, entries 1-3). Further lowering of temperature (−50 °C) showed no improvement in enantioselectivity (Table 13, entry 4). Among various temperatures examined, the temperature −40 °C produced the better result. To identify the appropriate base for the enantioselective allylation reaction catalysed by (−)-38, the experiments were performed using 4-methoxybenzaldehyde, allyltrichlorosilane, TBAI, (−)-38 (0.5 mol%) and in presence of various bases such as DIPEA, DMAP, Et₃N and DMPU in dichloromethane at −40 °C. When the allylation reaction was carried out in the absence of base the reaction failed to generate the product (Table 14, entry 1). Among various bases examined, the base, disopropylethylamine (DIPEA) exhibited the promising results. The use of DIPEA (5 equiv.) displayed the 100% conversion of 4-methoxybenzaldehyde and the homoallylic alcohol was obtained in 58% ee (Table 14, entry 2).
Table 13. Effect of temperature on efficiency and enantioselectivity in presence of (–)-38a

<table>
<thead>
<tr>
<th>entry</th>
<th>temp (°C)</th>
<th>time</th>
<th>conversion (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>10 min</td>
<td>100</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>–20</td>
<td>20 min</td>
<td>100</td>
<td>44</td>
</tr>
<tr>
<td>3</td>
<td>–40</td>
<td>1 h</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>–50</td>
<td>4.5 h</td>
<td>100</td>
<td>58</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (–)-38 (0.5 mol), (i-Pr)2NEt (5 equiv.) and TBAI (1 equiv.) in dichloromethane (0.8 mL) at various temperatures.
b. Determined from 1H NMR.
c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tR = 18.3 min [(S)-3a], tR = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (R)-(+)-configuration, as revealed by the comparison of HPLC retention times, with the literature value.40a

After identifying the appropriate base, the reactions were conducted with different equivalent of DIPEA to achieve good yield and ee of homoallylic alcohol (Table 14, entries 2 & 6-10).

Table 14. Effect of base on efficiency and enantioselectivity in presence of (–)-38a

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>base (equiv.)</th>
<th>time (h)</th>
<th>conversion (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nil</td>
<td>5</td>
<td>24</td>
<td>nr</td>
<td>nd</td>
</tr>
<tr>
<td>2</td>
<td>DIPEA</td>
<td>5</td>
<td>1</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>3</td>
<td>DMAP</td>
<td>5</td>
<td>24</td>
<td>38</td>
<td>rac</td>
</tr>
<tr>
<td>4</td>
<td>Et3N</td>
<td>5</td>
<td>24</td>
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<td>DMPU</td>
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<tr>
<td>6</td>
<td>DIPEA</td>
<td>1</td>
<td>24</td>
<td>64</td>
<td>56</td>
</tr>
<tr>
<td>7</td>
<td>DIPEA</td>
<td>3</td>
<td>1</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>8</td>
<td>DIPEA</td>
<td>10</td>
<td>1.5</td>
<td>100</td>
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<tr>
<td>9</td>
<td>DIPEA</td>
<td>15</td>
<td>3</td>
<td>100</td>
<td>53</td>
</tr>
<tr>
<td>10</td>
<td>DIPEA</td>
<td>20</td>
<td>4</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>

a. All the reactions were performed with 4-methoxybenzaldehyde (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), catalyst (–)-38 (0.5 mol), TBAI (1 equiv.) and various bases and different equivalents of DIPEA in dichloromethane (0.8 mL) at –40°C.
b. Determined from 1H NMR.
c. Enantiomeric excess were determined by chiral HPLC analysis (Chiral stationary phase: Daicel-Chiralpak OD, Mobile phase: hexane and isopropyl alcohol 98/2, 1 mL/min, tR = 18.3 min [(S)-3a], tR = 21.3 min [(R)-3a]). The product 3a produced in all experiments are of (R)-(+)-configuration, as revealed by the comparison of HPLC retention times, with the literature value.40a nr = no reaction, nd = not determined.
When increasing the base equivalent from 1 equiv. to 3 equiv., the conversion of aldehyde to homoallylic alcohol increased from 64% to 100% with slight improvement in enantioselectivity (Table 14, entries 6 & 7). Further increase of base equivalent from 5 equiv. to 20 equiv., the time required for 100% conversion increased from 1 h to 4 h and selectivity of the homoallylic alcohol diminished from 58% ee to 50% ee (Table 14, entries 8-10). Hence, the best condition to obtain good yield and selectivity of homoallylic alcohol was found to be with 3 equiv. of DIPEA (Table 14, entry 2).

After extensive experimentations based on the above variables, the best condition for allylation reaction was found to be 0.5 mol% of catalyst (−)-38 loading with 1 equiv. of TBAI as additive and 3 equiv. of DIPEA as base in dichloromethane at −40 °C to generate homoallylic alcohol in good yield and enantiomeric excess (Scheme 23).

Scheme 23. Optimized condition for allylation reaction in the presence of (−)-38

Based on this condition, the versatility of catalyst bipyridine N,N'-dioxide (−)-38, was examined for the enantioselective allylation reaction with various electron rich and electron deficient and heterocyclic aldehydes (Table 15).

Table 15. Asymmetric allylation of aldehydes in presence of (−)-38a

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehyde</th>
<th>R</th>
<th>time (h)</th>
<th>yieldb (%)</th>
<th>eec (%)</th>
<th>configurationd</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>4-MeO-C6H4</td>
<td>1</td>
<td>92</td>
<td>58</td>
<td>R</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>C6H5</td>
<td>2</td>
<td>84</td>
<td>35</td>
<td>R</td>
</tr>
<tr>
<td>3</td>
<td>1g</td>
<td>4-NO2-C6H4</td>
<td>36</td>
<td>86</td>
<td>25</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td>1i</td>
<td>2-thienyl</td>
<td>36</td>
<td>76</td>
<td>62</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>1j</td>
<td>3-thienyl</td>
<td>8</td>
<td>87</td>
<td>82</td>
<td>R</td>
</tr>
</tbody>
</table>

a. All reactions were performed with aldehydes (0.25 mmol, 1 equiv.), allyltrichlorosilane (1.2 equiv.), 0.5 mol% of catalyst (−)-38, (i-Pr)2NEt (5 equiv.) and TBAI (1 equiv.) in dichloromethane (0.8 ml) at −40 °C.
b. Yields are of isolated product.
c. Enantiomeric excess were determined by chiral HPLC analysis.
d. Absolute configurations were assigned by comparing the HPLC retention time with the literature data.
Interestingly, aldehydes, 1a, 1c, 1g, 1i and 1j generated the corresponding homoallylic alcohols in good yield at –40°C. Electron rich 4-methoxybenzaldehyde produced the corresponding homoallylic alcohols in 92% yield with 58% ee (Table 5, entry 1) and benzaldehyde generated the homoallylic alcohol in 84% yield with 35% ee (Table 15, entry 2). The electron withdrawing group containing benzaldehyde such as 4-nitrobenzaldehyde generated the corresponding homoallylic alcohol in good yield (86%) with very low enantiomeric purity, 25% ee (Table 15, entry 3). The efficiency of the catalyst was further examined with electron rich heterocyclic carboxaldehydes such as 2-thiophenecarboxaldehyde 1l and 3-thiophenecarboxaldehydes 1j. These aldehydes, 1l and 1j, successfully furnished the homoallylic alcohols 3l and 3j in moderate enantioselectivity (Table 15, entries 4-5).
2.4. CONCLUSIONS

In conclusion, we have designed and synthesized a series of enantiomerically pure chiral pyridine N-oxides and evaluated their ability to promote the Sakurai–Hosomi–Denmark-type allylation reaction of aldehydes with allyltrichlorosilane. An electron-rich pyridine N-oxide 35 is a prerequisite for high enantioselectivity and good yield of homoallylic alcohol. The notable observation of the present work contemplates the beneficial effect of a mixture of solvents on the enantioselectivity. The stabilizing effect of a partial positive charge on the β-carbon by the lone pair electrons of the S/O atoms of the heterocycles in 2-thiophenecarbaldehyde and 2-furancarbaldehyde respectively, accounts for the excellent enantioselectivity and opposite configuration of the homoallylic alcohol produced. Also we may not rule out the possible coordination of lone pair of electrons on S/O to silicon atom of allylsilanes. Theoretical studies are in progress to ascertain this hypothesis. The catalyst (+)-35 was not a successful catalyst to generate homoallylic alcohol with good enantiomeric purity from electron deficient 4-nitrobenzaldehyde. Hence, to improve the yield and enantiomeric excess of homoallylic alcohols obtained from electron deficient aldehydes, the $C_2$-symmetric chiral bipyridine $N,N'$-dioxide 38 was designed, synthesized and evaluated for allylation reaction. The $C_2$-symmetric chiral bipyridine $N,N'$-dioxide 38 was found to be very reactive catalyst but produced homoallylic alcohols with poor enantiomeric purity.
2.5. EXPERIMENTAL SECTION

2.5.1. General Experimental Conditions

The general experimental conditions mentioned in chapter I are strictly followed in this chapter also.

The low temperature experiments 0 °C to –90 °C) were carried out using Julabo FT902 cooling system, Germany. Enantiomeric excess of the samples were determined on a Shimadzu HPLC systems using the appropriate Daicel Chiralpak AD-H, OD, AS or OJ-H columns.

2.5.1.2. Solvents and Reagents

Allylchlorosilane, crotylbromide (E/Z: 85/15), trichlorosilane Pd(PPh3)4 and NiCl2 were purchased from Sigma-Aldrich and used without further purification. All the aldehydes were purchased from Sigma-Aldrich and purified by distillation under reduced pressure. Anthracene-9-carboxaldehyde was prepared following the reported procedure. Boronic acids were prepared according to the literature procedure. Solvents used for the reactions were dried using standard procedures.

2.5.2 Synthesis of 6-chloropyridine and 4-chloropyridine derivatives:

To the stirred solution of (−)-21 (3.71 g, 10 mmol) in 75 mL of chloroform was added phosphorous oxychloride (27.5 mL, 300 mmol) under nitrogen atmosphere and the mixture was stirred at 90 °C for 24 h. The solution was then poured into ice-cold aqueous Na2CO3 and extracted with dichloromethane (75 mL × 3) and the organic extract was washed with brine, dried over anhydrous MgSO4, and filtered. The solvent was removed under reduced pressure and the resulting residue was purified through silica gel column chromatography using hexane/dichloromethane (30:70) as eluent to afford 6-chloro derivative (−)-22 and 4-chloro derivative (−)-23 as colourless solid. Similarly the opposite isomer (+)-22 and (+)-23 were synthesized from (+)-21.

Data for the compound (−)-22

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield</td>
<td>2.30 g (59%)</td>
</tr>
<tr>
<td>[α]25</td>
<td>−91.64 (c 1.00, CHCl3)</td>
</tr>
<tr>
<td>Mp</td>
<td>118.8-120.8 °C</td>
</tr>
</tbody>
</table>
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IR (KBr, cm\(^{-1}\)) : 3072, 2972, 1727, 1579, 1439, 1270, 748

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta_H 7.41-7.36\) (m, 3H), 7.31-7.29 (m, 1H), 7.17-7.10 (m, 3H), 7.07 (d, \(J = 8.0\) Hz, 1H), 7.01 (td, \(J = 8.0, 1.2\) Hz, 1H), 6.97-6.95 (m, 1H), 6.51 (d, \(J = 7.6\) Hz, 1H), 4.81 (d, \(J = 2.8\) Hz, 1H), 4.52 (d, \(J = 2.4\) Hz, 1H), 4.13-4.00 (m, 2H), 3.91 (dd, \(J = 5.2, 2.8\) Hz, 1H), 1.19 (t, \(J = 7.2\) Hz, 3H) ppm (Spectrum No. 5)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta_C 172.8, 162.9, 150.3, 143.2, 142.5, 140.4, 140.3, 138.6, 126.5, 126.3, 126.2, 126.0, 125.8, 124.9, 123.8, 123.6, 122.0, 120.4, 61.1, 50.5, 50.3, 49.7, 47.4, 14.4 ppm (Spectrum No. 6)

HRMS-ESI (m/z) : Found 390.1262 and calculated 390.1261 for \(C_{24}H_{21}ClNO_2^+\) (M+H)

Data for the compound (−)-23

Yield : 1.05 g (27%)

\([\alpha]_{D}^{25}\) : −55.81 (c 2.46, CHCl\(_3\))

Mp : 99-101 °C

IR (KBr, cm\(^{-1}\)) : 3068, 2967, 1714, 1570, 1464, 1226, 755

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta_H 8.25\) (d, \(J = 5.2\) Hz, 1H), 7.41 (d, \(J = 7.2\) Hz, 1H), 7.38-7.35 (m, 1H), 7.31-7.29 (m, 1H), 7.17-7.10 (m, 3H), 7.04 (dd, \(J = 5.2, 2.0\) Hz, 1H), 7.00 (td, \(J = 7.2, 1.2\) Hz, 1H), 6.93 (d, \(J = 7.2\) Hz, 1H), 6.78 (d, \(J = 1.6\) Hz, 1H), 4.82 (d, \(J = 2.8\) Hz, 1H), 4.49 (d, \(J = 2.4\) Hz, 1H), 4.14-4.00 (m, 2H), 3.89 (dd, \(J = 5.2, 2.4\) Hz, 1H), 3.52 (dd, \(J = 5.2, 2.8\) Hz, 1H), 1.20 (t, \(J = 7.2\) Hz, 3H) ppm (Spectrum No. 7)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta_C 172.9, 163.4, 149.6, 144.1, 143.3, 142.6, 140.4, 140.3, 126.5, 126.3, 126.2, 125.6, 124.9, 123.6, 122.7, 121.9, 61.0, 50.6, 49.9, 49.8, 47.3, 14.4 ppm (Spectrum No. 8)

HRMS-ESI (m/z) : Found 390.1263 and calculated 390.1261 for \(C_{24}H_{21}ClNO_2^+\) (M+H)

2.5.3. General procedure: Synthesis of 25(a-c), 28(a-c), 32 & 33

6-Chloro pyridine derivative (+)-22 (1.95 g, 5 mmol) was added to a degassed toluene solution (10 mL) containing Pd(PPh\(_3\))\(_4\) (0.46 g, 0.4 mmol). To this mixture a degassed solution of aryl boronic acid (6 mmol) in methanol (5 mL) and a degassed
solution of NaHCO$_3$ (1.26 g, 15 mmol) in water (5 mL) were added successively under nitrogen atmosphere. After heating for 15 h at 90 °C, the reaction mixture was cooled to room temperature, extracted with ethyl acetate (10 mL x 3) and dried over anhydrous MgSO$_4$. The solvent was removed under reduced pressure and the resulting residue was purified through silica gel column chromatography using hexane/ethyl acetate as eluent to afford the corresponding biaryl product.

2.5.3.1. Synthesis of (+)-25a

Following the general procedure, the reaction of (+)-22 (1.95 g, 5 mmol) with phenyl boronic acid (0.73 g, 6 mmol) furnished the biaryl (+)-25a as a colourless solid after silica gel column purification (hexane/ethyl acetate = 90:10).

**Yield** : 2.06 g (96%)

$[\alpha]_{D}^{25}$ : +49.40 (c 1.0, CHCl$_3$)

**Mp** : 46.5-48.5 °C

**IR (KBr, cm$^{-1}$)** : 3037, 2976, 1724, 1575, 1453, 1200, 759

**$^1$H NMR (400 MHz, CDCl$_3$)** : $\delta$ H 7.63-7.59 (m, 3H), 7.51-7.49 (m, 2H), 7.44-7.34 (m, 5H), 7.24-7.14 (m, 3H), 7.03 (d, $J$ = 7.6 Hz, 1H), 7.01 (td, $J$ = 7.6, 1.2 Hz, 1H), 6.94 (d, $J$ = 6.8 Hz, 1H), 4.89 (d, $J$ = 2.8 Hz, 1H), 4.51 (d, $J$ = 2.4 Hz, 1H), 4.18-4.01 (m, 2H), 3.94 (dd, $J$ = 5.6, 2.4 Hz, 1H), 3.82 (dd, $J$ = 5.6, 2.8 Hz, 1H), 1.22 (t, $J$ = 7.2 Hz, 3H) ppm (Spectrum No. 9)

**$^{13}$C NMR (100 MHz, CDCl$_3$)** : $\delta$ C 173.5, 161.0, 155.8, 143.9, 142.9, 140.9, 140.7, 139.3, 136.9, 129.6,128.8, 128.4, 126.9, 126.3, 126.0, 125.9, 125.6, 124.9, 123.5, 121.2, 117.8, 115.4, 60.8, 51.2, 50.1, 49.9, 47.6, 14.4 ppm (Spectrum No. 10)

**HRMS-ESI (m/z)** : Found 432.1966 and calculated 432.1964 for C$_{30}$H$_{26}$NO$_2$$^+$ (M+H)

2.5.3.2. Synthesis of (−)-25b

Following the general procedure, the reaction of (−)-22 (1.95 g, 5 mmol) with 1-naphthyl boronic acid (1.03 g, 6 mmol) furnished the biaryl (−)-25b as a viscous liquid after silica gel column purification (hexane/ethyl acetate = 90:10).
Yield : 2.26 g (94%)

$[\alpha]_D^{25} : -120.05$ (c 0.60, CHCl$_3$)

IR (KBr, cm$^{-1}$) : 3052, 2975, 1727, 1577, 1445, 1270, 756

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$H 7.88-7.84 (m, 2H), 7.68-7.64 (m, 2H), 7.49-7.45 (m, 2H), 7.42 (d, $J = 7.2$ Hz, 1H), 7.40-7.36 (m, 2H), 7.33-7.28 (m, 3H), 7.19 (td, $J = 7.6$, 1.2 Hz, 1H), 7.16-7.08 (m, 2H), 7.04 (td, $J = 7.6$, 1.2 Hz, 1H), 7.01 (d, $J = 7.6$ Hz, 1H), 6.97 (d, $J = 6.8$ Hz, 1H), 4.82 (d, $J = 2.8$ Hz, 1H), 4.59 (d, $J = 2.4$ Hz, 1H), 4.09-3.96 (m, 3H), 3.93 (dd, $J = 5.2$, 2.4 Hz, 1H), 1.16 (t, $J = 7.2$ Hz, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta$C 173.4, 160.9, 157.9, 143.7, 143.0, 140.9, 140.8, 138.7, 136.5, 134.0, 131.2, 128.8, 128.3, 127.9, 126.5, 126.3, 126.2, 126.1, 126.0, 125.9, 125.8, 125.4, 125.3, 124.9, 123.8, 123.7, 122.9, 120.9, 60.8, 51.6, 50.0, 48.7, 47.4, 14.4 ppm

HRMS-ESI (m/z) : Found 504.1927 and calculated 504.1939 for C$_{34}$H$_{27}$NO$_2$.Na$^+$

2.5.3.3. Synthesis of (−)-25c

Following the general procedure, the reaction of (−)-22 (1.95 g, 5 mmol) with 9-anthracenyl boronic acid (1.33 g, 6 mmol) furnished the biaryl (−)-25c as a colourless solid after silica gel column purification (hexane/ethyl acetate = 90:10).

Yield : 1.91 g (72%)

$[\alpha]_D^{25} : -156.27$ (c 1.00, CHCl$_3$)

Mp : 87.2-89.1 °C

IR (KBr, cm$^{-1}$) : 3056, 2928, 1726, 1578, 1458, 1271, 752

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$H 8.51 (s, 1H), 8.06-8.01 (m, 2H), 7.71 (t, $J = 8.0$ Hz, 1H), 7.50-7.42 (m, 3H), 7.39-7.27 (m, 5H), 7.21 (d, $J = 7.2$ Hz, 1H), 7.13-7.09 (m, 4H), 7.07-6.90 (m, 3H), 4.80 (d, $J = 2.4$ Hz, 1H), 4.72 (d, $J = 2.8$ Hz, 1H), 4.11 (dd, $J = 5.2$, 2.8 Hz, 1H), 4.08-3.94 (m, 2H), 3.87 (dd, $J = 5.2$, 2.8 Hz, 1H), 1.14 (t, $J = 7.2$ Hz, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta$C 173.4, 161.6, 157.0, 143.5, 142.7, 140.9, 140.8, 136.3, 135.6, 131.53, 131.50, 130.1, 128.5, 128.3, 127.4, 126.5, 126.4, 126.3, 126.2, 126.1, 126.0, 125.9, 125.7, 125.5, 125.2, 124.9,
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124.6, 123.9, 123.8, 120.9, 60.9, 51.3, 50.0, 48.7, 47.4, 14.4 ppm

HRMS-ESI (m/z) : Found 532.2261 and calculated 532.2277 for C_{38}H_{30}NO_2^+ (M+H)

2.5.3.4. Synthesis of (−)-28a

Following the general procedure, the reaction of (−)-22 (1.95 g, 5 mmol) with 2-methoxyphenyl boronic acid (0.91 g, 6 mmol) furnished the biaryl (−)-28a as a colourless solid after silica gel column purification (hexane/ethyl acetate = 88:12).

Yield : 2.19 g (95%)

[α]_{D}^{25} : −65.35 (c 1.53, CHCl_3)

Mp : 62.9-63.6 °C

IR (KBr, cm\(^{-1}\)) : 3064, 2970, 1727, 1578, 1456, 1259, 755

\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) : δ_H 7.69 (dd, J = 8.0, 0.8 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.44 (d, J = 7.2 Hz, 1H), 7.38-7.36 (m, 1H), 7.32-7.27 (m, 2H), 7.18 (td, J = 7.2, 1.2 Hz, 1H), 7.17-7.08 (m, 3H), 7.00 (td, J = 7.2, 1.2 Hz, 1H), 6.95-6.90 (m, 4H), 4.83 (d, J = 2.4 Hz, 1H), 4.47 (d, J = 2.4 Hz, 1H), 4.08-3.97 (m, 2H), 3.91 (dd, J = 5.4, 2.4 Hz, 1H), 3.82 (s, 3H), 3.80 (dd, J = 5.4, 2.4 Hz, 1H), 1.18 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 13)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : δ_C 173.5, 160.6, 157.1, 154.2, 144.0, 143.0, 141.0, 140.9, 135.8, 132.0, 129.7, 128.9, 126.3, 126.0, 125.9, 125.6, 124.9, 123.61, 123.58, 122.7, 120.8, 120.7, 111.3, 60.8, 55.6, 51.4, 49.9, 49.8, 47.6, 14.4 ppm (Spectrum No. 14)

HRMS-ESI (m/z) : Found 462.2062 and Calculated 462.2069 for C_{31}H_{28}NO_3^+ (M+H)

2.5.3.5. Synthesis of (−)-28b

Following the general procedure, the reaction of (−)-22 (1.95 g, 5 mmol) with 3-methoxyphenyl boronic acid (0.91 g, 6 mmol) furnished the biaryl (−)-28b as a viscous liquid after silica gel column purification (hexane/ethyl acetate = 88:12).

Yield : 2.28 g (99%)

[α]_{D}^{25} : −37.62 (c 2.78, CHCl_3)

IR (KBr, cm\(^{-1}\)) : 3436, 2935, 1727, 1571, 1460, 1267, 755
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$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$H 7.56 (t, $J$ = 7.6 Hz, 1H), 7.45-7.41 (m, 2H), 7.36-7.34 (m, 1H), 7.31-7.29 (m, 1H), 7.24-7.21 (m, 1H), 7.18-7.16 (m, 2H), 7.13-7.08 (m, 3H), 6.97 (d, $J$ = 7.6 Hz, 1H), 6.93 (td, $J$ = 7.6, 1.2 Hz, 1H), 6.88-6.85 (m, 2H), 4.82 (d, $J$ = 2.4 Hz, 1H), 4.46 (d, $J$ = 2.4 Hz, 1H), 4.10-3.95 (m, 2H), 3.81 (s, 3H), 3.80-3.78 (m, 1H), 1.16 (t, $J$ = 7.2 Hz, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta$C 173.4, 160.9, 160.0, 155.5, 143.9, 143.0, 140.9, 140.7, 136.9, 129.4, 126.3, 126.0, 125.97, 125.6, 124.9, 123.5, 123.4, 121.4, 119.4, 118.0, 114.6, 112.3, 60.8, 55.6, 51.2, 49.9, 49.8, 47.5, 14.4 ppm

HRMS-ESI (m/z) : Found 462.2076 and Calculated 462.2069 for C$_{31}$H$_{28}$NO$_3$+ (M+H)

2.5.3.6. Synthesis of (−)-28c

Following the general procedure, the reaction of (−)-22 (1.95 g, 5 mmol) with 4-methoxyphenyl boronic acid (0.91 g, 6 mmol) furnished the biaryl (−)-28c as a colourless solid after silica gel column purification (hexane/ethyl acetate = 88:12).

Yield : 2.07 g (90%)

[α]$_D^{25}$ : −41.35 (c 1.50, CHCl$_3$)

Mp : 118.4-120.2 °C

IR (KBr, cm$^{-1}$) : 3068, 2988, 1725, 1575, 1447, 1246, 752

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$H 7.58-7.52 (m, 3H), 7.48 (d, $J$ = 7.2 Hz, 1H), 7.42 (d, $J$ = 8.0 Hz, 1H), 7.40-7.37 (m, 1H), 7.35-7.33 (m, 1H), 7.20-7.12 (m, 3H), 7.01-6.95 (m, 2H), 6.92 (d, $J$ = 7.2 Hz, 1H), 6.90-6.86 (m, 2H), 4.86 (d, $J$ = 2.4 Hz, 1H), 4.47 (d, $J$ = 2.4 Hz, 1H), 4.15-3.99 (m, 2H), 3.88 (dd, $J$ = 5.2, 2.4 Hz, 1H), 3.85 (s, 3H), 3.78 (dd, $J$ = 5.2, 2.4 Hz, 1H), 1.21 (t, $J$ = 7.2 Hz, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta$C 173.5, 160.8, 160.4, 155.4, 144.0, 143.0, 141.0, 140.8, 136.9, 132.1, 128.2, 126.3, 126.0, 125.8, 125.7, 125.0, 123.51, 123.48, 120.6, 117.0, 113.8, 60.8, 55.5, 51.2, 50.1, 49.9, 47.6, 14.4 ppm

HRMS-ESI (m/z) : Found 462.2046 and calculated 462.2069 for C$_{31}$H$_{28}$NO$_3$+ (M+H)
2.5.3.7. Synthesis of (+)-32

Following the general procedure, the reaction of (+)-22 (1.95 g, 5 mmol) with 2,6-dimethoxyphenyl boronic acid (1.09 g, 6 mmol) furnished the biaryl (+)-32 as a colourless solid after silica gel column purification (hexane/ethyl acetate = 75:25).

Yield: 2.31 g (94%)

$[\alpha]_D^{25}$: +99.64 (c 1.00, CHCl$_3$

Mp: 197.1-198.5 °C

IR (KBr, cm$^{-1}$): 3068, 2974, 1721, 1585, 1463, 1250, 751

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 7.43-7.35 (m, 3H), 7.32-7.27 (m, 2H), 7.14-7.07 (m, 3H), 7.04 (dd, $J = 7.6$, 0.8 Hz, 1H), 6.99 (td, $J = 7.2$, 1.2 Hz, 1H), 6.94 (dd, $J = 7.2$, 1.2 Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 2H), 6.27 (d, $J = 8.0$ Hz, 1H), 4.79 (d, $J = 2.8$ Hz, 1H), 4.64 (d, $J = 2.4$ Hz, 1H), 4.08-3.96 (m, 3H), 3.72 (s, 6H), 3.40 (dd, $J = 5.6$, 2.8 Hz, 1H), 1.13 (t, $J = 7.2$ Hz, 3H) ppm (Spectrum No. 17)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$C 173.1, 161.1, 153.7, 153.7, 143.7, 143.7, 142.6, 141.2, 140.5, 135.7, 129.6, 126.2, 126.0, 125.92, 125.90, 124.7, 124.0, 123.7, 123.5, 119.9, 119.1, 104.7, 60.8, 56.2, 50.7, 50.2, 50.1, 47.8, 14.3 ppm (Spectrum No. 18)

HRMS-ESI (m/z): Found 492.2179 and calculated 492.2175 for C$_{32}$H$_{30}$NO$_4$+ (M+H)

2.5.3.8. Synthesis of (+)-33

Following the general procedure, the reaction of (+)-22 (1.95 g, 5 mmol) with 2,4,6-trimethoxyphenyl boronic acid (1.27 g, 6 mmol) furnished the biaryl (+)-33 as a colourless solid after silica gel column purification (hexane/ethyl acetate = 70:30).

Yield: 2.06 g (79%)

$[\alpha]_D^{25}$: +97.04 (c 0.82, CHCl$_3$

Mp: 183.5-185.4 °C

IR (KBr, cm$^{-1}$): 3072, 2971, 1723, 1589, 1457, 1210, 757

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 7.41-7.36 (m, 3H), 7.29-7.27 (m, 1H), 7.14-7.07 (m, 3H), 7.03 (dd, $J = 7.6$, 0.4 Hz, 1H), 6.99 (td, $J = 7.2$, 1.2 Hz, 1H), 6.96-6.94 (m, 1H), 6.25 (d, $J = 7.6$ Hz, 1H), 6.22 (s, 2H), 4.79 (d, $J = 2.8$ Hz, 1H), 4.64 (d, $J = 2.4$ Hz, 1H), 4.06-3.96 (m, 3H), 3.86 (s, 3H), 3.70 (s, 6H), 3.41 (dd, $J = 5.6$, 2.8 Hz, 1H),
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1.14 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 21)

$^{13}$C NMR (100 MHz, CDCl$_3$) : δ$_C$ 173.1, 161.3, 161.0, 159.0, 153.6, 143.7, 142.6, 141.2, 140.5, 135.6, 126.2, 126.0, 125.90, 125.87, 124.7, 124.2, 124.0, 123.5, 118.9, 113.0, 91.4, 60.8, 56.2, 55.5, 50.7, 50.2, 50.0, 47.8, 14.3 ppm (Spectrum No. 22)

HRMS-ESI (m/z) : Found 522.2289 and calculated 522.2280 for C$_{33}$H$_{32}$NO$_5^+$ (M+H)

2.5.4. General procedure for the preparation of N-oxides, 26(a-c), 29(a-c), 34 & 35

To the stirred solution of pyridine compound (2.5 mmol) in CH$_2$Cl$_2$ (10 mL) at 0 °C, m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) in CH$_2$Cl$_2$ (5 mL) was added drop-wise via double ended needle at 0 °C and the mixture was stirred at room temperature for 6 h under the atmosphere of nitrogen. The reaction mixture was washed with saturated NaHCO$_3$ (10 mL × 3) and the aqueous layer was extracted with dichloromethane (10 mL × 2). The combined organic layer was washed with brine, dried over anhydrous MgSO$_4$ and filtered. The solvent was evaporated under reduced pressure. The resulting residue was purified through silica gel column chromatography to afford the corresponding N-oxides.

2.5.4.1. Synthesis of (+)-21

Following the general procedure, the reaction of (+)-20 (0.89 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (+)-21 as a colourless solid after silica gel column purification (ethyl acetate/methanol = 95:5).

Yield : 0.88 g (95%)

$[\alpha]^{25}_D$ : +130.06 (c 1.00, CHCl$_3$)

Mp : 133.5-135.5 °C

IR (KBr, cm$^{-1}$) : 3041, 2977, 1728, 1478, 1287, 867, 760

$^1$H NMR (400 MHz, CDCl$_3$) : δ$_H$ 8.28 (dd, J = 6.4, 0.8 Hz, 1H), 7.44-7.43 (m, 1H), 7.41 (d, J = 7.2 Hz, 1H), 7.31-7.29 (m, 1H), 7.19-7.11 (m, 3H), 7.08-7.04 (m, 1H), 7.03 (td, J = 7.2, 1.2 Hz, 1H), 6.96 (d, J = 6.8 Hz, 1H), 6.90 (td, J = 8.0, 1.2 Hz, 1H), 6.17 (dd, J = 8.0, 2.0 Hz, 1H), 4.78 (d, J = 2.8 Hz, 1H), 4.69 (dd, J = 5.6, 2.4 Hz, 1H), 4.61 (d, J = 2.4 Hz, 1H), 4.06-3.98 (m, 2H), 2.92 (dd, J = 5.6, 2.8 Hz, 1H), 1.11 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 3)
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Experimental Section

$^{13}$C NMR (100 MHz, CDCl$_3$) : δC 172.1, 153.1, 142.7, 142.5, 140.8, 139.9, 139.7, 126.7, 126.6, 126.31, 126.28, 125.9, 125.1, 125.0, 124.2, 123.9, 123.8, 123.6, 123.5, 61.2, 50.5, 47.4, 46.7, 41.3, 14.3 ppm (Spectrum No. 4)

HRMS-ESI (m/z) : Found 372.1600 and calculated 372.1600 for C$_{24}$H$_{22}$NO$_3$+ (M+H)

2.5.4.2. Synthesis of (+)-26a

Following the general procedure, the reaction of (+)-25a (1.08 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (+)-26a as a colourless solid after silica gel column purification (hexane/ethyl acetate = 55:45).

Yield : 1.06 g (95%)

$[\alpha]_{D}^{25}$ : +294.64 (c 1.01, CHCl$_3$)

Mp : 89.1-91.1 °C

IR (KBr, cm$^{-1}$) : 3040, 2973, 1731, 1562, 1467, 1256, 841, 758

$^1$H NMR (400 MHz, CDCl$_3$) : δH 7.83-7.81 (m, 2H), 7.50-7.41 (m, 5H), 7.31-7.29 (m, 1H), 7.24 (dd, J = 7.6, 2.0 Hz, 1H), 7.17 (td, J = 7.6, 1.2 Hz, 1H), 7.16-7.09 (m, 2H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 6.92 (t, J = 7.6 Hz, 1H), 6.07 (dd, J = 8.0, 2.0 Hz, 1H), 4.82-4.80 (m, 2H), 4.68 (d, J = 2.4 Hz, 1H), 4.02 (q, J = 7.2 Hz, 2H), 2.99 (dd, J = 5.6, 2.4 Hz, 1H), 1.12 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 11)

$^{13}$C NMR (100 MHz, CDCl$_3$) : δC 172.2, 153.5, 149.5, 143.0, 142.4, 141.1, 139.8, 133.5, 129.7, 129.5, 128.3, 126.7, 126.5, 126.3, 126.2, 126.0, 125.0, 124.9, 124.3, 124.2, 123.7, 122.5, 61.1, 50.7, 47.6, 46.6, 41.8, 14.3 ppm (Spectrum No. 12)

HRMS-ESI (m/z) : Found 448.1914 and calculated 448.1913 for C$_{30}$H$_{26}$NO$_3$+ (M+H)

2.5.4.3. Synthesis of (−)-26b

Following the general procedure, the reaction of (−)-25b (1.20 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (−)-26b as a pale yellow solid after silica gel column purification (hexane/ethyl acetate = 55:45).

Yield : 1.18 g (95%)
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\[\alpha\]_{D}^{25} : \ -345.15 (c 1.00, CHCl₃)

Mp : \ 212.0-214.1 \ ^\circ\text{C}

IR (KBr, cm\(^{-1}\)) : \ 3064, 2970, 1728, 1560, 1466, 1246, 845, 772

\(^1\)H NMR (400 MHz, CDCl₃) : \ \delta_H \ 7.97-7.88 (m, 2H), 7.61-7.55 (m, 3H), 7.51-7.46 (m, 2H), 7.42-7.33 (m, 3H), 7.30-7.27 (m, 1H), 7.23-7.18 (m, 1H), 7.13-7.06 (m, 3H), 7.03-6.95 (m, 2H), 6.24-6.20 (m, 1H), 4.85-4.84 (m, 1H), 4.79-4.67 (m, 2H), 4.06-3.97 (m, 2H), 3.09-3.02 (m, 1H), 1.16-1.06 (m, 3H) ppm [observance of multiplets may be due to the presence of atropisomerism due to naphthalene group]

\(^{13}\)C NMR (100 MHz, CDCl₃) : \ \delta_C \ 172.1, 153.6, 150.1, 143.2, 140.0, 133.6, 130.1, 129.8, 128.8, 128.6, 128.0, 127.9, 126.9, 126.7, 126.6, 126.4, 126.3, 126.2, 126.0, 125.8, 125.5, 125.3, 124.9, 124.5, 124.2, 123.8, 123.7, 123.0, 61.1, 50.9, 47.3, 46.7, 42.1, 14.2 ppm [recorded at 50 \ ^\circ\text{C}]

HRMS-ESI (m/z) : Found 498.2068 and calculated 498.2069 for C\(_{34}\)H\(_{28}\)NO\(_3\)\(^+\) (M+H)

2.5.4.4. Synthesis of (-)-26c

Following the general procedure, the reaction of (-)-25c (1.32 g, 2.5 mmol) with \(m\)-chloroperbenzoic acid (70\%, 0.65 g, 3.75 mmol) furnished the N-oxide (-)-26c as a pale yellow solid after silica gel column purification (hexane/ethyl acetate = 60:40).

Yield : \ 0.55 g (40%)

\[\alpha\]_{D}^{25} : \ -281.33 (c 0.33, CHCl₃)

Mp : \ 122.0-124.1 \ ^\circ\text{C}

IR (KBr, cm\(^{-1}\)) : \ 3060, 2928, 1731, 1565, 1459, 1254, 849, 748

\(^1\)H NMR (400 MHz, CDCl₃) : \ \delta_H \ 8.59 (s, 1H), 8.11-8.05 (m, 2H), 7.53-7.51 (m, 3H), 7.48-7.43 (m, 3H), 7.39-7.35 (m, 2H), 7.32-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.15-7.13 (m, 1H), 7.10-7.06 (m, 4H), 6.38 (dd, \(J = 8.0, 2.0 \ \text{Hz}, 1\H), 4.86 (d, \(J = 2.4 \ \text{Hz}, 1\H), 4.79 (d, \(J = 2.0 \ \text{Hz}, 1\H), 4.76 (dd, \(J = 5.6, 2.0 \ \text{Hz}, 1\H), 4.01 (q, \(J = 7.2 \ \text{Hz}, 2\H), 3.12 (dd, \(J = 5.6, 2.4 \ \text{Hz}, 1\H), 1.09 (t, \(J = 7.2 \ \text{Hz}, 3\H) \ \text{ppm}
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**13C NMR (100 MHz, CDCl₃)**: δC 172.2, 153.9, 148.1, 142.8, 142.5, 141.4, 139.9, 131.8, 131.5, 130.1, 130.0, 129.1, 128.92, 128.89, 127.9, 127.7, 126.9, 126.8, 126.6, 126.4, 126.2, 125.8, 125.51, 125.46, 125.4, 125.08, 125.06, 124.4, 123.9, 123.5, 123.3, 61.1, 50.3, 47.4, 46.5, 42.2, 14.2 ppm

**HRMS-ESI (m/z)**: Found 548.2217 and calculated 548.2226 for C₃₈H₃₀NO₃⁺ (M+H)

**2.5.4.5. Synthesis of (−)-29a**

Following the general procedure, the reaction of (−)-28a (1.15 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (−)-29a as a colourless solid after silica gel column purification (hexane/ethyl acetate = 40:60).

**Yield**: 1.07 g (90%)

**[α]D²⁵**: −133.34 (c 1.26, CHCl₃)

**Mp**: 84.0-85.6 °C

**IR (KBr, cm⁻¹)**: 3072, 2973, 1730, 1589, 1468, 1249, 849, 755

**1H NMR (400 MHz, CDCl₃)**: δH 7.44-7.40 (m, 4H), 7.31-7.28 (m, 1H), 7.19-7.15 (m, 2H), 7.14-7.10 (m, 2H), 7.08-7.06 (m, 1H), 7.04-7.01 (m, 2H), 6.97 (d, J = 7.2 Hz, 1H), 6.90 (t, J = 8.0 Hz, 1H), 6.12 (dd, J = 8.0, 1.6 Hz, 1H), 4.80 (d, J = 2.8 Hz, 1H), 4.75 (dd, J = 5.6, 2.4 Hz, 1H), 4.72 (d, J = 2.4 Hz, 1H), 4.01 (q, J = 7.2 Hz, 2H), 3.83 (s, 3H), 3.00 (dd, J = 5.6, 2.8 Hz, 1H), 1.10 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 15)

**13C NMR (100 MHz, CDCl₃)**: δC 172.2, 157.4, 153.0, 148.1, 143.0, 142.4, 141.2, 140.0, 130.9, 130.8, 126.6, 126.4, 126.2, 126.1, 126.0, 125.9, 124.9, 124.3, 123.7, 123.1, 122.5, 120.7, 111.5, 61.0, 56.0, 50.5, 47.6, 46.5, 41.8, 41.4 ppm (Spectrum No. 16)

**HRMS-ESI (m/z)**: Found 478.2015 and calculated 478.2018 for C₃₁H₂₈NO₄⁺ (M+H)

**2.5.4.6. Synthesis of (−)-29b**

Following the general procedure, the reaction of (−)-28b (1.15 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (−)-29b as a colourless solid after silica gel column purification (hexane/ethyl acetate = 40:60).
Yield : 1.15 g (97%)
$[\alpha]_{D}^{25}$ : $-151.59$ (c 1.38, CHCl$_3$)
Mp : 74.1-75.5 °C
IR (KBr, cm$^{-1}$) : 3068, 2970, 1732, 1586, 1469, 1254, 859, 769
$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$ $H$ 7.44-7.42 (m, 2H), 7.40-7.34 (m, 3H), 7.31-7.29 (m, 1H), 7.24 (dd, $J$ = 8.0, 2.0 Hz, 1H), 7.19-7.09 (m, 3H), 7.03 (td, $J$ = 7.6, 1.2 Hz, 1H), 7.00-6.90 (m, 3H), 6.07 (dd, $J$ = 8.0, 2.0 Hz, 1H), 4.82-4.80 (m, 2H), 4.70 (d, $J$ = 2.0 Hz, 1H), 4.03 (q, $J$ = 7.2 Hz, 2H), 3.85 (s, 3H), 2.99 (dd, $J$ = 5.6, 2.4 Hz, 1H), 1.13 (t, $J$ = 7.2 Hz, 3H) ppm
$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta$ $C$ 172.2, 159.5, 153.6, 149.4, 142.9, 142.4, 141.1, 139.8, 134.7, 129.3, 126.7, 126.5, 126.3, 126.0, 125.1, 124.9, 124.3, 123.7, 122.6, 122.2, 115.6, 115.1, 61.1, 55.6, 50.7, 47.5, 46.6, 41.8, 14.3 ppm
HRMS-ESI (m/z) : Found 478.2019 and calculated 478.2018 for C$_{31}$H$_{28}$NO$_4$\(^+\) (M+H)

2.5.4.7. Synthesis of (−)-29c

Following the general procedure, the reaction of (−)-28c (1.15 g, 2.5 mmol) with $m$-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (−)-29c as a colourless solid after silica gel column purification (hexane/ethyl acetate = 40:60).

Yield : 0.97 g (81%)
$[\alpha]_{D}^{25}$ : $-217.49$ (c 1.00, CHCl$_3$)
Mp : 63.7-65.2 °C
IR (KBr, cm$^{-1}$) : 3072, 2970, 1731, 1568, 1473, 1255, 833, 755
$^1$H NMR (400 MHz, CDCl$_3$) : $\delta$ $H$ 7.85-7.82 (m, 2H), 7.44-7.42 (m, 2H), 7.31-7.29 (m, 1H), 7.23 (dd, $J$ = 7.6, 2.0 Hz 1H), 7.18-7.09 (m, 3H), 7.05-6.98 (m, 3H), 6.96-6.94 (m, 1H), 6.89 (t, $J$ = 8.0 Hz, 1H), 6.03 (dd, $J$ = 8.0, 2.0 Hz, 1H), 4.82-4.80 (m, 2H), 4.69 (d, $J$ = 2.4 Hz, 1H), 4.03 (q, $J$ = 7.2 Hz, 2H), 3.86 (s, 3H), 2.99 (dd, $J$ = 5.6, 2.8 Hz, 1H), 1.12 (t, $J$ = 7.2 Hz, 3H) ppm
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^{13}C NMR (100 MHz, CDCl_3) : δC 172.2, 160.5, 153.3, 149.1, 143.0, 142.4, 141.1, 139.9, 131.2, 126.6, 126.4, 126.2, 126.1, 126.0, 125.8, 124.9, 124.6, 124.3, 124.0, 123.6, 121.9, 113.7, 61.1, 55.5, 50.7, 47.6, 46.6, 41.9, 14.3 ppm

HRMS-ESI (m/z) : Found 478.1997 and calculated 478.2018 for C_{31}H_{28}NO_4 (+M+H)

2.5.4.8. Synthesis of (+)-34

Following the general procedure, the reaction of (+)-32 (1.23 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (+)-34 as a colourless solid after silica gel column purification (hexane/ethyl acetate = 35:65).

Yield : 1.18 g (93%)

[α]^{25}_D : +215.09 (c 1.00, CHCl_3)

Mp : 114.4-116.4 °C

IR (KBr, cm^{-1}) : 3068, 2950, 1731, 1591, 1470, 1255, 842, 754

^{1}H NMR (400 MHz, CDCl_3) : δH 7.45-7.41 (m, 2H), 7.36 (t, J = 8.4 Hz, 1H), 7.29-7.27 (m, 1H), 7.17-7.08 (m, 4H), 7.03 (td, J = 7.2, 1.2 Hz, 1H), 6.94 (d, J = 6.8 Hz, 1H), 6.86 (t, J = 8.0 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 6.46 (d, J = 8.4 Hz, 1H), 6.15 (dd, J = 8.0, 2.0 Hz, 1H), 4.78 (d, J = 2.8 Hz, 1H), 4.76 (d, J = 2.4 Hz, 1H), 4.70 (dd, J = 5.2, 2.4 Hz, 1H), 4.00 (q, J = 7.2 Hz, 2H), 3.84 (s, 3H), 3.73 (s, 3H), 3.00 (dd, J = 5.2, 2.8 Hz, 1H), 1.08 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 19)

^{13}C NMR (100 MHz, CDCl_3) : δC 172.3, 158.6, 158.2, 152.7, 145.4, 143.0, 142.4, 141.5, 140.1, 130.9, 126.9, 126.5, 126.3, 126.2, 126.0, 125.9, 124.8, 124.4, 123.7, 123.1, 122.2, 112.1, 104.4, 104.3, 61.0, 56.3, 56.2, 50.2, 47.7, 46.4, 41.9, 14.2 ppm (Spectrum No. 20)

HRMS-ESI (m/z) : Found 508.2128 and calculated 508.2124 for C_{32}H_{30}NO_5 (+M+H)

2.5.4.9. Synthesis of (+)-35

Following the general procedure, the reaction of (+)-33 (1.30 g, 2.5 mmol) with m-chloroperbenzoic acid (70%, 0.65 g, 3.75 mmol) furnished the N-oxide (+)-35 as a colourless solid after silica gel column purification (hexane/ethyl acetate = 30:70).
Yield : 0.94 g (70%)
\([\alpha]_D^{25}\) : +98.34 (c 1.41, CHCl₃)
Mp : 113.1-114.5 °C
IR (KBr, cm⁻¹) : 3068, 2945, 1732, 1598, 1464, 1262, 837, 755

**¹H NMR (400 MHz, CDCl₃)** : δH 7.45-7.41 (m, 2H), 7.29-7.27 (m, 1H), 7.17-7.08 (m, 4H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 6.95 (d, J = 7.2 Hz, 1H), 6.84 (t, J = 8.0 Hz, 1H), 6.25 (d, J = 2.0 Hz, 1H), 6.21 (d, J = 2.0 Hz, 1H), 6.14 (dd, J = 8.0, 2.0 Hz, 1H), 4.78 (d, J = 2.8 Hz, 1H), 4.75 (d, J = 2.4 Hz, 1H), 4.69 (dd, J = 5.6, 2.4 Hz, 1H), 4.00 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 3.82 (s, 3H), 3.71 (s, 3H), 2.99 (dd, J = 5.6, 2.8 Hz, 1H), 1.09 (t, J = 7.2 Hz, 3H) ppm (Spectrum No. 23)

**¹³C NMR (100 MHz, CDCl₃)** : δC 172.3, 162.5, 159.4, 158.9, 152.6, 145.3, 143.0, 142.4, 141.5, 140.1, 127.3, 126.5, 126.3, 126.2, 126.0, 125.9, 124.8, 124.4, 123.6, 122.8, 122.0, 105.1, 91.2, 91.1, 60.9, 56.2, 56.1, 55.6, 50.2, 47.7, 46.4, 42.0, 14.2 ppm (Spectrum No. 24)

HRMS-ESI (m/z) : Found 538.2230 and calculated 538.2230 for C₃₃H₃₂NO₆⁺ (M+H)

### 2.5.5. General procedure for allylation of aldehydes in presence of (+)-35

Allyltrichorosilane (44 µL, 0.3 mmol) was added drop-wise to the solution of catalyst (+)-35 (26.8 mg, 0.05 mmol), diisopropylethylamine (0.21 mL, 1.25 mmol), *tetra-n*-butylammonium iodide (92.3 mg, 0.25 mmol) and aldehyde 1 (0.25 mmol) in 1:1 mixture of chloroform: tetrachloroethane (0.76 mL) under nitrogen atmosphere at -78 °C with stirring. After 24 h the reaction mixture was quenched with aqueous saturated NaHCO₃ (2 mL). Organic layer was separated and then the aqueous layer was extracted with diethyl ether (5 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated in rotary evaporator under reduced pressure. The residue was purified through silica gel column chromatography to afford the homoallylic alcohols.

#### 2.5.5.1. Reaction of 1a with 2b in presence of (+)-35 (Table 9, Entry 1)

Following the general procedure, the 4-methoxybenzaldehyde (34 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(4-methoxyphenyl)but-3-en-1-ol 3a as a colourless oil after silica gel column purification (hexane/ethyl acetate = 85:15).
The configuration of the homoallylic alcohol (−)-3a was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\textsuperscript{40a}

Yield : 37.4 mg (84%)

IR (neat, cm\textsuperscript{-1}) : 3405 (br), 3075, 2935, 1640, 1612, 1514, 1442, 1247, 1036, 918, 832

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) : δ\textsubscript{H} 7.29-7.25 (m, 2H), 6.89-6.86 (m, 2H), 5.78 (ddt, J = 17.6, 10.4, 7.2 Hz, 1H), 5.17-5.10 (m, 2H), 4.67 (td, J = 6.4, 3.2 Hz, 1H), 3.79 (s, 3H), 2.51-2.47 (m, 2H), 2.10 (d, J = 3.2 Hz, 1H) ppm

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) : δ\textsubscript{C} 159.0, 136.2, 134.7, 127.2, 118.1, 113.8, 73.1, 55.3, 43.8 ppm

HPLC data : Column : Chiralcel OD (4.6 mm x 250 mm)
Enantiomeric excess : 87% [(S)-3a]
Retention time : t\textsubscript{R} = 18.3 min, t\textsubscript{S} = 21.3 min
Mobile phase : 98:2
(hexanes: isopropanol)
Flow rate : 1 mL/min
Wavelength (λ) : 220 nm

2.5.5.2. Reaction of 1b with 2b in presence of (+)-35 (Table 9, Entry 2)

Following the general procedure, the 2-methoxybenzaldehyde (34 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(2-methoxyphenyl)but-3-en-1-ol 3b as a colourless oil after silica gel column purification (hexane/ethyl acetate = 85:15).

The configuration of the homoallylic alcohol (−)-3b was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\textsuperscript{40a}

Yield : 42.3 mg (95%)

IR (neat, cm\textsuperscript{-1}) : 3447 (br), 3071, 1637, 1588, 1438, 1240, 1030, 915, 754

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) : δ\textsubscript{H} 7.34 (dd, J = 7.6, 1.6 Hz, 1H), 7.27-7.23 (m, 1H), 6.96 (td, J = 7.6, 1.2 Hz, 1H), 6.88 (dd, J = 8.0, 0.8 Hz, 1H), 5.90-5.80 (m, 1H), 5.17-5.09 (m, 2H), 4.98-4.95 (m, 1H), 3.86 (s, 3H), 2.63-2.47 (m, 3H) ppm

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) : δ\textsubscript{C} 156.6, 135.4, 131.9, 128.5, 127.0, 120.8, 117.7, 110.6, 69.9, 55.4, 42.0 ppm
HPLC data
- Column: Chiralcel OD (4.6 mm x 250 mm)
- Enantiomeric excess: 80% [(S)-3b]
- Retention time: t_S = 14.4 min, t_R = 15.8 min
- Mobile phase (hexanes: isopropanol): 98:2
- Flow rate: 1 mL/min
- Wavelength (λ): 220 nm

2.5.5.3. Reaction of 1c with 2b in presence of (+)-35 (Table 9, Entry 3)

Following the general procedure, the benzaldehyde (26.5 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(phenyl)but-3-en-1-ol 3c as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (–)-3c was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.

Yield: 32.0 mg (87%)

IR (neat, cm⁻¹): 3389 (br), 3077, 2906, 1641, 1493, 1454, 1050, 987, 916, 758

¹H NMR (400 MHz, CDCl₃): δ_H 7.37-7.33 (m, 4H), 7.30-7.27 (m, 1H), 5.87-5.76 (m, 1H), 5.20-5.13 (m, 2H), 4.76-4.73 (m, 1H), 2.58-2.46 (m, 2H), 2.07 (s, 1H) ppm

¹³C NMR (100 MHz, CDCl₃): δ_C 144.0, 134.6, 128.5, 127.6, 125.9, 118.3, 73.4, 43.8 ppm

HPLC data
- Column: Chiralcel OD (4.6 mm x 250 mm)
- Enantiomeric excess: 83% [(S)-3c]
- Retention time: t_R = 15.7 min, t_S = 18.1 min
- Mobile phase (hexanes: isopropanol): 98:2
- Flow rate: 1 mL/min
- Wavelength (λ): 220 nm

2.5.5.4. Reaction of 1d with 2b in presence of (+)-35 (Table 9, Entry 4)

Following the general procedure, the 9-anthracenecarboxaldehyde (51.5 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(anthracen-9-yl)but-3-en-1-ol 3d as a pale yellow semi solid after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (–)-3d was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.
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Yield : 38.5 mg (62%)

IR (neat, cm⁻¹) : 3416, 3050, 2924, 2855, 1665, 1445, 1304, 1285, 1033, 917, 731

¹H NMR (400 MHz, CDCl₃) : δ_H 8.67-8.66 (m, 2H), 8.41 (s, 1H), 8.02-8.00 (m, 2H), 7.52-7.44 (m, 4H), 6.33-6.29 (m, 1H), 6.02-5.92 (m, 1H), 5.28-5.23 (m, 1H), 5.17-5.14 (m, 1H), 3.25-3.17 (m, 1H), 2.90-2.83 (m, 1H), 2.38 (d, J = 2.0 Hz, 1H) ppm

¹³C NMR (100 MHz, CDCl₃) : δ_C 135.3, 134.1, 131.8, 129.4, 129.3, 128.3, 125.7, 124.9, 118.0, 70.7, 42.2 ppm

HPLC data : Column : Chiralcel AD-H (4.6 mm x 250 mm)
Enantiomeric excess : 92% [(S)-3d]
Retention time : t_R = 16.8 min, t_S = 20.0 min
Mobile phase (hexanes:isopropanol) : 95:5
Flow rate : 1 mL/min
Wavelength (λ) : 220 nm

2.5.5.5. Reaction of 1e with 2b in presence of (+)-35 (Table 9, Entry 5)

Following the general procedure, the piperonal (37.5 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)- 1-(benzo[d][1,3]dioxol-5-yl)but-3-en-1-ol 3e as a pale yellow oil after silica gel column purification (hexane/ethyl acetate = 85:15).

*The configuration of the homoallylic alcohol (−)-3e was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.*

Yield : 27.8 mg (58%)

IR (neat, cm⁻¹) : 3386 (br), 3076, 2979, 1641,1609, 1504, 1443, 1041, 927, 813

¹H NMR (400 MHz, CDCl₃) : δ_H 6.87 (d, J = 0.8 Hz, 1H), 6.81-6.76 (m, 2H), 5.95 (s, 2H), 5.79 (ddt, J = 17.6, 10.4, 7.2 Hz, 1H), 5.18-5.12 (m, 2H), 4.66-4.63 (m, 1H), 2.49-2.45 (m, 2H), 2.04 (s, 1H) ppm

¹³C NMR (100 MHz, CDCl₃) : δ_C 147.9, 147.0, 138.1, 134.5, 119.3, 118.5, 108.2, 106.5, 101.1, 73.3, 44.0 ppm

HPLC data : Column : Chiralcel OD (4.6 mm x 250 mm)
Enantiomeric excess : 81% [(S)-3e]
Retention time : t_R = 25.5 min, t_S = 28.2 min
Mobile phase (hexanes:isopropanol) : 98:2
Flow rate : 1 mL/min
Wavelength (λ) : 220 nm
2.5.5.6. Reaction of 1f with 2b in presence of (+)\-35 (Table 9, Entry 6)

Following the general procedure, the 3,4-dimethoxybenzaldehyde (41.5 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(3,4-dimethoxyphenyl)but-3-en-1-ol 3f as a colourless solid after silica gel column purification (hexane/ethyl acetate = 75:25).

The configuration of the homoallylic alcohol (\(-\))\-3f was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40e

| Yield       | : 42.1 mg (81%) |
| IR (KBr, cm\(^{-1}\)) | : 3400 (br), 3068, 2958, 2910, 1641, 1518, 1462, 1024, 922, 804 |
| Mp          | : 93-95 \(^\circ\)C       |
| \(^1\)H NMR (400 MHz, CDCl\(_3\)) | : \(\delta\)\(_\text{H}\) 6.92 (d, \(J = 1.6\) Hz, 1H), 6.89-6.86 (m, 1H), 6.83 (d, \(J = 8.4\) Hz, 1H), 5.80 (ddt, \(J = 17.6, 10.4, 7.2\) Hz, 1H), 5.19-5.11 (m, 2H), 4.68 (t, \(J = 6.4\) Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 2.52-2.48 (m, 2H), 2.06 (s, 1H) ppm |
| \(^13\)C NMR (100 MHz, CDCl\(_3\)) | : \(\delta\)\(_\text{C}\) 149.1, 148.5, 136.7, 134.7, 118.4, 118.2, 111.1, 109.1, 73.3, 56.1, 56.0, 43.9 ppm |
| HPLC data   | Column : Chiralcel AS (4.6 mm x 250 mm) |
|             | Enantiomeric excess : 94\% [(S)-3f] |
|             | Retention time : \(t_S = 15.4\) min, \(t_R = 16.8\) min |
|             | Mobile phase : 99.5:0.5 |
|             | (hexanes: isopropanol) |
|             | Flow rate : 0.75 mL/min |
|             | Wavelength (\(\lambda\)) : 220 nm |

2.5.5.7. Reaction of 1g with 2b in presence of (+)\-35 (Table 9, Entry 7)

Following the general procedure, the 4-nitrobenzaldehyde (37.8 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(4-nitrophenyl)but-3-en-1-ol 3g as a yellow oil after silica gel column purification (hexane/ethyl acetate = 75:25).

The configuration of the homoallylic alcohol (\(-\))\-3g was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40f

| Yield       | : 22.7 mg (47%) |
| IR (neat, cm\(^{-1}\)) | : 3424 (br), 3078, 2931, 2853, 1641, 1605, 1518, 1347, 1109, 1055, 921, 854 |
| \(^1\)H NMR | : \(\delta\)\(_\text{H}\) 8.22 (d, \(J = 8.8\) Hz, 2H), 7.54 (d, \(J = 8.8\) Hz, 2H), 5.84-5.74 (m, 1H), 5.22-5.17 (m, 2H), 4.89-4.85 (m, 1H), 2.60-2.54 (m,
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(400 MHz, CDCl₃) 1H), 2.49-2.42 (m, 1H), 2.20 (d, J = 3.2 Hz, 1H) ppm

¹³C NMR:  δC 151.2, 147.4, 133.3, 126.7, 123.7, 119.7, 72.3, 44.0 ppm

HPLC data : Column: Chiralcel AD-H (4.6 mm x 250 mm)
Enantiomeric excess: 25% [(S)-3g]
Retention time: tₘ = 46.0 min, tₛ = 48.4 min
Mobile phase (hexanes: isopropanol) 20:1
Flow rate: 0.4 mL/min
Wavelength (λ): 220 nm

2.5.5.8. Reaction of 1h with 2b in presence of (+)-35 (Table 9, Entry 8)

Following the general procedure, the 4-chlorobenzaldehyde (35.1 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(4-chlorophenyl)but-3-en-1-ol 3h as a colourless oil after silica gel column purification (hexane/ethyl acetate = 85:15).

The configuration of the homoallylic alcohol (−)-3h was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.⁴⁰f

Yield: 44.6 mg (98%)
IR (neat, cm⁻¹): 3386 (br), 3078, 2979, 2932, 1641, 1597, 1500, 1493, 1411, 1014, 919, 830

¹H NMR: δH 7.33-7.28 (m, 4H), 5.83-5.73 (m, 1H), 5.19-5.14 (m, 2H), 4.72 (dd, J = 7.6, 5.2 Hz, 1H), 2.54-2.41 (m, 2H), 2.12 (s, 1H) ppm

¹³C NMR: δC 142.4, 134.1, 133.3, 128.7, 127.3, 119.0, 72.7, 44.0 ppm

HPLC data: Column: Chiralcel OJ-H (4.6 mm x 250 mm)
Enantiomeric excess: 76% [(S)-3h]
Retention time: tₛ = 21.6 min, tₘ = 23.9 min
Mobile phase (hexanes: isopropanol) 98:2
Flow rate: 0.7 mL/min
Wavelength (λ): 210 nm

2.5.5.9. Reaction of 1i with 2b in presence of (+)-35 (Table 9, Entry 9)

Following the general procedure, the 2-thiophenecarboxaldehyde (28 mg, 0.25 mmol) furnished the homoallylic alcohol, (R)-1-(thiophen-2-yl)but-3-en-1-ol 3i as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).
The configuration of the homoallylic alcohol (+)-3i was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\textsuperscript{40c}

<table>
<thead>
<tr>
<th>Yield</th>
<th>27.3 mg (71%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (neat, cm(^{-1}))</td>
<td>3387 (br), 3075, 2930, 2906, 1641, 1435, 1035, 918, 851</td>
</tr>
<tr>
<td>(^1)H NMR (400 MHz, CDCl(_3))</td>
<td>(\delta_H) 7.25 (dd, (J = 4.4, 1.6) Hz, 1H), 6.99-6.96 (m, 2H), 5.83 (ddt, (J = 17.6, 10.4, 7.2) Hz, 1H), 5.22-5.14 (m, 2H), 5.00-4.96 (m, 1H), 2.64-2.60 (m, 2H), 2.32 (s, 1H) ppm</td>
</tr>
<tr>
<td>(^{13})C NMR (100 MHz, CDCl(_3))</td>
<td>(\delta_C) 147.9, 133.9, 126.7, 124.6, 123.8, 118.7, 69.4, 43.8 ppm</td>
</tr>
</tbody>
</table>

**HPLC data**
- Column: Chiralcel OJ-H (4.6 mm x 250 mm)
- Enantiomeric excess: 92\% [(R)-3i]
- Retention time: \(t_R = 20.8\) min, \(t_S = 23.3\) min
- Mobile phase: (hexanes: isopropanol)
- Flow rate: 0.5 mL/min
- Wavelength (\(\lambda\)): 220 nm

2.5.5.10. Reaction of 1j with 2b in presence of (+)-35 (Table 9, Entry 10)

Following the general procedure, the 3-thiophenecarboxaldehyde (28 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(thiophen-3-yl)but-3-en-1-ol 3j as a pale yellow oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (–)-3j was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\textsuperscript{40g}

<table>
<thead>
<tr>
<th>Yield</th>
<th>25.8 mg (67%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (neat, cm(^{-1}))</td>
<td>3389 (br), 3077, 2907, 1641, 1418, 1053, 914, 852</td>
</tr>
<tr>
<td>(^1)H NMR (400 MHz, CDCl(_3))</td>
<td>(\delta_H) 7.30 (dd, (J = 5.0, 3.0) Hz, 1H), 7.20-7.19 (m, 1H), 7.08 (dd, (J = 5.0, 1.2) Hz, 1H), 5.81 (ddt, (J = 17.6, 10.4, 7.2) Hz, 1H), 5.20-5.13 (m, 2H), 4.83 (dd, (J = 7.6, 5.2) Hz, 1H), 2.60-2.50 (m, 2H), 2.02 (s, 1H) ppm</td>
</tr>
<tr>
<td>(^{13})C NMR (100 MHz, CDCl(_3))</td>
<td>(\delta_C) 145.5, 134.3, 126.1, 125.7, 120.8, 118.5, 69.7, 43.0 ppm</td>
</tr>
</tbody>
</table>

**HPLC data**
- Column: Chiralcel OD (4.6 mm x 250 mm)
- Enantiomeric excess: 89\% [(S)-3j]
- Retention time: \(t_R = 11.3\) min, \(t_S = 11.7\) min
Mobile phase 95:5
(hexanes: isopropanol)
Flow rate 0.8 mL/min
Wavelength (λ) 220 nm

2.5.5.11. Reaction of 1k with 2b in presence of (+)-35 (Table 9, Entry 11)

Following the general procedure, the 2-furancarboxaldehyde (24 mg, 0.25 mmol) furnished the homoallylic alcohol, (R)-1-(2-furan-2-yl)-but-3-en-1-ol 3k as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (+)-3k was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\(^{40h}\)

Yield : 17.9 mg (52%)
IR (neat, cm\(^{-1}\)) : 3396 (br), 3078, 2912, 1643, 1434, 1061, 921, 861
\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta_H 7.37\) (d, \(J = 0.8\) Hz, 1H), 6.33-6.32 (m, 1H), 6.24 (d, \(J = 3.2\) Hz, 1H), 5.80 (ddt, \(J = 17.6, 10.4, 7.2\) Hz, 1H), 5.19-5.12 (m, 2H), 4.74 (t, \(J = 6.4\) Hz, 1H), 2.68-2.57 (m, 2H), 2.20 (s, 1H) ppm
\(^13\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta_C 156.2, 142.1, 133.8, 118.6, 110.2, 106.2, 67.1, 40.2\) ppm

HPLC data : Column Chiralcel AD-H (4.6 mm x 250 mm)
Enantiomeric excess : 93\% [(R)-3k]
Retention time : \(t_S = 65.5\) min, \(t_R = 69.9\) min
Mobile phase : 99.5:0.5
(hexanes: isopropanol)
Flow rate : 0.5 mL/min
Wavelength (λ) : 220 nm

2.5.5.12. Reaction of 1l with 2b in presence of (+)-35 (Table 9, Entry 12)

Following the general procedure, the trans-cinnamaldehyde (33 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-(E)-1-Phenylhexa-1,5-dien-3-ol 3l as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (−)-3l was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\(^{40h}\)
**Yield**: 16.1 mg (37%)

**IR (neat, cm⁻¹)**: 3420 (br), 2952, 2924, 1636, 1461, 967, 750, 916, 696

**¹H NMR (400 MHz, CDCl₃)**: δ_H 7.39-7.37 (m, 2H), 7.33-7.29 (m, 2H), 7.25-7.21 (m, 1H), 6.60 (dd, J = 16.0, 0.4 Hz, 1H), 6.24 (dd, J = 16.0, 6.4 Hz, 1H), 5.86 (ddt, J = 17.6, 10.4, 7.2 Hz, 1H), 5.21-5.14 (m, 2H), 4.38-4.33 (m, 1H), 2.48-2.34 (m, 2H), 1.92 (br. s, 1H) ppm

**¹³C NMR (100 MHz, CDCl₃)**: δ_C 136.8, 134.2, 131.7, 130.5, 128.7, 127.8, 126.6, 118.6, 71.8, 42.1 ppm

**HPLC data**: Column: Chiralcel OD (4.6 mm x 250 mm)
Enantiomeric excess: 71% [([S]-3l]
Retention time: t_R = 8.4 min, t_S = 13.3 min
Mobile phase (hexanes: isopropanol): 90:10
Flow rate: 1 mL/min
Wavelength (λ): 254 nm

2.5.5.13. Reaction of 1m with 2b in presence of (→)+35 (Table 9, Entry 13)

Following the general procedure, the cyclohexanecarboxaldehyde (28 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-cyclohexylbut-3-en-1-ol 3m as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (→)-3m was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.⁴⁰j

**Yield**: 24.7 mg (64%)

**IR (neat, cm⁻¹)**: 3405 (br), 3075, 2916, 2852, 1640, 1450, 892

**¹H NMR (400 MHz, CDCl₃)**: δ_H 5.88-5.78 (m, 1H), 5.15-5.10 (m, 2H), 3.40-3.35 (m, 1H), 2.35-2.28 (m, 1H), 2.15-2.08 (m, 1H), 1.87-1.62 (m, 6H), 1.38-0.96 (m, 6H) ppm

**¹³C NMR (100 MHz, CDCl₃)**: δ_C 135.6, 118.0, 74.9, 43.2, 38.9, 29.2, 28.2, 26.6, 26.4, 26.3 ppm

**HPLC data**: Column: Chiralcel OD (4.6 mm x 250 mm)
Enantiomeric excess: 33% [([S]-3m]
Retention time: t_R = 7.4 min, t_S = 7.8 min
Mobile phase (hexanes: isopropanol): 99.9:0.1
Flow rate : 1 mL/min
Wavelength (λ) : 220 nm

2.5.5.14. Reaction of 1a with 2c in presence of (–)-35 (Scheme 13)

Crotyltetrachlorosilane (71 mg, 0.38 mmol, E/Z: 82/18)\(^{51}\) was added drop-wise to the solution of catalyst (+)-35 (26.8 mg, 0.05 mmol), diisopropylethylamine (0.21 mL, 1.25 mmol), \textit{t}etra-\textit{n}-butylammonium iodide (92.3 mg, 0.25 mmol) and 4-methoxybenzaldehyde 1a (0.25 mmol) in 1:1 mixture of chloroform: tetrachloroethane (0.76 mL) under nitrogen atmosphere at -78 °C with stirring. After 24 h the reaction mixture was quenched with aqueous saturated NaHCO\(_3\) (2 mL). Organic layer was separated and then the aqueous layer was extracted with diethyl ether (5 mL \(\times\) 3). The combined organic layer was washed with brine, dried over anhydrous Na\(_2\)SO\(_4\), filtered and the solvent was evaporated in rotary evaporator under reduced pressure. The residue was purified through silica gel column chromatography (hexane/ethyl acetate = 90:10) to afford the homoallylic alcohol (1\(R\),2\(R\))-1-(4-methoxyphenyl)-2-methyl-3-en-1-ol 36 as a colourless oil.

\textit{The configuration of the homoallylic alcohol (+)-36 was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.\(^{40k}\)}

\begin{itemize}
  \item **Yield** : 30.2 mg (64%)
  \item **IR (neat, cm\(^{-1}\))** : 3449, 3077, 2972, 2932, 2836, 1639, 1612, 1513, 1461, 831
  \item **\(^1\)H NMR (400 MHz, CDCl\(_3\))** : \(\delta\)H 7.27-7.21 (m, 2H), 6.90-6.86 (m, 2H), 5.80 (ddd, \(J = 17.2, 10.0, 8.0\) Hz, 1H), 5.23-5.16 (m, 2H), 4.30 (d, \(J = 8.0\) Hz, 1H), 3.80 (s, 3H), 2.52-2.35 (m, 1H), 0.85 (d, \(J = 6.8\) Hz, 3H) ppm
  \item **\(^1\)C NMR (100 MHz, CDCl\(_3\))** : \(\delta\)C 158.9, 140.4, 134.8, 127.7, 115.4, 113.5, 77.1, 55.3, 44.7, 14.4 ppm
  \item **HPLC data** : Column : Chiralcel AD-H (4.6 mm x 250 mm)
    Diastereomeric ratio : 81:19 (anti/syn)
    Enantiomeric excess : 83%
    Retention time : \(t\text{R,R} = 43.7\) min, \(t\text{S,S} = 54.0\) min
    Mobile phase (hexanes: isopropanol) : 96:4
    Flow rate : 0.3 mL/min
    Wavelength (λ) : 230 nm
\end{itemize}
2.5.6. Synthesis of \( C_2 \)-symmetric bipyridine derivative (--)\textsuperscript{-39} 

Zinc powder (309 mg, 4.76 mmol) was added to a stirred solution of NiCl\(_2\) (617 mg, 4.76 mmol) and triphenylphosphine (4.99 g, 19.04 mmol) in degassed solution of degassed dry DMF (100 mL) under N\(_2\) atmosphere at 70 °C. The mixture stirred for 2 h, during which period the colour changed from blue to red. Then a solution of (--)\textsuperscript{-22} (1.85 g, 4.76 mmol) in DMF (5 mL) was added. After heating for 12 h at 50 °C, the reaction mixture was poured into 10% aqueous ammonia solution (20 mL) and extracted with dichloromethane (3 x 40 mL). The combined organic layer was removed under reduced pressure to afford the colourless solid. The crude material was purified through silica gel column chromatography using hexane/ethyl acetate (90:10) as eluent to afford (--)\textsuperscript{-39} as a colourless solid.

Yield: 1.33 g (79%)

\([\alpha]_D^{25}\) : -351.35 (c 0.50, CHCl\(_3\))

Mp: 132-134 °C

IR (KBr, cm\(^{-1}\)) : 3023, 2976, 2929, 1732, 1459, 1263, 1221, 750

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta\)H 7.54-7.43 (m, 4H), 7.40-7.31 (m, 6H), 7.19-7.12 (m, 6H), 7.03-6.96 (m, 4H), 6.94-6.88 (m, 2H), 4.83 (d, \(J = 2.2\) Hz, 2H), 4.44 (d, \(J = 2.2\) Hz, 2H), 3.64 (dd, \(J = 5.4, 2.2\) Hz, 2H), 1.18 (t, \(J = 7.2\) Hz, 6H) ppm (Spectrum No. 25)

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta\)C 173.4, 160.2, 155.1, 144.0, 143.0, 141.0, 140.7, 136.7, 126.4, 126.1, 126.0, 125.80, 125.77, 125.0, 123.5, 123.4, 122.6, 119.0, 60.8, 51.1, 50.5, 49.9, 47.5, 14.4 ppm (Spectrum No. 26)

HRMS-ESI (m/z) : Found 709.3088 and calculated 709.3066 for \(C_{48}H_{41}N_2O_4^+\) (M+H)

2.5.7. Synthesis of bipyridine mono N-oxide (--)\textsuperscript{-40} and bipyridine N,N'-dioxide (--)\textsuperscript{-38}

To the stirred solution of compound (--)\textsuperscript{-39} (1.29 g, 1.82 mmol) in CH\(_2\)Cl\(_2\) (10 mL) at 0 °C, \(m\)-chloroperbenzoic acid (70%, 0.94 g, 5.46 mmol) in CH\(_2\)Cl\(_2\) (20 mL) was added drop-wise via double ended needle at 0 °C and the mixture was stirred at 0 °C for 12 h under the atmosphere of nitrogen. The reaction mixture was washed with saturated NaHCO\(_3\) (15 mL x 3) and the aqueous layer was extracted with dichloromethane (20 mL.
× 3). The combined organic layer was washed with brine, dried over anhydrous MgSO₄ and filtered. The solvent was evaporated under reduced pressure. The resulting residue was purified through silica gel column chromatography using hexane/ethyl acetate (30:70) as eluent to afford (-)-40 and (-)-38 as pale yellow colour solid.

**Data for the compound (-)-40**

- **Yield**: 0.13 g (10%)
- **[α]D²⁵**: -171.07 (c 1.00, CHCl₃)
- **Mp**: 138-140 °C
- **IR (KBr, cm⁻¹)**: 3069, 2957, 1731, 1570, 1467, 1267, 835, 750
- **¹H NMR (400 MHz, CDCl₃)**: δ_H 8.70 (dd, J = 7.8, 0.6 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.45-7.39 (m, 3H), 7.37-7.28 (m, 4H), 7.18-7.09 (m, 6H), 7.02 (td, J = 7.2, 1.2 Hz, 1H), 6.95 (td, J = 7.2, 1.2 Hz, 1H), 6.91 (d, J = 7.2 Hz, 1H), 6.84-6.82 (m, 2H), 6.76 (t, J = 7.8 Hz, 1H), 6.00 (dd, J = 8.0, 2.0 Hz, 1H), 4.84 (d, J = 2.4 Hz, 1H), 4.80 (d, J = 2.8 Hz, 1H), 4.78 (dd, J = 5.6, 2.2 Hz, 1H), 4.56 (d, J = 2.4 Hz, 1H), 4.35 (d, J = 2.4 Hz, 1H), 4.13-3.99 (m, 4H), 3.89 (dd, J = 5.2, 2.4 Hz, 1H), 3.80 (dd, J = 5.2, 2.4 Hz, 1H), 2.94 (dd, J = 5.6, 2.8 Hz, 1H), 1.91 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H) ppm
- **¹³C NMR (100 MHz, CDCl₃)**: δ_C 173.2, 172.2, 160.5, 153.0, 149.0, 147.5, 143.7, 143.2, 143.0, 142.4, 140.9, 140.7, 139.8, 136.5, 126.7, 126.5, 126.4, 126.24, 126.18, 126.1, 126.0, 125.7, 125.6, 125.1, 125.0, 124.2, 123.9, 123.6, 123.51, 123.46, 122.8, 61.1, 60.9, 51.8, 50.7, 49.9, 49.8, 47.5, 47.4, 46.7, 41.6, 14.4, 14.3 ppm
- **HRMS-ESI (m/z)**: Found 725.3016 and calculated 725.3015 for C₄₈H₄₁N₂O₅⁺ (M+H)

**Data for the compound (-)-38**

- **Yield**: 1.09 g (81%)
- **[α]D²⁵**: -346.75 (c 1.00, CHCl₃)
- **Mp**: 157-159 °C
- **IR (KBr, cm⁻¹)**: 3069, 3041, 2977, 1732, 1468, 1458, 1253, 1221, 844, 749
1H NMR (400 MHz, CDCl₃) : δ_H 7.53 (dd, J = 7.6, 1.6 Hz, 2H), 7.45-7.42 (m, 4H), 7.30-7.28 (m, 2H), 7.20-7.10 (m, 6H), 7.06-7.05 (m, 4H), 6.95 (t, J = 8.0 Hz, 2H), 6.16 (dd, J = 8.0, 2.0 Hz, 2H), 4.79 (d, J = 2.8 Hz, 2H), 4.77 (dd, J = 5.6, 2.4 Hz, 2H), 4.68 (d, J = 2.4 Hz, 2H), 4.02 (q, J = 7.2 Hz, 4H), 2.97 (dd, J = 5.6, 2.8 Hz, 2H), 1.11 (t, J = 7.2 Hz, 6H) ppm (Spectrum No. 27)

13C NMR (100 MHz, CDCl₃) : δ_C 172.1, 153.4, 142.9, 142.8, 142.4, 140.9, 139.9, 126.7, 126.6, 126.34, 126.28, 126.2, 124.9, 124.3, 124.1, 123.7, 123.4, 61.2, 50.8, 47.6, 46.7, 41.5, 29.8, 14.3 ppm (Spectrum No. 28)

HRMS-ESI (m/z) : Found 741.2904 and calculated 741.2965 for C₄₈H₄₁N₂O₆⁺ (M+H)

2.5.8. General procedure for allylation of aldehydes in presence of (–)-38 (0.5 mol%)

Allyltrichlorosilane (44 µL, 0.3 mmol) was added drop-wise to the solution of catalyst (–)-38 (0.93 mg, 0.00125 mmol), diisopropylethylamine (0.13 mL, 0.75 mmol), tetra-n-butylammonium iodide (92.3 mg, 0.25 mmol) and aldehyde 1 (0.25 mmol) in dichloromethane (0.8 mL) under nitrogen atmosphere at −40 °C. The reaction mixture was stirred at −40 °C until the reaction was complete (as monitored by TLC). After appropriate time the reaction mixture was quenched with aqueous saturated NaHCO₃ (2 mL). Organic layer was separated and then the aqueous layer was extracted with diethyl ether (5 mL × 3). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated in rotary evaporator under reduced pressure. The residue was purified through silica gel column chromatography to afford the homoallylic alcohols.

2.5.8.1. Reaction of 1a with 2b in presence of (–)-38 (Table 15, Entry 1)

Following the general procedure, the 4-methoxybenzaldehyde (34 mg, 0.25 mmol) furnished the homoallylic alcohol, (R)-1-(4-methoxyphenyl)but-3-en-1-ol in 41 mg (92%, 58% ee) as a colourless oil after silica gel column purification (hexane/ethyl acetate = 85:15).

The configuration of the homoallylic alcohol (+)-3a was assigned by comparing the reported retention time of the literature data of HPLC chromatogram.⁴⁰a
2.5.8.2. Reaction of 1c with 2b in presence of (−)-38 (Table 15, Entry 2)

Following the general procedure, the benzaldehyde (26.5 mg, 0.25 mmol) furnished the homoallylic alcohol, (R)-1-(phenyl)but-3-en-1-ol 3c in 31 mg (84%, 35% ee) as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (+)-3c was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40b

2.5.8.3. Reaction of 1g with 2b in presence of (−)-38 (Table 15, Entry 3)

Following the general procedure, the 4-nitrobenzaldehyde (37.8 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(4-nitrophenyl)but-3-en-1-ol 3g in 41.5 mg (86%, 25% ee) as a yellow oil after silica gel column purification (hexane/ethyl acetate = 75:25).

The configuration of the homoallylic alcohol (−)-3g was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40f

2.5.8.4. Reaction of 1i with 2b in presence of (−)-38 (Table 15, Entry 4)

Following the general procedure, the 2-thiophene carboxaldehyde (28 mg, 0.25 mmol) furnished the homoallylic alcohol, (S)-1-(thiophen-2-yl)but-3-en-1-ol 3i in 29.3 mg (76%, 62% ee) as a colourless oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (−)-3i was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40c

2.5.8.5. Reaction of 1j with 2b in presence of (−)-38 (Table 15, Entry 5)

Following the general procedure, the 3-thiophene carboxaldehyde (28 mg, 0.25 mmol) furnished the homoallylic alcohol, (R)-1-(thiophen-3-yl)but-3-en-1-ol in 34.5 mg (87%, 82% ee) as a pale yellow oil after silica gel column purification (hexane/ethyl acetate = 90:10).

The configuration of the homoallylic alcohol (+)-3j was assigned by comparing the reported retention time of the literature data of HPLC chromatogram. 40g
2.6. REFERENCES


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References


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41. These crystallographic data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. and CCDC numbers for the crystals, (a) (+)-22 = CCDC No.: 862192; (b) (+)-23 CCDC No.: 862198; (c) (+)-25a = CCDC No.: 862194; (d) (−)-25c = CCDC No.: 862197; (e) (−)-26b = CCDC No.: 862196; (f) (−)-28 = CCDC No.: 862193; (g) (+)-33 = CCDC No.: 862195.


44. Prepared as an 82/18 trans/cis mixture via the CuCl-catalysed reaction of crotol bromide with HSiCl3.

45. Theoretical studies are in progress to ascertain this hypothesis.


