Chapter 6

A synthetic approach for the enantiopure bromohydrins using Evans chiral auxiliary as chiral precursor and TsNBr₂ as brominating agent
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6.1. Introduction

Asymmetric synthesis, the science and art of assembling complex molecules as single enantiomers from relatively simple starting materials, is a critical topic in modern organic chemistry.¹⁻² Nowadays enantiomerically pure compounds are in widespread use. Pharmaceuticals, vitamins, agrochemicals, flavors, and fragrances are often from multifunctional molecules bearing stereocenters.³ In the pharmaceutical industry, for example, single enantiomer drugs have become increasingly important; currently almost all newly introduced chiral drugs are marketed as single enantiomers.⁴ There are four general approaches to the selective synthesis of one enantiomeric form of a target molecule. They involve (i) resolution, (ii) use of “chiral pool” starting materials, (iii) temporary installation of chiral auxiliaries, and (iv) asymmetric catalysis.⁵⁻⁶ The use of chiral auxiliaries in the synthesis of enantiomerically pure compounds has found wide application for a variety of reactions over the last three decades. Despite the extensive developments in this area by many academic and industrial research groups, new auxiliary controlled reactions continue to evolve frequently.⁷⁻⁸ One of the most utilized type of auxiliaries is the class of chiral oxazolidinones initially developed in the Evans group.⁹ Although a number of chiral auxiliaries have been developed the class of chiral oxazolidinones developed by David Evans has proved to be the gold standard to which all others are compared.¹⁰⁻¹¹ These chiral imides have been applied to a wide range of asymmetric transformations and the methodology developed has been most successful in the stereoselective construction of numerous chiral
building blocks, as well as natural products, antibiotics and medicinally important compounds.

Vicinal halohydrins are versatile building blocks and key intermediates for the synthesis of many bioactive compounds, and the development of methods for their asymmetric synthesis has therefore attracted much attention.\textsuperscript{12-14} Though a number of methods are known, there is still need of a general approach to the enantioselective synthesis of cyclic \textit{cis} vicinal halohydrins.
6.2. Review of literature

Potentially asymmetric halohydroxylation of alkenes is a very straightforward method. But, in literature limited examples are found. In 1998, El-Qisairi et al. first reported palladium(II)-catalyzed enantioselective hydroxychlorination of terminal alkenes with a metal chloride-mechanistically it is a hydroxychlorination to alkenes and there is no involvement of halonium (X⁺) intermediate. Pd (II) catalysts containing chiral auxiliaries produced optically active products. They used monodentate chiral amines such as (CH₃)₂C*NH(CH₃)Ph (Scheme 6.1).¹⁵

Scheme 6.1

Sudalai et al. described NaIO₄ mediated oxidative enantioselective halohydrination of alkenes (encapsulated in β-cyclodextrin) using alkali metal halides with moderate enantioselectivity.¹⁶

Barluenga et al describe a novel strategy to propagate the chirality of a terpene through the combination of the powerful chemistry of boroxycarbene complexes to activate C-H bonds with the ability of IPy₂BF₄ reagent in addition reactions to unsaturated systems (Scheme 6.2).¹⁷

Scheme 6.2

Later Hajra et al. reported silver (I)-promoted asymmetric halohydrin reaction of chiral N-enoyl-2-oxazolidinones.¹⁸

There are a few methods for the stereoselective synthesis of the α-halo-β hydroxycarboxylic acid derivatives. Reagent controlled aldol reaction of chiral α-halogenated
imide enolates with suitable aldehydes provide selectively both anti- and syn-α halo-β-hydroxycarboxylic acid derivatives.\textsuperscript{19}

Zaidlewicz et al prepared asymmetric bromohydrins as intermediate compound for asymmetric synthesis of (S)-bufuralol and a propafenone analogue.\textsuperscript{20} Yanagi et al. synthesised optically active bromohydrin by the asymmetric borane reduction of the prochiral phenacyl bromide using a catalyst prepared from aluminum triethoxide and a chiral amino alcohol.\textsuperscript{21} Raghavan et al. synthesised bromohydrins from β-Methyl-γ,δ-unsaturated sulfoxides with high 1,2-asymmetric induction.\textsuperscript{22} Hull et al. investigated the asymmetric reduction of a bromomethyl ketone with oxazaborolidine under a variety of conditions. The best results were obtained using 20 mole percent of the oxazaborolidine catalyst while performing the reaction at room temperature (Scheme 6.3).\textsuperscript{23}

![Scheme 6.3](image)

Similarly, Zaidlewicz et al. also synthesised chlorohydrins by enantioselective reduction of benzofuryl halomethyl ketones.\textsuperscript{24} Rodrigues did bioreduction of 3-bromo-2-oxoalkanoates with Saccharomyces cerevisiae entrapped in calcium alginate pellets with double gel layers, syn-(2R,3S)-β-bromo-α-hydroxy esters were obtained regioselectively in high yields and high ee.\textsuperscript{25}

Ros et al. synthesised vicinal halohydrins via dynamic kinetic resolution method. Expanding the scope of enantioselective catalysis via DKR, transfer hydrogenation of a variety of cyclic α-halo ketones was accomplished using the Noyori/Ikariya (R,R)- or (S,S)-I catalysts and either HCO$_2$H/Et$_3$N or HCO$_2$Na/n-Bu$_4$NBr in H$_2$O/CH$_2$Cl$_2$ as the hydrogen sources. Good yields of vicinal bromo-, chloro-, and fluorohydrins with excellent de and ee levels were achieved in most cases after a simple tuning of reaction conditions.\textsuperscript{26} Another method of bromohydrin synthesis is the ring opening reaction of epoxides. For this chiral lewis base is used. For example, the ring opening of meso epoxides using enantiomerically pure chiral phosphoramides with SiCl$_4$ affords enantiomerically enriched chlorohydrins in excellent yield.\textsuperscript{27} The NaIO$_4$ -mediated asymmetric bromohydroxylation of α,β-unsaturated carboxamides was achieved using lithium bromide as the bromine source under acidic
conditions at room temperature to afford the corresponding chiral α-bromo-β-hydroxy carboxamide.\textsuperscript{28}

Lewis acid Yb(OTf)\textsubscript{3} catalyzed asymmetric halohydrin reactions (halohydroxylation as well as halomethoxylation) of chiral α,β-unsaturated carboxylic acid derivatives were also performed using \textit{N}-halosuccinimide (NXS; X = Br, I) as the halogen source.\textsuperscript{29}
6.3. Present work

6.3.1. Objective

Very few numbers of works are reported in this regard and the known methods are also not free from drawbacks. Therefore, we thought for a better method using chiral auxiliary. Our group had already developed a stereoselective bromohydroxylation method using TsNBr$_2$.\textsuperscript{30} So, under a suitable experimental condition it is possible to synthesize chiral bromohydrins using this existing methodology. In this regard, we intended a possible pathway for the synthesis of enantiopure bromohydrins. We have chosen chiral precursor such as Evans Chiral auxiliary for the synthesis of optically pure bromohydrins (Scheme 6.4).

\[
\begin{align*}
\text{R} \overset{\text{(COCl)}_2}{\longrightarrow} \text{R} \overset{\text{DCM}}{\longrightarrow} \text{R} \overset{\text{Ph}}{\longrightarrow} \text{R} \overset{\text{BuLi, THF}}{\longrightarrow} \\
\text{O} \overset{\text{BuLi, THF}}{\longrightarrow} \text{N} \overset{\text{BuLi, THF}}{\longrightarrow} \text{O} \overset{\text{BuLi, THF}}{\longrightarrow} \\
\text{H} \overset{\text{BuLi, THF}}{\longrightarrow} \text{Br} \overset{\text{BuLi, THF}}{\longrightarrow} \\
\text{O} \overset{\text{BuLi, THF}}{\longrightarrow} \text{N} \overset{\text{BuLi, THF}}{\longrightarrow} \text{O} \overset{\text{BuLi, THF}}{\longrightarrow}
\end{align*}
\]

Scheme 6.4
6.3.2. Results and discussion

The experiment started with the preparation of the acid chlorides from various acids containing a double bond. Initially, 2-butenoic acid was taken for study. For this, 1 equiv. of acid was dissolved in dichloromethane and then 2 equiv. of oxalyl chloride was added to it under nitrogen atmosphere. The mixture was stirred at room temperature to give the acid chloride. In the second step of the reaction the acid chloride was coupled with the chiral auxiliary ((S)-4-(Phenylmethyl)-2-oxazolidinone). The chiral auxiliary (S)-4-(Phenylmethyl)-2-oxazolidinone was prepared using a literature procedure.\textsuperscript{31} The coupling reaction was done in presence of BuLi following the procedure available in literature.\textsuperscript{32} After the isolation of the coupled product, we have tried for the bromohydrine product. To a solution of olefin (1.1 mmol) in acetonitrile-water (4:1) (5 ml) was added TsNBr\textsubscript{2} (1.2 mmol) at room temperature. But, the results were not satisfactory. Therefore it was again examined at low temperature (-40°C) modifying the acetonitrile-water ratio to 9:1. This ratio was modified since at high water ratio, the reaction mixture was solidified at low temperature. The reaction was instantaneous and after 5 minutes stirring it was taken to room temperature and again stirred for another 10 minutes. The reaction was taken up in ethyl acetate and purified by column chromatography. Then the reaction was extended with various cinnamic acids (Table 6.1).

Table 6.1 synthesis of enantiopure bromohydrins

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield\textsuperscript{a}</th>
</tr>
</thead>
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<td>1</td>
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<td>m-BrC\textsubscript{6}H\textsubscript{4}</td>
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<td>5</td>
<td>p-FC\textsubscript{6}H\textsubscript{4}</td>
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</tr>
<tr>
<td>6</td>
<td>p-CH\textsubscript{3}C\textsubscript{6}H\textsubscript{4}</td>
<td>68</td>
</tr>
</tbody>
</table>

\textsuperscript{a}isolated yield after chromatographic separation
6.3.3. Spectral Data Analysis

After getting the products, these structures are characterized by $^1$H and $^{13}$C NMR spectral analysis.

$^1$H NMR spectra:

In the proton NMR spectra of these bromoalcohols, all aromatic protons were appeared in the range 8 ppm -7 ppm as multiplets. For the group -$CH$(OH)- the proton signal came out as a doublet in the region around 5.7 ppm and the proton signal for the group -$CH$Br- came out as another doublet at around 5 ppm. The hydrogen of the group -$NCH$- appeared as a multiplet at around 4.6-4.5 ppm. Then, the two hydrogens of -$CH_2$O- gave a multiplet at 4.2-4.1 ppm. The remaining two hydrogen of the group Ph$CH_2$- gave two separate multiplets in between 3-2.5 ppm.

$^{13}$C NMR spectra:

In the $^{13}$C NMR spectra, the two carbonyl carbons were visible at around 169 ppm (\[\text{BrHC} \overset{\text{O}}{\text{-}} \text{N}\overset{\text{O}}{\text{-}}\]) and 152 ppm (\[\text{N} \overset{\text{O}}{\text{C}} \overset{\text{O}}{\text{H}} \overset{\text{O}}{\text{-}}\]). All the signals in the region around 137-127 ppm were due to the aromatic carbons. The appearance of the signal at about 75 ppm was due to the carbon where -OH group was attached. The signal of the carbon where Br atom was attached appeared at around 55 ppm. The remaining carbons of the groups -$OCH_2$-, -$NCHCH_2$- and Ph$CH_2$- were appeared at 66 ppm, 45 ppm, and 37 ppm respectively.
Fig 6.1 $^1$H NMR Spectra of (4S)-4-benzyl-3-[(2E)-but-2-enoyl]-1, 3-oxazolidin-2-one

Fig 6.2 $^{13}$C NMR Spectra of (4S)-4-benzyl-3-[(2E)-but-2-enoyl]-1, 3-oxazolidin-2-one
Fig 6.3 $^1$H NMR Spectra of (4S)-4-benzyl-3-(2-bromo-3-hydroxybutanoyl)-1, 3-oxazolidin-2-one

Fig 6.4 $^{13}$C NMR Spectra of (4S)-4-benzyl-3-(2-bromo-3-hydroxybutanoyl)-1, 3-oxazolidin-2-one
Fig 6.5 $^1$H NMR Spectra of (4S)-4-benzyl-3-\[(2E)-3-(4-chlorophenyl)prop-2-enoyl\]-1,3-oxazolidin-2-one

Fig 6.6 $^{13}$C NMR Spectra of (4S)-4-benzyl-3-\[(2E)-3-(4-chlorophenyl)prop-2-enoyl\]-1,3-oxazolidin-2-one
Fig 6.7 $^1$H NMR Spectra of (4S)-4-benzyl-3-[2-bromo-3-(4-chlorophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one

Fig 6.8 $^{13}$C NMR Spectra of (4S)-4-benzyl-3-[2-bromo-3-(4-chlorophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one
6.3.4. Probable Mechanism

Most probably, a three-membered cyclic brominium ion intermediate is formed at the initial stage of the reaction due to electrophilic addition of the Br⁺ ion (generated from TsNBr₂) onto the olefin. The intermediate undergoes ring opening by the nucleophile via the S₈₂ pathway. The S₈₂ opening is responsible for anti stereoselectivity of the product. The regoselectivity can be explained by considering the fact that the β-position is more positive than the α-position due to the presence of the aromatic ring. Nucleophilic opening of the cyclic bromonium intermediate is most likely from the more positive β-position (Scheme 6.5).

Scheme 6.5

6.4. Conclusion

Bromohydrin formation reaction was examined for substrates containing Evans chiral auxiliary. Reaction at room temperature was found to be sluggish giving a number of products. However, the reaction was successful at -40 °C producing corresponding bromohydrins in high yield.
6.5. Experimental Section

6.5.1. General procedure for the synthesis of acid chloride

To a solution of α,β unsaturated acid (1 eqv.) in dichloromethane, oxalyl chloride (2 eqv.) was added at 0°C and stirred at nitrogen atmosphere for overnight. Then solvent was evaporated to get the acid chloride.

6.5.2. General procedure for the synthesis of the auxiliary\textsuperscript{31}

Preparation of (S)-Phenylalanol

To a solution of (S)-phenylalanine (16.5 g, 0.1 mol) in dry THF (50 ml) under nitrogen atmosphere, freshly distilled boron trifluoride etherate (12.3 ml, 0.1 mol) was added dropwise over a period of 30 minutes with constant stirring. The reaction mixture was heated at reflux for 2 hour, resulting in a colorless, homogeneous solution. Then, borane–dimethyl sulfide complex (8.8 g, 0.12 mol) was added carefully to the refluxing solution over a period of 100 minutes. Then it was refluxed for another 6 hours. The reaction mixture was allowed to cool to room temperature and quenched by the slow addition of a 1:1 tetrahydrofuran–water solution (12.5 ml.), followed aqueous sodium hydroxide (75 ml of 5 M). The resulting two-phase mixture was heated at reflux for 12 hour, cooled to room temperature, and filtered. The residual solids were washed with tetrahydrofuran (5 ml), and the filtrate was evaporated to remove the tetrahydrofuran. The resulting slurry was extracted with dichloromethane several times (20 X 5). The organic extracts are dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation to get white crystalline solid which was further recrystallized from ethyl acetate (mp 88.5-91°C, 75% yield).

Preparation of (S)-4-(Phenylmethyl)-2-oxazolidinone

(S)-phenylalanol (10 g, 0.07 mol), anhydrous potassium carbonate (0.97 g, 0.007 mol), and diethyl carbonate (17.5 ml, 0.15 mol) was mixed under nitrogen atmosphere. The mixture was distilled at 135°C with stirring and ethanol was collected from the reaction over a period of 2.5 hour. The light-yellow solution was cooled to ambient temperature and it was extracted with dichloromethane (75 ml), dried over anhydrous magnesium sulfate, filtered,
and concentrated to get the white crystalline solid. It was recrystallised with hot ethyl acetate-hexane (mp 84.5-86.5°C).

6.5.3. General procedure for coupling of chiral auxilliary to the acid chloride

To a stirred, -78°C precooled solution of (S)-4-(Phenylmethyl)-2-oxazolidinone (6 mmol, 1.00 eqv.) in dry THF (30 ml) was added BuLi (6.00 mmol, 1.00 eqv.) by syringe. The resulting solution was stirred at this temperature for 20 minute, and the acid chloride (6.6 mmol, 1.10 eqv.) was added to the resulting slurry. The mixture was stirred at -78°C for 30 minute and at 0°C for 2 hour when a saturated solution of NH₄Cl (25 ml) was added. The resulting suspension was allowed to warm to room temperature and the volatiles were evaporated. EtOAc (25 ml) was added and the organic layer separated and washed with a saturated solution of NaHCO₃ (2 x 25 ml) and brine (25 ml). The organic solution was dried over sodium sulphate, filtered, evaporated and chromatographed (7:3 petroleum ether/EtOAc).

6.5.4. General procedure for synthesis of the bromohydrin

To a solution of chiral oxilliary coupled α,β unsaturated substrate (1.1 mmol) in acetonitrile-water (9:1) (10 ml) at -40°C was added TsNBr₂ (1.2 mmol). The color of TsNBr₂ as well as the olefin disappears immediately. After stirring for 5 minute, the temperature of the reaction was raised to room temperature and stirred for another 10 minute and then sodium thiosulfate (200 mg approximately) was added and the reaction mixture was stirred for 20 minute. The reaction mixture was taken up in ether, washed with brine, dried (Na₂SO₄), and concentrated. Purification of the crude product by flash chromatography on silica gel (230-400 mesh) with petroleum ether- EtOAc (30%) as eluent gave the pure product.

6.5.5. Experimental data

¹H NMR and ¹³C spectra were recorded in bruker 400 MHz instrument. Chemical shifts are given in δ units relative to the tetramethylsilane (TMS) signal as an internal reference in CDCl₃. Coupling constants (J) are reported in hertz. IR spectra were recorded in Perkin – Elmer Spectrum RXI FT-RI spectrometer. Silica gel (230-400 mesh) was used for column chromatography.
1. (4S)-4-benzyl-3-[(2E)-but-2-enoyl]-1, 3-oxazolidin-2-one

\( ^1\text{HNMR (CDCl}_3, 400 \text{ MHz}) \delta: 7.47-7.44 (m, 1H), 7.43 (d, 1H, } J = 7.6 \text{ Hz}), 7.41-7.32 (m, 5H), 4.86-4.82 (m, 1H), 4.34-4.26 (m, 2H), 3.46-3.42 (m, 1H), 2.94-2.88 (m, 1H), 2.1 (d, 3H, } J = 5.2 \text{ Hz). } ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz}) \delta: 164.9, 153.4, 146.9, 135.3, 129.4, 128.9, 127.3, 121.8, 66.1, 55.2, 37.8, 18.5. \)

(4S)-4-benzyl-3-(2-bromo-3-hydroxybutanoyl)-1, 3-oxazolidin-2-one

\( ^1\text{HNMR (CDCl}_3, 400 \text{ MHz}) \delta: 7.28-7.19 (m, 5H), 5.38 (d, } J = 8.4 \text{ Hz), 4.67-4.64 (m, 1H), 4.22-4.18 (m, 1H), 4.16-4.09 (m, 1H), 4.08-4.01 (m, 1H), 3.27-3.19 (m, 1H), 2.79-2.67 (m, 1H), 1.41 (d, } J = 6 \text{ Hz). } ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz}) \delta: 169.1, 152.5, 134.7, 129.4, 129.0, 127.5, 68.9, 66.3, 55.7, 46.5, 37.7, 20.1. \)

2. (4S)-4-benzyl-3-[(2E)-3-(4-chlorophenyl)prop-2-enoyl]-1,3-oxazolidin-2-one

\( ^1\text{HNMR (CDCl}_3, 400 \text{ MHz}) \delta: 7.83 (d, 2H, } J = 10.4 \text{ Hz), 7.52 (d, 2H, } J = 8.4 \text{ Hz), 7.34-7.18 (m, 7H), 4.77-4.73 (m, 1H), 4.23-4.15 (m, 2H), 3.34-3.30 (m, 1H), 2.83-2.80 (m, 1H). } ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz}) \delta: 164.9, 153.5, 144.9, 136.6, 135.3, 133.0, 129.8, 129.5, 129.2, 129.0, 127.4, 117.5, 66.2, 55.4, 37.9. \)

(4S)-4-benzyl-3-[2-bromo-3-(4-chlorophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one

\( ^1\text{HNMR (CDCl}_3, 400 \text{ MHz}) \delta: 7.36-7.19 (m, 9 H), 5.78 (d, 1H, } J = 8.4 \text{ Hz), 5.15 (d, 1H, } J = 8.4 \text{ Hz), 4.69-4.64 (m, 1H), 4.19-4.14 (m, 2H), 3.23 (dd, 1H, } J_1 = 3.2 \text{ Hz, } J_2 = 13.4 \text{ Hz), 2.77 (dd, 1H, } J_1 = 9.2 \text{ Hz, } J_2 = 13.6 \text{ Hz). } ^{13}\text{C NMR (CDCl}_3, 100 \text{ MHz}) \delta: \)
168.8, 152.5, 137.5, 134.6, 134.51, 129.41, 129.0, 128.7, 128.6, 127.5, 74.4, 66.3, 55.1, 44.8, 37.0.

3. (4S)-4-benzyl-3-[(2E)-3-(4-bromophenyl) prop-2-enoyl]-1, 3-oxazolidin-2-one

\[\begin{align*}
\text{HNMR (CDCl}_3, 400 \text{ MHz)} \delta: & \ 7.89-7.76 (m, 2H), 7.52-7.43 (m, 4H), 7.35-7.17 (m, 5H), 4.72-4.29 (m, 1H), 4.24-4.15 (m, 2H), 3.34-3.30 (m, 1H), 2.84-2.77 (m, 1H). \\
\text{C NMR (CDCl}_3, 100 \text{ MHz)} \delta: & \ 153.5, 144.9, 135.2, 133.4, 132.2, 132.0, 130.0, 129.5, 128.9, 128.7, 127.4, 117.6, 66.2, 55.4, 37.9.
\end{align*}\]

(4S)-4-benzyl-3-[2-bromo-3-(4-bromophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one

\[\begin{align*}
\text{HNMR (CDCl}_3, 400 \text{ MHz)} \delta: & \ 7.41-6.97 (m, 9H), 7.58 (d, 1H, J = 8 \text{ Hz}), 5.05 (d, 1H, J = 7.6 \text{ Hz}), 4.61-4.50 (m, 1H), 4.21-4.11 (m, 2H), 3.07-3.03 (m, 1H), 2.66-2.60 (m, 1H). \\
\text{C NMR (CDCl}_3, 100 \text{ MHz)} \delta: & \ 168.9, 152.5, 138.1, 134.4, 132.1, 131.6, 129.3, 129.0, 128.8, 127.5, 74.3, 66.2, 55.5, 44.2, 37.4.
\end{align*}\]

4. (4S)-4-benzyl-3-[(2E)-3-(3-bromophenyl)prop-2-enoyl]-1,3-oxazolidin-2-one

\[\begin{align*}
\text{HNMR (CDCl}_3, 400 \text{ MHz)} \delta: & \ 7.79 (d, 1H, J = 16 \text{ Hz}), 7.69 (d, 1H, J = 16 \text{ Hz}), 7.44-7.40 (m, 2H), 2.25-7.11 (m, 7H), 4.71-4.66 (m, 1H), 4.17-4.08 (m, 2H), 3.27-3.23 (m, 1H), 2.77-2.71(m, 1H). \\
\text{C NMR (CDCl}_3, 100 \text{ MHz)} \delta: & \ 164.8, 158.0, 153.5, 144.6, 136.6, 133.5, 131.3, 130.4, 129.4, 128.9, 127.4, 127.2, 123.0, 118.4, 66.2, 55.4, 37.8.
\end{align*}\]
(4S)-4-benzyl-3-[2-bromo-3-(3-bromophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one

\[
\text{\includegraphics{structure.png}}
\]

\(^1\)HNMR (CDCl\(_3\), 400 MHz) \(\delta\): 7.37-7.01 (m, 9H), 5.73 (d, 1H, \(J = 8 \text{ Hz}\)), 5.03 (d, 1H, \(J = 4.8 \text{ Hz}\)), 4.57-4.53 (m, 1H), 4.11-3.95 (m, 2H), 3.13-2.99 (m, 1H), 2.69-2.56 (m, 1H).\(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\): 168.9, 152.4, 141.6, 134.5, 131.8, 130.3, 130.1, 129.4, 128.9, 127.5, 125.9, 122.6, 74.7, 66.2, 55.5, 44.7, 37.4.

5. (4S)-4-benzyl-3-[2-bromo-3-(4-fluorophenyl)-3-hydroxypropanoyl]-1,3-oxazolidin-2-one

\[
\text{\includegraphics{structure.png}}
\]

\(^1\)HNMR (CDCl\(_3\), 400 MHz) \(\delta\): 7.38-7.16 (m, 9H), 5.81 (d, 1H, \(J = 8 \text{ Hz}\)), 5.10 (d, 1H, \(J = 8.4 \text{ Hz}\)), 4.66-4.60 (m, 1H), 4.12-4.04 (m, 2H), 3.12-3.07 (m, 1H), 2.71-2.63 (m, 1H).\(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\): 169.2, 163.9, 158.4, 134.9, 129.0, 128.9, 127.5, 115.7, 74.8, 66.6, 47.9, 42.6, 41.2.

6. (4S)-4-benzyl-3-[(2E)-3-(4-methylphenyl)prop-2-enoyl]-1,3-oxazolidin-2-one

\[
\text{\includegraphics{structure.png}}
\]

\(^1\)HNMR (CDCl\(_3\), 400 MHz) \(\delta\): 7.49 (d, 2H, \(J = 8.4 \text{ Hz}\)), 7.32-7.13 (m, 9H), 4.78-4.73 (m, 1H), 4.22-4.14 (m, 2H), 3.33 (dd, 1H, \(J_1 = 3.2 \text{ Hz}, J_2 = 13.6 \text{ Hz}\)), 2.80 (dd, 1H, \(J_1 = 9.6 \text{ Hz}, J_2 = 13.4 \text{ Hz}\)), 2.34 (s, 3H).\(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\): 165.3, 153.6, 146.6, 141.3, 135.4, 131.8, 129.6, 129.5, 128.9, 128.7, 127.3, 115.8, 66.1, 55.4, 37.9, 21.5.
(4S)-4-benzyl-3-[2-bromo-3-hydroxy-3-(4-methylphenyl)propanoyl]-1,3-oxazolidin-2-one

$^1$HNMR (CDCl$_3$, 400 MHz) δ: 7.29-7.08 (m, 9H), 5.89 (d, 1H, $J = 7.6$ Hz), 5.10 (d, 1H, $J = 3.2$ Hz), 4.66-4.58 (m, 1H), 4.18-4.07 (m, 2H), 3.06-2.97 (m, 1H), 2.76-2.63 (m, 1H), 2.27 (s, 3H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ: 169.3, 152.5, 138.6, 136.1, 134.6, 129.4, 129.3, 128.9, 127.4, 126.9, 75.3, 66.2, 55.4, 45.1, 37.4, 21.2.
6.6. References


