CHAPTER 5

SYNTHESIS AND CHARACTERIZATION OF CHIRAL ANALOGUE OF POLYANILINE

Contents

5.1 Introduction

Chiral conjugated polymers have remained one of the most attractive topics in polymer science with wide applications in materials science, chemical and biological sensors, catalysis, pharmaceutics, enantioselective separation etc.[1] Natural polymers such as polysaccharides, proteins and nucleic acids are chiral. Besides natural chiral macromolecular compounds, a family of synthetic optically active polymers are known.[2] The synthesis of such chiral conjugated polymers is an interesting topic in polymer science. One of the methods known for preparing optically active conjugated polymers include the polymerization of optically active monomers. Koeckelberghs *et al.* synthesized poly(N-substituted dithieno[3,2-*b*:2',3'-*d*]pyrrole)s (PDTPs) and chiral poly(3-(3,7-dimethyloctyloxy)thiophene)s conjugated polymers as shown in Figure 1. They have studied the chiroptical properties of both chiral polymers in neutral and oxidized form.[3]

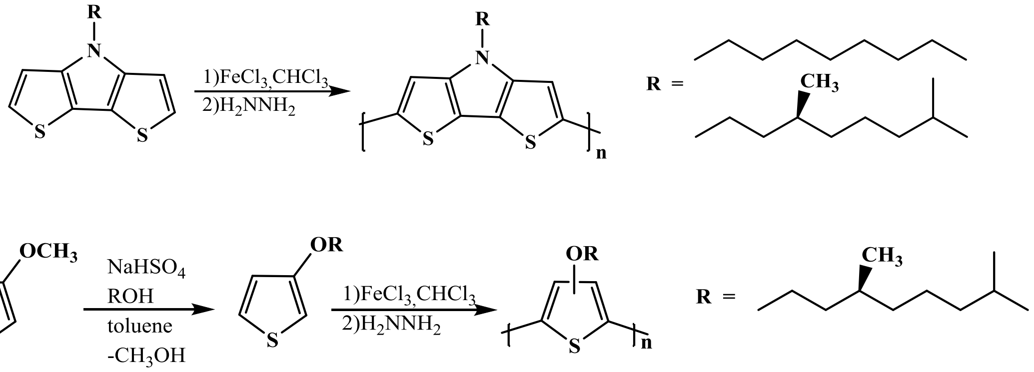


Figure 1 : Chiral poly(N-substituted dithieno[3,2-*b*:2',3'-*d*]pyrrole)s (PDTPs) and chiral poly(3-(3,7-dimethyloctyloxy)thiophene)s conjugated polymers

Another method for preparing chiral polymer is by introducing a chiral group into an optically-inactive polymer by a suitable reaction. Yashima *et al.* reported the introduction of helicity in a stereoregular, *cis-transoidal* poly((4-carboxyphenyl)acetylene) (poly-**1**) as shown in Figure 2. In the presence of optically active amines such as (*R*)-**2** and (*S*)-**3** as shown in Figure 2 has capability of interacting with the polymer's carboxy groups, a dynamic, one handed macromolecular helicity is induced in the polymer, resulting in optical activity. They also showed that the helicity can be memorized when the chiral amine is replaced by different achiral amines. Small structural changes in the achiral amines manipulate the effectiveness of helicity retention noticeably.[4]

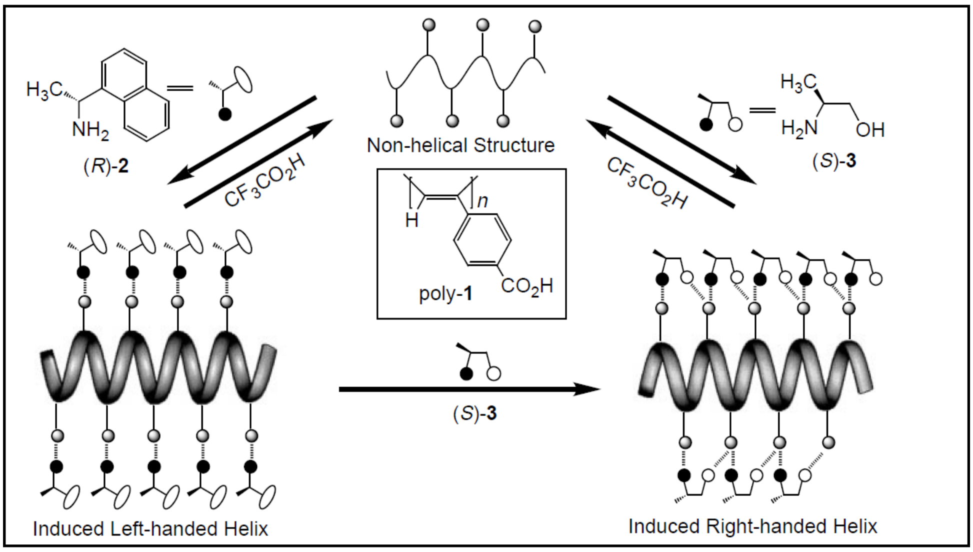


Figure 2: Introduction of helicity in poly((4-carboxyphenyl)acetylene) (poly-**1**)

Among chiral polymers, chiral conducting polymers have attracted great attention. Especially, there has been increased interest in synthesizing chiral conducting polyaniline (PANI) due to the high environmental stability, simple synthesis and low cost.[5] Chiral polyaniline (PANI) were synthesized usually by using chiral inducer. Majidi *et al.* were first to report synthesis of chiral PANI by electrochemical polymerization of aniline in the presence of enantiomers of 10-camphorsulfonic acid as well as by co-dissolving PANI and chiral acid in common solvents.[6] Thiyagarajan *et al.* reported biocatalytic route for synthesis of polymer nanocomposites. Template assisted (poly(acrylicacid), PAA) enzymatic synthesis was done where horseradish peroxidase (HRP) showed direct influence on stereospecificity of the polyaniline (PANI) in the nanocomposites PAA/PANI/(+) CSA, PAA/PANI/(-) CSA.[7] Moreover W. Li *et al.* used aniline oligomers to accelerate the synthesis of chiral PANI nanofibers which can have many applications in chiral separations and biological sensors.[8]

Synthesis of chiral polyaniline catalysed by micellar peroxidise in which dodecylbenzenesulfonicacid (DBSA) was used as surfactant as it can form micelles and simultaneously dope with PANI. The catalytic efficiency of horseradish and palm tree peroxidases was examined in presence of DBSA.[9]

Water soluble chiral PAA poly(acrylic acid)/PANI (Polyaniline) nanocomposites were synthesized using a simplified template-guided synthetic procedure using a chiral camphorsulfonic acid (CSA) as chiral inducing agent and poly(acrylic acid) as a template as shown in Figure 3. They suggest that polyaniline and the polyelectrolyte are bounded mainly by electrostatic interaction.[10]

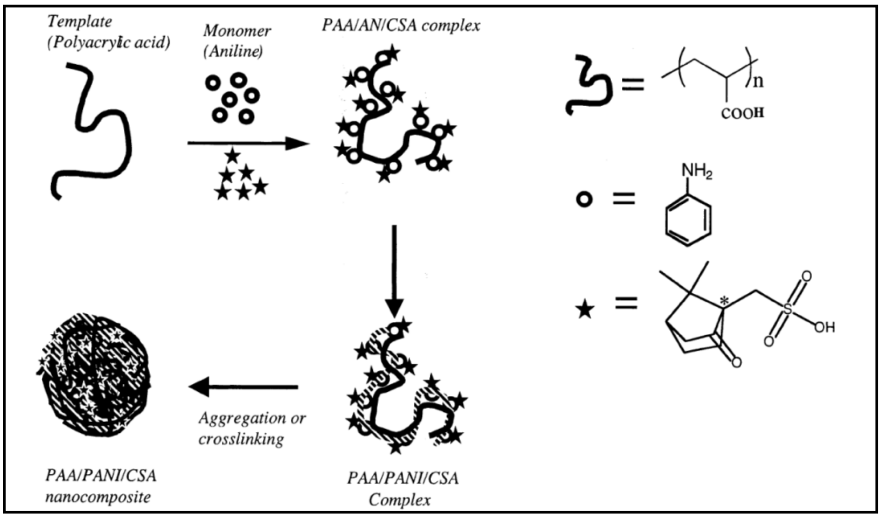


Figure 3: Synthesis of chiral PAA poly(acrylic acid)/PANI (Polyaniline) nanocomposites

Nagarajan *et al*. reported enzymatic polymerization of aniline in the presence of DNA as anionic polyelectrolyte template and found that in the presence of DNA the chirality is induced in PANI by formation of intermacromolecular complex.[11] Yuan *et al.* used dextran sulfate (DSA) as macromolecular dopant in the formation of intermacromolecular complex with the polyaniline derivatives as shown in Figure 4, which was confirmed by the CD spectra.[12]

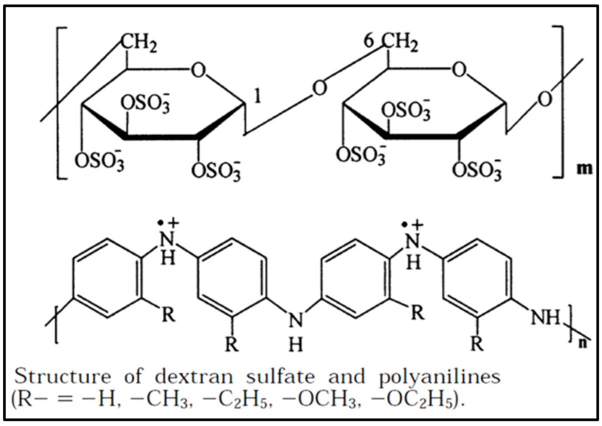


Figure 4: Structure of dextran sulphate and polyanilines

Recently a novel method for the synthesis of chiral conducting polyaniline was developed by Guo *et al*. They reported a protein-induced synthesis of chiral conducting PANI as shown in Figure 5. Proteins such as bovine hemoglobin and bovine serum albumin were used as chiral inducer as they had the ability to direct enantio specificity of PANI which may be ascribed to the α-helix structure within the proteins. The synthesis of chiral conducting PANI was carried out at room temperature in dodecylbenzenesulfonic acid (DBSA) micelle solutions. Oxidant (H_2O_2 or ammonium persulfate) was added to initiate the polymerization of aniline. The achieved chiral conducting polyaniline exhibited nanometered, spherical shape according to scanning electron microscopy and transmission electron microscopy images.[13]

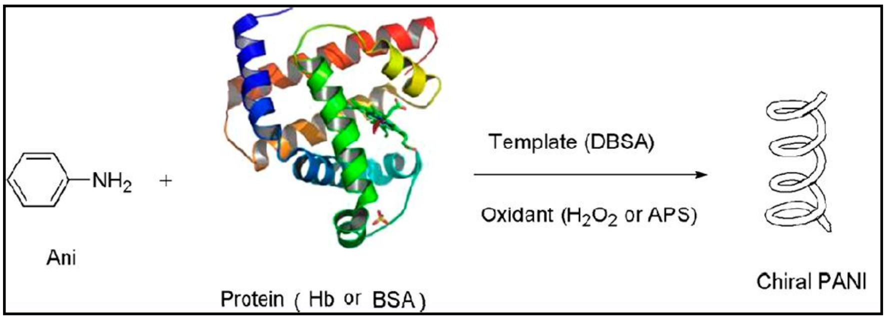


Figure 5: Protein-induced synthesis of chiral conducting PANI

Shen et al. induced chirality in polyaniline by complexation with chiral palladium complex as shown in Figure 6. By crystal study of the polyaniline and N,N-bis(4'-dimethylaminophenyl)-1,4-benzoquinonediimine complex of palladium, it was found that a chiral propeller twist conformation of the π-conjugated moiety was formed. They claimed that these type of systems can become potential candidate for asymmetric catalysts.[14]

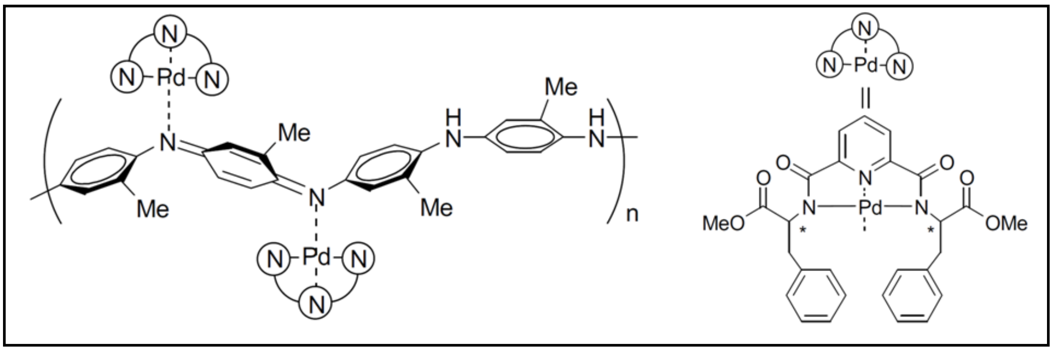


Figure 6: Chirality in polyaniline by complexation with chiral palladium complex

Feng *et al.* used (+)- and (-)-PANI based electrodes to detect the configuration of D- or L-Ala using cyclic voltammetry (CV), tafel (TAF), and open circuit potential (OCP) techniques.[15] There have been very few reports on polyaniline bearing chiral alkyl groups *via* covalent bonds. Alam *et al.* for the first time reported polymerization and characterization of aniline bearing chiral alkyl group on ring *via* covalent bond poly[(+/-)-2-(sec-butyl)aniline].[16]

In this portion of work we wish to synthesize chiral polyaniline by attaching chiral group at appropriate position, like at *ortho* or *meta* to amino. These chiral anilines which can be used as monomers, for polymerization which will result in chiral derivatives of PANI.

It is an important and challenging area for synthesis of chiral molecules as a single enantiomer which has been recognized by chemist for development of targeted chiral molecules. An active research in organic synthesis is done for new and efficient methods for synthesis and resolution of chirally pure compounds.[17] One of the methods for producing optically active compound is chiral resolution.

Introduction to Chiral resolution

Chiral resolution is defined as process for separation of the enantiomers from a racemic mixture. Several advancements have been made in asymmetric synthesis for resolution of racemates into both of its pure form.[18] Chiral resolution can be classified in two ways, first one is classical method based on physical separation of diastereomeric forms and other method is based on kinetic resolution. The most well-designed way of performing kinetic resolution is use of biocatalyst or enzyme.[19]

As compared to conventional form of organic reactions, biological transformation catalysed by biocatalyst has received great attention.[20] Enzymatic reaction is a reaction catalysed by particular enzyme for conversion of one molecule (substrate) to another (product) by microorganism. Enzymes are the most refined catalysts in existence as they are highly selective, catalysing the reaction of only one isomer of the racemic compound at a specific reaction site with defined stereochemistry including enantioselectively.[21]

Enzyme-catalyzed reactions are divide into six types out of which Hydrolases, are the most frequently used enzymes due to their broad substrate spectrum and considerable stability in organic solvents. Among the hydrolases, lipases are considered the most popular and useful enzymes for asymmetric synthesis. Lipases are compatible with the range of organic solvents.[22]

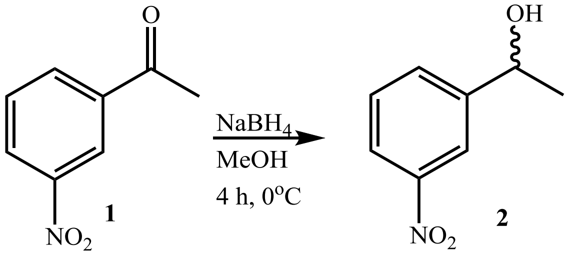
One of the application of lipase is acylation of alcohols, which is most currently used process in biocatalysts.[23] In literature there are many examples of the resolution of primary[24] and secondary alcohols,[25] although the resolution with tertiary alcohols is more difficult and very few examples have been reported.[26] Reactions are easily carried out using lipase at room temperature using common organic solvents, moreover handling the reaction conditions is also safe and no specific apparatus are needed.

5.2 Results and discussion

In this chapter we present synthesis of chiral substituted aniline monomer from achiral starting material by enzymatic resolution, which is further polymerized to chiral polymer. This chiral analogue of polyaniline was characterized and studied for asymmetric reaction.

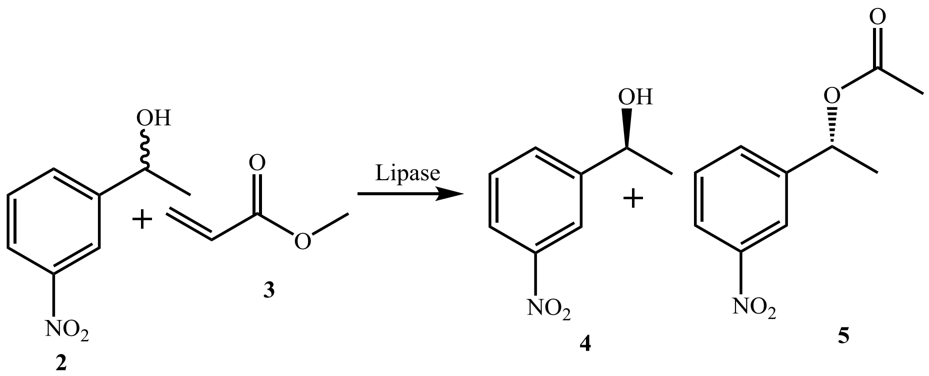
5.2.1 Synthesis and characterization of chiral analogue of polyaniline

To introduce chiral substitution in aniline moiety, a chiral group needs to be attached. Polymerisation of such aniline containing a chiral group, can furnish chiral PANI. With this idea, molecule **2** was chosen. The synthesis of **2** should begin with 3-nitro acetophenone. It was reduced with sodium borohydride at 0°C to yield 1-(3-nitrophenyl)ethan-1-ol in excellent yield generating a chiral center.



Scheme 1: Reduction of 3-nitro acetophenone

The enantiomers were separated by enzymatic kinetic resolution using lipase as shown in Scheme 2. The enantiomers of alcohols were separated by selecting biocatalyst which allows one of them to react much faster compared to the other, undergoing acylation reaction with vinyl acetate. Biocatalysts available commercially such as immobilized lipases were screened for effectively convert one isomer to acetyl derivative. Optimization study were done by changing the amount of vinyl acetate and time as shown in Table 1. Enantiomeric purity of the product as well as unreacted alcohol was determined by chiral phase HPLC analysis. (Solvent system: 5% IPA-Hexane; Flow rate: 1 ml/min; Detector: UV-254 nm ; Chiral Column: Amylose)



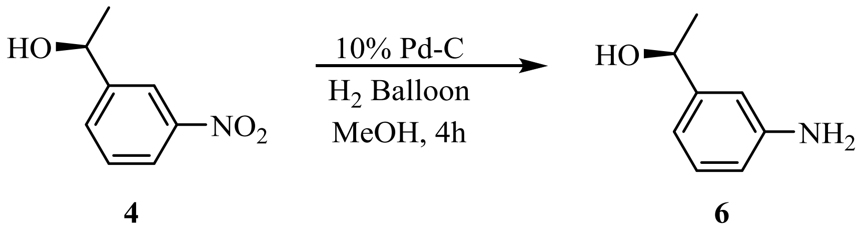
Scheme 2: Enzymatic kinetic resolution of enantiomers using lipase

Table 1: Optimization study

Entry	Vinyl acetate	Reaction time (days)	% yield of acetate	% yield of alcohol	ee of acetate	ee of alcohol
1	5.4 mmol	4	23	70	98.57	29.32
2	10.8 mmol	8	45	53	93.00	84.16
3	**5.4 mmol**	**10**	**47**	**52**	**96.73**	**82.28**
4	10.8 mmol	10	49	51	92.51	86.80

Conditions : 1-(3-nitrophenyl)ethan-1-ol (0.3 g, 1.8 mmol), Lipase (0.2 g), diethyl ether, room temperature

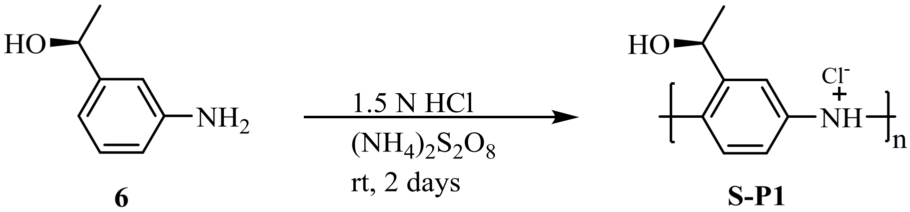
From the above Table it was observed that with 5.4 mmol of vinyl acetate in 10 days best ee of 1-(3-nitrophenyl)ethyl acetate is obtained (entry 3), while ee of 1-(3-nitrophenyl)ethan-1-ol was 82.28 which was improved to 100 % ee by crystallization. Specific optical rotation was found to be -40.33 (c=1 in $CHCl_3$) which indicates it to be an S-isomer of alcohol, as compared to the literature data.[27] The *S* isomer of 1-(3-nitrophenyl)ethan-1-ol was further treated with 10% Pd/C using hydrogen balloon to yield (*S*)-1-(3-aminophenyl)ethan-1-ol **6** in 98% yield.



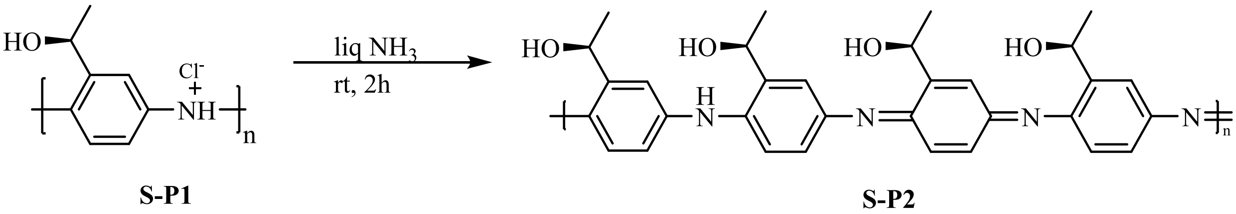
Scheme 3: Reduction of *S* 1-(3-nitrophenyl)ethan-1-ol

After the reduction of nitro, (*S*)-1-(3-aminophenyl)ethan-1-ol was subjected to chemical oxidation using ammonium persulphate from its hydrochloride salt to yield polymer

S-P1. Further neutralization with aqueous ammonia gave final polymer *S*-P2 with chiral substituent as shown in Scheme 5.

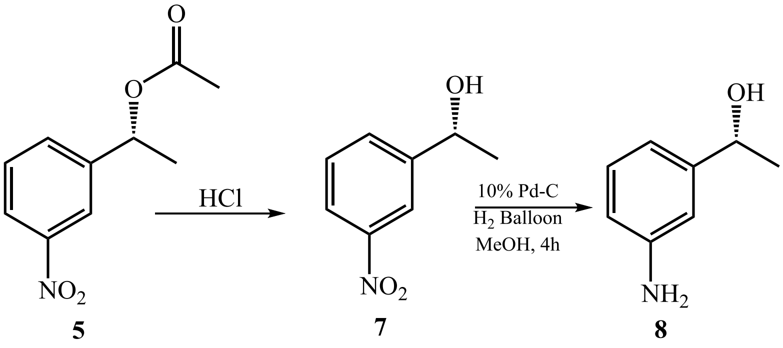


Scheme 4: Polymerisation of (*S*)-1-(3-aminophenyl)ethan-1-ol



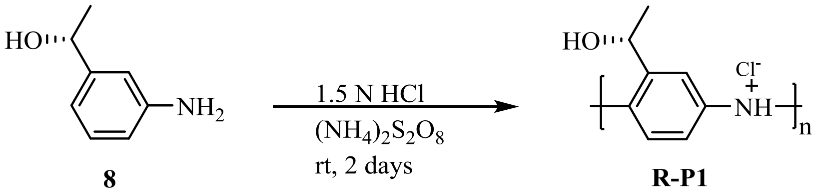
Scheme 5: Neutralization of polymer

Similarly (*R*)-1-(3-nitrophenyl)ethyl acetate was reduced to 1-(3-aminophenyl)ethyl acetate which was further polymerized by same method, but unfortunately a gummy material was obtained. So we decided to hydrolyse acetate to alcohol as shown in Scheme 6, which was further reduced to (*R*)-1-(3-aminophenyl)ethan-1-ol, whose configuration was confirmed by specific optical rotation [+41.21 (c=1 in $CHCl_3$), based on the literature for known *R*-isomer of alcohol].[27] while the HPLC analysis showed its ee to be 98.6 %.

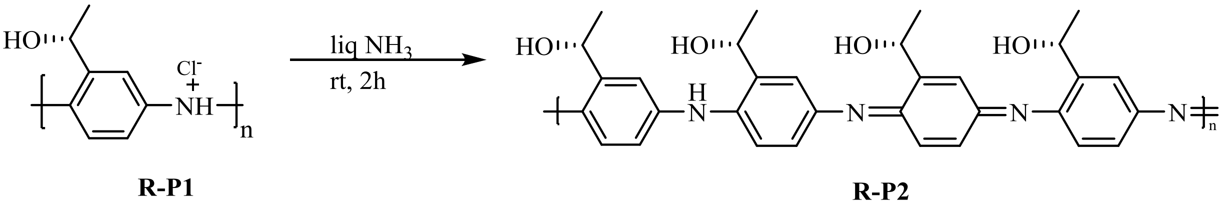


Scheme 6: Synthesis of (*R*)-1-(3-aminophenyl)ethan-1-ol

Polymerization of compound 8 was performed similarly as discussed above to get polymer R-P1. The resulted polymer on neutralization gives polymer R-P2.



Scheme 7: Polymerisation of (R)-1-(3-aminophenyl)ethan-1-ol



Scheme 8: Neutralization of polymer

Initial characterization of chiral PANI derivatives was done by IR, UV-Vis and circular dichromism spectroscopy. The spectrum of chiral PANI *S*-P2 displays a broad band at 3357 cm,$^{-1}$ may be attributed to merged O-H and N-H stretching mode of aromatic amine, absorption bands at 1599 and 1492 cm,$^{-1}$ may be assigned to the C=C stretching vibration of quinonoid and benzenoid units of PANI chain, band at 1300 cm^{-1} may be attributed to C-N stretching in aromatic amine and an absorption at 1072 cm^{-1}, which is attributed to the plane bending vibration of C–H, related to the quinonoid (N=Q=N).

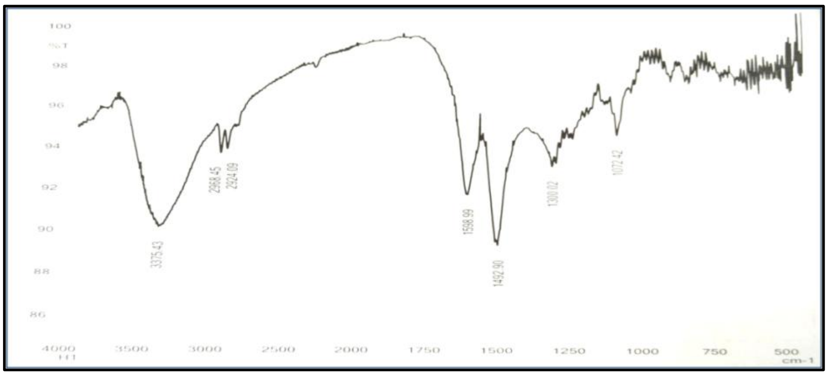


Figure 7: IR spectra of **S-P2**

In UV-visible spectral analysis, the peak wavelengths (λ_{max}) of *R*-P1 and *S*-P1 at 270 nm, attributable to the π–π* transition of the benzene ring in THF solution (Figure 8, left). The colour of the solution changed visibly from red to blue after reduction of polymer *S*-P1 to *S*-P2 in THF solution as shown in (Figure 8, right), polymer *S*-P2 display new peak at 570 nm. The de-doping procedure therefore appears to change the charge state of the polyaniline derivative.[28]

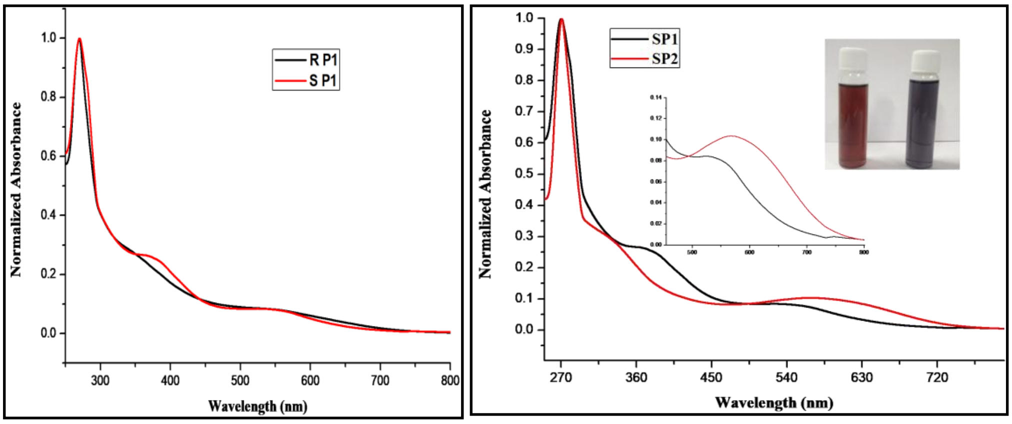


Figure 8: Absorption spectra of *R*-P1 and *S*-P1 (left), Absorption spectra of *S*-P1 and *S*-P2 (right)

Circular dichroism (CD) measurements were done for polymer *R*-P2 and *S*-P2. It is difficult to obtain a completely reduced form of the polyaniline derivative by base treatment. Partial oxidation of polyaniline along the main chain produces an incomplete reduction state. Therefore, the preparation of a polyaniline derivative with a perfect mirror image Cotton effect in the CD of the reduced state is very difficult.[28] Figure 9 shows the CD spectra of *R*-P2 and *S*-P2, display a image with opposite Cotton effect which proves it’s optically active. The circular dichroism in the UV-visible region may be attributed to the predominantly formation of one handed helix of the polyaniline derivative.

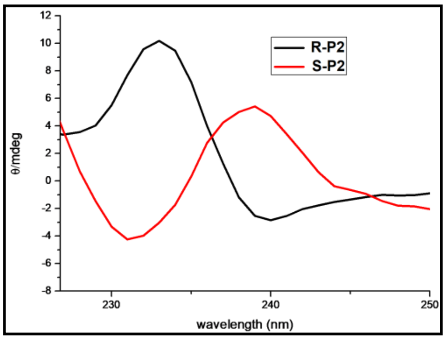
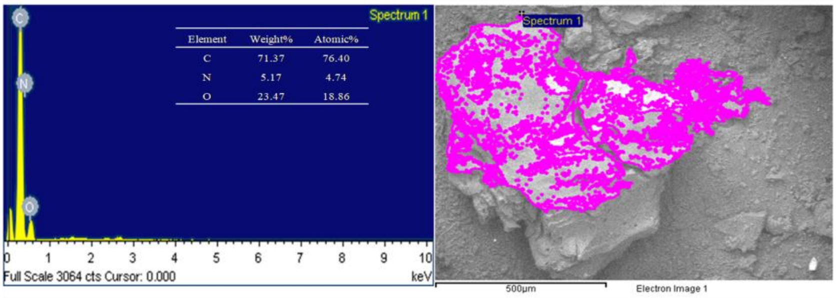


Figure 9: CD Spectra of *R*-P2 and *S*-P2

5.2.2 Applications of catalyst for asymmetric reactions

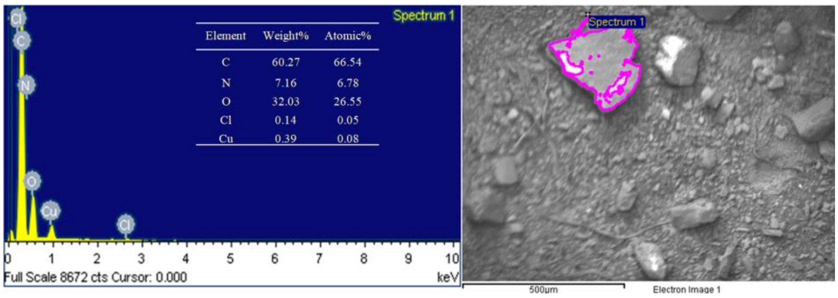
In this portion of work we present our findings for the immobilization of $Cu(OAc)_2$, $FeCl_3$ and $PdCl_2$ onto chiral PANI (***S*-P2**) and explore the catalyst for asymmetric Henry reaction, Biginelli reaction and hydrogenation reaction respectively. The sample of chiral

PANI (***S*-P2**) free from oligomers was then exposed to a solution of Cu, Fe and Pd salts in acetonitrile to immobilize the metal ions on the support. The catalysts Chiral PANI-Cu(OAc)$_2$, Chiral PANI-FeCl$_3$, Chiral PANI-PdCl$_2$ were separated dried and initial characterization was done by EDX technique to find the composition of the catalyst. Loading of metal chlorides on chiral PANI is confirmed by EDX analysis as shown in Figure 10 a-d.



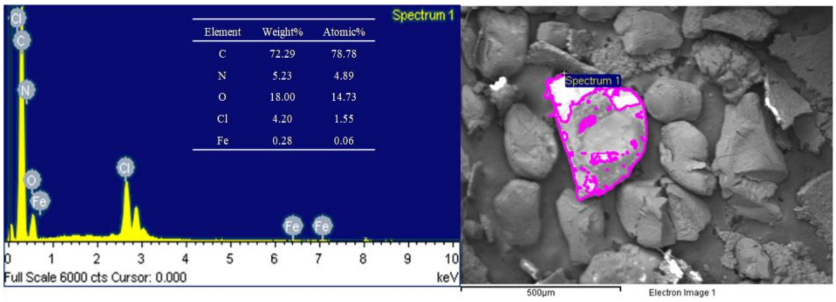
Element	Weight%	Atomic%
C	71.37	76.40
N	5.17	4.74
O	23.47	18.86

Figure 10a: EDX of Chiral PANI S-P2



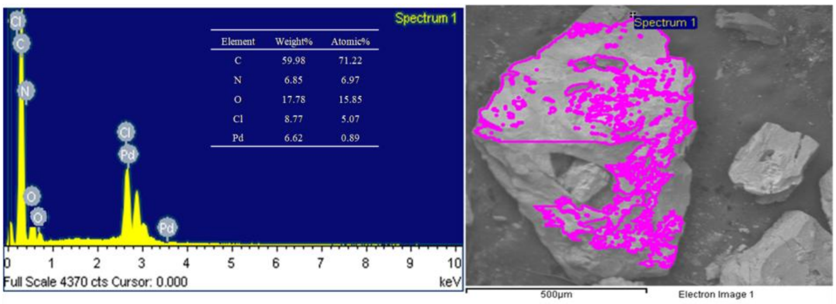
Element	Weight%	Atomic%
C	60.27	66.54
N	7.16	6.78
O	32.03	26.55
Cl	0.14	0.05
Cu	0.39	0.08

Figure 10b: EDX of Chiral PANI-Cu(OAc)$_2$



Element	Weight%	Atomic%
C	72.29	78.78
N	5.23	4.89
O	18.00	14.73
Cl	4.20	1.55
Fe	0.28	0.06

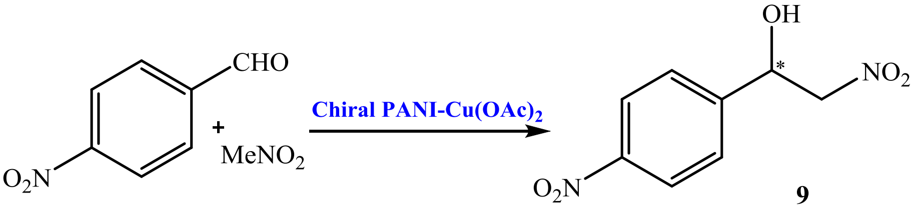
Figure 10c: EDX of Chiral PANI-FeCl$_3$



Element	Weight%	Atomic%
C	59.98	71.22
N	6.85	6.97
O	17.78	15.85
Cl	8.77	5.07
Pd	6.62	0.89

Figure 10d: EDX of Chiral PANI-PdCl$_2$

The synthesized Chiral PANI-Cu(OAc)$_2$ catalyst was examined for the asymmetric Henry reaction with nitomethane and 4-nitro benzaldehyde shown in Scheme 9.



Scheme 9: Asymmetric Henry reaction using Chiral PANI-Cu(OAc)$_2$

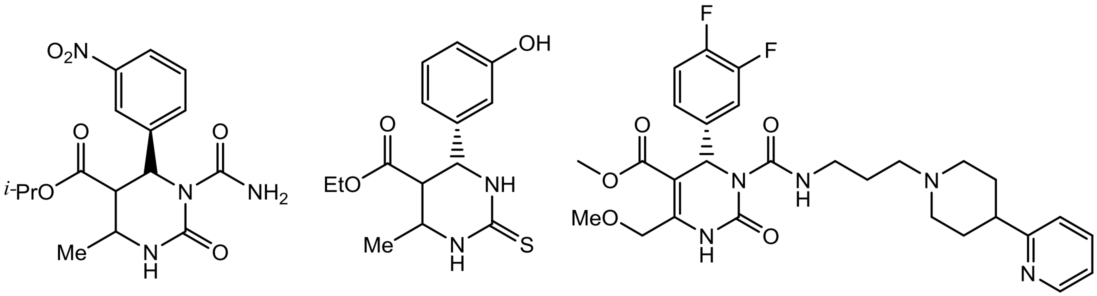
Among various C-C bond forming reactions, nitro aldol (Henry) reaction is one of the important reactions in organic chemistry[29] as nitro aldol products find increasing applications in synthesis of various natural products. Moreover, Henry products can be easily converted into useful synthetic intermediates which include dehydration to yield nitroalkenes, oxidation of secondary alcohol to give nitroketones or reduction of nitro group to give β-amino alcohols. This reaction has also found its applications in synthesis of various pharmaceuticals like β-blocker (S)-propranolol[30]. Amprenavir, HIV protease inhibitor, L-Ascsamine[31] etc. Many metal based catalysts were known for asymmetric nitroaldol reaction out of which copper salts have been most widely used as they are less toxic, relatively cheaper and have excellent chelating properties. Gong *et. al.* has screened this reaction with Cu (II) and N,N-chiral ligands, which were synthesized from (-)-exo- bornylamine and from (+)-menthylamine.[32]

We examined the Chiral PANI-Cu(OAc)$_2$ catalyst for the asymmetric Henry reaction with nitromethane and 4-nitro benzaldehyde by varying three different solvents at room temperature in water bath for 72 h as shown in the Table-2. Unfortunately we did not get any enatiomeric excess in the cases studied.

Table 2: Solvent study

Sr. No.	Solvent	Catalyst	% yield	ee
1.	Ethnaol	Chiral PANI-Cu(OAc)$_2$	46	Racemic
2.	DCE	Chiral PANI-Cu(OAc)$_2$	35	Racemic
3.	Acetone	Chiral PANI-Cu(OAc)$_2$	59	Racemic

As seen in the previous chapter the well-known Biginelli reaction, is one of the most useful multicomponent reactions, which offers straightforward access to multifunctionalized 3,4-dihydropyrimidin-2-(1H)-ones (DHPMs) and related compounds, through the simple condensation reaction of an aldehyde, a urea or thiourea, and an easily enolizable carbonyl compound. It can be noted that the DHPM has one chiral canter and the asymmetric version of the reaction is also known. In the last decades, many improved procedures with new catalysts for Biginelli reaction have been reported.[33] However, most of the reported methods only resulted in racemic DHPMs. But ccompounds containing the DHPM moiety are chiral molecules, and it has been revealed that the configuration at the stereogenic carbon C(4) determines their biological properties as enantiomers shows different or opposite pharmaceutical activities. For example, only the enantiomer (*R*)-SQ 32926 exhibits an antihypertensive effect,[34] and (*S*)-Monastrol shows potential anticancer activity.[35] While *S*-L-771688 is more potent and selective α_{1a} receptor antagonist for the treatment of benign prostatic hyperplasia (BPH) versus its *R*-enantiomer.[36] Other biologically active compounds bearing dihydropyrimidine moiety were also reported.[37] Therefore, an efficient method for the preparation of optically pure DHPMs is of considerable interest.

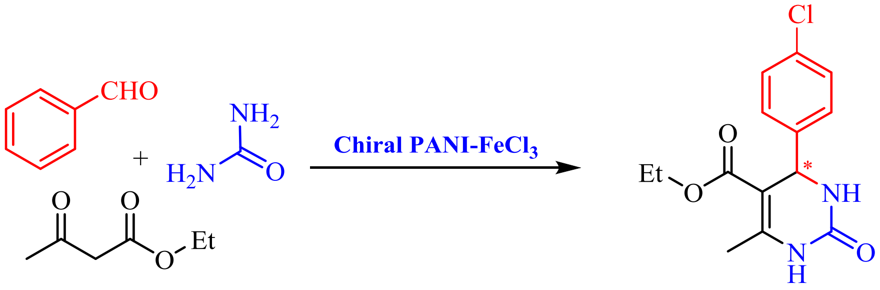


(R)-SQ 32926 **(S)-Monastrol** **S-L-771688**

Figure 11: Chiral Compounds containing the DHPM moiety

The catalytic asymmetric Biginelli reaction for the synthesis of enantioselective DHPMs are not much explored. Y.J. Huang *et al.* synthesize DHPMs using a recyclable new chiral ytterbium catalyst.[38] X.H. Chen *et al.* for the first time reported first organocatalytic highly enantioselective Biginelli reaction using a BINOL-derived phosphoric acids as catalyst.[39] Some secondary amines and Bronsted acids were also employed as catalyst to promote the Biginelli reaction with moderate to good enantioselectivities.[40] Saha *et al.* reported a proline-derived secondary amine as catalyst in the enantioselective Biginelli reaction.[41] In contrast, although primary amines are also known to participate as catalysts in asymmetric synthesis that involve enamine intermediates, there were few examples on the use of chiral amines as catalysts in the asymmetric synthesis of DHPMs.[42] In spite of these few examples, it is still desirable to develop other new catalysts for this important transformation.

As a part of our continuing interests in synthesis asymmetric small-molecule catalysis, here, we wish study our synthesized Chiral PANI-$FeCl_3$ as catalysts in the asymmetric synthesis of DHPMs through the Biginelli reaction as shown in Scheme 10.



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Scheme 10: Asymmetric Biginelli reaction Chiral PANI-$FeCl_3$

We examined chiral PANI-$FeCl_3$ catalyst for the asymmetric Biginelli reaction with ethylacetoacetate, urea and 4-chloro benzaldehyde by two solvents, at room temperature in water bath (72 h) as shown in below table. Unfortunately in this case also we did not get any enantiomeric excess.

Table 3: Solvent study

Sr. No.	Solvent	Catalyst	% yield	ee
1.	Ethnaol	Chiral PANI-$FeCl_3$	68	Racemic
2.	DCE	Chiral PANI-$FeCl_3$	30	Racemic

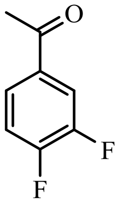
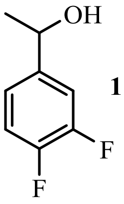
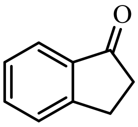
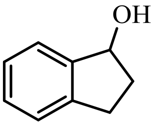
The catalytic asymmetric hydrogenation has been known as one of the most significant methods for the synthesis of various chiral compounds. Knowles and Noyori were awarded the Nobel Prize in Chemistry in 2001 for their pioneering work in catalytic asymmetric hydrogenation.[43] During the last few decades several efficient and selective methods have been reported for catalytic asymmetric reduction of carbonyl compounds.[44] Asymmetric Hydrogenation of ketones, has been used in a number of industrial process for the synthesis of pharmaceuticals, agrochemicals etc.[45] Palladium has increasingly emerged popular metal for asymmetric hydrogenation of ketones.[46] Wang *et al.* for the first time reported Pd-catalyzed asymmetric hydrogenation of ketones, in the presence of

$Pd(CF_3COO)_2$/(R,R)-Me-Duphos, a variety of aryl and alkyl substituted phthalimide ketones were hydrogenated to furnish the corresponding secondary alcohols with up to 92% enantiomeric excess (ee).[47]

So we decided to explored our Chiral PANI-$PdCl_2$ catalyst for the asymmetric hydrogenation reaction of ketones using hydrogen balloon under atmospheric conditions as shown in scheme 11. So initially we did reaction with 3,4- difluoro acetophenone in presence of catalyst at room temperature in methanol under hydrogen balloon. The reduced product as shown in below table (entry 1) was further converted to acetate to find its enatiomeric excess by chiral phase HPLC column, but regrettably did not get enatiomeric excess. The catalyst was also explored for bulky starting material, 1-indenone (entry 2). As a result of this reaction reduced product was obtained in good yield, however, we were not succeeded to get any enantiomeric excess.

Scheme 11: Asymmetric hydrogenation reaction using Chiral PANI-$PdCl_2$

Table 4: Hydrogenation of ketone by Chiral PANI-$PdCl_2$

Sr. No.	Substrate	Product	% Yield	ee
1.		 **11**	84 %	Racemic*
2.		 **12**	79 %	Racemic

* Alcohol was converted to acetate
Reaction condition: MeOH, H_2 balloon, 48 h, Chiral PANI-$PdCl_2$

5.3 Conclusion

In this section, we discussed about synthesis of chiral monomer by enzymatic resolution, which was polymerized to get both *R* and *S* chiral analogue of polyaniline. After initial characterization, its applications as a heterogeneous catalyst for chiral Henry, Biginelli and hydrogenation reaction were tried by loading different metal salts, but unfortunately we were unable to get eniatiomeric excess.

5.4 Experimental section

Thin Layer Chromatography was performed on silica gel plates coated on aluminium sheets. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography on silica gel (60-120 mesh) and neutral alumina. NMR Spectra were recorded on 400 MHz Spectrometer with $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were recorded on GCMS instrument. IR Spectra were recorded as KBr pallets. Energy Dispersive X-ray Spectroscopy (EDX) analysis were using Jeol5610LV. Specific optical rotations were measured on JACSO P-2000 Polarimeter. For the HPLC analysis Amylose and Chiralpak OD-H column were used.

Synthesis of 1-(3-nitrophenyl)ethan-1-ol (Scheme 1) :

250 mL round bottom flask was charged with 3-nitroacetophenone (10 g, 0.06 moles) in 100 ml MeOH and kept in ice bath. Sodium borohydride (2.3 g, 0.06 moles) was added in portion wise at 0 ^{o}C in an ice bath resulting in vigorous evolution of hydrogen. After stirring for 4 h at room temperature, the reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic phase was washed with water and dried over anhydrous sodium sulfate. Solvent was removed in vacuum and the crude product was purified by column chromatography on silica gel to afford 1-(3-nitrophenyl)ethan-1-ol **(2)** (9.6 g, 95%) as pale yellow solid.

General procedure for resolution of alcohol (Scheme 2) :

To a solution of racemic alcohol (**2**) (0.30 g, 1.79 mmol) in dry ether (10 mL), lipase (0.1 g, 66% w/w) and vinyl acetate (0.5 mL, 5.37 mmol) were added and resultant reaction mixture was stirred for 4-10 days at room temperature. The material was filtered and the filtrate was concentrated in vacuum. Separation was carried out by column chromatography over silica gel using ethyl acetate and petroleum ether as the eluent. The (*R*)-1-(3-nitrophenyl)ethyl acetate (**5**) was eluted with 10 % ethyl acetate- petroleum ether and (S)-1-(3-nitrophenyl)ethan-1-ol (**4**) with 20 % ethyl acetate- petroleum ether.

(*R*)-1-(3-nitrophenyl)ethyl acetate **(5)**

^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.57-1.59 (d, *J*=6.8 Hz, 3H), 2.12 (s, 3H), 5.92-5.96 (q, *J*=6.8 Hz, 1H), 7.52-7.56 (t, *J*=7.6 Hz, 1H), 7.67-7.69 (d, *J*=7.6 Hz, 1H), 8.14-817 (m, 1H), 8.23-8.24 (m, 1H).

HPLC Condition: Amylose column, 5% *Iso*-propanol in hexane, Flow = 1 mL/min, UV = 215 nm, Retention time = 10.57 min for (*R*)-isomer, 12.56 min for (*S*)-isomer.

(*S*)-1-(3-nitrophenyl)ethan-1-ol (**4**)

^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.54-1.56 (d, 6.4 Hz), 5.02-5.06 (q, 6.4 Hz), 7.52-7.56 (t, *J*=8 Hz, 1H), 7.72-7.74 (d, *J*=8 Hz, 1H), 8.13-815 (d, *J*=8.4 Hz, 1H), 8.26 (s, 1H).

HPLC Condition: Amylose column, 5% *Iso*-propanol in hexane, Flow = 1 mL/min, UV = 215 nm, Retention time = 20.0 min for (*R*)-isomer, 23.75 min for (*S*)-isomer.

General procedure for synthesis of 1-(3-aminophenyl)ethan-1-ol (6 & 8) :

In 100 ml round bottom flask 1-(3-nitrophenyl)ethan-1-ol (1.8 g, 10.7 mmol) was taken. To that 10% Pd/C (0.18 g, 10%w/w) was added and stirred for 6 h under hydrogen balloon at room temperature in methanol. The catalyst was filtered and the filtrate was concentrated in vacuum and purification was done by filter column chromatography to yield 1-(3-aminophenyl)ethan-1-ol in 98 % yield which was immediately used for polymerization.

Procedure for Synthesis of Chiral analogue Polyaniline

(S)-1-(3-aminophenyl)ethan-1-ol (3 g, 22.0 mmol) was dissolved in aqueous HCl (1.5 M, 25 mL), and a solution of ammoniumpersulfate (5 g, 22.0 mmol) in HCl (1.5 M, 25 mL) was added to it at 0 °C. Since aniline polymerization is strongly exothermic, the oxidant must be added slowly over a period of 1 h. After the addition of the oxidant, the reaction was stirred (two days). The precipitated polyaniline hydrochloride (**S-P1)** was separated by filtration and washed consecutively with water. To remove the oligomers and low molecular weight polymers soxhlet was done in THF and MeOH. The soluble portion of polymer were used for UV-Visible, CD-Spectra and GPC analysis, while the undissolved portion of polymer was then vacuum-dried and treated with aqueous ammonia (3 wt %) for 2 h. Deprotonated polymer was again washed with water, methanol and dried to get final polymer **S-P2** (1.2 g). Similarly **R-P1** and **R-P2** polymer were synthesized.

Preparation of metal loaded PANI:

Metal salts (300 mg) and chiral PANI **S-P2** (300 mg) were added to a solution acetonitrile and stirred at ambient temperature (48 h) under nitrogen atmosphere. The resultant catalyst was filtered and washed thoroughly with acetonitrile and acetone until the filtrate was colorless. The resulting residue was dried to afford the catalyst as black powder. The above process was employed for $Cu(OAc)_2$, $FeCl_3$, and with minor modification for $PdCl_2$ (150 mg for 300 mg PANI).

General procedure for Henry reaction:

In a clean dry 10 ml flask, 4-nitro benzaldehyde (0.15 g, 0.993 mol), nitromethane (0.625, 9.93 mmol) were dissolved in appropriate solvent (4 ml) at room temperature in water bath. To that Chiral PANI-$Cu(OAc)_2$ catalyst (50 mg) was added and stirred for 72 h. Solvent was evaporated and purified by column chromatography to afford Henry product as mentioned in table 2 which were characterized by NMR Spectroscopy and entiomeric excess was determine by chiral phase HPLC column.

2-nitro-1-(4-nitrophenyl)ethan-1-ol **(9)**

^{1}H-NMR (400 MHz, $CDCl_3$): 4.60-4.65 (m, 2H), 5.62-5.65 (m, 1H), 7.64-7.66 (d, *J*=8.8 Hz, 2H), 8.28-8.30 (d, *J*=8.8 Hz, 2H).

HPLC Condition: Chirapak OD-H column, 15% IPA in hexane, Flow = 0.8 mL/min, UV = 254 nm, Retention time = 21.10 min and 26.10 min.

General procedure for Biginelli reaction:

The Chiral PANI-$FeCl_3$ was screened for the three component classical one-pot Biginelli reaction. In a small round bottom 10 ml flask 4-chloro bennzaldehyde (0.1 g, 0.7 mmol), ethyl acetoacetate (0.1 ml, 0.7 mmol), urea (0.05 g, 0.84 mmol), and Chiral PANI-$FeCl_3$ (50 mg) in appropriate solvent (4 ml) and stirred in water bath at room temperature 72 h. The reactions were monitored by thin layer chromatography, catalyst was separated by filtration and the product was purified by column chromatography over silica gel. The yields mentioned refer to the isolated yield and the products have been characterized by NMR Spectroscopy and entiomeric excess was determine by chiral phase HPLC column.

Ethyl-4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(10)**

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16-1.20(t, J= 7.2Hz, 3 H, $-CH_3$), 2.36(s, 3H, $-CH_3$), 4.05-4.13(m, 2H, $-CH_2$), 5.42-5.42(d, *J*= 2Hz, 1H, -CH), 5.74(br s, -NH), 7.33-7.34(m, 4H, Ar-H), 8.11(br s, -NH).

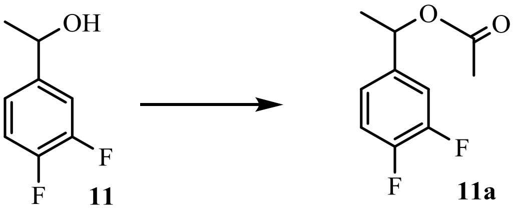
HPLC Condition: Chirapak OD-H column, 30% IPA in hexane, Flow = 0.5 mL/min, UV = 254 nm, Retention time = 9.81 min and 11.67 min.

General procedure for hydrogenation reaction:

In a clean dry 10 ml flask starting material ketone (0.1 g) and Chiral PANI-$PdCl_2$ catalyst (50 mg) were taken in methanol (10 ml) under H_2 balloon at room temperature for 48 h. The reaction was monitored by performing thin layer chromatography, catalyst was simply separated by filtration and the products were purified by filter column chromatography over silica gel. The yields mentioned refer to the isolated yield and the products have been characterized by NMR Spectroscopy and enantiomeric excess was determine by chiral phase HPLC column.

1-(3,4-difluorophenyl)ethan-1-ol **(11)**

^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.47-1.49 (d, J=6.4 Hz, 3H), 2.02 (br s, 1H), 4.86-4.90 (q, J=6.4 Hz, 1H), 7.08-7.22 (m, 3H)



Synthesis of 1-(3,4-difluorophenyl)ethyl acetate **(11a)**

In a clean dry round bottom flask, 1-(3,4-difluorophenyl)ethan-1-ol (0.075, 0.47 mmol) was dissolved in dichloro methane (10 ml). To that solution acetic anhydride (0.05 ml, 0.57 mmol), triethyl amine (0.10 ml, 0.76 mmol) and 4-dimethyl amino pyridine was added in catalytic amount and stirred reaction at room temperature. After 5 h reaction was quenched and purified by column chromatography to afford 1-(3,4-difluorophenyl)ethyl acetate in 94% yield.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.51-1.53 (d, J = 6.8 Hz, 3H), 2.01 (s, 3H), 5.80-5.85 (d, J = 6.8 Hz, 3H), 7.08-7.22 (m, 3H).

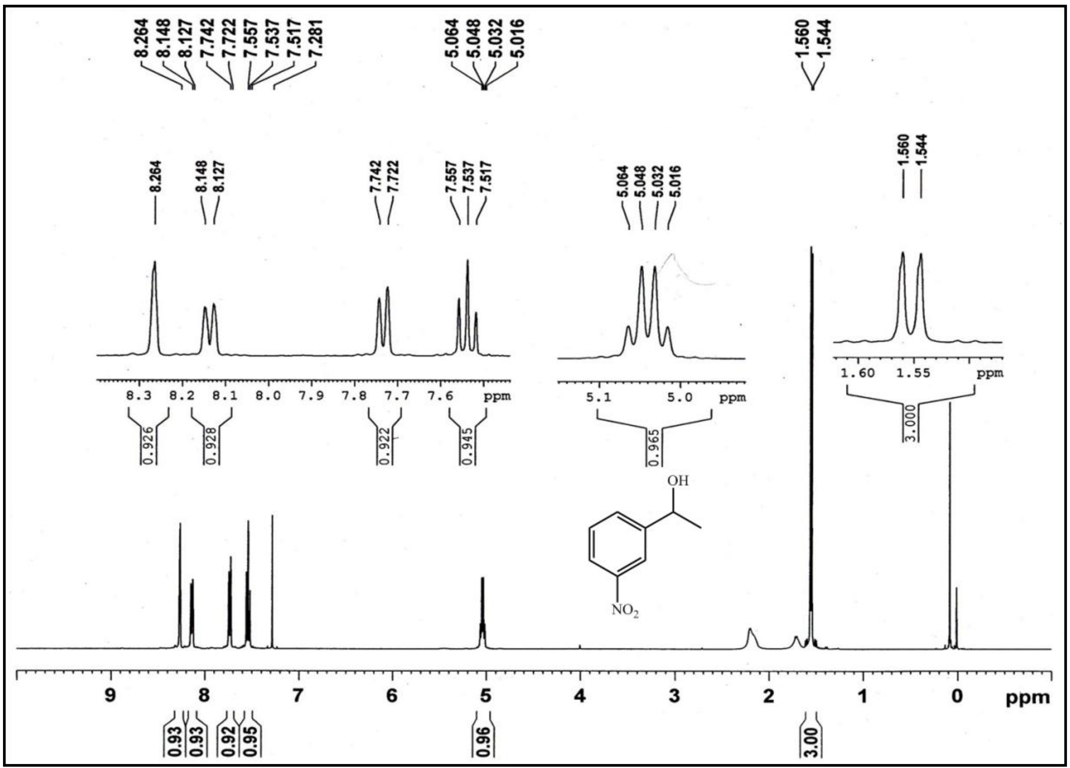
HPLC Condition: Amylose column, 7% IPA in hexane, Flow = 0.5 mL/min, UV = 254 nm, Retention time = 8.64 min and 9.19 min.

2,3-dihydro-1H-inden-1-ol **(12)**

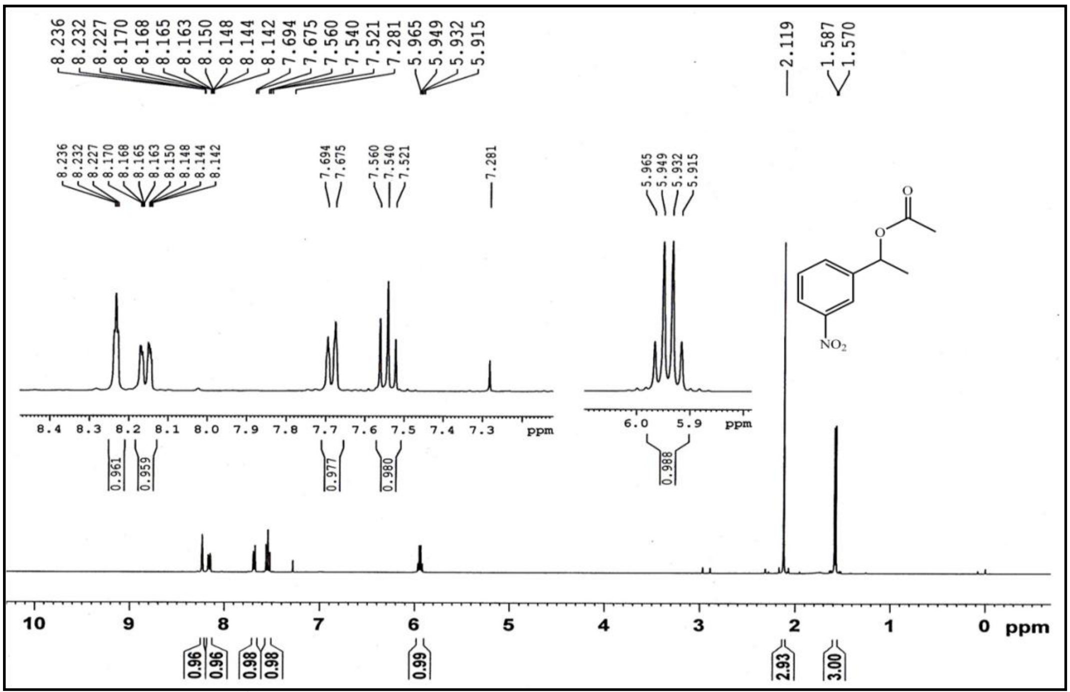
^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.92-1.99 (m, 2H), 2.01- 2.55 (m, 1H), 2.80-2.88 (m, 1H), 3.04-3.43 (m, 1H), 5.25-5.27 (t, J = 6 Hz, 1H), 7.26-7.29 (m, 3H), 7.43-7.45 (m, 1H).

HPLC Condition: Amylose column, 5% IPA in hexane, Flow = 1 mL/min, UV = 254 nm, Retention time = 8.75 min and 9.87 min.

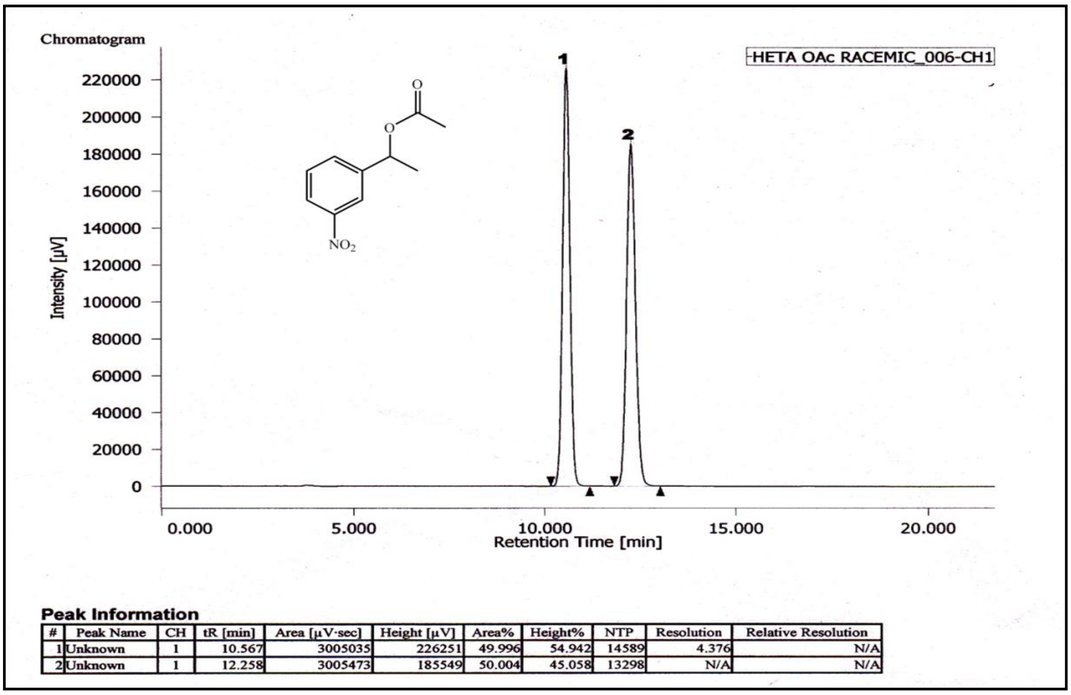
Spectral Data:



^{1}H-NMR of 1-(3-nitrophenyl)ethan-1-ol (**4**)



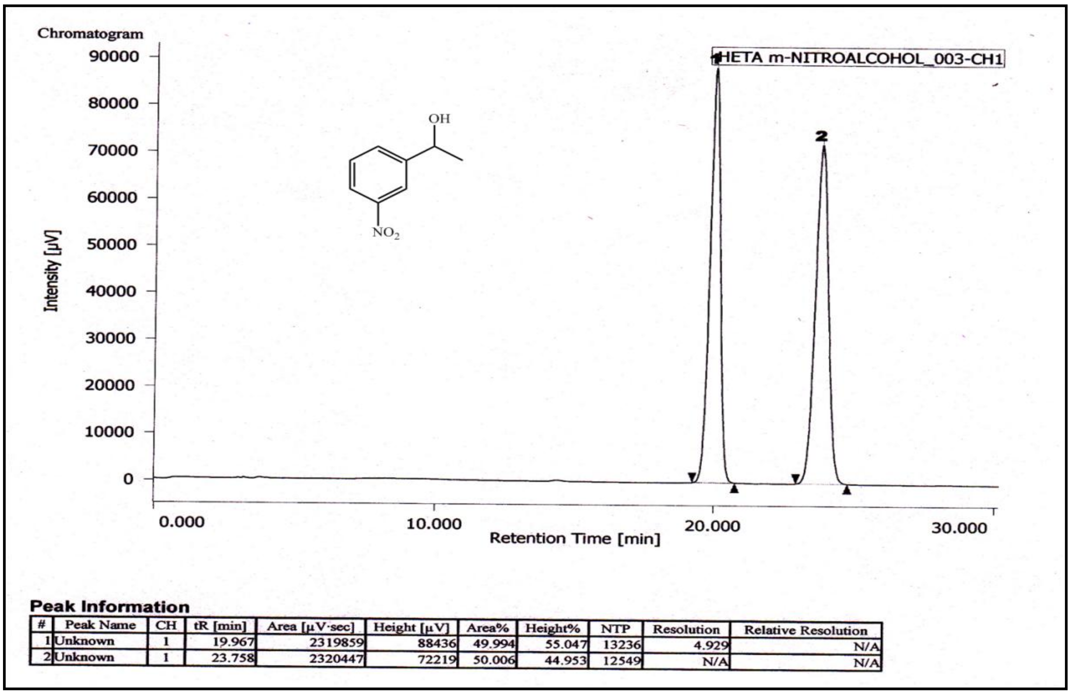
^{1}H-NMR of 1-(3-nitrophenyl)ethyl acetate **(5)**



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	NTP	Resolution	Relative Resolution
1	Unknown	1	10.567	3005035	226251	49.996	54.942	14589	4.376	N/A
2	Unknown	1	12.258	3005473	185549	50.004	45.058	13298	N/A	N/A

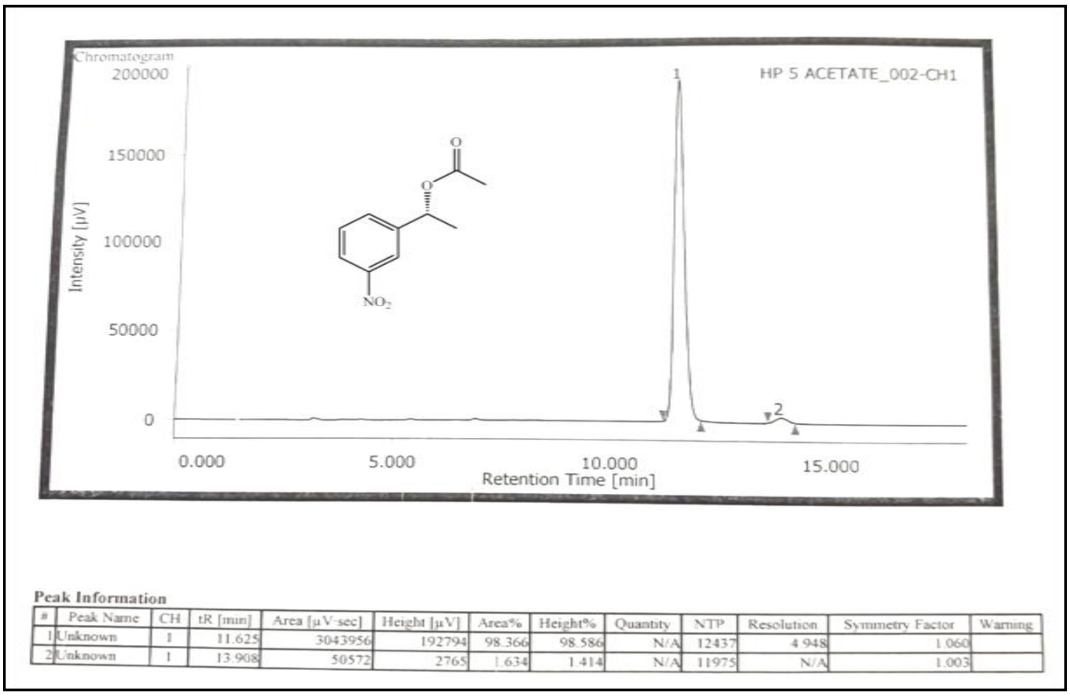
HPLC chromatograph of racemic 1-(3-nitrophenyl)ethyl acetate
Solvent system: 5% IPA-Hexane; Flow rate: 1 ml/min; Detector: UV-254 nm ;
Chiral Column: Amylose.



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	NTP	Resolution	Relative Resolution
1	Unknown	1	19.967	2319859	88436	49.994	55.047	13236	4.929	N/A
2	Unknown	1	23.758	2320447	72219	50.006	44.953	12549	N/A	N/A

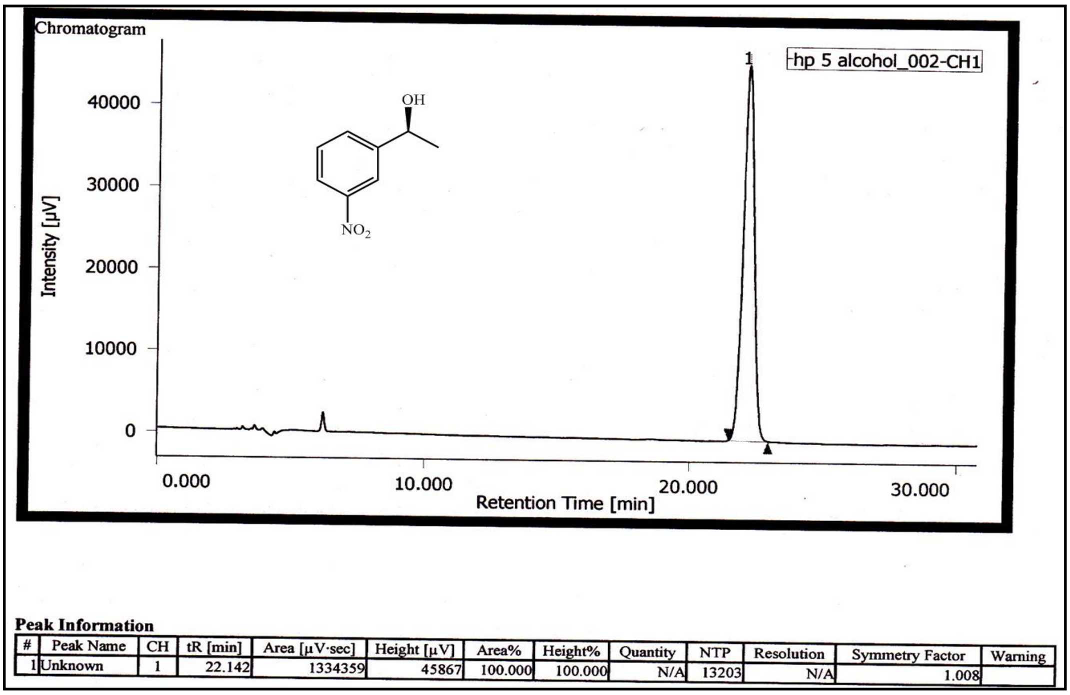
HPLC chromatograph for racemic 1-(3-nitrophenyl)ethan-1-ol
Solvent system: 5% IPA-Hexane; Flow rate: 1 ml/min; Detector: UV-254 nm ;
Chiral Column: Amylose.



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	11.625	3043956	192794	98.366	98.586	N/A	12437	4.948	1.060	
2	Unknown	1	13.908	50572	2765	1.634	1.414	N/A	11975	N/A	1.003	

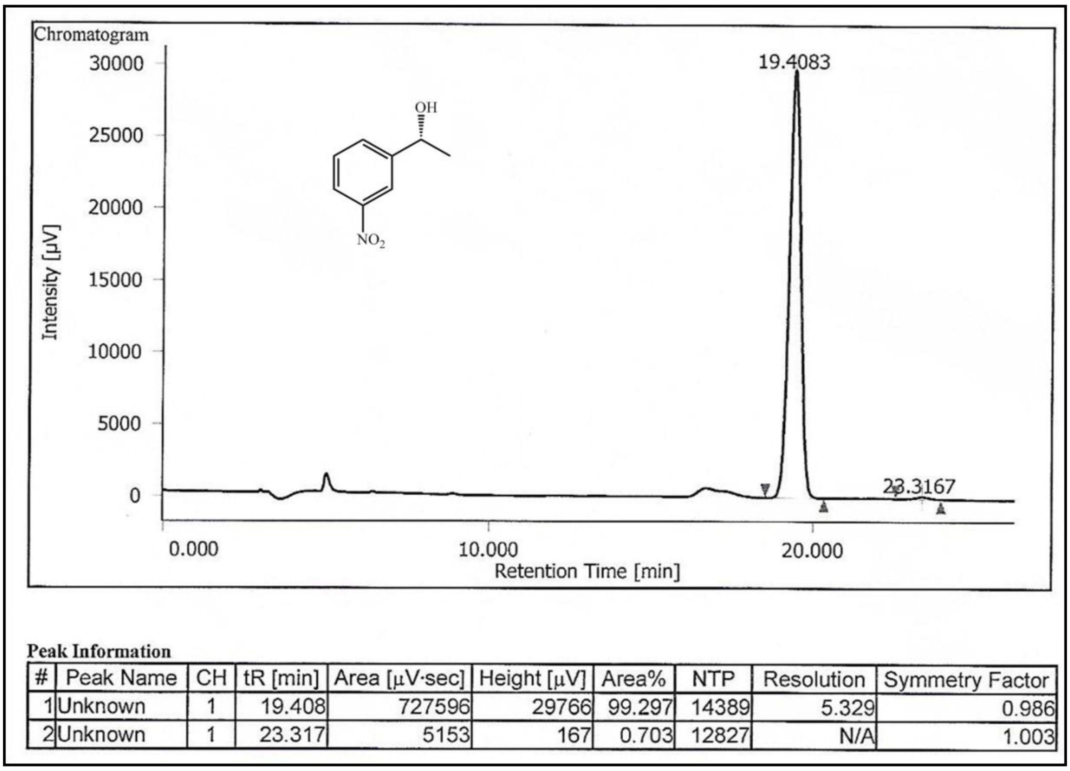
HPLC chromatograph of (*R*)-1-(3-nitrophenyl)ethyl acetate [Entry 3, Table 1]



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	22.142	1334359	45867	100.000	100.000	N/A	13203	N/A	1.008	

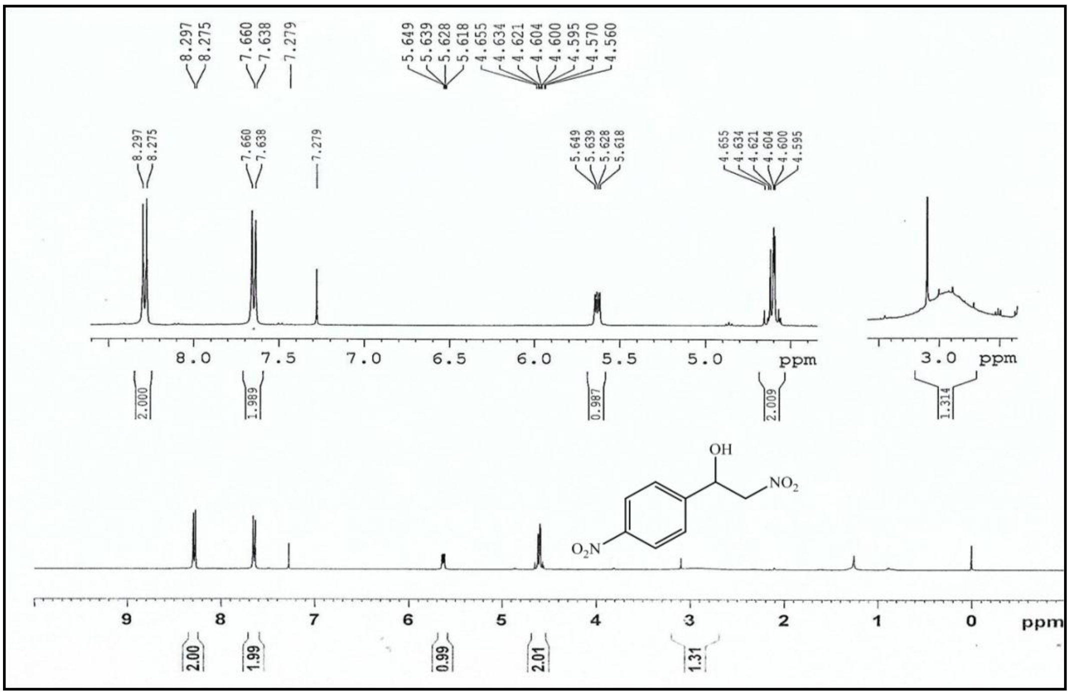
HPLC chromatograph for (*S*)-1-(3-nitrophenyl)ethan-1-ol



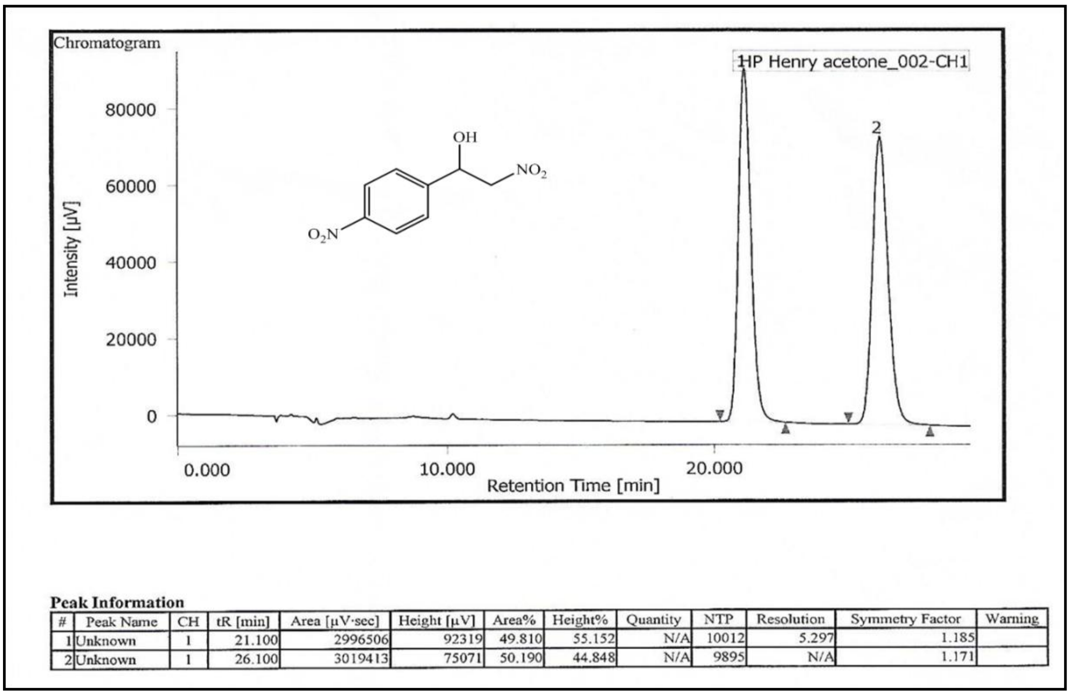
Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	NTP	Resolution	Symmetry Factor
1	Unknown	1	19.408	727596	29766	99.297	14389	5.329	0.986
2	Unknown	1	23.317	5153	167	0.703	12827	N/A	1.003

HPLC chromatograph for (*R*)-1-(3-nitrophenyl)ethan-1-ol



^{1}H-NMR of compound **(9)**

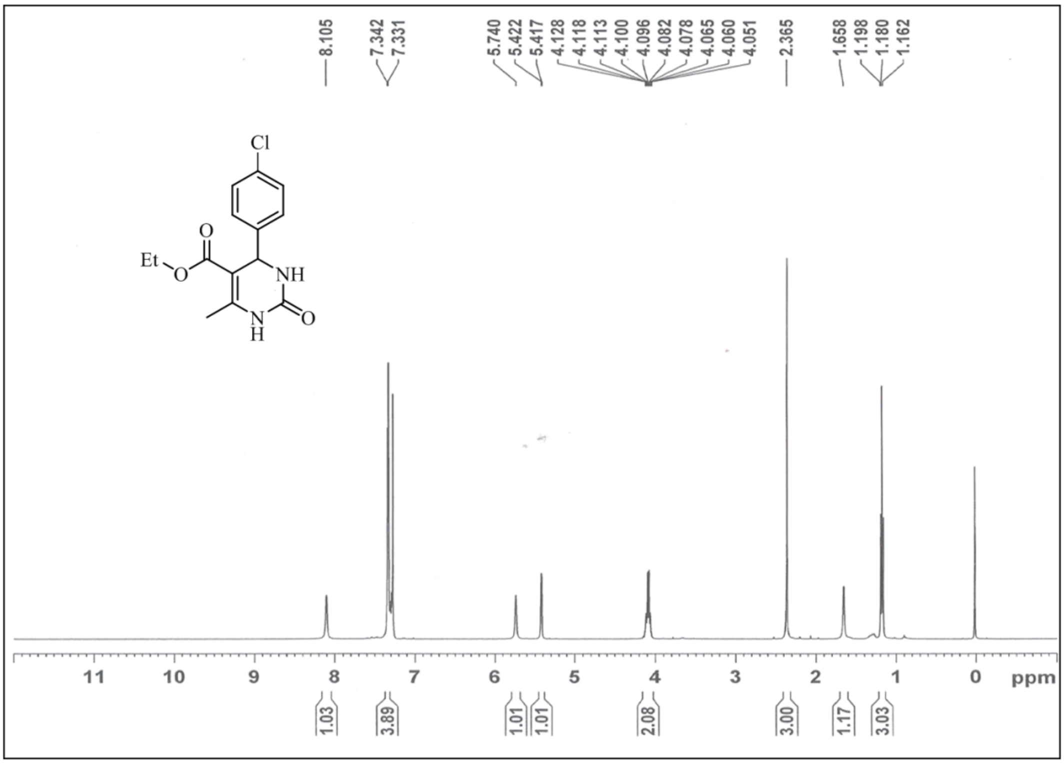


Peak Information

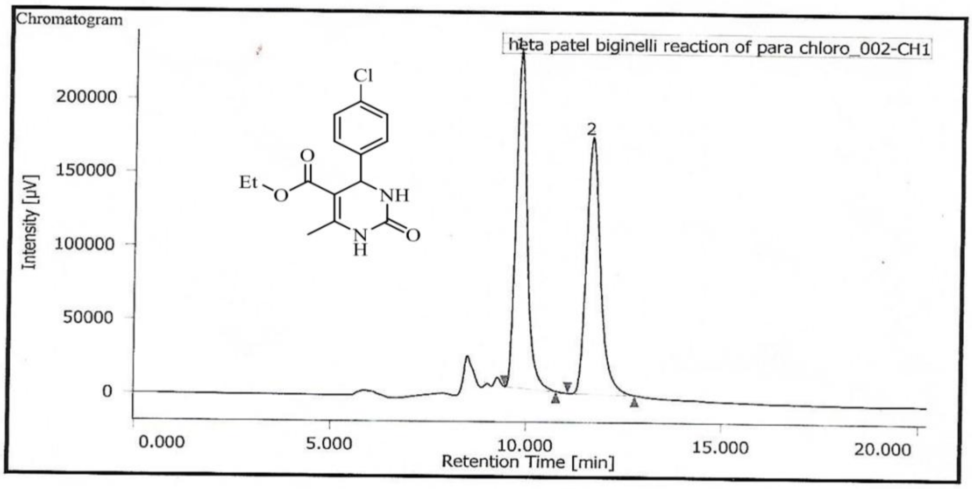
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	21.100	2996506	92319	49.810	55.152	N/A	10012	5.297	1.185	
2	Unknown	1	26.100	3019413	75071	50.190	44.848	N/A	9895	N/A	1.171	

HPLC chromatograph of 2-nitro-1-(4-nitrophenyl)ethan-1-ol

Solvent system: 15% IPA-Hexane; Flow rate: 0.8 ml/min; Detector: UV-254 nm ; Chiral Column: Chirapak OD-H.



^{1}H-NMR of compound **(10)**

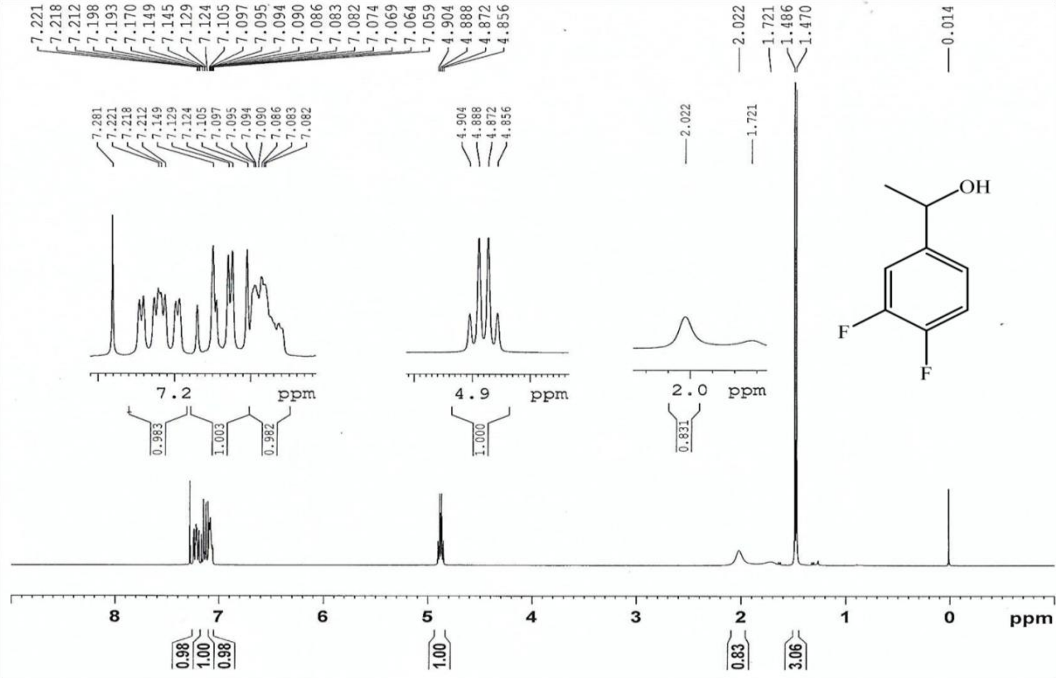


Peak Information

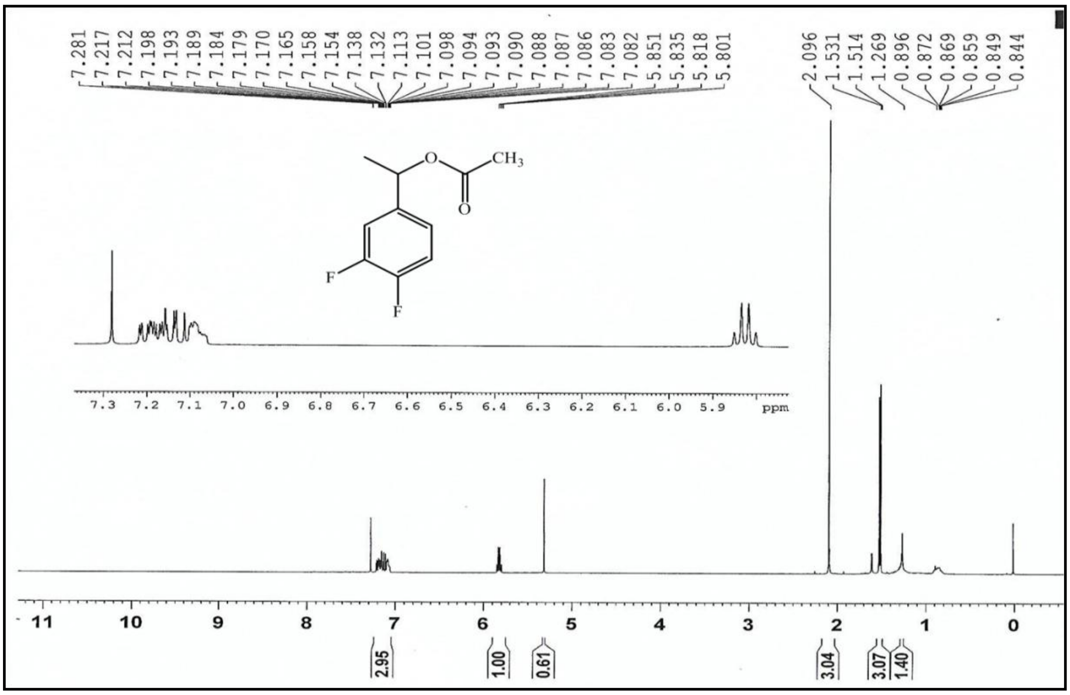
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	9.808	4528112	229390	51.082	56.841	N/A	6204	3.315	1.460	
2	Unknown	1	11.667	4336281	174174	48.918	43.159	N/A	5556	N/A	1.434	

HPLC chromatograph of Ethyl-4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**10**)

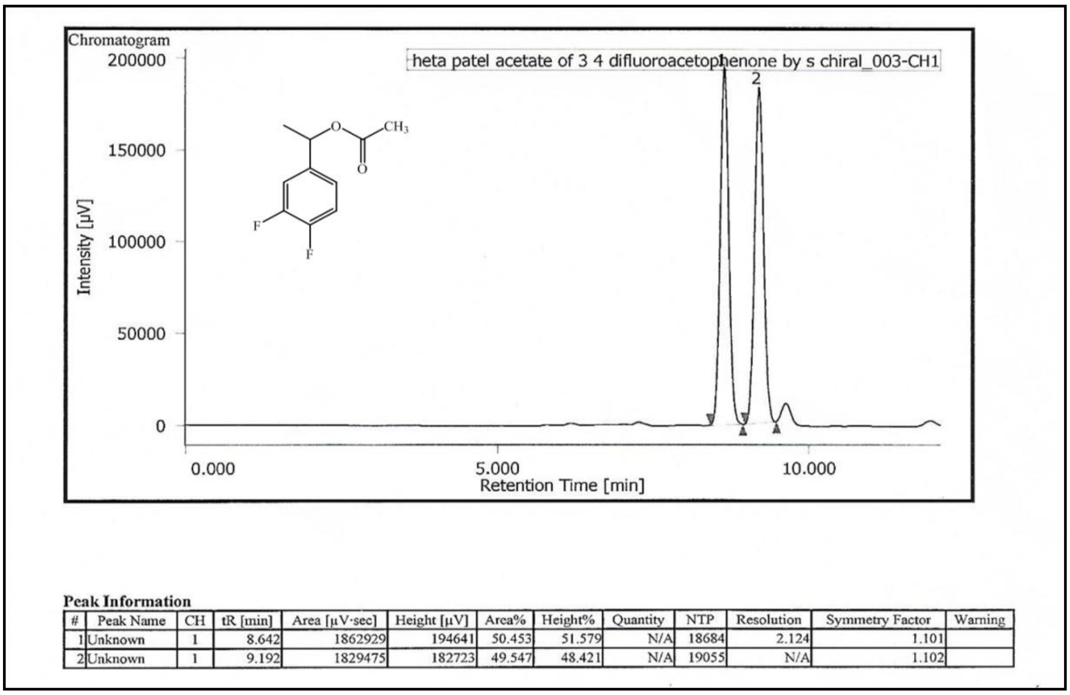
Solvent system: 30% IPA-Hexane; Flow rate: 0.5 ml/min; Detector: UV-254 nm ; Chiral Column: Chiralpak OD-H.



^{1}H-NMR of compound **(11)**



^{1}H-NMR of compound **(11a)**

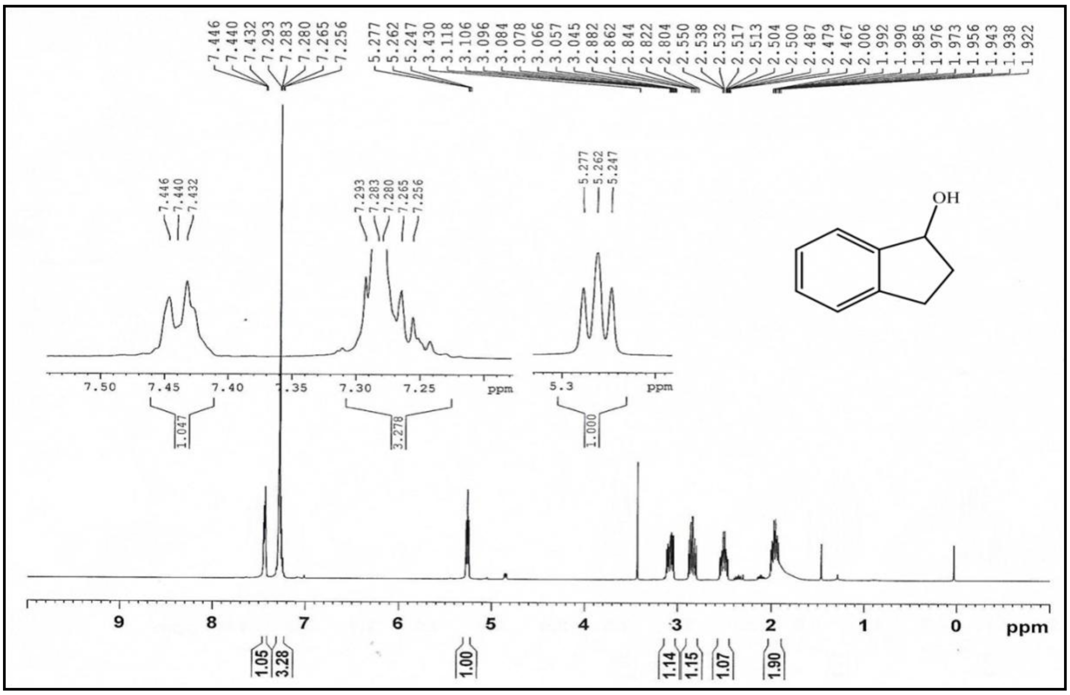


Peak Information

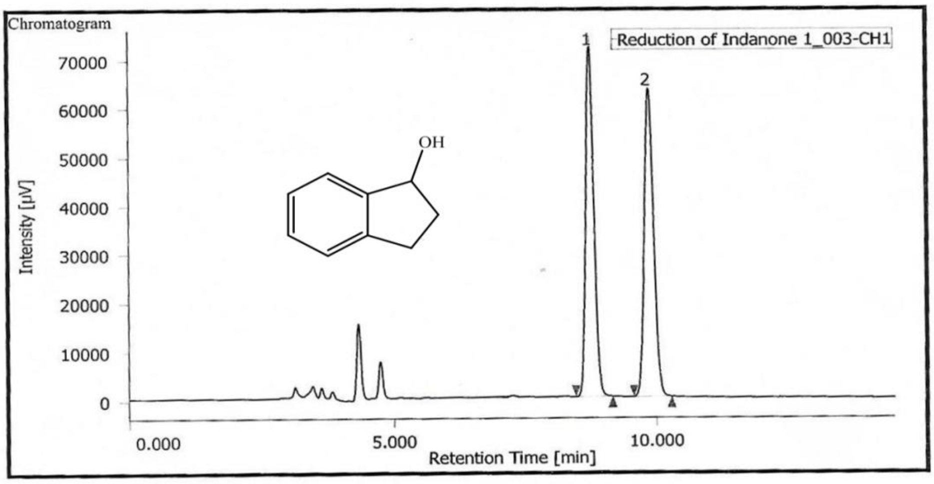
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	8.642	1862929	194641	50.453	51.579	N/A	18684	2.124	1.101	
2	Unknown	1	9.192	1829475	182723	49.547	48.421	N/A	19055	N/A	1.102	

HPLC chromatograph of 1-(3,4-difluorophenyl)ethyl acetate (**11a**)

Solvent system: 7% IPA-Hexane; Flow rate: 0.5 ml/min; Detector: UV-254 nm ; Chiral Column: Amylose.



^{1}H-NMR of compound **(12)**



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	8.750	771488	71889	50.006	53.234	N/A	15353	3.702	1.075	
2	Unknown	1	9.867	771318	63155	49.994	46.766	N/A	14984	N/A	1.094	

HPLC chromatograph of 2,3-dihydro-1H-inden-1-ol **(12)**

Solvent system: 5% IPA-Hexane; Flow rate: 1 ml/min; Detector: UV-254 nm ; Chiral Column: Chiralpak OD-H.

5.5 References

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