4.1 Introduction

In organic synthesis, hydrogen bond catalysis has proven to be an effective technique, notably in enantioselective organocatalysis.[1] Small chiral organic compounds with hydrogen bond donor functions are frequently used in the organocatalytic method to encourage asymmetric reactions. A special family of organocatalysts created along these principles are thiourea derivatives.[2] The capacity of these compounds to establish double H-bonds with molecules, which can advantageously organize and activate the reacting partners, is widely considered to be a prerequisite for the catalytic activity of these compounds.[3] Moreover, the reaction's anionic species and transition states (TSs) can be greatly stabilized by several H-bonding interactions, opening up kinetically more favorable paths.

Thiourea-based organocatalysts are distinctive and well-liked among the other organocatalysts because of their non-covalent supramolecular interactions. Jacobsen,[4] Schreiner[5], and Takemoto[6] catalysts, as depicted in Figure 1, are pioneering examples of thiourea-based organocatalysts.

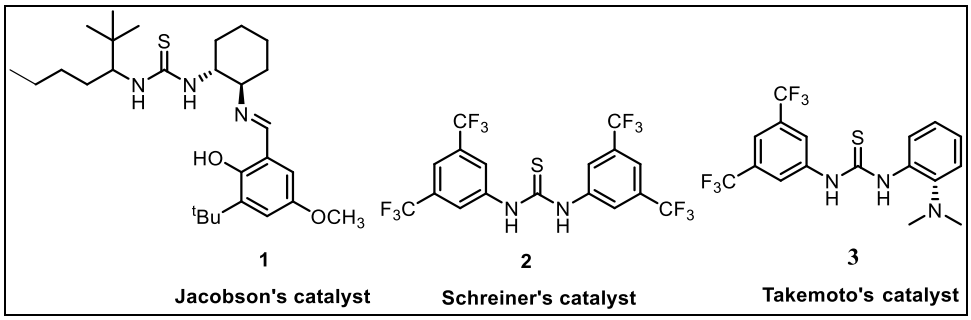


Figure 1: pioneering examples of thiourea-based organocatalysts.

A broad range of chiral thiourea organocatalysts are identified in the literature to accelerate diverse synthetically effective asymmetric organocatalytic transformations e.g., Michael addition, nitro-Mannich reaction, amination reaction, sulfa-Michael addition, Domino aza-Michael-Henry reaction, α-alkylation of aldehydes, Mannich-type reactions, Diels-Alder reaction, intramolecular [5 + 2] cycloadditions, vinylogous aldol reactions, etc.[7-13]

Due to their simultaneous activation of both electrophiles and nucleophiles, bifunctional chiral thiourea-amine organocatalysts have grown in popularity in recent years. These organocatalysts' primary role is to activate nucleophiles, while the thiourea group also uses double hydrogen bonding to stimulate electrophiles. As a result, it improves enantioselectivity as well as reaction rates.

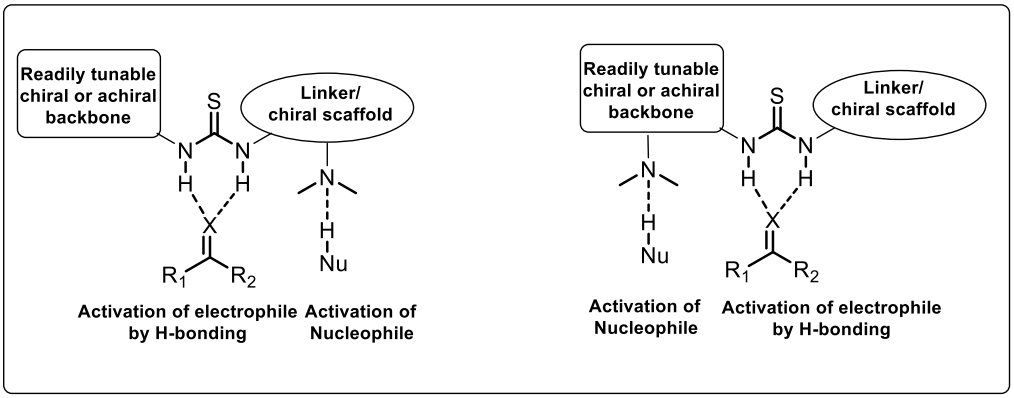


Figure 2: Mechanistic illustration of dual activation of bifunctional thiourea-amine organocatalyst

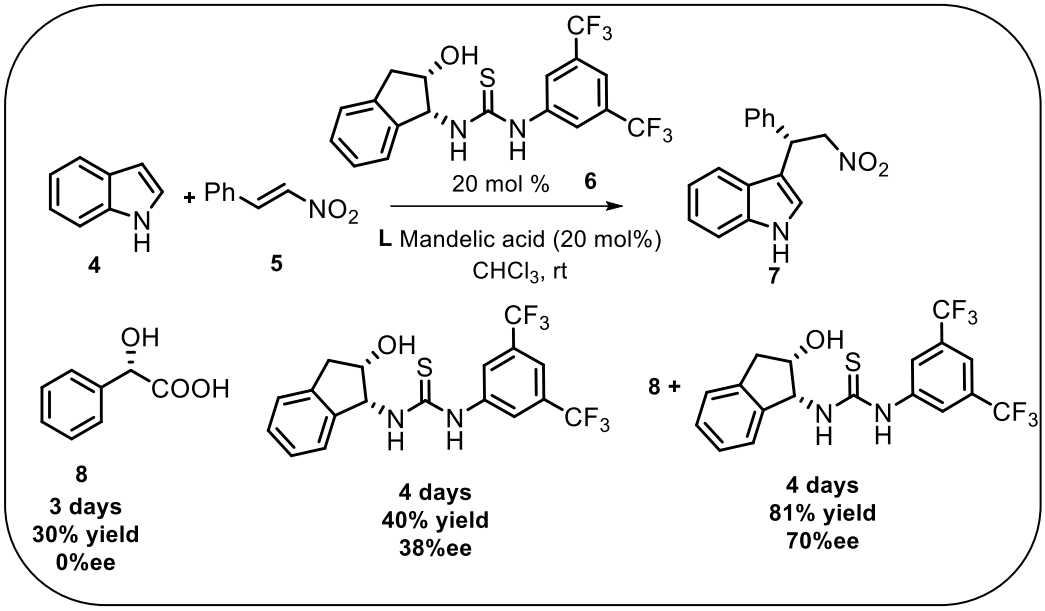
4.1.1 Friedel–Crafts Alkylation of Indoles

For the creation of new carbon-carbon bonds, the Friedel-Crafts alkylation reaction[14] has garnered a lot of interest and grown into a potent tool in organic synthesis. New catalytic enantioselective variations have received a lot of attention in this field.[15,16]

Given that the indole framework has been found in many natural and synthetic products as well as pharmaceuticals with intriguing biological activities, the addition of indole derivatives to electron-deficient olefins allows easy accessibility to 3-substituted indole analogues with potential applications.[17]

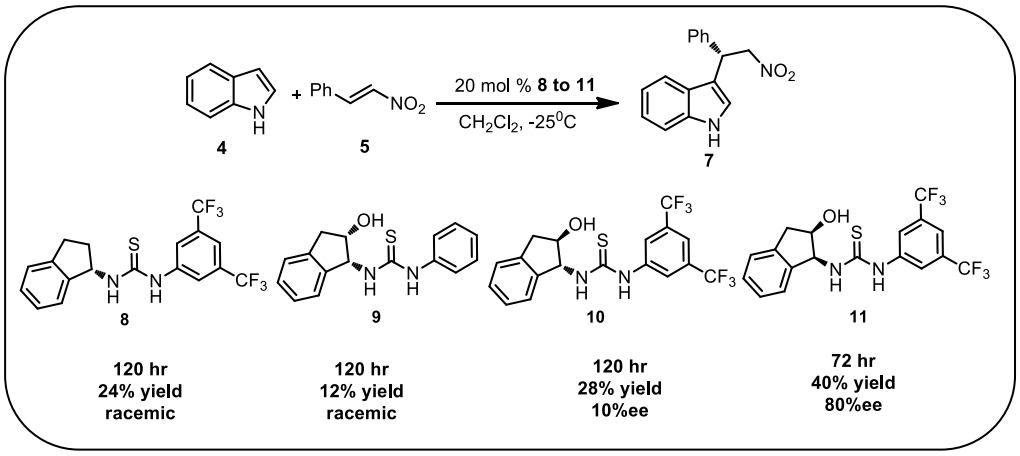
The outcomes demonstrate the high efficiency of Bronsted acid assisted thiourea catalysts for the enantioselective Friedel-Crafts reaction of indoles with nitroalkenes.

The combined influence of the two species is greater than the effect of each species acting alone. The donor hydrogen of the thiourea catalyst, can easily have its chiral environment and pKa tuned by simply changing the type of the acid.



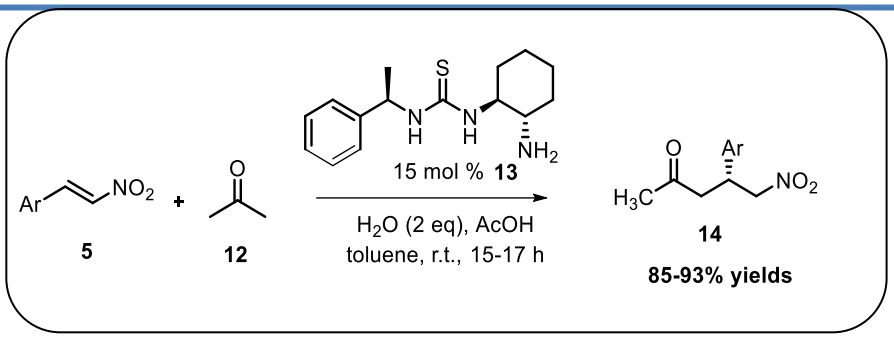
Scheme 1: Friedel–Crafts Alkylation of Indoles catalysed by thiourea

Harrera et-al did a comparison study a for the outcomes of the Friedel-Crafts alkylation reaction between indole **4** and nitrostyrene **5** at low temperatures with these catalysts. Nonetheless, the same trend has been seen in other processes when similar catalysts have been applied.[18]



Scheme 2: Thiourea-Catalyzed Friedel-Crafts Alkylation Reaction

Tsogoeva et al. in (2006) described the dual function of an organocatalyst with a thiourea and amine group as a potent catalyst to the various different aromatic nitro olefins **5** with propane-2-one **12** for the production of chiral scaffolds as γ-nitro ketones in high conversion and enantioselectivities (Scheme 3).[19-24]



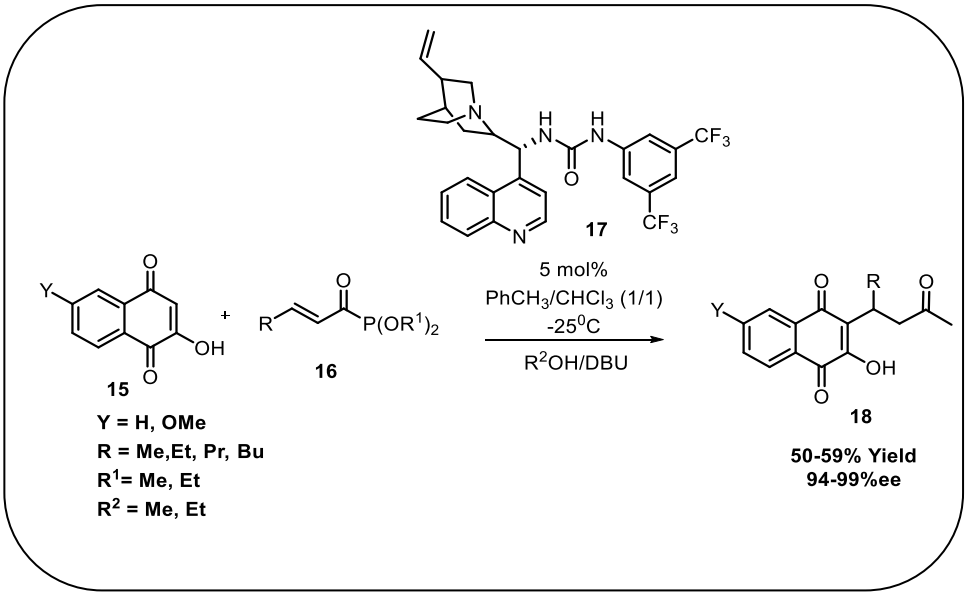
Scheme 3: Thiourea-Catalyzed Alkylation Reaction of Propane 2-one and Nitro-olefine

4.1.2 Enantioselective Michael Addition

One of the most significant processes for creating carbon–carbon bonds in organic synthesis is the Michael addition.[25] Throughout the years, a lot of work has been put into developing asymmetric catalytic forms of the process. Recent years have seen significant advancements in the organocatalyst-mediated Michael addition due to the demand for ecologically favorable and metal-free reactions.[26,27] Chiral bifunctional amine-thioureas, one of the established organocatalysts, have proven to be effective and have been used in asymmetric catalytic Michael addition reactions.[28]

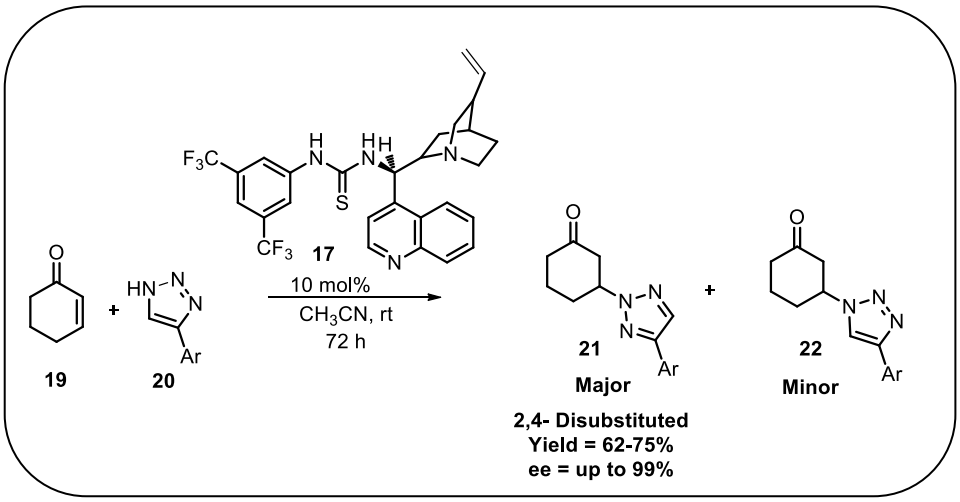
Due to the readily available and high reactivity of nitroalkenes, the capacity of the nitro functionality to accept hydrogen bonds from properly designed catalyst systems, and the high synthetic application of the nitroalkane adducts, the asymmetric Michael addition of different carbon nucleophiles to nitrolefins is proving to be a particularly interesting target.[29-31]

Using a cinchona-based thiourea catalyst, Wang and Zhou et al. developed an asymmetric Michael addition reaction **17**. (**Scheme 4**).[32] The corresponding -substituted carboxylates **18** were produced via the reaction of 2-hydroxy-1,4-naphthoquinone **15** and α,β-unsaturated ketophosphonates **16** in the presence of **17**, after which they were treated with alcohol in the presence of DBU. They were able to convert in to products with high degrees of enantioselectivities in moderate to good yields.



Scheme 4: Chiral thiourea catalyzed asymmetric synthesis of β-substituted carboxylates

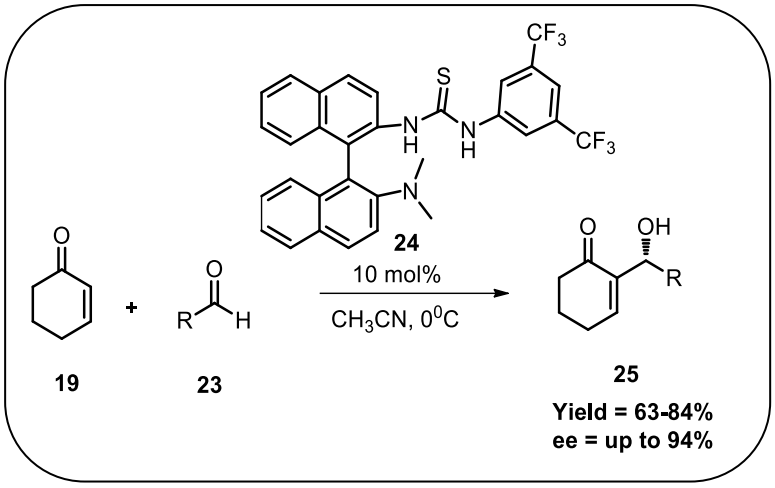
bifunctional thiourea organocatalysts' catalytic activity in the direct aza-Michael addition of 4-aryl-NH-1,2,3-triazoles **20** to different cyclic enones. It has been noted that the enantioselective aza-Michael addition was significantly aided by the cinchonine-derived thiourea organocatalyst **17**. In order to produce 2,4-disubstituted 1,2,3-triazoles **21** as principal Michael adducts in good to high chemical yield with outstanding enantioselectivity as well as minor 1,4-disubstituted 1,2,3-triazoles **22**, the catalytic procedure first involved the specific addition of N_2 to triazoles.[33]



Scheme 5: Organocatalytic Aza-Michael Addition of 4-Aryl-NH-1,2,3-triazoles 2 with 2-Cyclohexen-1-One

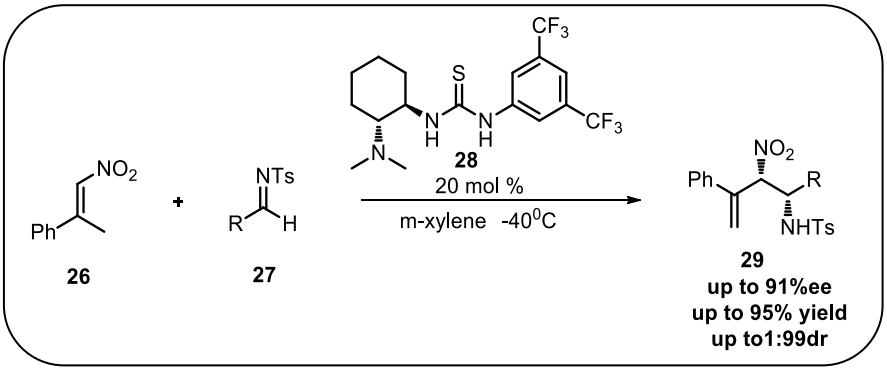
4.1.3 Morita-Baylis-Hillman (MBH) reaction

The MBH reaction, which produced structurally diverse chiral allylic alcohols and novel C-C bonds, has drawn a lot of interest in organic synthesis. The development of catalytic, enantioselective versions of the processes has so received a lot of attention, which is not surprising. Few chiral thiourea-based amines, though, were employed as MBH reaction catalysts. Wang and colleagues described the chiral naphthidine-derived thiourea-amine organocatalyst for the first time in 2005. they employed the chiral thiourea-amine to catalyse cyclohexenone's **19** highly enantioselective MBH reactions with a variety of aldehydes **23** (**Scheme 5**).[34]



Scheme 6: MBH reaction catalyzed by binaphthyl-derived thiourea-amine Organocatalyst.

Xu and colleagues reported the aza-MBH-type conversion of nitroalkenes **26** to N-tosylimines **29** later in 2009. (**Scheme 7**). They produced highly diastereoselective and enantioselective compounds using N-cyclohexanediamine derivatives **28** (Takemoto's catalyst). This reaction, in contrast to typical aza-MBH reactions, undergoes a unique intramolecular proton shift to produce unusual products.[34]



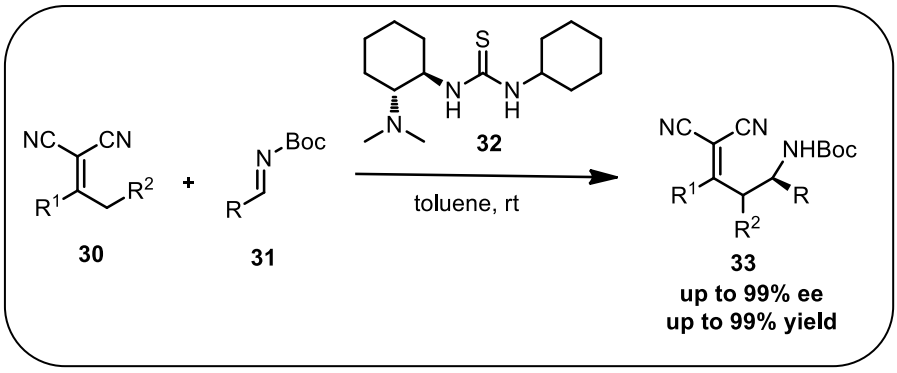
Scheme 7: Abnormal MBH reaction catalyzed by Takemoto's catalyst.

4.1.4 Mannich reaction

There are numerous successful instances of the use of bifunctional organic compounds as organocatalysts for the Mannich reaction that have a tertiary amine and a thiourea component (**Scheme 8**). These chiral molecular scaffolds, which included cyclohexane-1,2-diamine, 1,1'-binaphthyl-2,2'-diamine, cinchona alkaloids, and other amino acids, were used to create these bifunctional catalysts.[35]

The Mannich reaction was utilised by researchers to quickly combine acyl-protected imine with β-substituted nitroacetates, vinylogous, aliphatic, and carbonyl compounds. In particular, Jacobsen synthesized the N-acyliminium ion from the N-Cbz -chloroglycine ethyl ester *in situ* before the subsequent addition.[36]

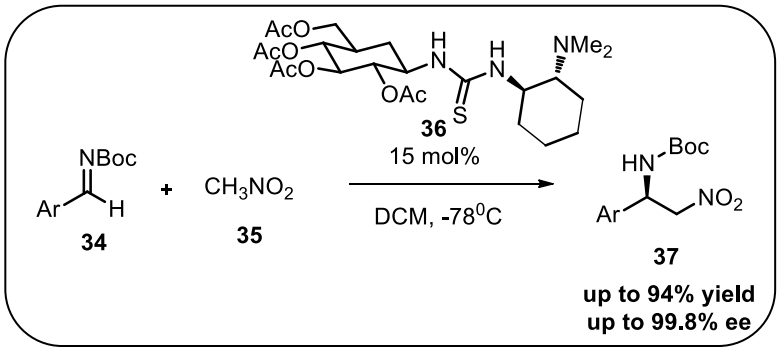
The first direct asymmetric vinylogous Mannich reaction was reported by Chen and colleagues, and it was assisted by a straightforward bifunctional thiourea-tertiary amine catalyst (Scheme 8). At ambient temperature, the unique reaction is highly regio- and stereoselective and feasible for a variety of substrates.[37]



Scheme 8: Mannich reaction catalyzed by Takemoto's catalyst.

4.1.5 Henry reaction

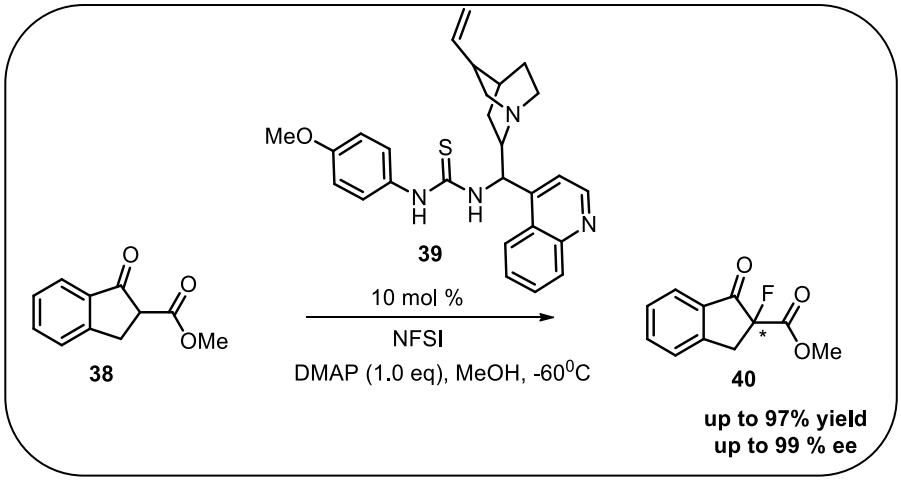
Lewis acid or an alkaline catalyst could both effectively catalyse the Henry reaction.[38] Zhou reported the first instance of Henry reaction catalysed by thiourea-based tertiary amine in 2008.[39] Starting with alpha-D-glucose, a new bifunctional chiral thiourea-amine organocatalyst **36** with a tertiary amine group and a glycosyl-thiourea framework was simply made. The asymmetric aza-Henry reaction between nitromethane and N-Boc imines was successfully catalysed by this chiral thiourea-amine catalyst, producing the respective products in high yields and ee values (**Scheme 9**).



Scheme 9: Henry reaction catalyzed by glucose derived thiourea-amine

4.1.6 C-X bond formation reactions catalysed by chiral thiourea-amine Organocatalysts

Relatively small organic compounds have been used as incredibly efficient and selective catalysts in a variety of processes. These frequently used catalysts could facilitate the creation of carbon-halogen bonds when combined with some halogenating chemicals, in addition to their utility in C-C bond formation processes (NBS, NIS, NFSI). Hu's laboratory originally reported in 2012 that chiral cinchona based thiourea-amine catalysts can be used to achieve good enantioselective fluorination processes (**Scheme 10**).

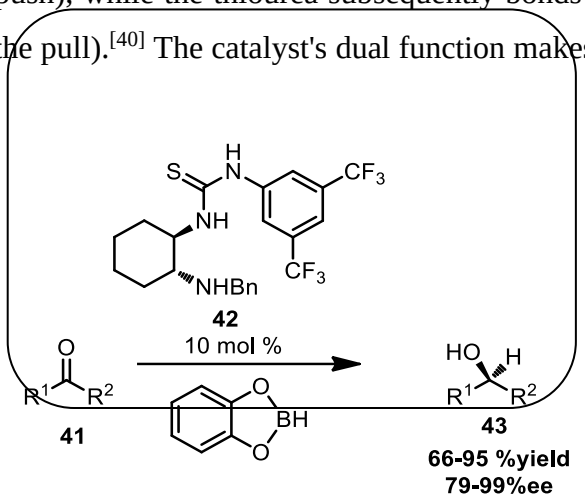


Scheme 10: Thiourea-catalyzed enantioselective fluorination of keto esters

4.1.7 Enantioselective reduction of ketones

Enantioselective organocatalytic reduction of ketones for the generation of C-H bonds might also be accomplished using bifunctional thiourea-amine catalysts. Falck predicted that the interaction of a chiral thiourea-amine organocatalyst with a borane would result in the formation of a stereochemically influenced boronate-amine complex (**Scheme 11**).

The amine group of the catalyst **42** gives the hydride in that structure a greater degree of nucleophilicity (the push), while the thiourea subsequently bonds well to and activates the carbonyl group (the pull).[40] The catalyst's dual function makes it possible to reduce the ketones.



Scheme 11: Thiourea-catalyzed enantioselective reduction of ketones

4.1.8 Thiourea catalyst as a Chiral solvating agent

Asymmetric synthetic techniques for producing chiral compounds in high yields as well as quick, simple, and precise strategies for determining the optical purities of chiral molecules using multivariate analytical techniques, such as HPLC, GC, CE, NMR, etc., have all been developed in response to the growing trend for chiral compounds in the chemical, biological, and pharmaceutical fields. NMR spectroscopy using chiral solvating agents (CSAs) to generate diastereomeric adducts with substrate through noncovalent interactions may be one of the simplest ways among them since it does not require chiral derivatization of the analyte or the use of special devices other than common NMR spectrometers and has the advantage of simplicity, accessibility, and ease of use.[41]

Chiral carboxylic acids are common structural components of organic compounds and pharmaceuticals as well as adaptable functional synthons. Several CSAs for carboxylic acids have been described over the past few decades. They include amines, lanthanide complexes, diamines, amides, macrocyclic compounds, amino alcohols, ureas, and thioureas.[42]

Simple class of chiral thioureas have been reported by Juaristi et al. to be effective receptors for chiral carboxylates. The ^{1}H NMR spectra of the diastereomeric compounds produced by this complexation exhibit distinct resolved signals that can be utilised to

assess the enantiomeric purity and assign the absolute configuration of the corresponding carboxylic acids.[43]

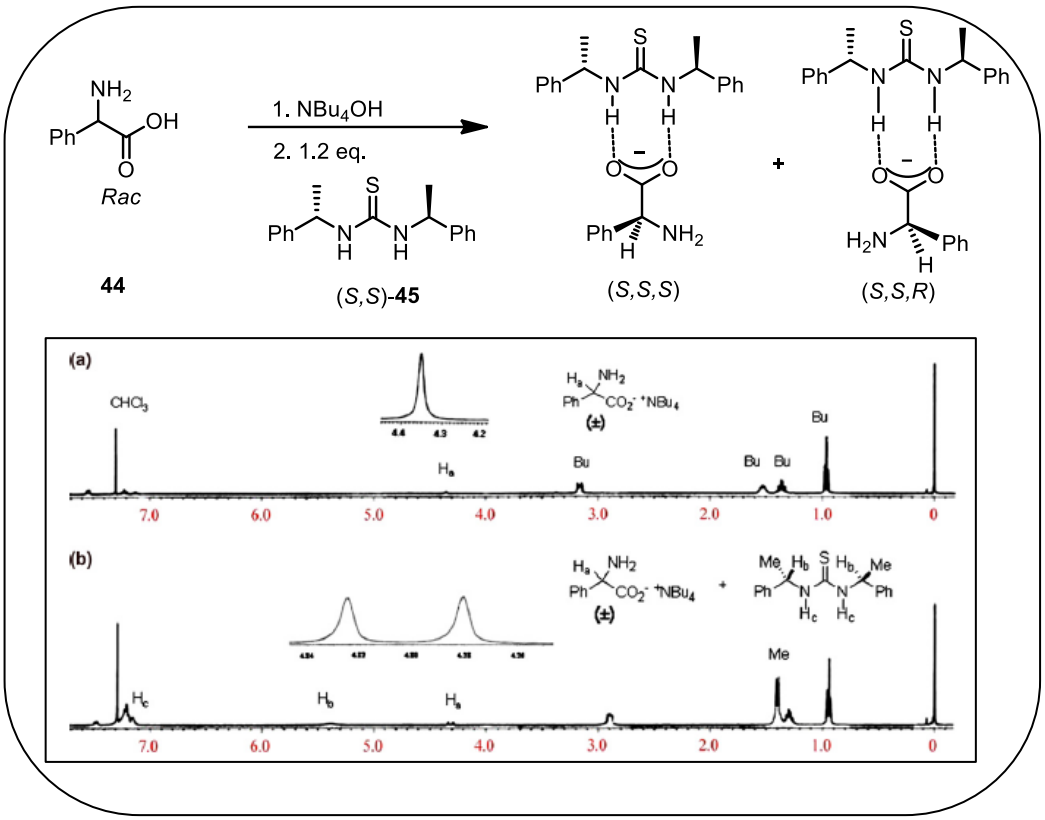
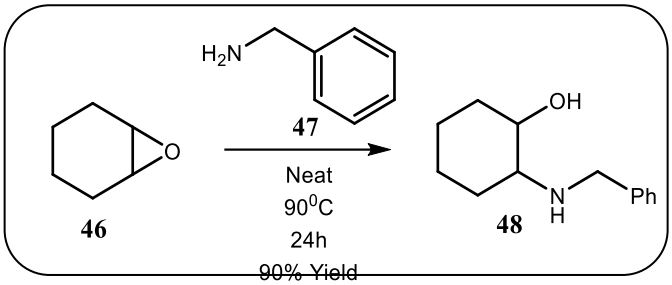


Figure 3: ^{1}H NMR spectra (400 MHz) of *Rac*-phenylglycine (a) before the Addition of (S,S)-**45** (b) followed by the addition of 1.2 equiv of (S,S)-**45**

4.2 Synthesis of ligand (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58**

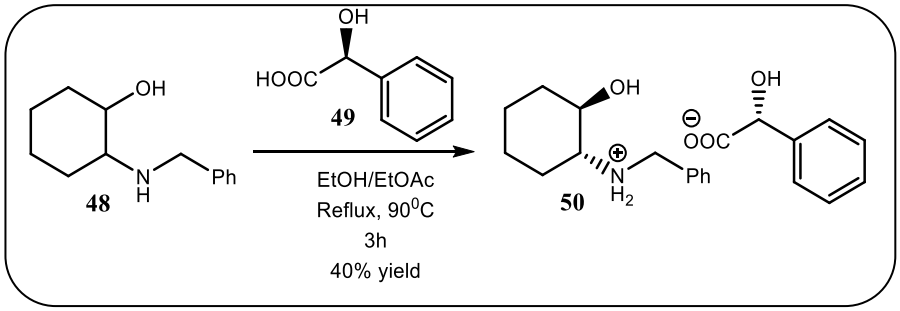
By studying a literature on thiourea based organic molecules which has many applications in the various fields like organocatalysis and work as a chiral solvating agent in organic chemistry, we have started our work to synthesize a thiourea based organic-molecules. To synthesize a effective thiourea based organocatalyst two different groups attached at two different nitrogen sites of thiourea should be such that it should easily form a interaction with substrate and favour a confirmation from a particular direction.

Synthesis of ligand (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** were started by epoxide ring opening reaction of epoxyclohexene **46** with the help of benzyl amine **47** to form a racemic 2-(benzylamino)cyclohexen-1-ol **48** product with 90% yield



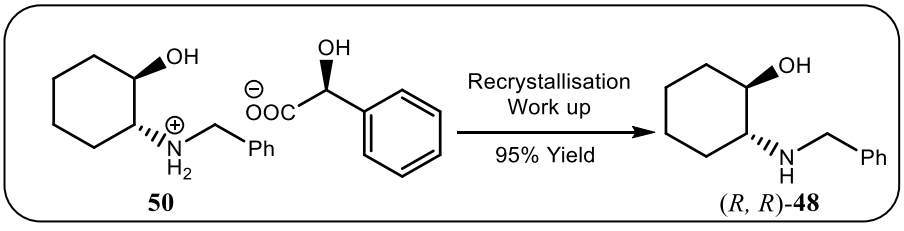
Scheme 12: Epoxide ring opening reaction of epoxyclohexene **46.**

As amino alcohols are potent to form a supramolecular interaction like H-bonding with suitable analytes due to availability of lone pair of electrons, racemic 2-(benzylamino)cyclohexen-1-ol **48** which contains equimolar mixture of (*R*,*R*) and (*S*,*S*) was resolved by the treatment with optically active *S*-mandelic acid **49** in a reflux condition. (*R*,*R*)- **48** form a diastereomeric salt with *S*-mandalic acid **49**. This diastereomeric salt then purified by recrystallisation with good yield. Solvent used for recrystallization was EtOH/EtOAc mixture in a (20:80) ratio.



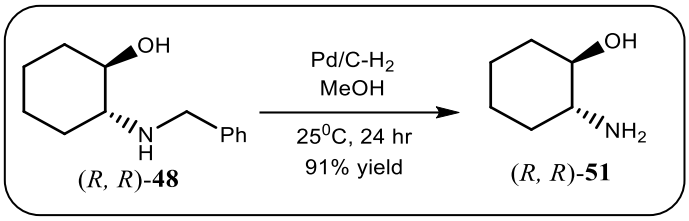
Scheme 13: Diastereomeric salt formation of racemic 2-(benzylamino) cyclohexen-1-ol **48.**

Compound **50** which is diastereomeric salt of (*R*,*R*) 2-(benzylamino)cyclohexen-1-ol and *S* mandelic acid. This diastereomeric salt **50** then cleaved in a EtOAc/H_2O (50:50) biphasic mixture to get enantioenriched (*R*,*R*) 2-(benzylamino)cyclohexen-1-ol. Optically pure (*R*,*R*)-**48** can be achieved by recrystallisation. Optical activity was measured in HPLC by chiral amylose column which indicate the purity of the compound **50** to be >99%



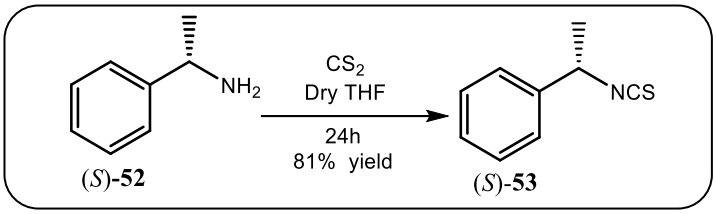
Scheme 14: Cleavage of (*R*,*R*)-2-(benzylamino)cyclohexen-1-ol **48** and *S*-mandelic acid**.**

Optically pure compound **48** then reduced in presence of Pd/C -H_2 for 24 hours at room temperature to get enantiomerically pure (*R,R*)- 2-aminocyclohexan-1-ol **51** with 91% yield.



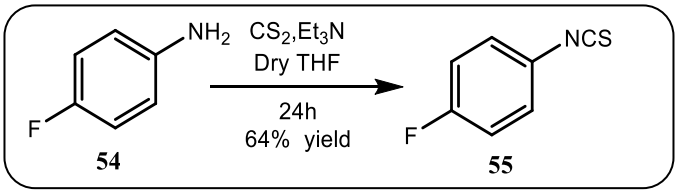
Scheme 15: Cleavage of (*R,R*) 2-(benzylamino)cyclohexen-1-ol **48** and *S*-Mandelic acid**.**

The isothiocyanates are very reactive. The (*S*)-1-phenylehane-1-amine is treated with carbon disulphide in the THF to get (*S*)-(1-isothiocyanatoethyl)benzene **53** with more then 80% yield.



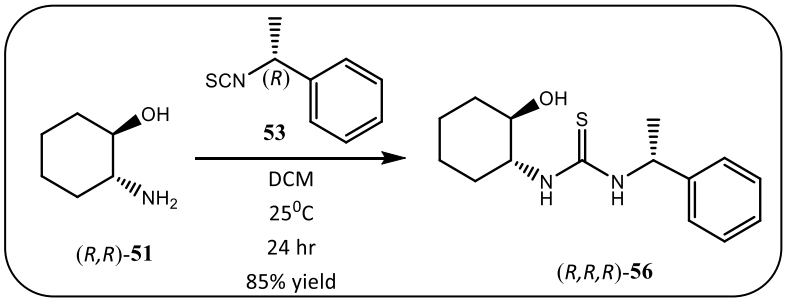
Scheme 16: Synthesis of (*S*)-(1-isothiocyanatoethyl)benzene **53**

1-fluoro-4-isothiocyanatobenzene **55** was synthesised by reacting 4-fluoroaniline **54** in presence of triethyl amine and carbon disulphide in dry THF.



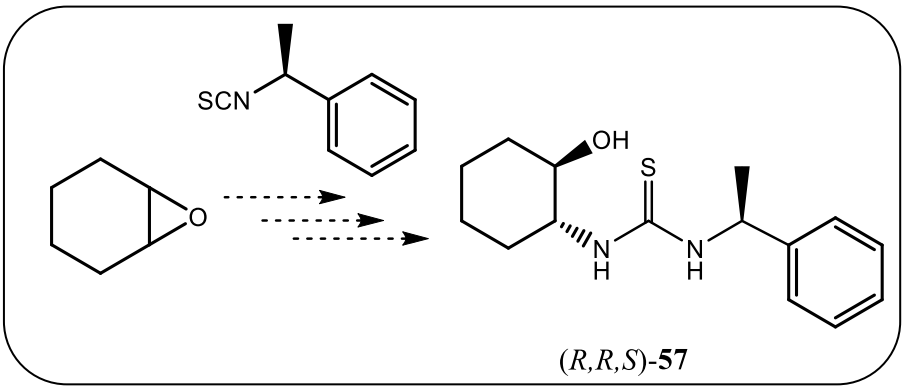
Scheme 17: Synthesis of 1-fluoro-4-isothiocyanatobenzene **55**

(*R,R*)- 2-aminocyclohexan-1-ol **51** is condensed with (*S*)-(1-isothiocyanatoethyl)benzene **53** in dichloromethane at ambient temperature for 24 hours to furnish 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**.

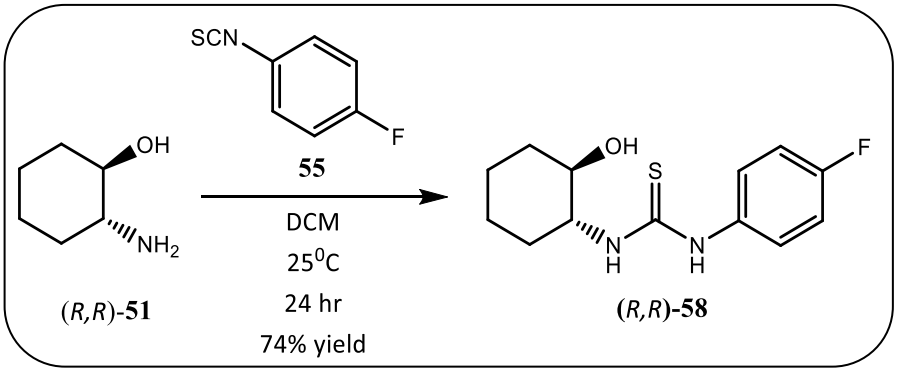


Scheme 17: Synthesis of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**

By applying same strategy, molecules 1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea **57** and 1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)urea **58** were also synthesized.



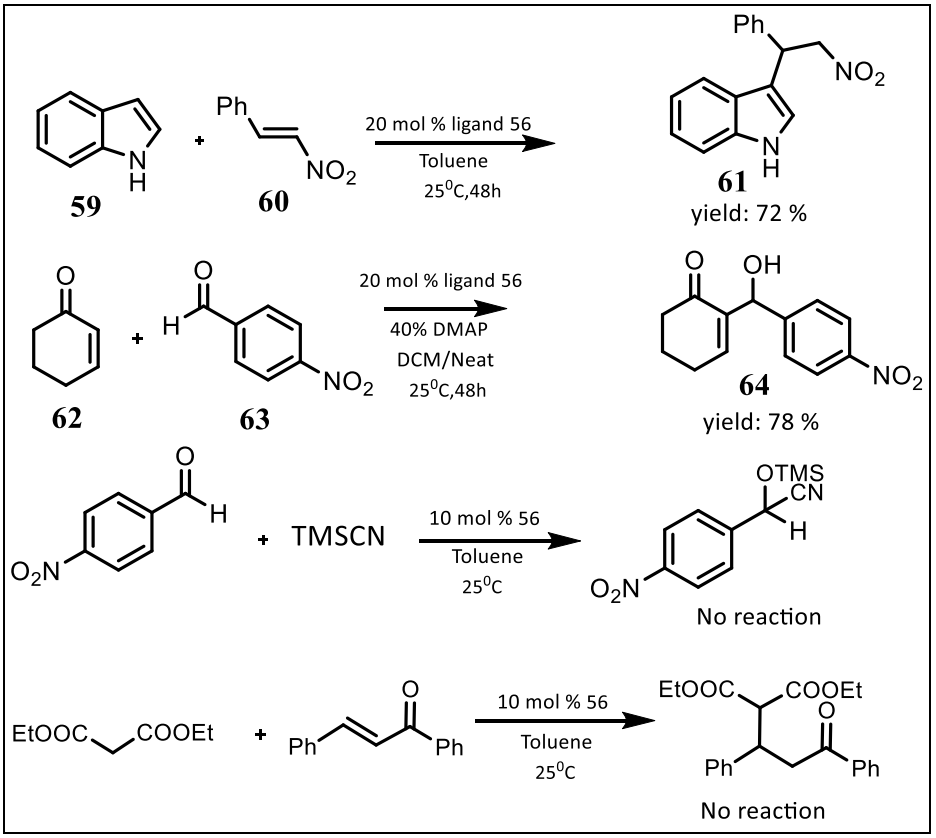
Scheme 18: Synthesis of compound **57.**



Scheme 19: Synthesis of compound 1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)thiourea **58**

These three ligands **56, 57, 58** contain thiourea moiety and cyclohexyl ring system which will allow them to interact with substrate molecules. Here both NH hydrogens of thiourea moity are acidic enough to make a supramolecular interaction with electron donating atoms like oxygen, sulfer or halogens while rigid cyclohexyl ring gives the substrate a particular cavity by which substrate molecule can form interaction in a particular direction with thiourea moity.

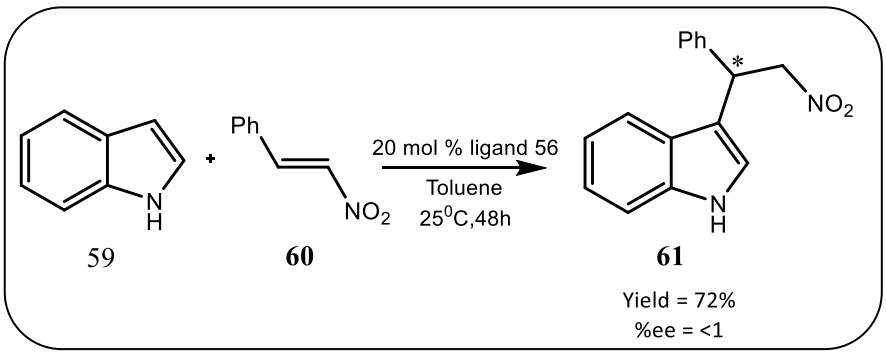
Having the possibility of supramolecular interaction of these ligands with different substrate molecules, we have screened these organic ligands in various organocatalytic reactions like aldol reaction, Morita Baylis Hillman reaction, Michael rection and Henry reaction.



Scheme 20: Different organocatalytic reaction mediated by (*R*,*R*,*R*)-**56**

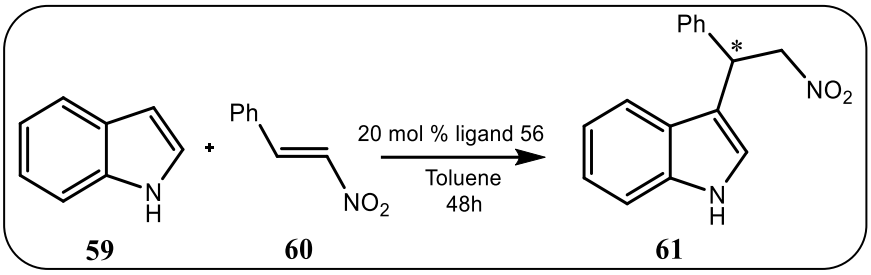
4.2.1 Asymmetric Michael reaction

Asymmetric Michael reaction is one of the very important reactions in organocatalysis. Here reaction 1 of the scheme 20 in which aldol condensation rection between indole **59** and E-nitrostyrene **60** was mediated by 20 mol% synthesized ligand (*R*,*R*,*R*)-**56** in an ambient temperature for 48 hours to get almost racemic 3-(2-nitro-1-phenylethyl)-1H-indole **61** with 72% yield and <1% ee.



Scheme 21: Asymmetric Michael reaction between indole and E-nitro styrene

In the beginning we had started our work of Asymmetric Michael reaction between indole **59** and E-nitro styrene **60** at room temperature without adding any ligand but reaction did not even proceed table 1 (entry 1). The same reaction was carried out in the presence of 20 mol% ligand **56** to get 72% yield but optical activity was <1%. this result clearly suggests the positive role of ligand **56** in the reaction (entry 2). As we further decreased the temperature from 25^0C to -60^0C for better interaction between ligand molecule **56** and substrate E-nitrostyrene **60** the optical activity marginally increases but the yield of the product decrease from 72% to 54%.

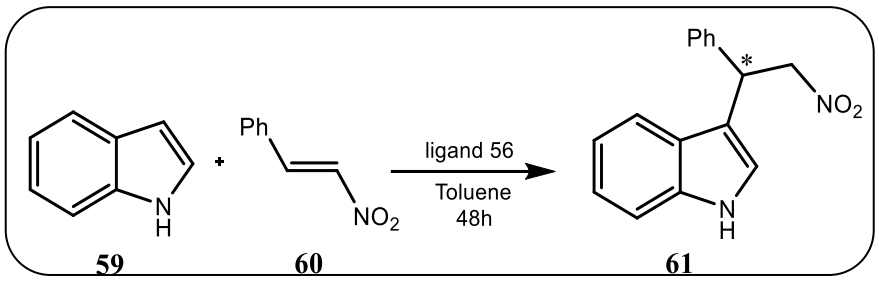


Scheme 22: Temperature study for Asymmetric Michael reaction

Table 1: Optimisation table of temperature study of Asymmetric Michael reaction

Ligand mol%	**Temp^{0}C**	**Time hr**	**%Yield**	**%ee**
-	25	48	-	-
20	25	48	72	<1
20	0	48	66	<2
20	-20	48	55	<2
20	-40	48	54	<2
20	-60	48	54	<2

Ligand optimisation study for the Asymmetric Michael reaction (Scheme 22) was done by taking 20 mol % of ligand **56**, reaction was done in toluene for 48 hours at -20^0C. the optical purity of the product increase up to 2% but no change in the product yield observed (Table 2) as we increase the amount of ligand from 20 mol% to 100 mol%, yet optical purity increases up to 3%

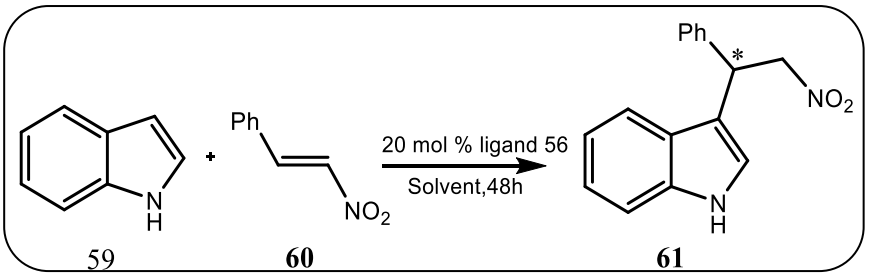


Scheme 23: Ligand study for Asymmetric Michael reaction

Ligand mol%	Temp^{0}C	Time hr	%Yield	%ee
-	-20	48	-	-
20	-20	48	55	<2
40	-20	48	57	<2
60	-20	48	57	<3
80	-20	48	56	<3
100	-20	48	57	<3

Table 2: Optimisation table of Ligand study of Asymmetric Michael reaction

The solvent optimisation study of the Asymmetric Michael reaction of indole and E-nitro styrene was done at -20^{0}C for 48 hours in toluene to get 72% of yield but the optical purity of the reaction was <1%. As changing of solvent for the same reaction condition from toluene to THF, the yield of a product decrease from 72 to 35 % yet optical purity of the product increase to up to 2%. further by changing solvent from toluene to dichloromethane or Acetonitrile the yield of the product was decrease up to 40% yet optical purity of the product does not exceed above 2%.



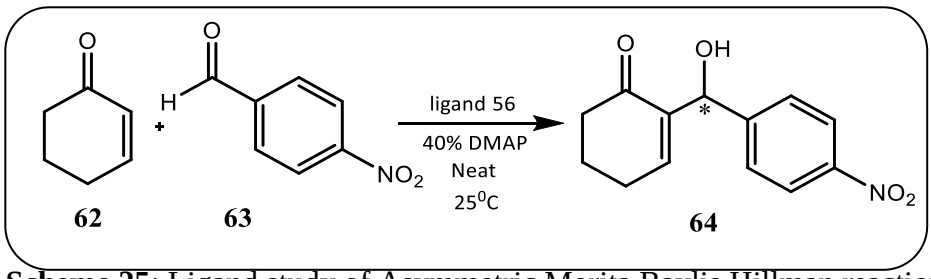
Scheme 24: Solvent study for Asymmetric Michael reaction

Table 3: Optimisation table of solvent study for the reaction

Ligand mol%	Solvent	Temp^{0}C	Time hr	%Yield	%ee
20	Toluene	-20	48	72	<2
20	THF	-20	48	35	<2
20	ACN	-20	48	50	<2
20	Dichloro Methane	-20	48	40	<2
20	Neat	-20	48	14	<2

4.2.2 Asymmetric Morita Baylis Hillman Reaction

Asymmetric Morita Baylis Hillman reaction is one of the most important reactions to synthesize optically active beta hydroxy ketones. we had tried Morita Baylis Hillman reaction of cyclohexanone **62** and 4-nitro benzaldehyde **63** in presence of 20 mol% of (*R*,*R*,*R*)-**56** and 40 %w/w DMAP in room temperature for 48 hours in a neat condition to get 78%yield of 2-(hydroxy(4-nitrophenyl)methyl)cyclohex-2-en-1-one **64.**

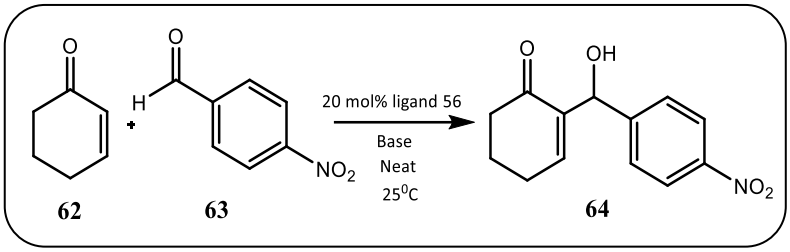


Scheme 25: Ligand study of Asymmetric Morita Baylis Hillman reaction

Table 4: ligand study for the Asymmetric Morita Baylis Hillman reaction

Ligand mol%	Temp^{0}C	Time (hr)	%Yield	%ee
-	25	24	17	Rac
20	25	24	78	<2
40	25	24	75	<2
60	25	24	74	<2
80	25	24	74	<2
100	25	24	73	<2

Ligand optimisation study of the Baylis Hillman reaction Scheme 25 was done by taking 20 mol% of ligand **56** at 25^0C for 24 hours to get 78% of product yet enantioselectivity is <2%. if the same reaction was done without adding catalyst **56** then the reaction did not even proceed after 24 hours. This result suggests the role of a catalyst in above reaction. As we increase the amount of ligand in a reaction from 20 to 100 mol% the product yield was decrease slightly but optical purity did not improve.



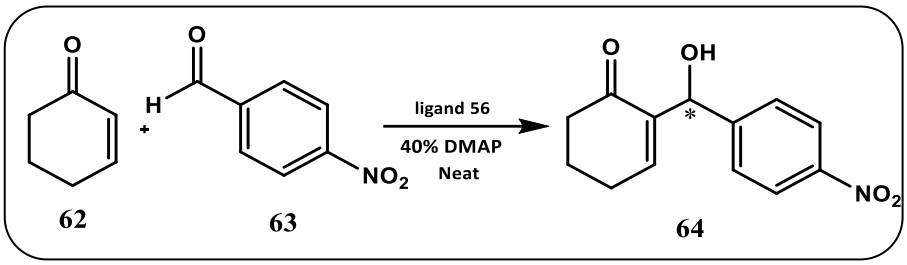
Scheme 26: Base study of Asymmetric Morita Baylis Hillman reaction

Asymmetric Morita Baylis Hillman reaction was done using different base. using standard reaction condition by taking 40 mol% DMAP and 20 mol% ligand at 25^0C for 24 hours conversion in product **64** was 78% with <2% optical purity. By changing base from DMAP to Et_3N with same reaction condition there was decrease in product conversion from 78% to 10% which indicates that DMAP works better in the above reaction than other organic bases. the optical purity of asymmetric Morita Baylis Hillman reaction did not improve by using different bases in the reaction.

Table 5: Optimisation table for Base study for the reaction

Base	**Temp^{0}C**	**Time hr**	**%Yield**	**%ee**
-	25	24	<1	Rac
DMAP	25	24	78	<2
DBU	25	24	40	<2
DABCO	25	24	45	<2
Et_3N	25	24	10	<2

Temperature study for asymmetric Morita Baylis Hillman reaction was done by taking 20 mol% of ligand **56** for 24 hours at 25^0C, 78% conversion of product was observed but optical purity was racemic. For the same reaction when the temperature was decrease from 25^0C to -78^0C the yield of the product decrease from 78 to 54% though optical purity of product **62** was not improve above 2%.



Scheme 27: Temperature study of Asymmetric Morita Baylis Hillman reaction

Table 6: Optimisation table of Temperature study for Asymmetric Morita Baylis Hillman reaction the reaction

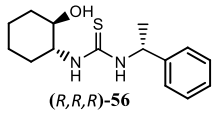
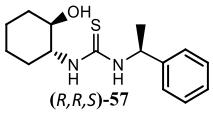
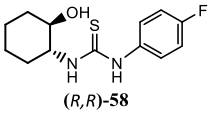
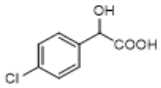
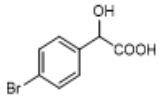
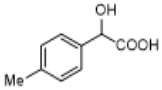
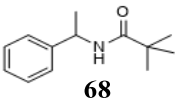
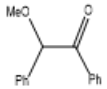
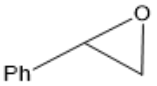
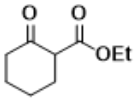
Ligand mol%	**Temp^{0}C**	**Time hr**	**%Yield**	**%ee**
20	25	24	78	<2
20	0	24	70	<2
20	-20	24	61	<2
20	-40	24	58	<2
20	-60	24	54	<3
20	-78	24	54	<3

4.2.3 Discrimination of Carboxylic acids, amide and other molecules

Thiourea molecules have a good potential to form supramolecular interaction with different molecules. We need to analyse several types of analytes to investigate the wider application of the usage of chiral solvating agents (CSA) for assessing optical purity by 1H NMR spectroscopy. Given that α-substituted acids represent a significant class of chiral chemicals, we explored the current CSA (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** for these molecules. CSAs are typically basic in nature and their method of interaction with substrates is based on the creation of diastereomeric complexes or salts.

Table 7: Study of CSA (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** for different analyte

(Δδ)= induced chemical shift, (ΔΔδ)= chemical shift nonequivalence

Δδ (ΔΔδ)	 (*R*,*R*,*R*)-**56**	 (*R*,*R*,*S*)-**57**	 (*R*,*R*)-**58**
 **65**	**0.053(0.005)**	**0.023**	**0.070**
 **66**	**0.051(0.005)**	**0.015**	**0.081**
 **67**	**0.042(0.004)**	**0.017**	**0.062**
 **68**	**0.014**	**0.012**	**0.005**
 **69**	**0.005**	**0.005**	**-**
 **70**	**0.014**	**0.014**	**0.013**
 **71**	**0.009**	**0.009**	**0.018**

We initially measured the 1H NMR of 10 mM racemic α-mandelic acids (MA) in the presence of 1 equivalent of chiral thiourea (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** as a CSA in

$CDCl_3$ to investigate the enantiomeric discriminating ability of this compound for carboxylic acids. As we investigate the (*R*,*R*,*R*)-**56** with para chloro mandelic acid **65,** the induced chemical shift (Δδ) 0.053 (table 7, entry 1) was observed while the α-H of mandelic acid get split to get chemical shift non equivalence (ΔΔδ) 0.005 (table 7, entry 1)**,** though baseline separation was not observed.

Then the (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** was also screened for the para chloro mandalic acid **65**, induced chemical shift 0.023 and 0.070 (table 7, entry 1) was observed respectively but no splitting of signal observed for the same**.** para bromo mandalic acid **66** and para methyl mandalic acid **67** was also investigate for (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** ligands to study electronic effect of analyte on the supramolecular interaction with ligands.

when para bromo mandelic acid **66** and para methyl mandelic acid **67** were scanned for (*R*,*R*,*R*)-**56** then α-H of mandelic acid get shifted (Δδ) 0.051 as well as split (ΔΔδ) 0.005 (table 7, entry 2,3) respectively. But when same **66** and **67** was scanned for (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** then α-H of mandelic acid only get shifted though no splitting of signals observed of para bromo mandelic acid **66** and para methyl mandelic acid **67** for (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** (table 7, entry 2,3) ligands.

Kagans type amide **60** was screen for the ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58,** α-H of amide was observed for analyte **68.** As the signal get shifted and induced chemical shift **(Δδ)** 0.014, 0.012 and 0.005 (table 7, entry 4) was observed respectively for (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58.**

Benzoin methyl ether **69** was scanned for (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** ligands as α-H of the ether group was shifted and induced chemical shift (Δδ) 0.005 (table 7, entry 5) for both the ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57,** but no shifting of signals observed for (*R*,*R*)-**58.** As no chemical shift non-equivalence **(ΔΔδ)** splitting of signals was observed for benzoin methyl ether by the ligands.

Analyte 2-phenyloxirane **70** was scanned for ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** as CSA, α-H of phenyl ring and oxygen get shifted and induced chemical shift **(Δδ)** 0.014 (table 7, entry 6)was observed for ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57** while 0.013 was observed for (*R*,*R*)-**58**.

The ethyl 2-oxocyclohexane-1-carboxylate was scanned for (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58**, α-H of the ketonic group gets shifted and induced chemical shift **(Δδ)** 0.009 (table 7, entry 7) was observed for ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57** each while 0.018 was observed for (*R*,*R*)-**58**.

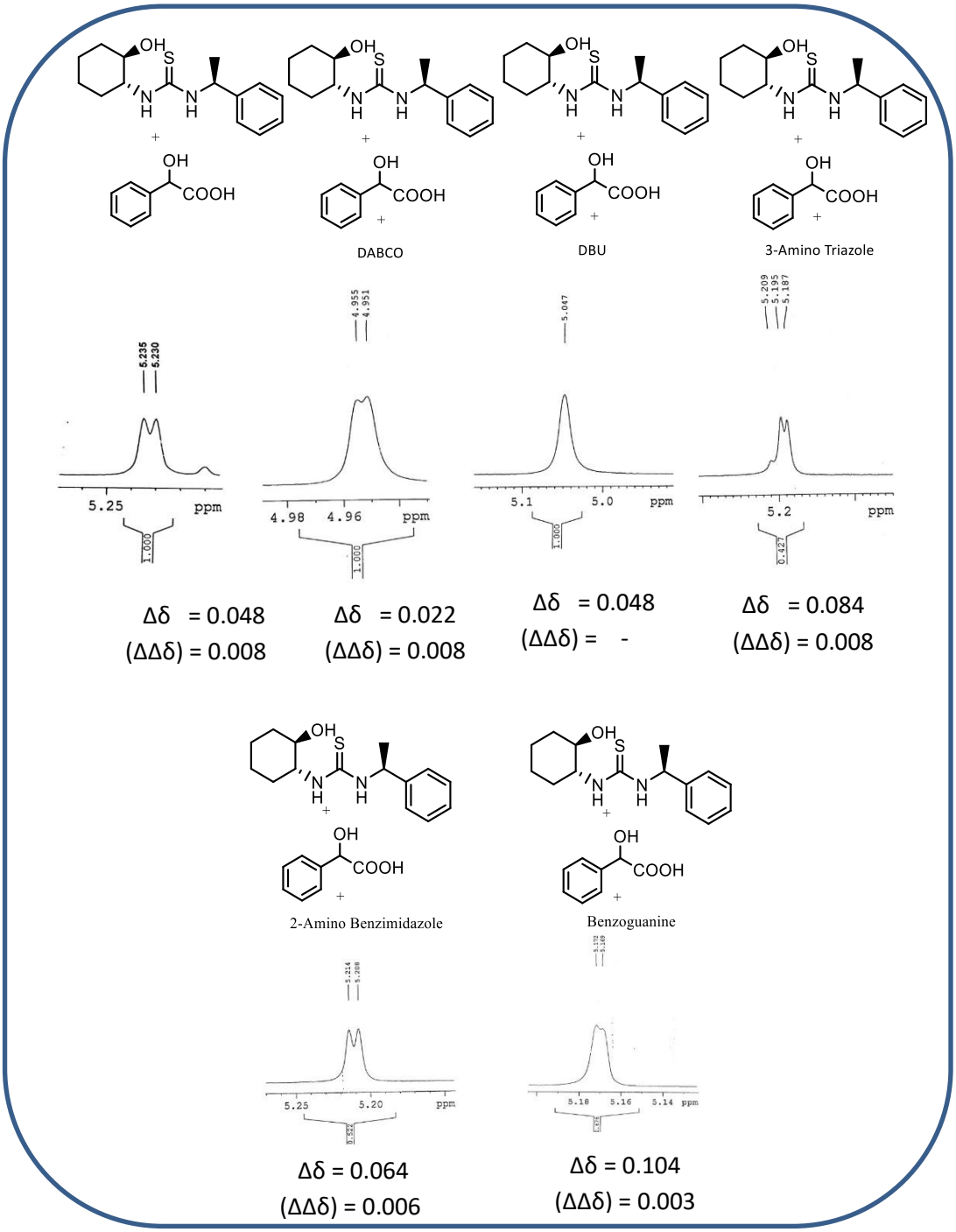
4.2.4 Optimisation study of different bases with CSA (*R,R,R*)-56.

Due to the involvement of H-bonding interactions between one chiral thiourea molecule and one ion pair of acid-base, we hypothesised that using a chiral thiourea as a CSA combined with a base for enantiodifferentiation of chiral carboxylic acids should give us a higher resolution of α-Hs of acids.

We initially recorded the ^{1}H NMR of 10 mM racemic mandelic acids (MAs) in the presence of 1 equiv of CSA (*R,R,R*)-**56** in $CDCl_3$ to investigate the enantiomeric discriminating capability of chiral thiourea (*R,R,R*)-**56** as a CSA for different carboxylic acids

It appears that there is only a very faint interaction between MA and CSA (*R,R,R*)-**56** because the shifts in the α-H signals of the two enantiomers of racemic MAs were small (Δδ=0.048, ΔΔδ=0.008) leading to inadequate baseline resolution (figure 1, entry 1).
With the addition of DABCO in the above solution, the two enantiomers of mandelic acid suffered less, and their α-H appeared as two signals in ^{1}H chemical shift nonequivalence (ΔΔδ= 0.008) value. For DABCO the baseline resolution was not obtained for mandelic acid. (figure 1, entry 2)
when we did the same experiment by adding DBU instead DABCO, the α-H of mandelic acid was shifted to get induced chemical shift (Δδ=0.048) but these signals was not get splitted as unable to observed the chemical shift non-equivalence **(ΔΔδ)** (figure 1, entry 3). As a part of CSA study addition of 1 equivalent of 3 amino triazole and 2 amino benzimidazole in a separate experiment instead of DABCO, the chemical shift non-equivalent **(ΔΔδ)** was observed 0.008 and 0.006 respectively but base line separation was not observed (figure 1, entry 4,5).

^{1}H NMR induced chemical shift (Δδ) *and nonequivalence* (ΔΔδ) *of analytes in presence of CSAs* All the spectra were recorded at 400 MHz in $CDCl_3$; at 10 mM concentration.



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4.3 Conclusion

We successfully synthesize chiral optically active thiourea ligands (*R*,*R*,*R*)-**56**, (*R*,*R*,*S*)-**57**, (*R*,*R*)-**58** and explore its application as a organocatalyst and also studied its supra molecular interaction as a (CSA) with different analytes. However, the preliminary results were not much exciting as although the thiourea derivatives managed to catalyse reactions, they were unable to produce products in enantiomerically enriched form. Similarly, the CSAs did not discriminate the signals of chiral analytes in NMR experiments.

Syntheic Procedure to synthesize Racemic trans-2-(N-benzyl)amino-1-cyclohexanol 48.

A two neck round bottom flask is charged with cyclohexene oxide **46** (5 mL, 4,85 g, 48 mmol, 1.1 equiv) and benzylamine **47** (4.87 mL, 4.77 g, 44 mmol, 1 equiv), equipped with a magnetic stirring bar, sealed and flushed with nitrogen. The reaction mixture is placed in a 140°C heated for overnight, then cooled to ambient temperature, diluted with dichloromethane (20 mL) and transferred into a 250-mL single-necked, round bottomed flask. The glass inlay is rinsed with dichloromethane (3×5 mL) and the combined organic phases are concentrated using a rotary evaporator (30 mmHg, ambient temperature). The residual cyclohexene oxide is removed under reduced pressure (1 mmHg) at room temperature over 11 h to yield 7.72 g (85%) amino alcohol **48** as a light yellow solid, which is suitable for use in the next step without further purification.

(S)-Mandelic acid salt of (1R,2R)-trans-2-(N-benzyl)amino-1-cyclohexanol

A 250 ml single-necked, round-bottomed flask containing a magnetic stirring bar is equipped with a pressure equalizing addition funnel fitted with an argon inlet. The flask is charged with amino alcohol **48** (4 g, 19 mmol, 1.0 equiv) dissolved in ethyl acetate (50 mL) and a solution of (S)-mandelic acid (1.48 g, 9.5 mmol, 0.5 equiv) in ethyl acetate (20 mL) and diethyl ether (10 mL) is added via the addition funnel over a period of 15 minutes at room temperature. After the addition is complete the dropping funnel is rinsed with diethyl ether (2 ×5 mL) and the reaction mixture is stirred overnight at ambient temperature, followed by 30 minutes at 0 °C. The precipitated ammonium salt is collected by suction filtration, then is washed with ethyl acetate (10 mL), followed by diethyl ether (2 ×10 mL), and dried in vacuo at room temperature over 1 hour to afford 2.57 g, 74% of the (S)-mandelic acid salt of (1R,2R)-trans-2-(N-benzyl)amino-1-cyclohexanol **50** as a colorless solid . The filtrate from the above procedure is transferred to a 2-L separatory funnel, then is washed with 1 N aq. NaOH solution (3×5 mL) and the aqueous layer is back-extracted with diethyl ether (3× 5 ml). The combined organic layers are dried ($MgSO_4$, approx. 10 g), filtered and concentrated under reduced pressure (40 ˚C, 100 mbar) to give 2.39 g of the crude amino alcohol *(1R,2R)*-**48** as a pale yellow oil.

Liberation of the amino alcohols from mandelic acid salt.

In a 100 ml separatory funnel, the mandelic acid and *(1R,2R)*-**48** salt **50** (50.04 g, 0.14 mol) is partitioned between ethyl acetate (20 mL) and 2 N aq. HCl solution (10 mL). Then, the mixture is manually and vigorously shaken until the salt is completely dissolved. The organic layer is additionally washed with 2 N aq. HCl solution (2 × 5 mL) and the combined aqueous phases are back-extracted with ethyl acetate (3 ×10 mL). The combined organic phases are dried (MgSO4, approx. 50 g), filtered and concentrated under reduced pressure to corresponding mandelic acid enantiomer. To a mixture of the acidic aqueous phase and diethyl ether (20 mL) in the same separatory funnel, 5 N NaOH (20 mL) is added carefully in small portions over a period of 45–60 minutes. After separation, the aqueous layer is extracted with diethyl ether (4 ×10 mL) and the combined organic phases are dried (MgSO4, approx. 5 g), filtered, and concentrated under reduced pressure (40 ˚C, 100 mbar) to yield 1.92 g (90–93%) of the corresponding trans-2-(N-benzyl)amino-1-cyclohexanol enantiomer *(1R,2R)*-**48** as a white solid.

Synthesis of (R, R)-2-aminocyclohexan-1-ol 51 from (1R, 2R)-trans-2-(N-benzyl)amino-1-cyclohexanol 50

To a 100ml three-necked, round-bottomed flask magnetic stir bar, fitted with rubber septa and a three-way glass adaptor connected to an argon inlet and a vacuum inlet (130 mm Hg, Note 27) are added *(R, R)* **50** (2 g, 5.5 mmol, 1.00 equiv) HPLC grade MeOH (20 mL).The argon flow sweeping through the round-bottomed flask is increased and a slurry consisting of 10 wt.% Pd-C (0.20 g) added to the reaction mixture over 15 min. fitted with a hydrogen balloon and a vacuum inlet (130 mmHg). The stirring reaction flask is evacuated, while keeping the balloon closed off, until the solvent starts to bubble, and then back-filled with hydrogen by closing the vacuum and opening the balloon to the flask. This process is repeated four times. The reaction mixture is stirred under hydrogen for another 24 h, After 24 h, the adaptor with the hydrogen balloon is replaced with the argon-vacuum adaptor. After 24 h, TLC analysis showed complete consumption of the starting material. The hydrogen balloon is removed, and the crude reaction mixture is filtered under vacuum (130 mmHg), through a pad of

Celite (15 g) packed into a Büchner funnel above the Celite bed. Then the Celite is washed with methanol (20 mL), and the organic layer is concentrated by rotary evaporation. The product is subjected to high vacuum until it reaches a constant weight to afford crude (R, R)-**51,** (1.3g, 80%) as a brown solid.

Representative procedure for *(R)* (1-isothiocyanatoethyl)benzene 53

A 50 mL round-bottom flask was charged with *(R)* α-methylamine (3 mL, 23 mmol), triethylamine (2.50 mL, 46 mmol), and THF (15 mL), then cooled with an ice bath under N2 atmosphere. Carbon disulphide (1.14 mL, 23.0 mmol) was then added to the reaction mixture by syringe pump over 0.5 h. After addition was completed, the mixture was stirred at room temperature. After 1 h 1 H NMR of an aliquot indicated that conversion into dithiocarbamate salt was complete. The reaction mixture was cooled with an ice bath, tosyl chloride (4.6 g, 23 mmol) was added, and the reaction allowed to warm to room temperature. After 0.5 h, 1N HCl (10 mL) and MTBE (10 mL) were added to the mixture. The aqueous layer was cut, and back extracted with MTBE (10 mL). The organic layers were then combined, dried over Na_2SO_4, and filtered. The filtrate was concentrated in vacuo to obtain an oil, which was passed through a silica plug using 100% hexane as eluent. 2.5 g of *(S)* (1-isothiocyanatoethyl)benzene **53** was obtained as a colourless oil, 75% yield.

Representative procedure for 1-fluoro-4-isothiocyanatobenzene 55

A 50 mL round-bottom flask was charged with p-Fluoroaniline **54** (3 g, 27 mmol), Et_3N (3.1 mL, 54 mmol) and THF (10 mL), then cooled with an ice bath under N2 atmosphere. CS_2 (1.05 mL, 27 mmol) was added using a syringe pump over 0.5 h. More CS_2 (1.05 mL, 27 mmol) and Et_3N (3.1 mL, 54 mmol) were added after 1 H NMR of an aliquot indicated incomplete conversion into the dithiocarbamate. Once conversion of the salt was completed, (18 h) the mixture was cooled with an ice bath and TsCl (5.2 g, 27 mmol) was added. The reaction was stirred at room temperature for 1 h. The material was subjected to work up (as above) and 1.9 g of 1-fluoro-4-phenyl isothiocyanate **55** was obtained; 81% yield.

General procedure for amide ligand (*R,R,R*)-56.

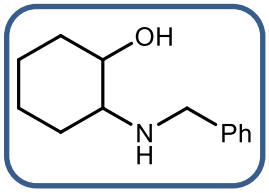
A 50 mL round-bottom flask was charged with *(R, R)*-**51** (0.5 g, 4 mmol), and THF (15 mL), then cooled with an ice bath under N_2 atmosphere. After which *(R)*-**53** (0.65 mL, 4 mmol) was then added to the reaction mixture by syringe pump over 0.5 h. After addition was completed, the mixture was stirred at room temperature for 24 h. After 24 h solvent was evaporated. The filtrate was concentrated in vacuo to obtain an oil, which was passed through a silica plug using 50% (ethyl acetate / petroleum ether) to get 0.67g (85%) yield of (*R,R,R*)-**56**

General procedure for amide ligand (*R,R,R*)-58

A 50 mL round-bottom flask was charged with *(R, R)*-**51** (0.5 g, 4 mmol), and THF (15 mL), then cooled with an ice bath under N_2 atmosphere. After which **55** (0.55 mL, 4 mmol) was then added to the reaction mixture by syringe pump over 0.5 h. After addition was completed, the mixture was stirred at room temperature for 24 h. After 24 h solvent was evaporated. The filtrate was concentrated in vacuo to obtain an oil, which was passed through a silica plug using 50% (ethyl acetate / petroleum ether) to get 0.58g (74%) yield of (*R, R*)-**58**

4.4 Experimental Data

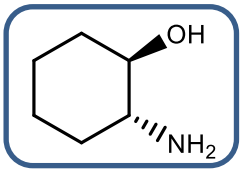
2-(benzylamino)cyclohexan-1-ol 48



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.350 (m, 4H), 3.970 (d, *J* = 12 Hz, 1H), 3.701 (d, *J* = 12 Hz, 1H), 3.221 (m, 1H), 2.361 (m, 1H), 2.188 (d, *J* = 6 Hz, 1H), 2.058 (s, 1H), 1.745 (d, *J* = 10 Hz, 2H), 1.277 (m, 3H), 1.105 (m, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 140.55, 128.46, 128.13, 127.04, 73.87, 63.08, 50.77, 33.27, 30.54, 25.17, 24.34. **IR (KBr)** υ 3294, 3060, 2936, 2856, 1602, 1498, 1430, 1221, 1197, 1152, 1077, 1028, 972, 880. cm^{-1}. Mass 205.05

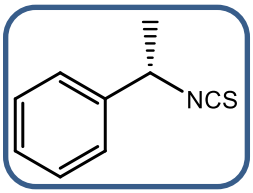
(1R,2R)-2-aminocyclohexan-1-ol 51

^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.449 (m, 1H), 3.050 (m, 1H), 2.466 (m, 1H), 1.651 (m, 5H), 1.267 (m, 5H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 85.83, 75.90, 52.80, 33.70, 30.76, 30.52, 24.60, 24.30, 23.41. **IR (KBr)** υ 3429, 2935, 2868, 1661, 1500, 1441, 1389, 1254, 843, 810. cm^{-1}. Mass 115.24

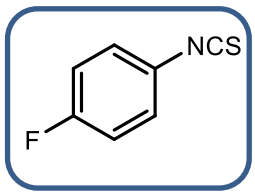


(S)-(1-isothiocyanatoethyl)benzene 53

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.434 (m, 2H), 7.439 (m, 2H), 4.947 (q, *J* = 6 Hz), 1.798 (d, *J* = 6 Hz).**^{13}C-NMR (100 MHz, $CDCl_3$)** δ 140.19, 128.98, 128.28, 125.47, 57.09, 25.07. **IR (KBr)** υ 3064, 3031, 2984, 2933, 2090, 1805, 1493, 1451, 1375, 1217, 1068, 949, 911 cm^{-1}. Mass 163.29



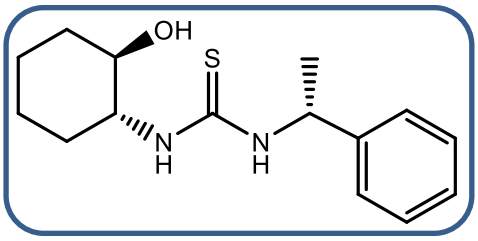
1-fluoro-4-isothiocyanatobenzene 55



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.249 (m, 2H), 7.066 (m, 2H). **IR (KBr)** υ 2186, 2099, 2058, 1501, 1229, 1151, 1092, 932, 832. cm^{-1}

1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea 57

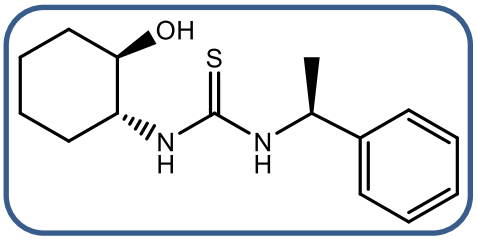
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.316 (m, 5H), 6.194 (broad, 1H), 5.333 (broad, 1H),



3.659 (broad, 2H), 3.154 (broad, 1H), 1.916 (m, 2H), 1.657 (m, 2H), 1.529 (d, *J* = 6Hz, 3H), 1.288 (4H, m). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 140.55, 128.46, 128.13, 127.04, 77.06, 73.87, 63.08, 50.77, 33.27, 30.54, 25.17, 24.34. **IR (KBr)** υ 3260, 3057, 2935, 2859, 1552, 1508, 1449, 1413, 1329, 1218, 1141, 1067, 947, 839. cm^{-1}. Mass 278.04.

1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea 56

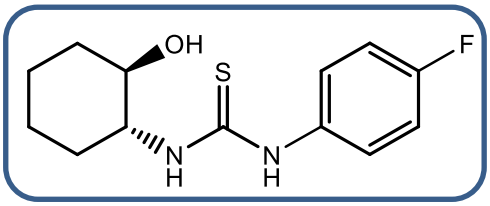
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.314 (m, 5H), 6.194 (broad, 1H), 5.341 (broad, 1H),



3.660 (broad, 2H), 3.154 (broad, 1H), 1.916 (m, 2H), 1.657 (m, 2H), 1.529 (d, *J* = 6Hz, 3H), 1.288 (4H,m). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 140.55, 128.46, 128.13, 127.04, 77.06, 73.87, 63.08, 50.77, 33.27, 30.54, 25.17, 24.34. **IR (KBr)** υ 3260, 3057, 2935, 2859, 1552, 1508, 1449, 1413, 1329, 1218, 1141, 1067, 947, 839. cm^{-1}. Mass 278.04.

1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)thiourea 58

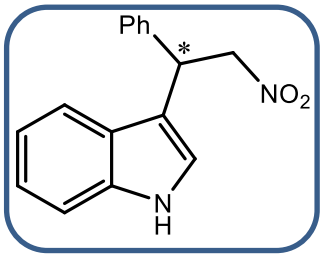
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.702 (broad, 1H), 7.111 (s, 4H), 6.803 (broad, 1H),



3.321 (broad, 1H), 1.439 (m, 6H). **IR (KBr)** υ 3260, 3057, 2935, 1552, 1508, 1449, 1413, 1329, 1269, 1218, 947, 883, 839. cm^{-1}. Mass 268.21

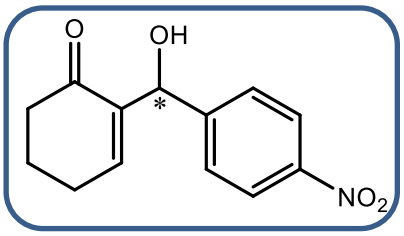
3-(2-nitro-1-phenylethyl)-1H-indole 61

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.484-7.462 (m, 1H), 7.393-7.306 (m, 5H), 7.293-7.206 (m, 1H), 7.124-7.087 (m, 1H), 7.065-7.058 (m, 1H), 5.241-5.201 (t, *J* = 8 Hz, 1H),



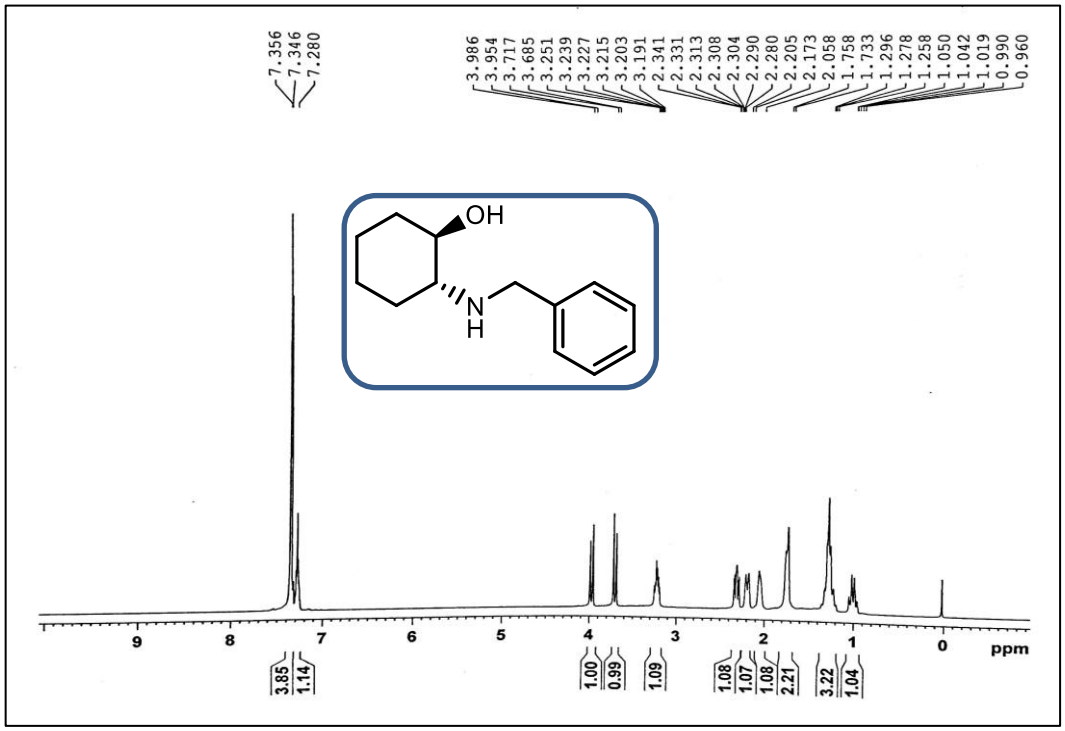
5.123-5.073 (dd, *J* = 8 Hz, 12 Hz, 1H), 4.997-4.945 (dd, *J* = 8 Hz, 12 Hz, 1H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 139.16, 136.47, 128,95, 127.79, 127.60, 126.09, 122.73, 121.61, 119.98, 118.95, 114.83, 111.40, 79.53, 46.55.

2-(hydroxy(4-nitrophenyl)methyl)cyclohex-2-en-1-one 64

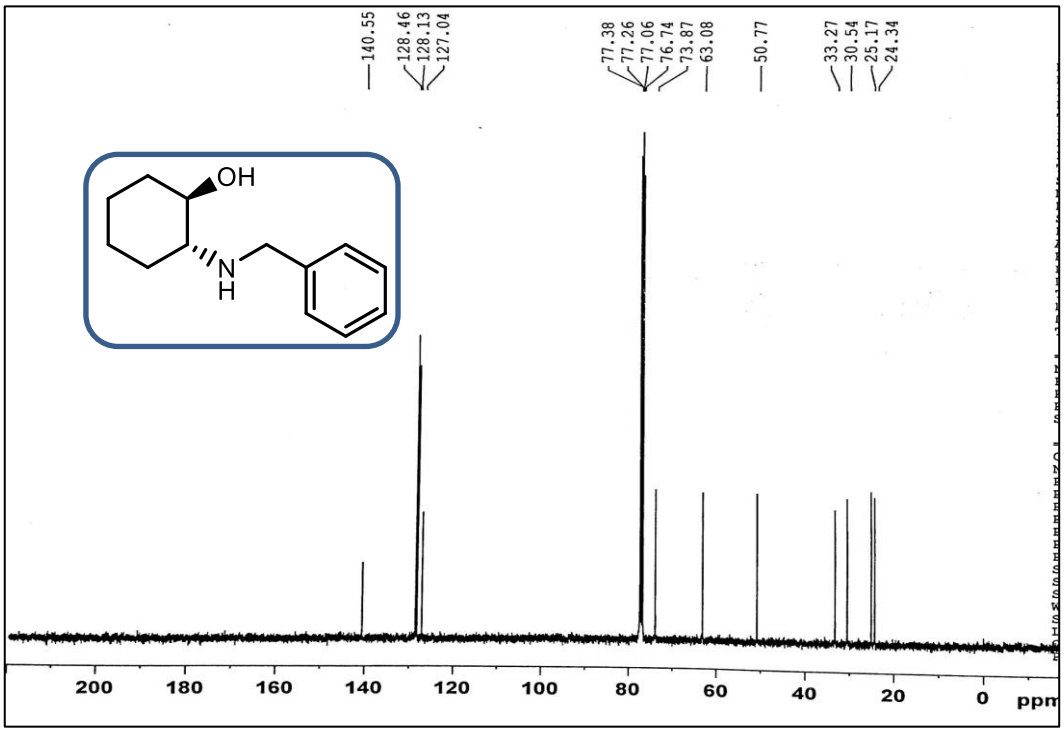


^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.219 (d, *J* = 8 Hz, 2H), 7.571 (d, *J* = 8 Hz, 2H), 6.835 (t, *J* = 4 Hz, 1H), 5.623 (d *J* = 6 Hz, 1H), 3.593 (d, *J* = 6 Hz, 1H), 2.474 (m, 4H), 2.035 (m, 2H). **^{13}C-NMR (100 MHz, $CDCl_3$)** δ 200.24, 149.24, 148.27, 147.24, 140.16, 127.14, 123.58, 72.16, 38.44, 25.80, 22.89.

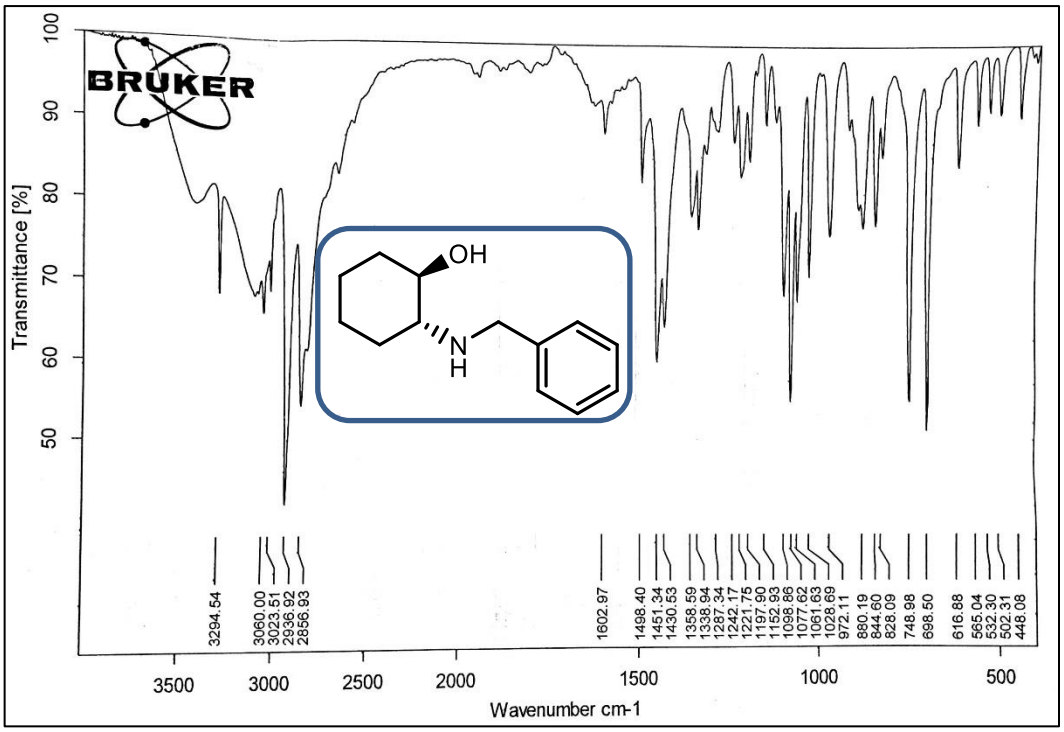
4.5 Spectral Data



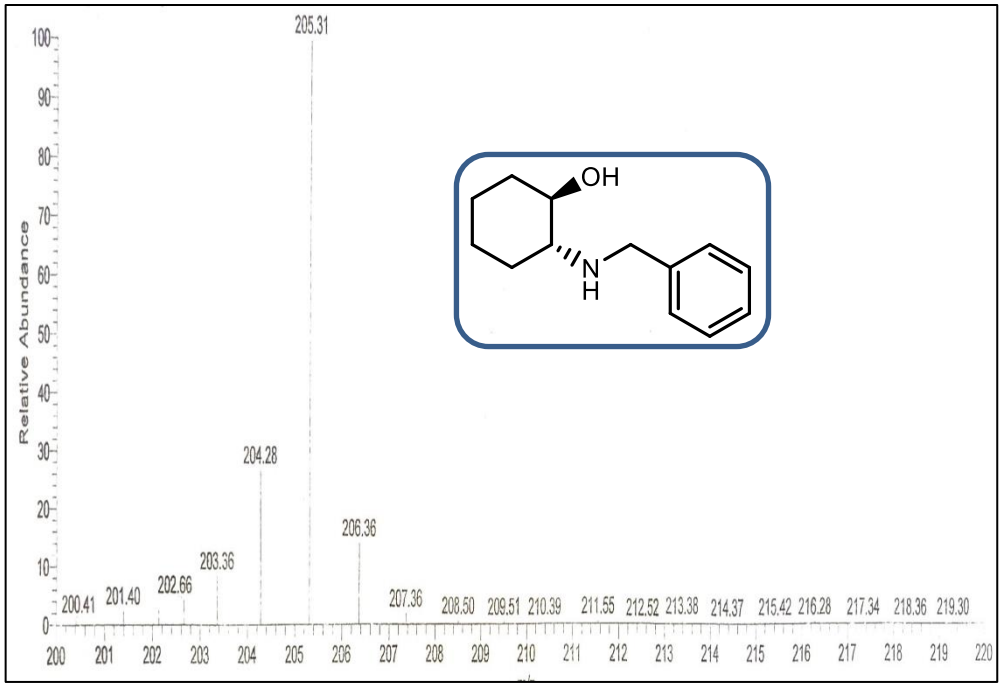
^{1}H NMR of (1R,2R)-2-(benzylamino)cyclohexan-1-ol **48**



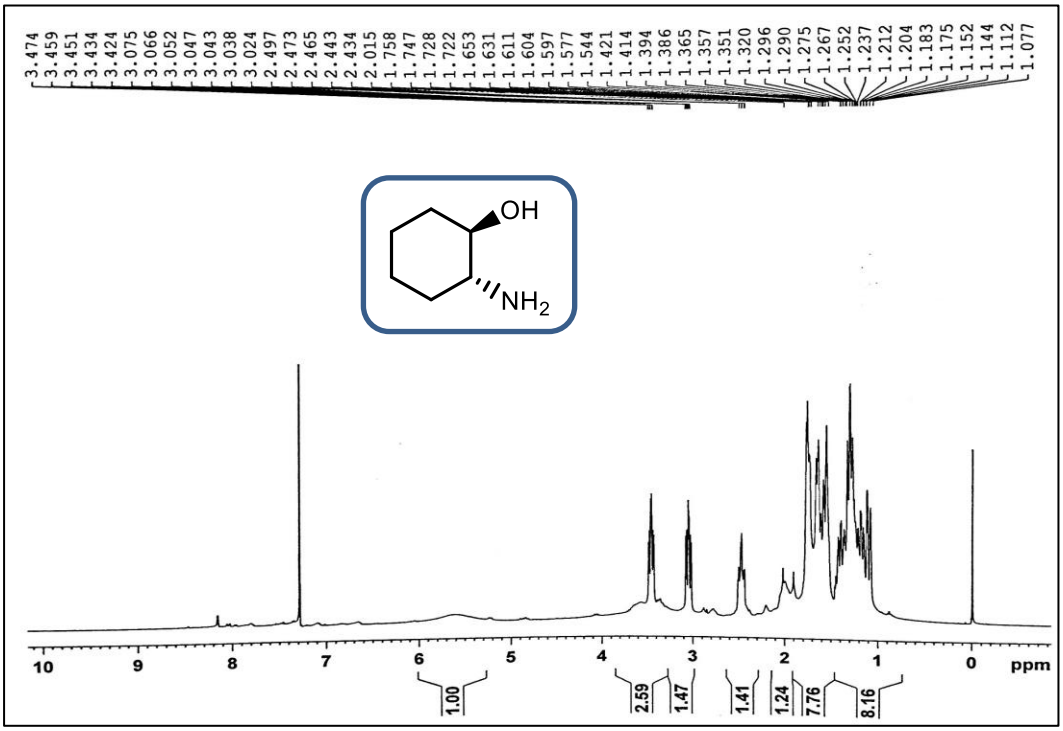
^{13}C NMR of (1R,2R)-2-(benzylamino)cyclohexan-1-ol **48**



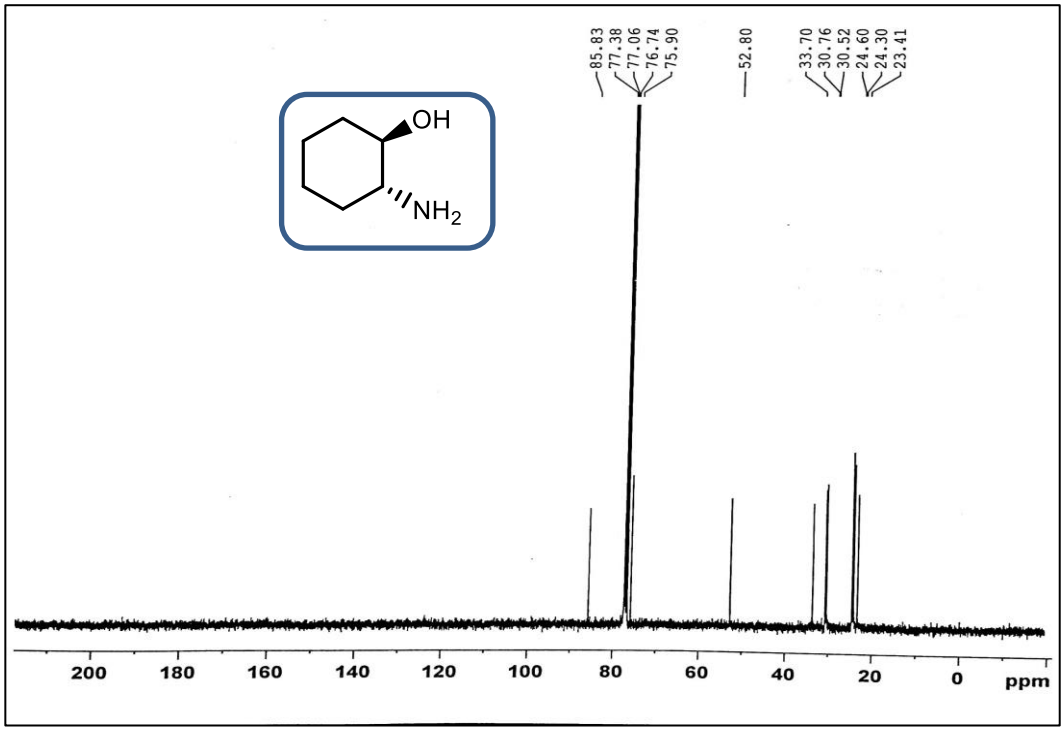
IR of (1R,2R)-2-(benzylamino)cyclohexan-1-ol **48**



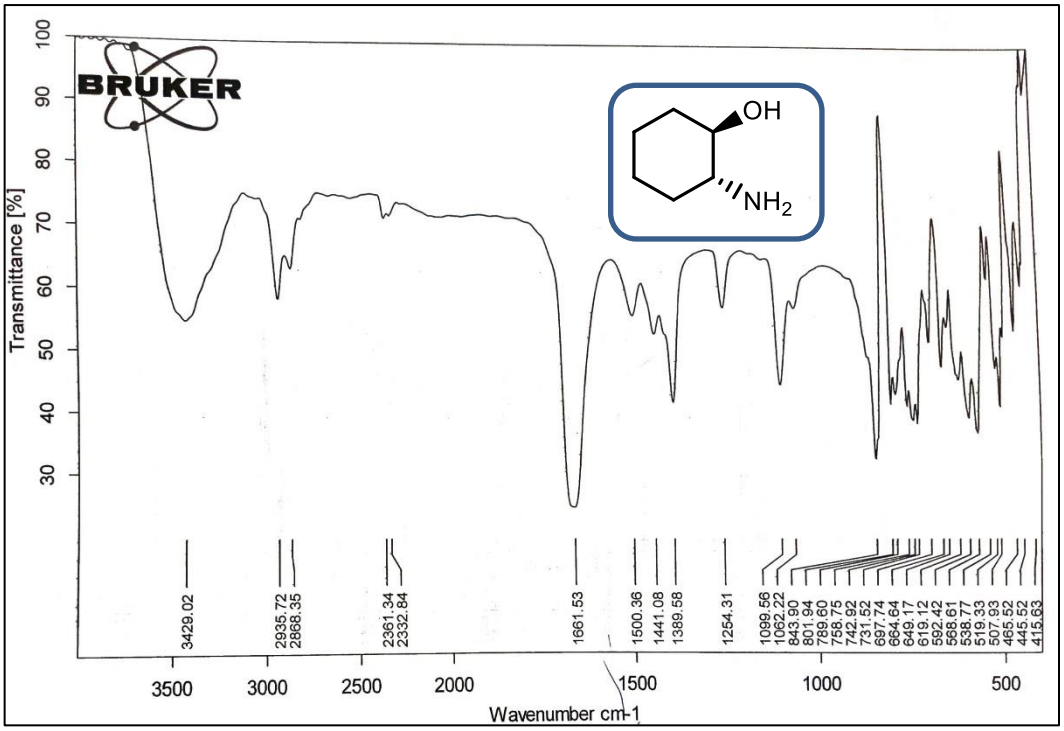
Mass of (1R,2R)-2-(benzylamino)cyclohexan-1-ol **48**



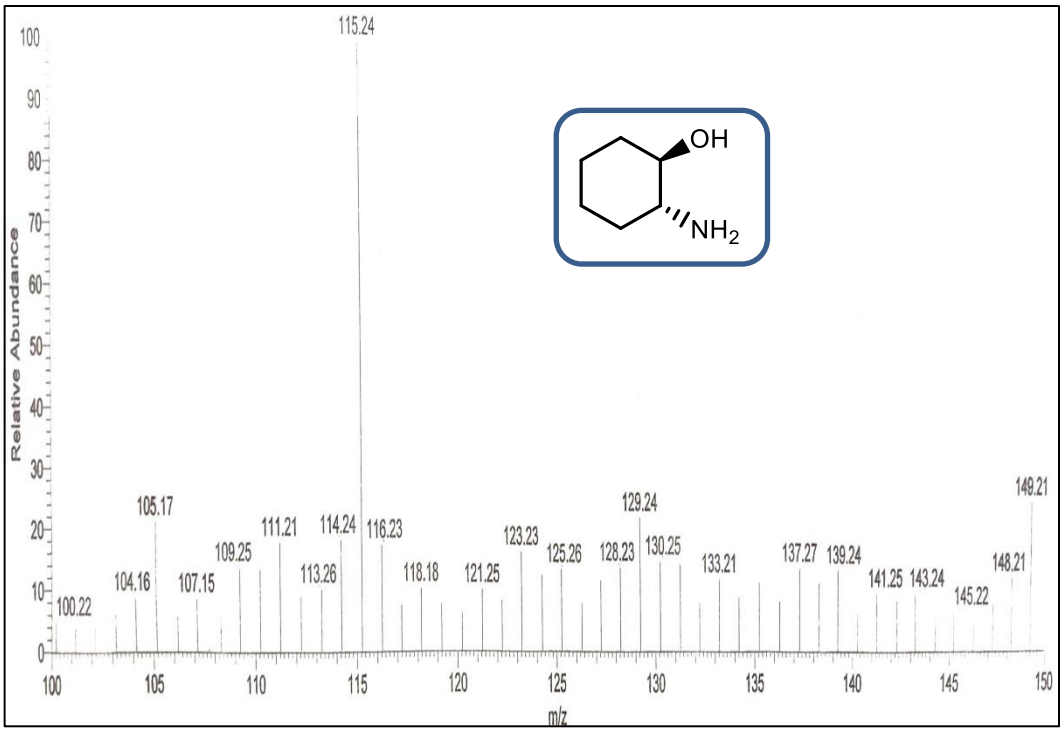
^{1}H NMR of (1R,2R)-2-aminocyclohexan-1-ol **51**



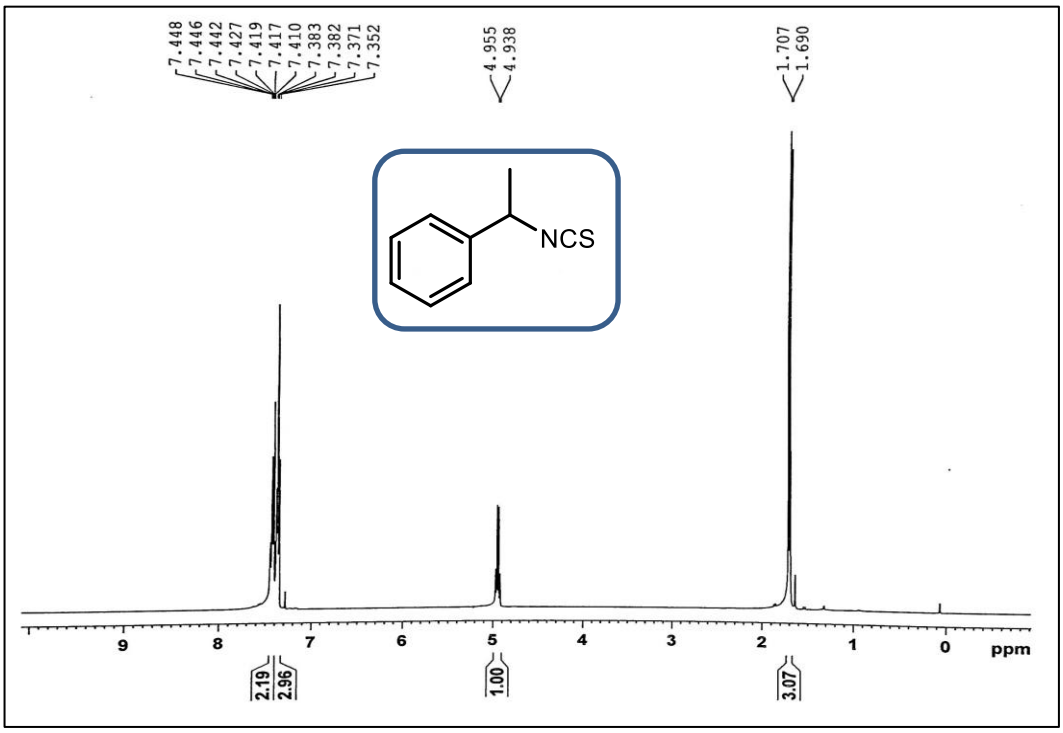
^{13}C NMR of (1R,2R)-2-aminocyclohexan-1-ol



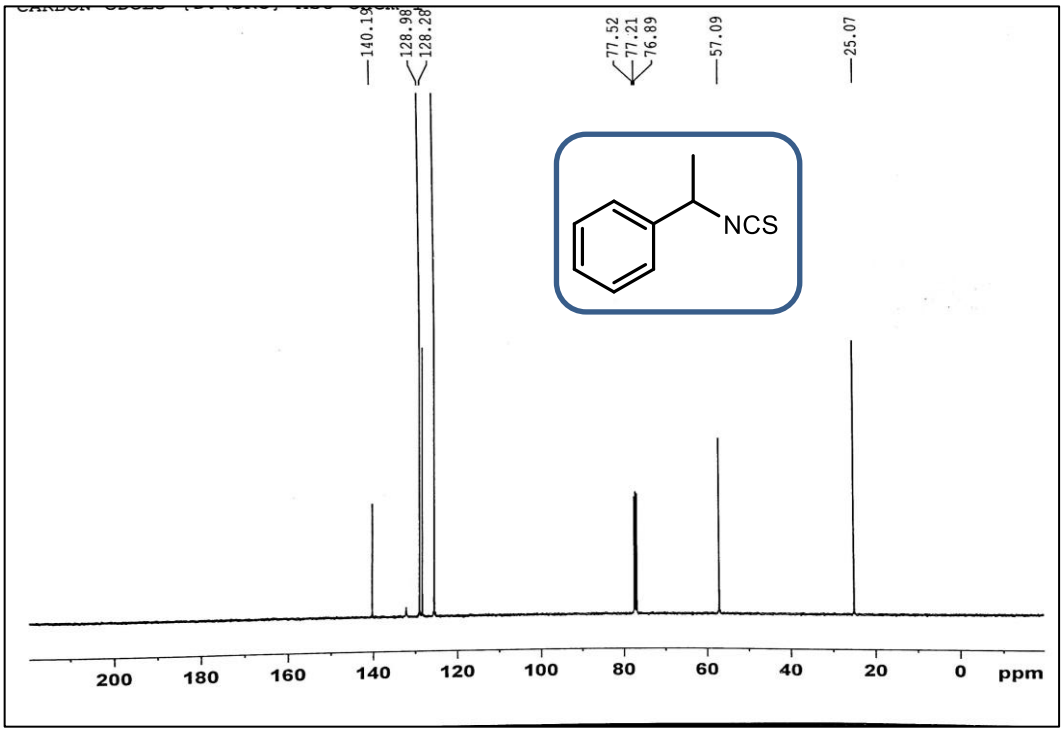
IR of (1R,2R)-2-aminocyclohexan-1-ol **51**



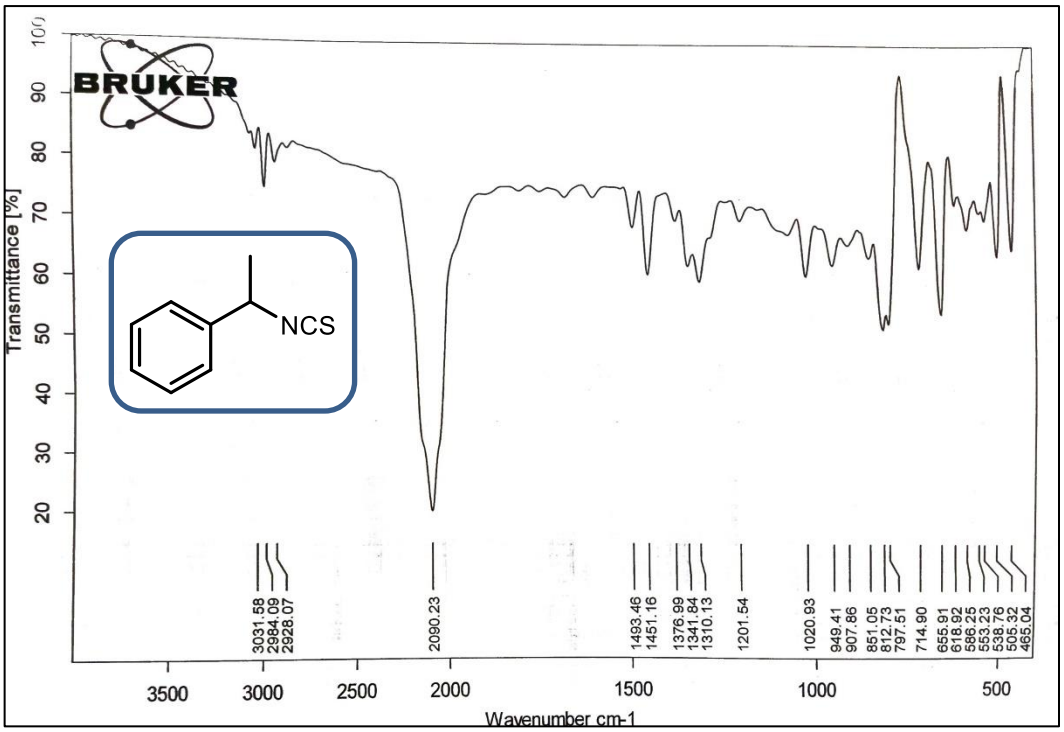
Mass of (1R,2R)-2-aminocyclohexan-1-ol **51**



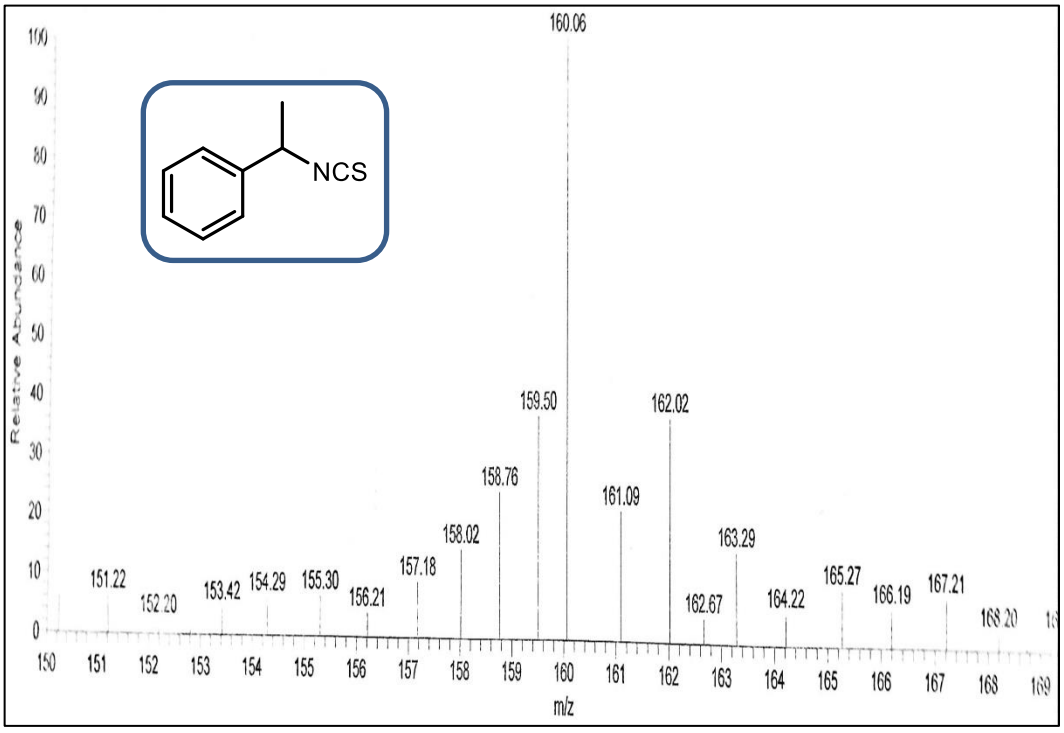
^{1}H NMR of (1-isothiocyanatoethyl)benzene **53**



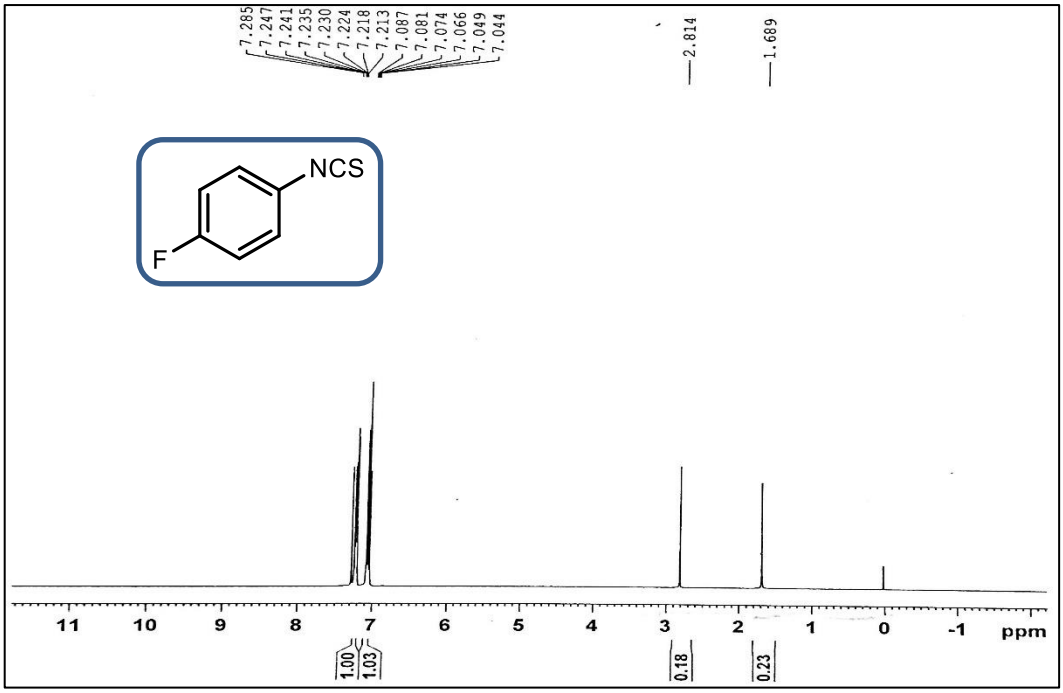
^{13}C NMR of (1-isothiocyanatoethyl)benzene **53**



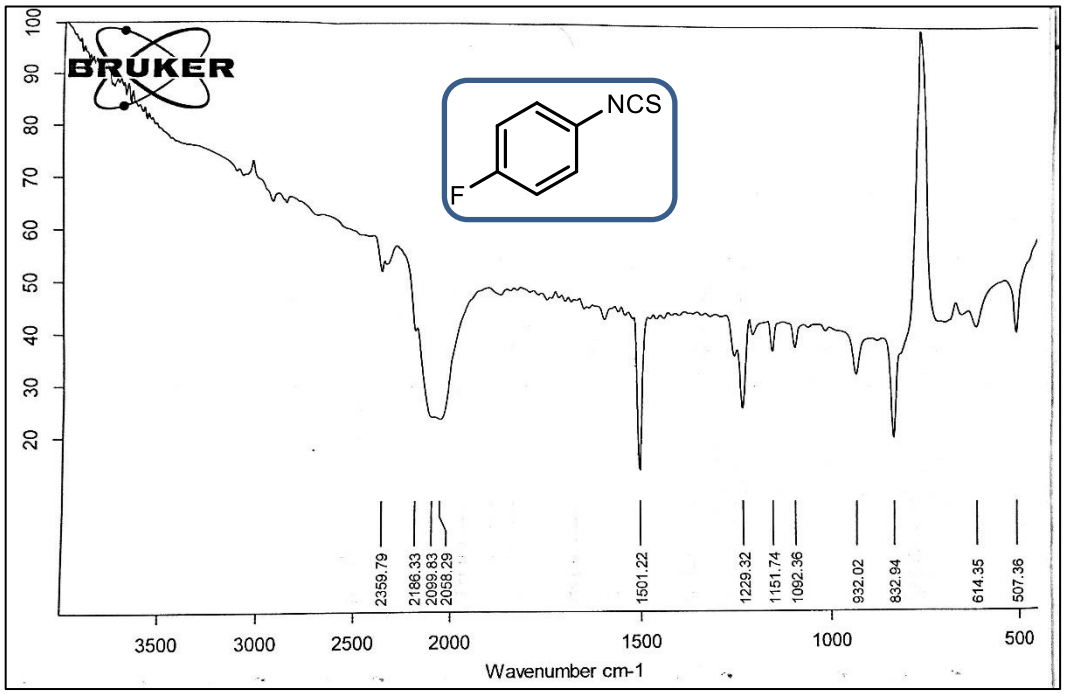
IR of 1-isothiocyanatoethyl)benzene **53**



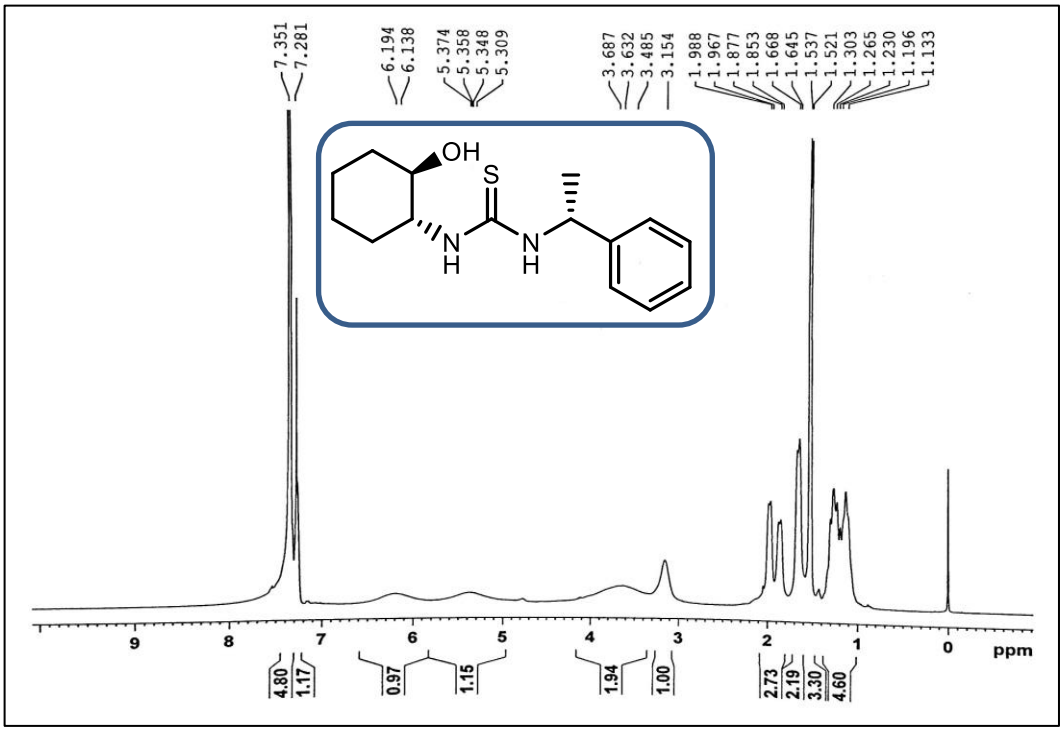
Mass of (S)-(1-isothiocyanatoethyl)benzene **53**



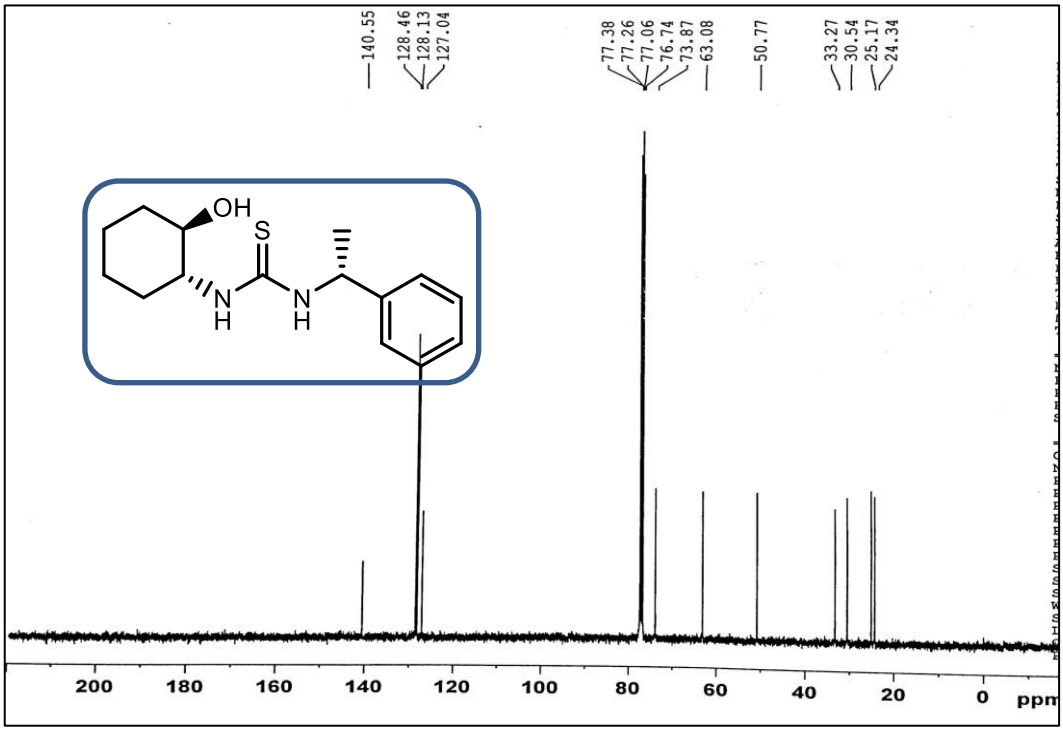
^{1}H NMR of 1-fluoro-4-isothiocyanatobenzene **55**



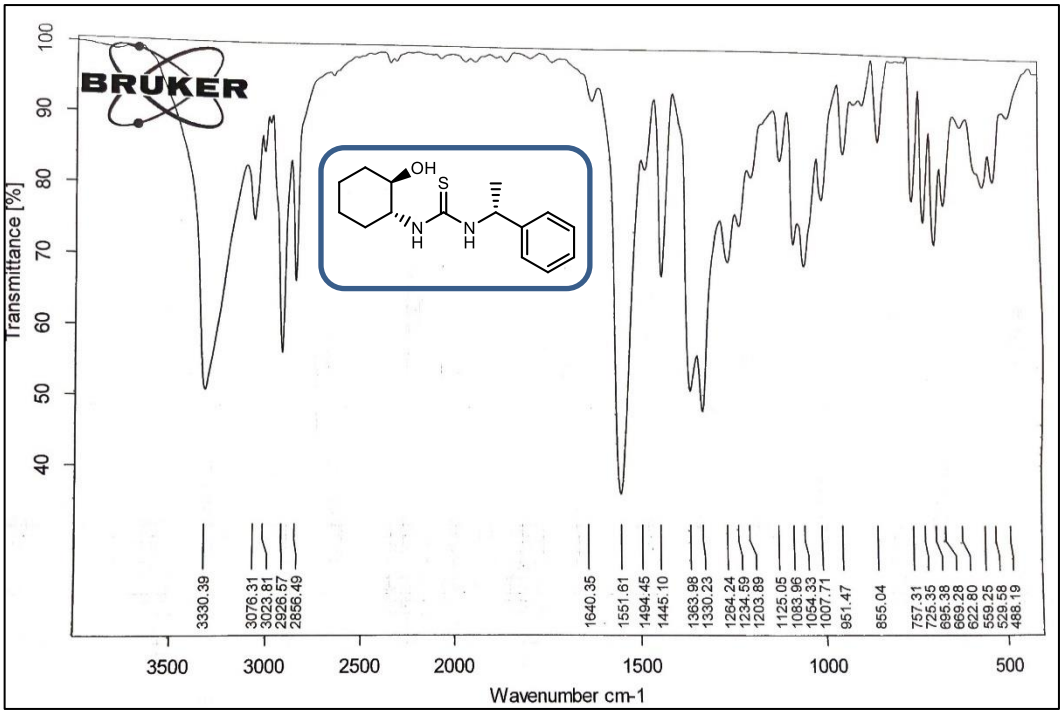
IR of 1-fluoro-4-isothiocyanatobenzene **55**



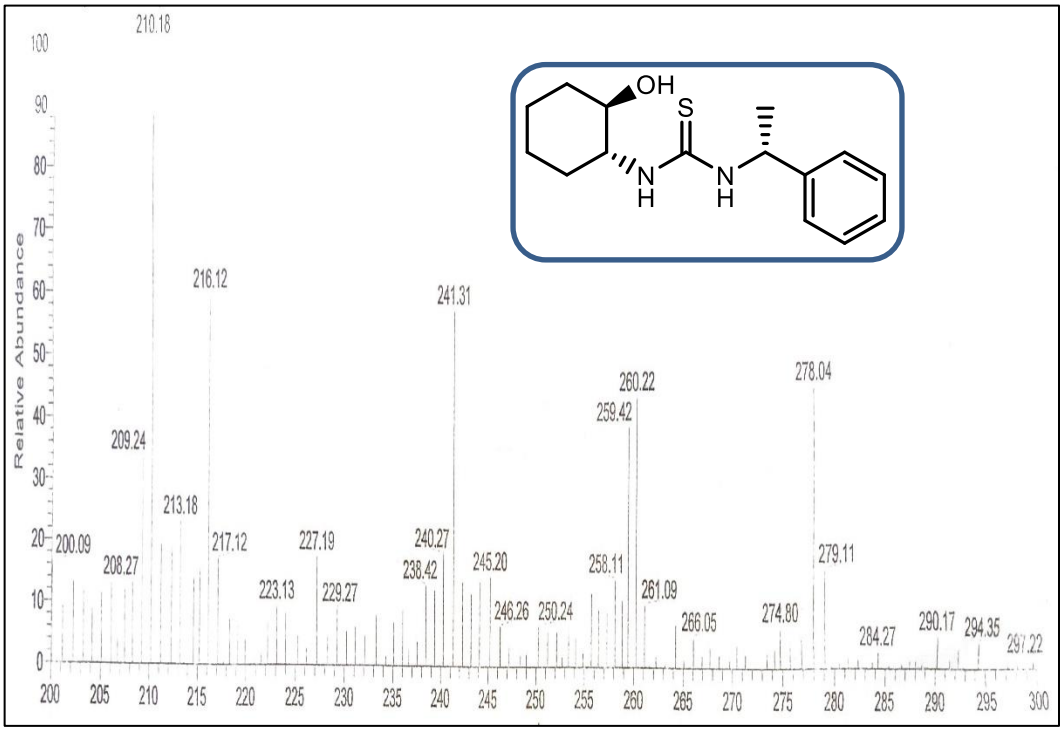
^{1}H NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea **57**



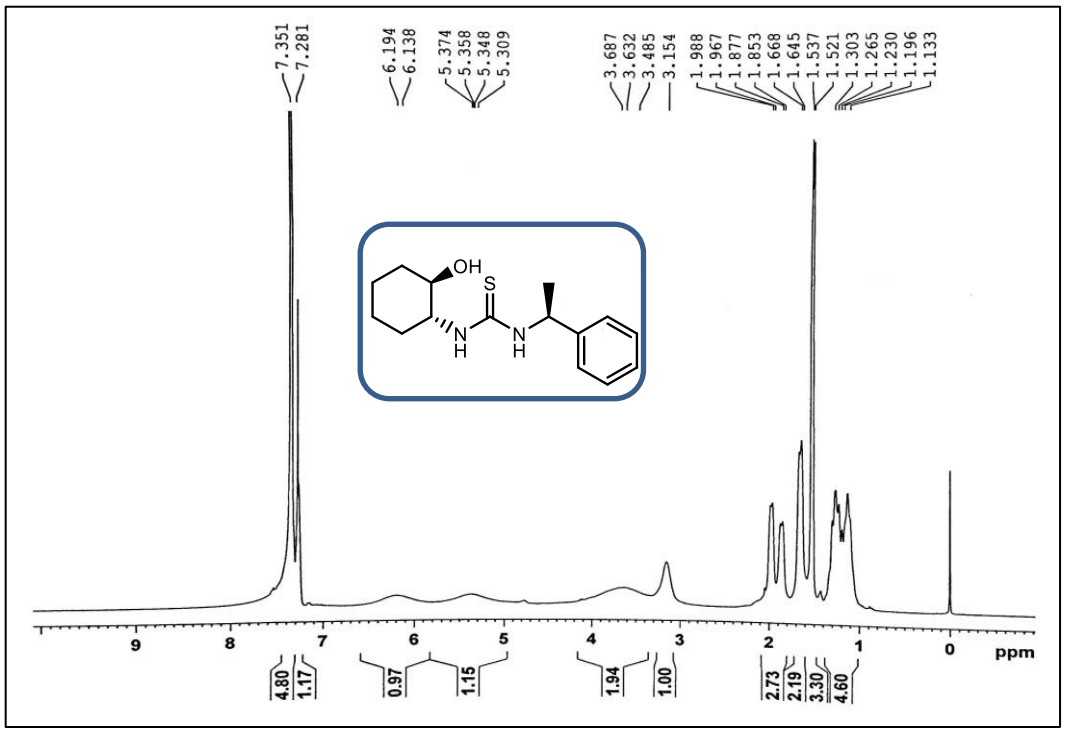
^{1}H NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea **57**



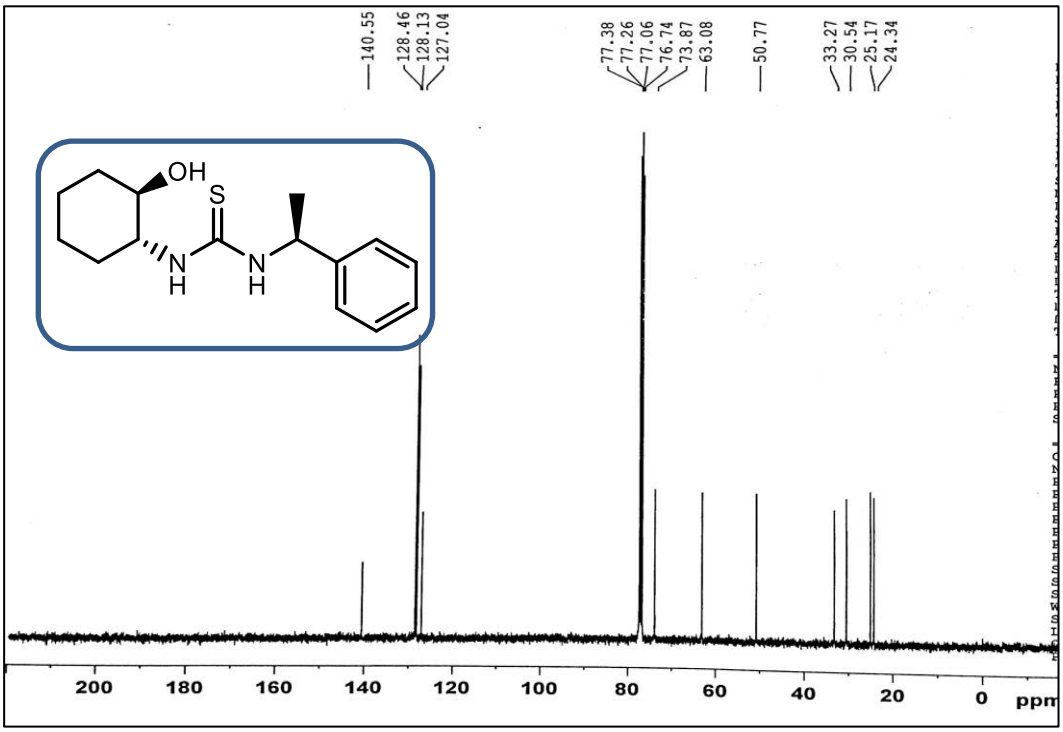
^{1}H NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea **57**



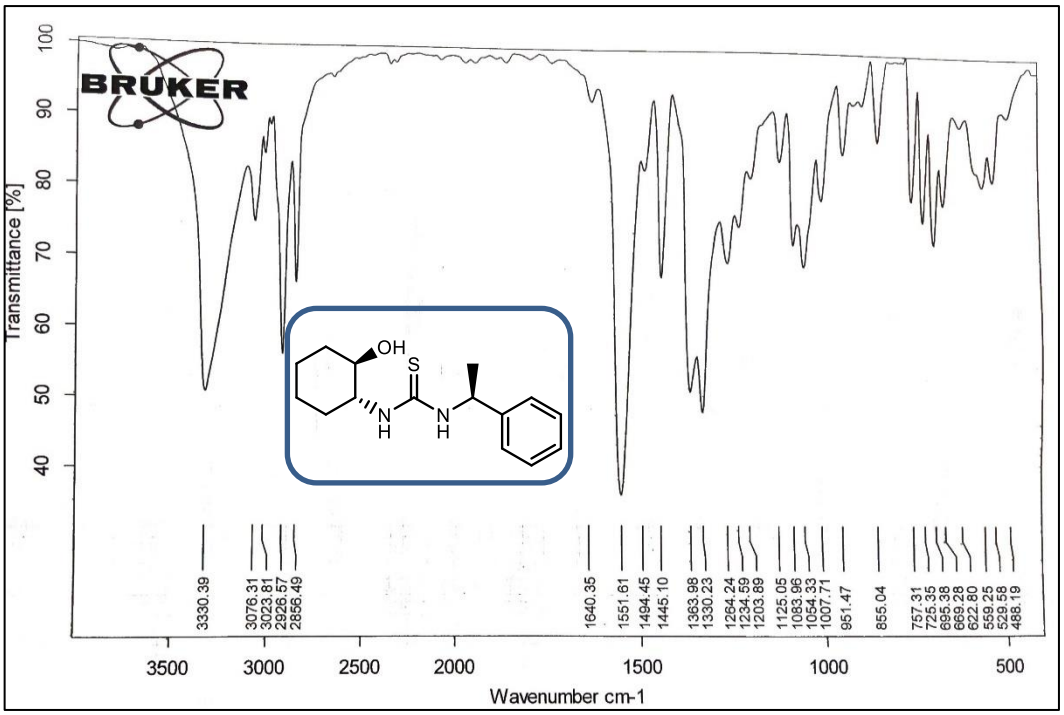
Mass of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((S)-1-phenylethyl)thiourea **57**



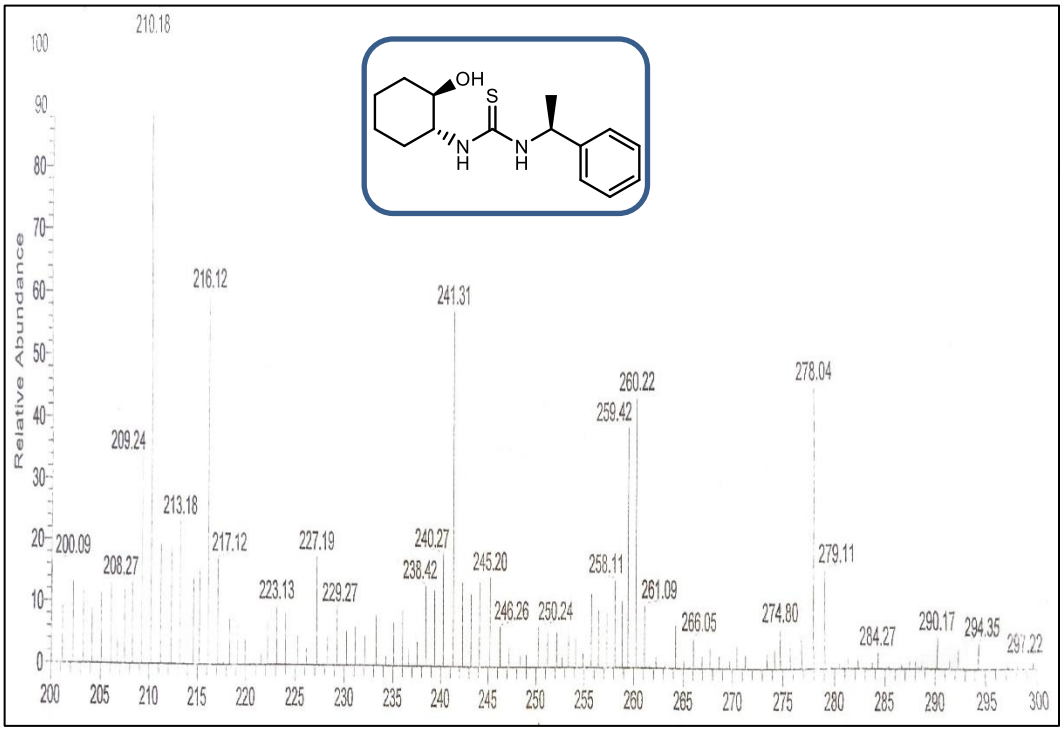
^{1}H NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**



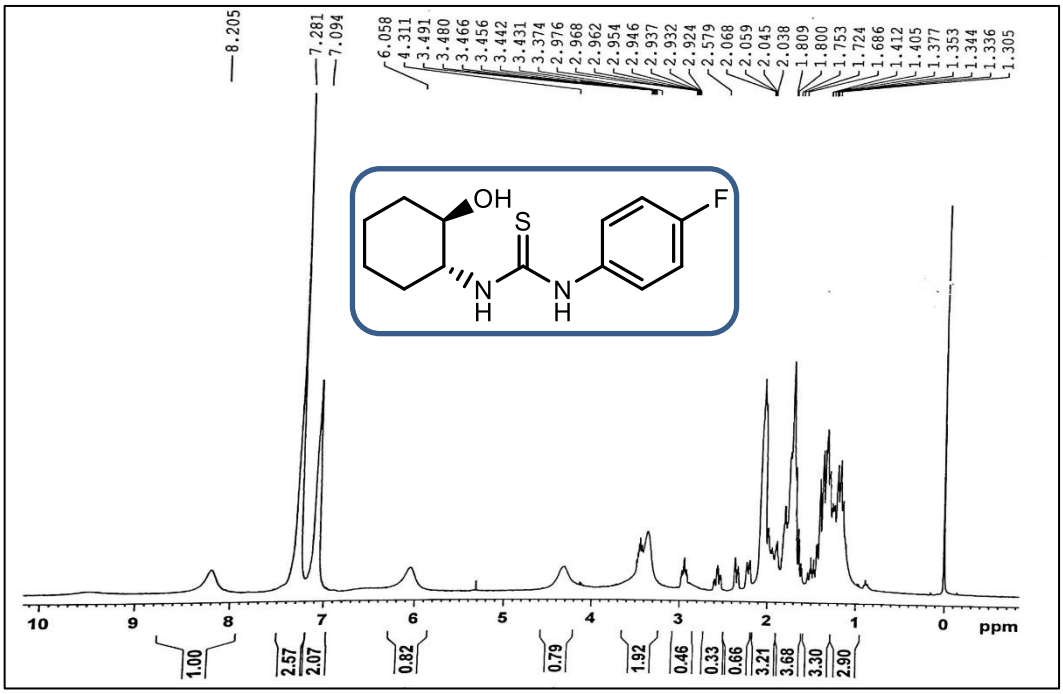
^{13}C NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**



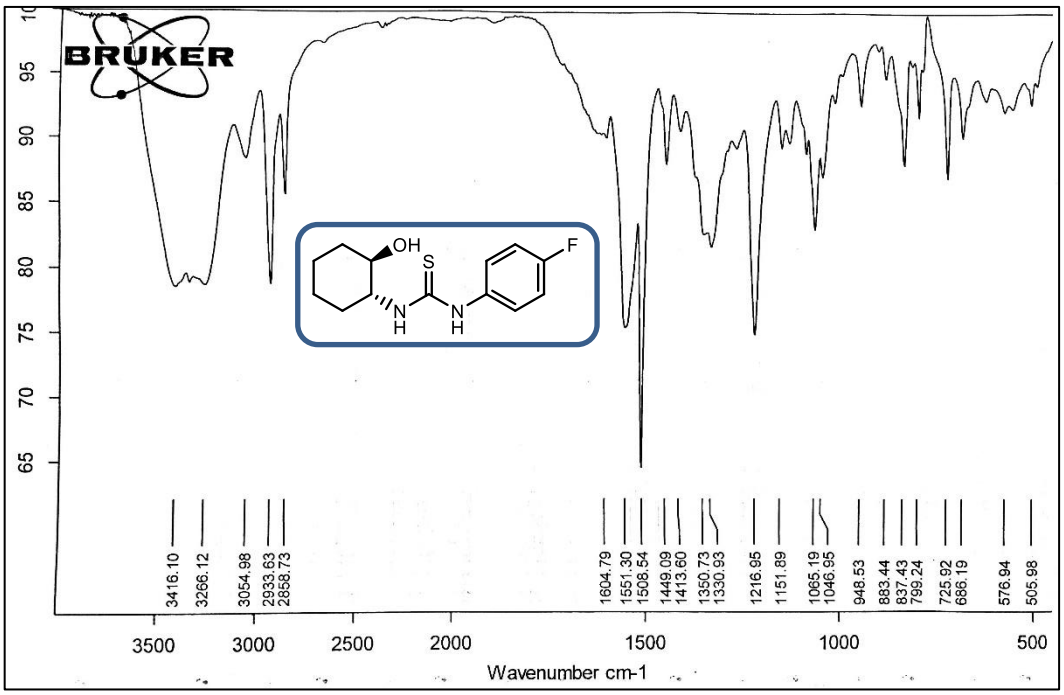
^{1}H NMR of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**



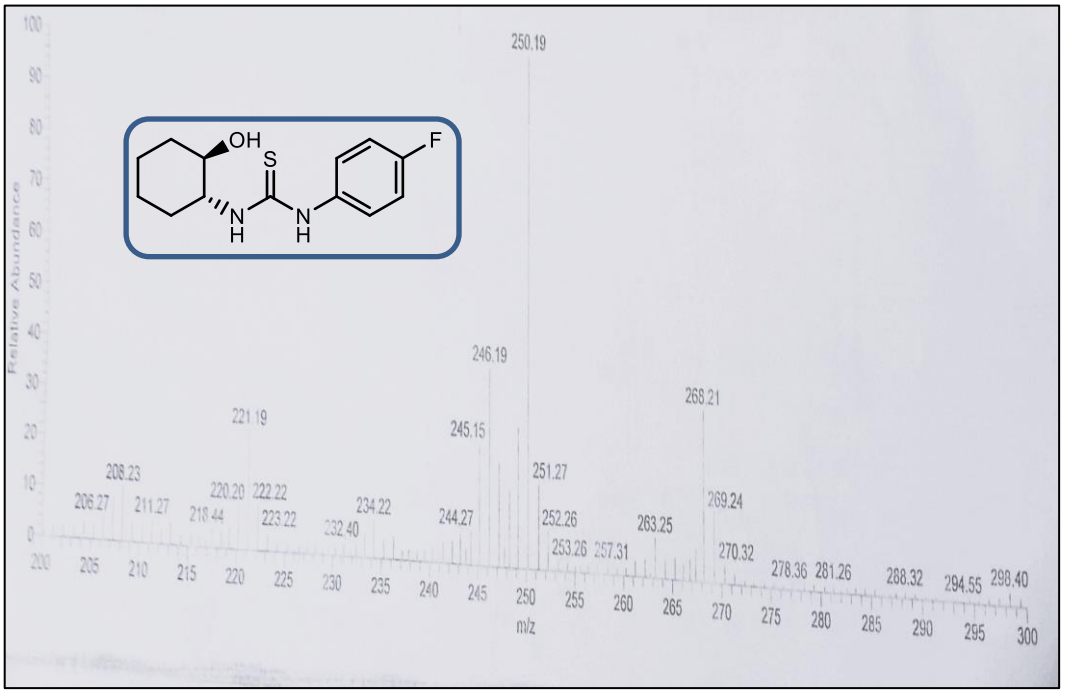
Mass of 1-((1R,2R)-2-hydroxycyclohexyl)-3-((R)-1-phenylethyl)thiourea **56**



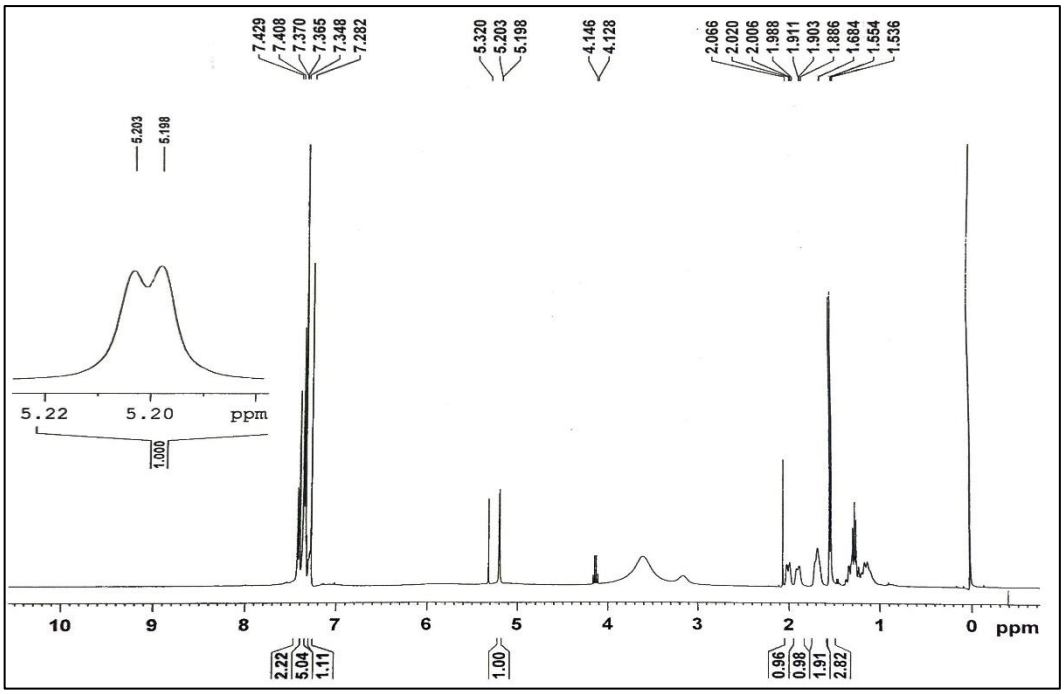
^{1}H NMR of 1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)thiourea **58**



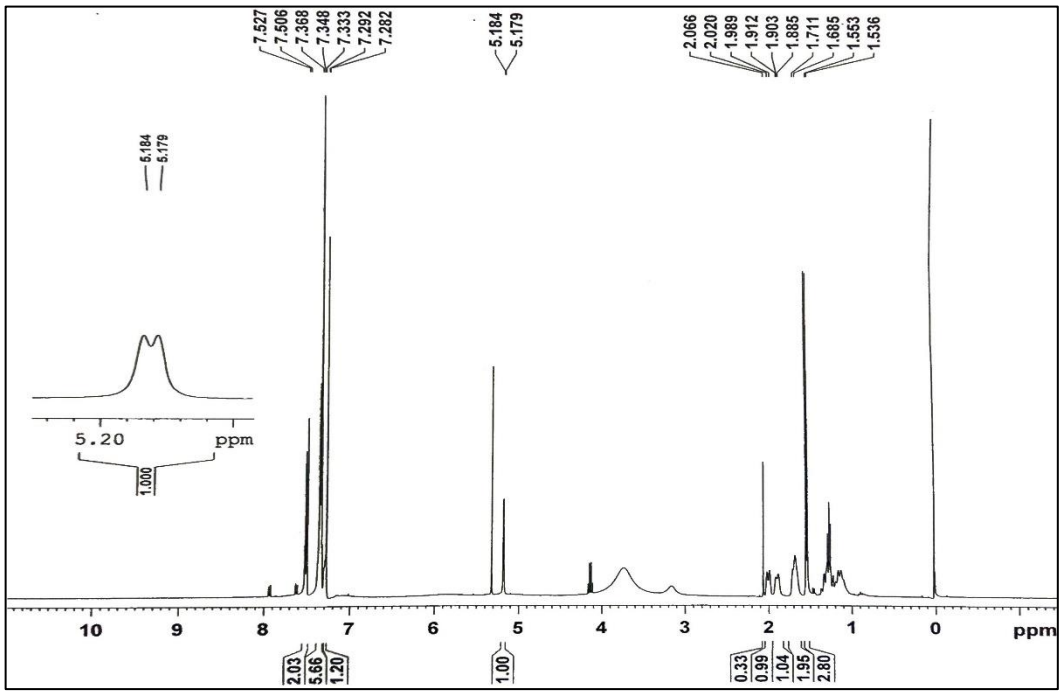
IR of 1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)thiourea **58**



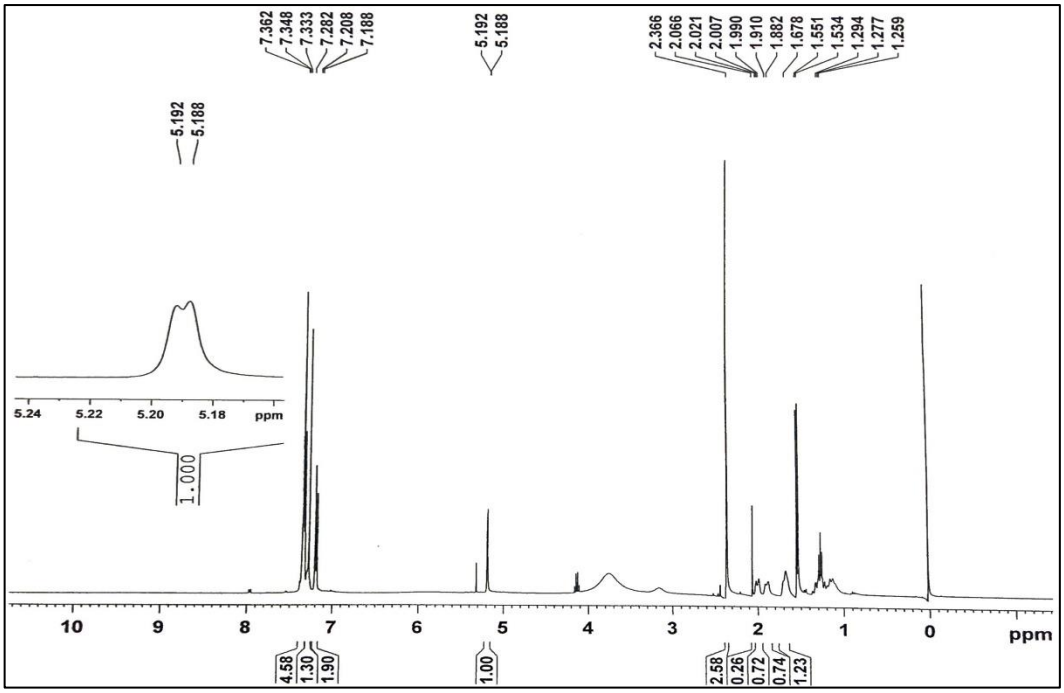
Mass of 1-(4-fluorophenyl)-3-((1R,2R)-2-hydroxycyclohexyl)thiourea **58**



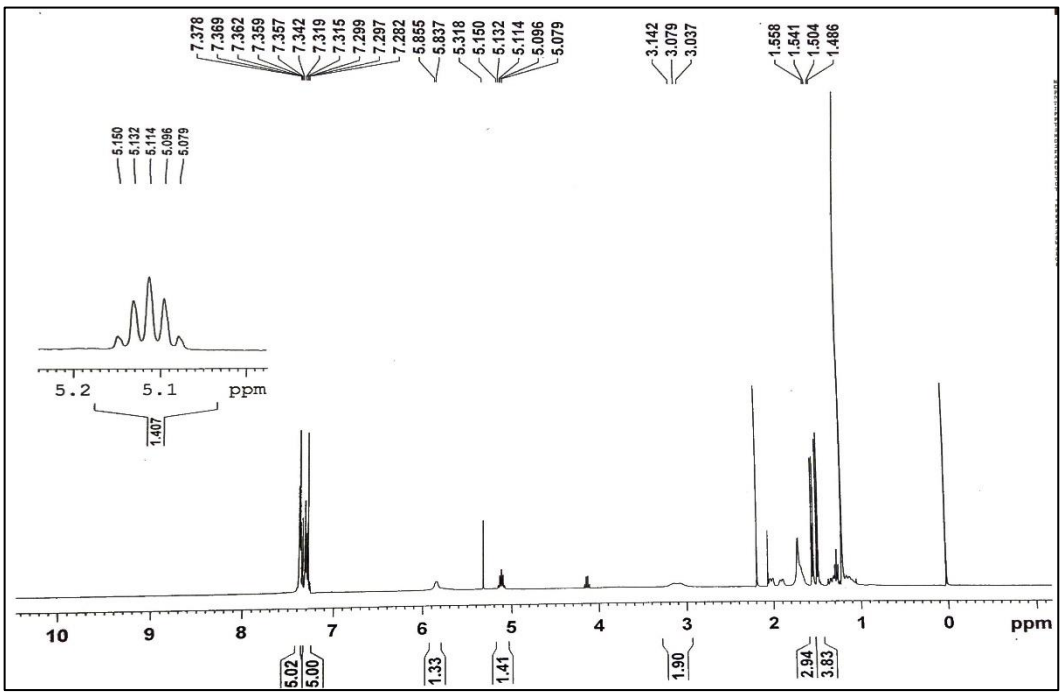
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **65**



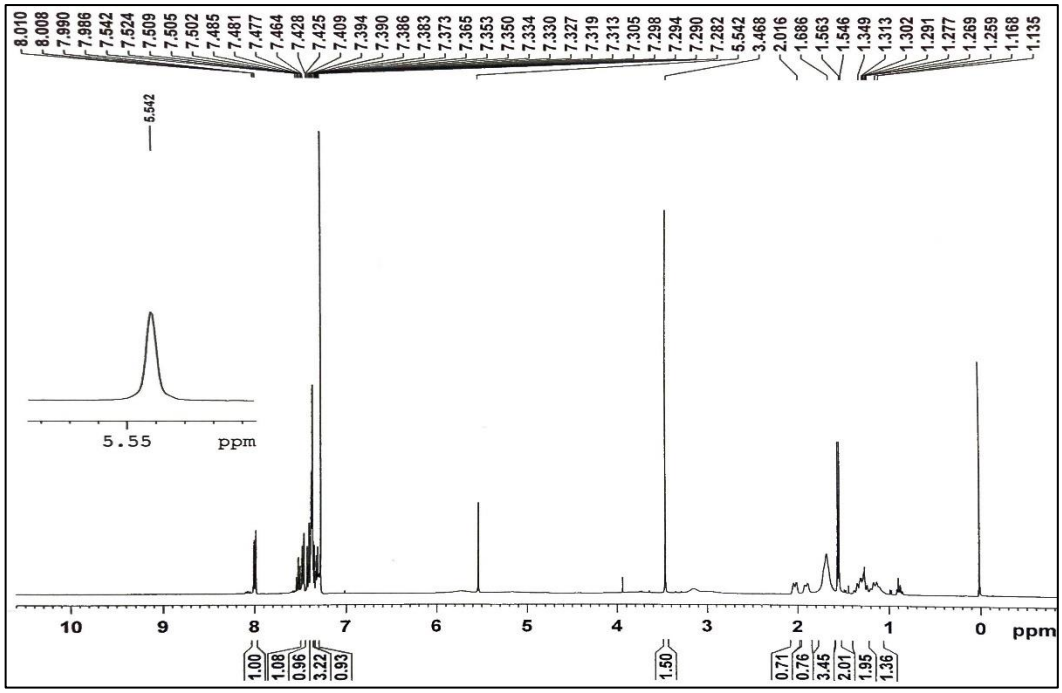
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **66**



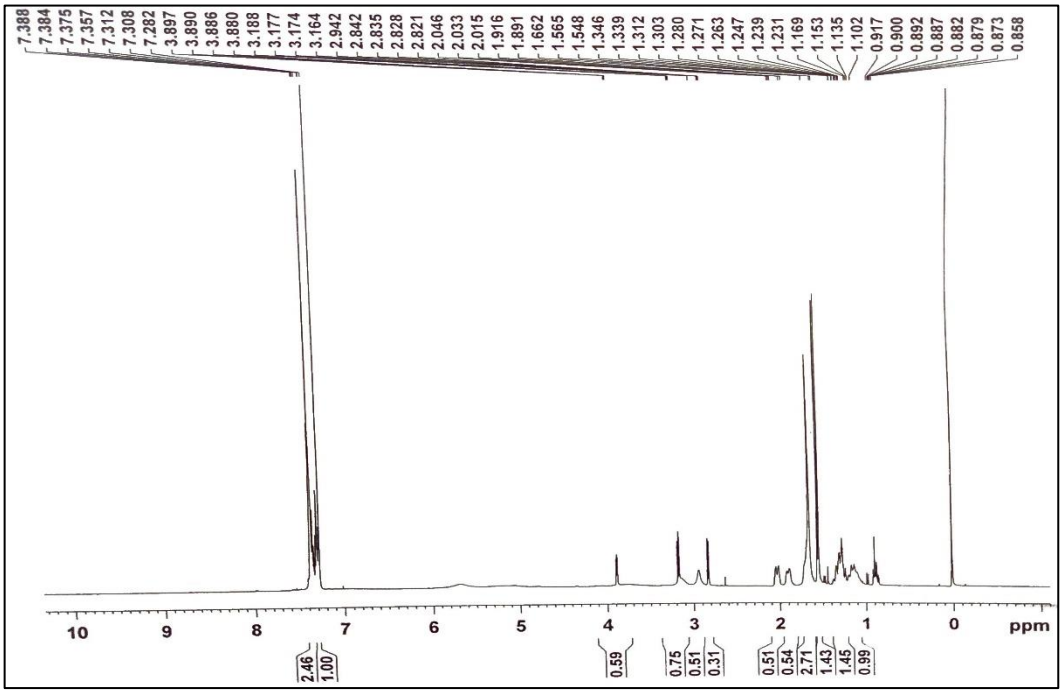
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **67**



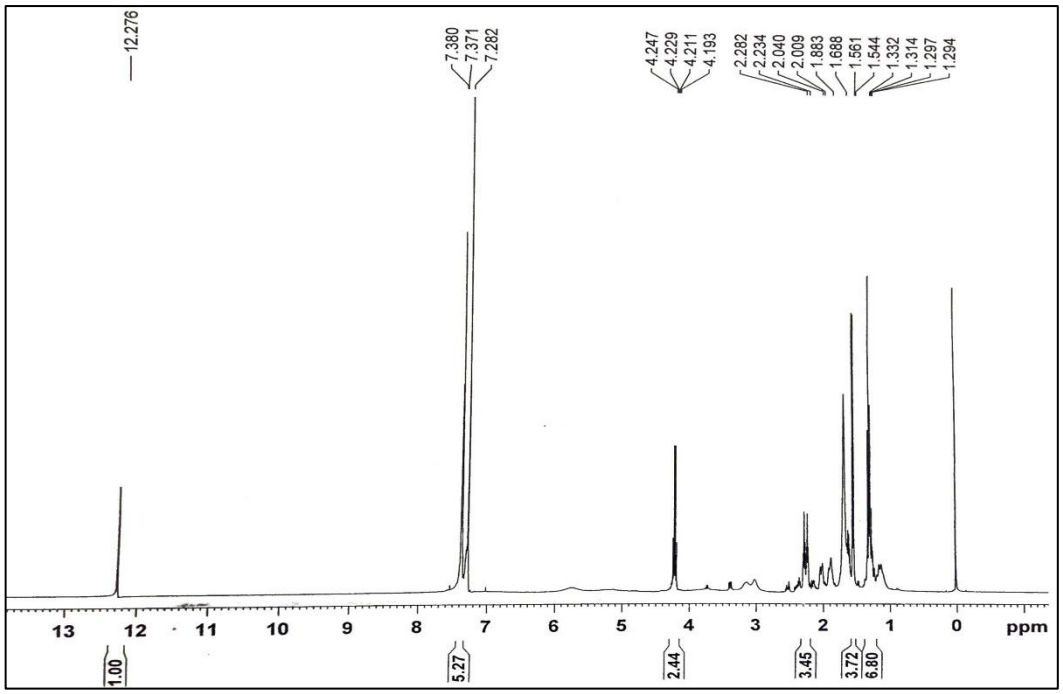
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **68**



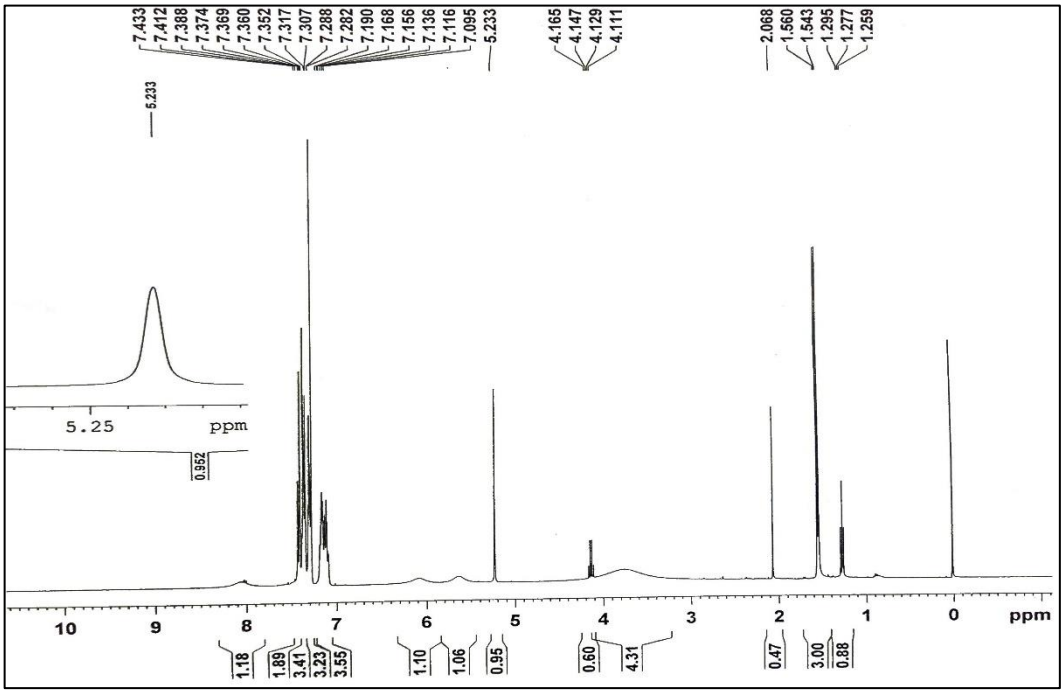
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **69**



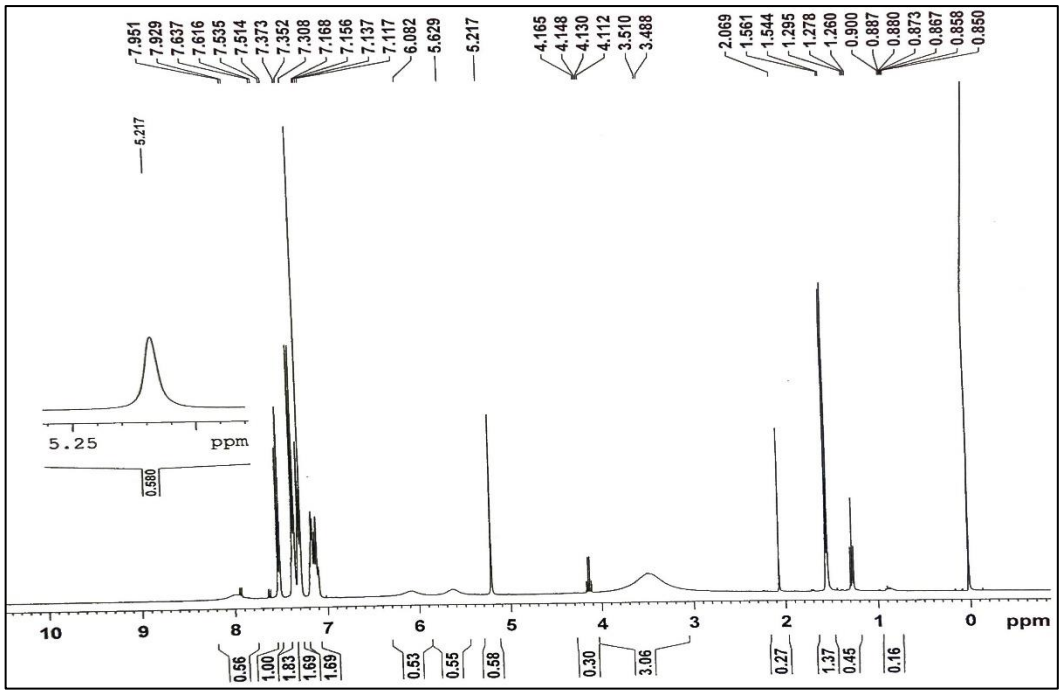
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **70**



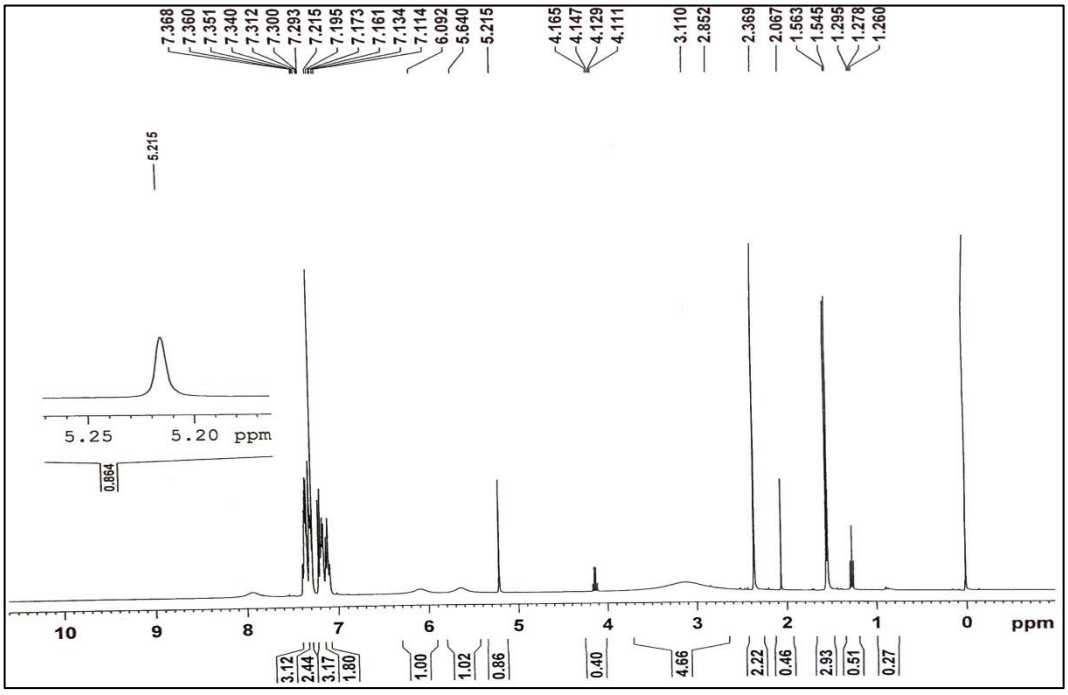
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + **71**



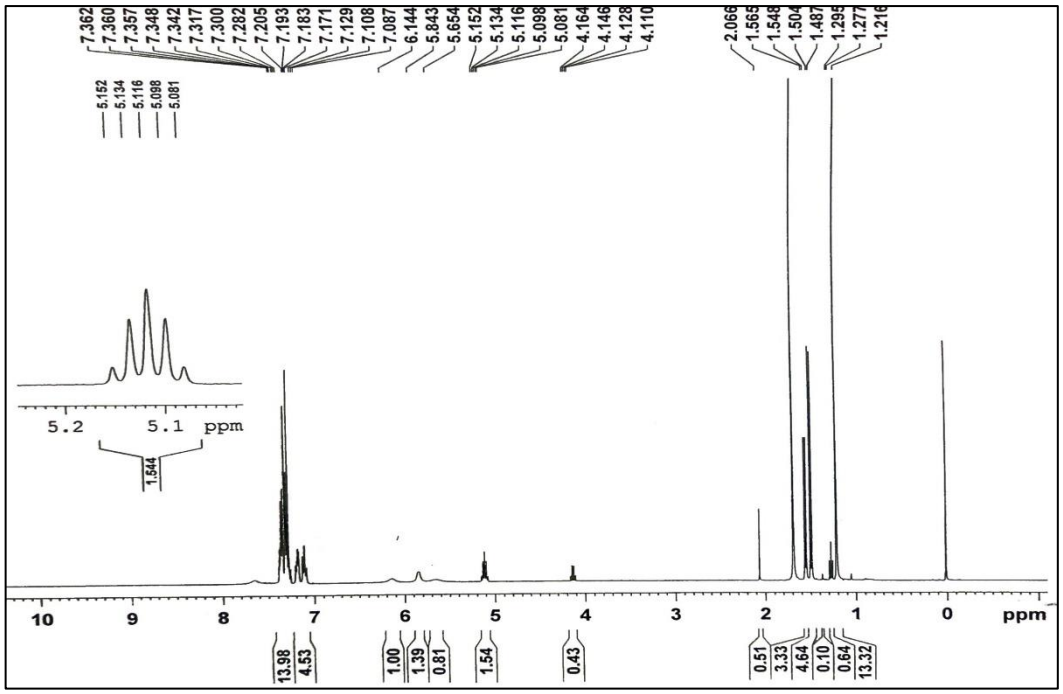
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **65**



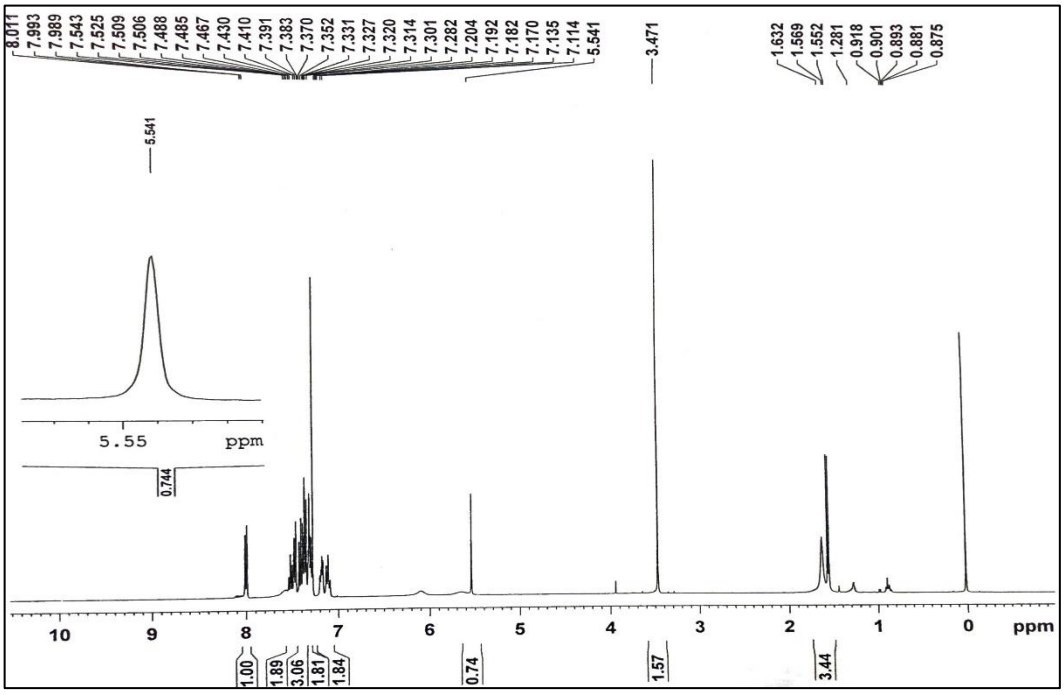
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **66**



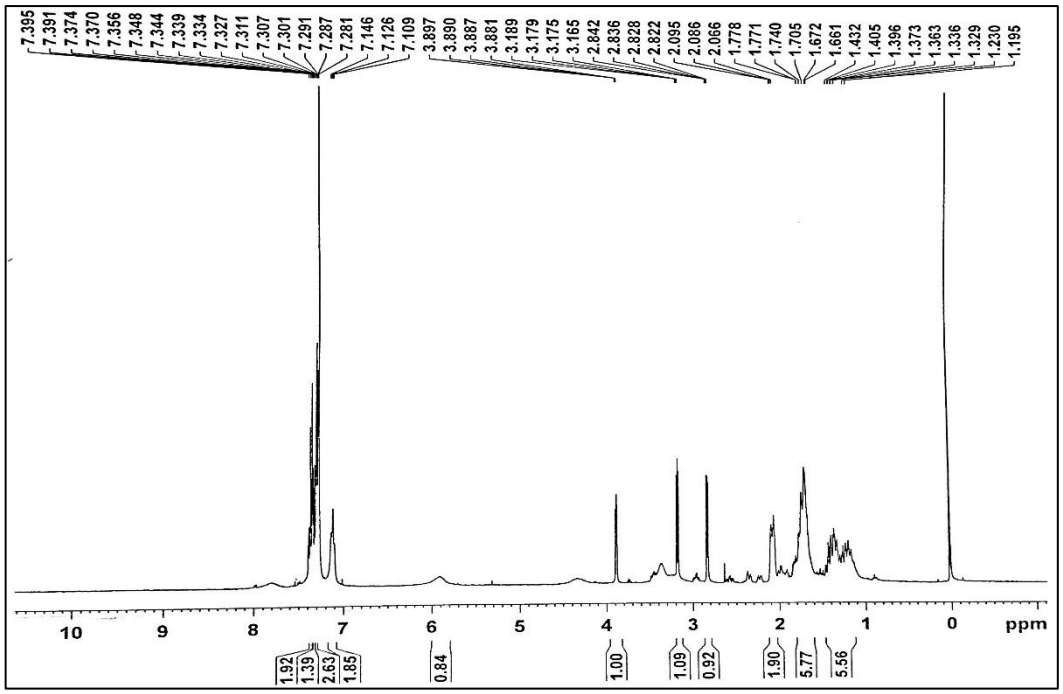
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **67**



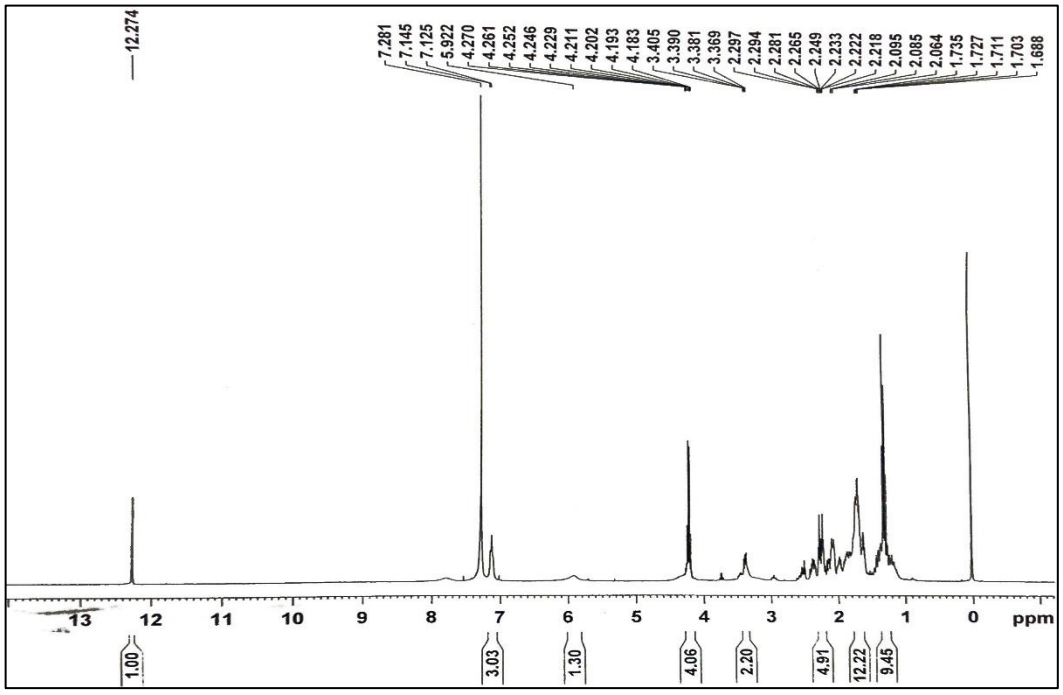
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **68**



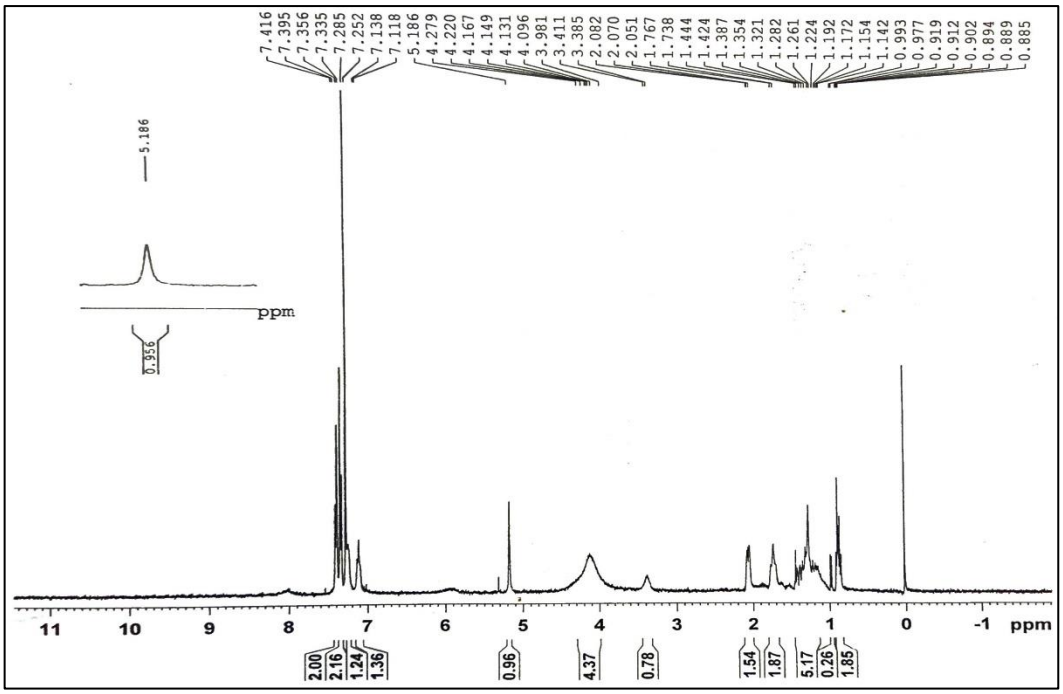
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **69**



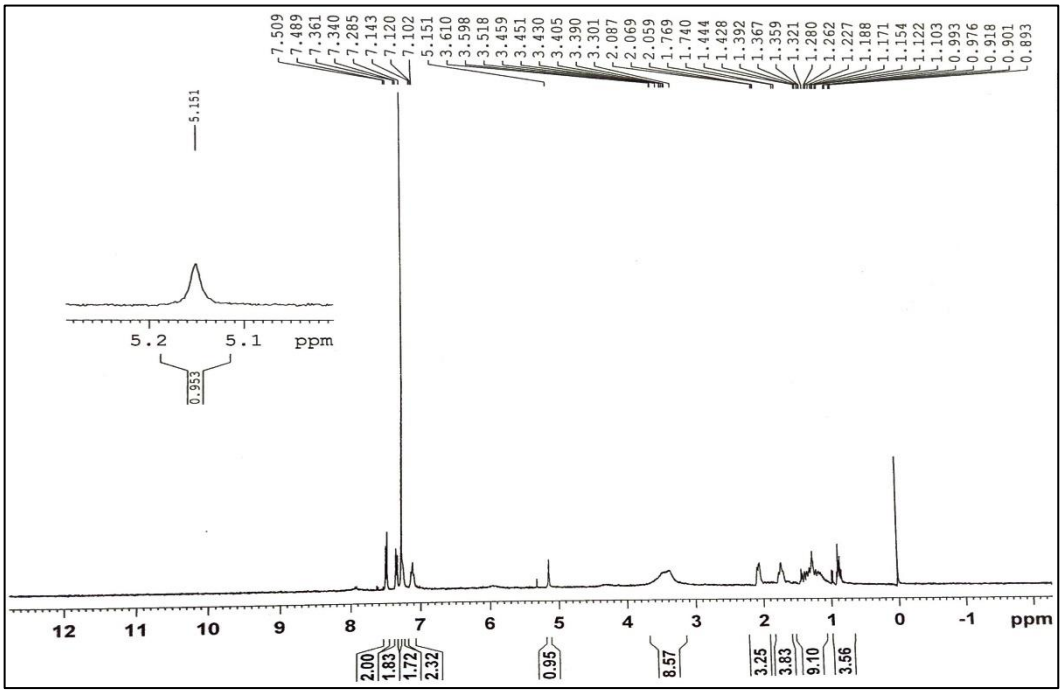
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **70**



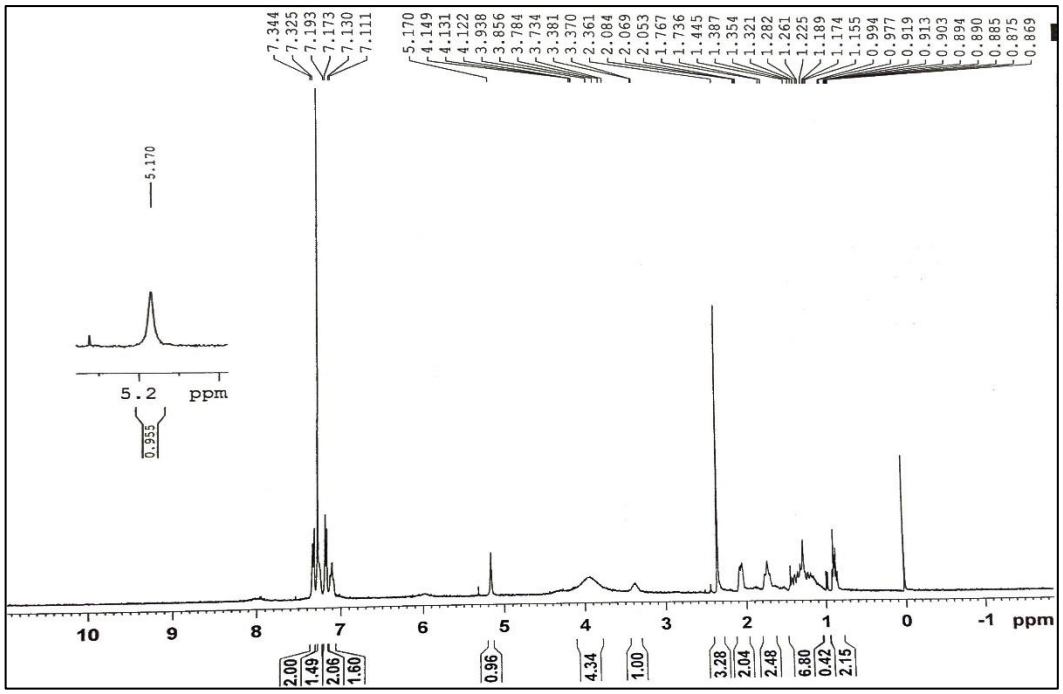
^{1}H NMR spectrum of (*R*, *R*, *S*)-**57** + **71**



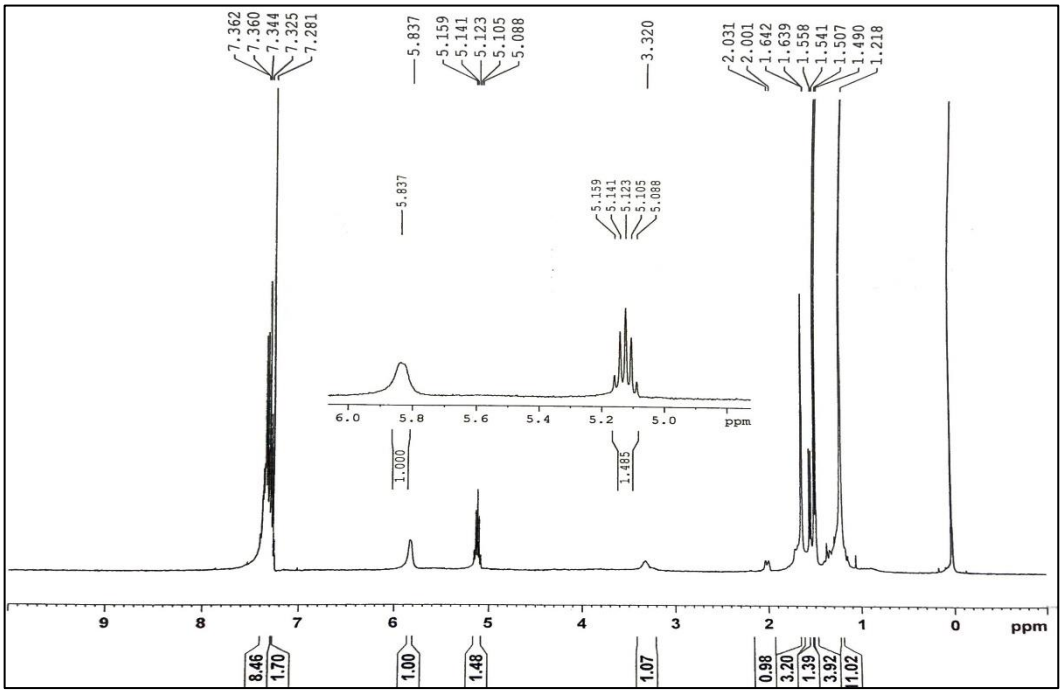
^{1}H NMR spectrum of (*R*, *R*)-**58** + **65**



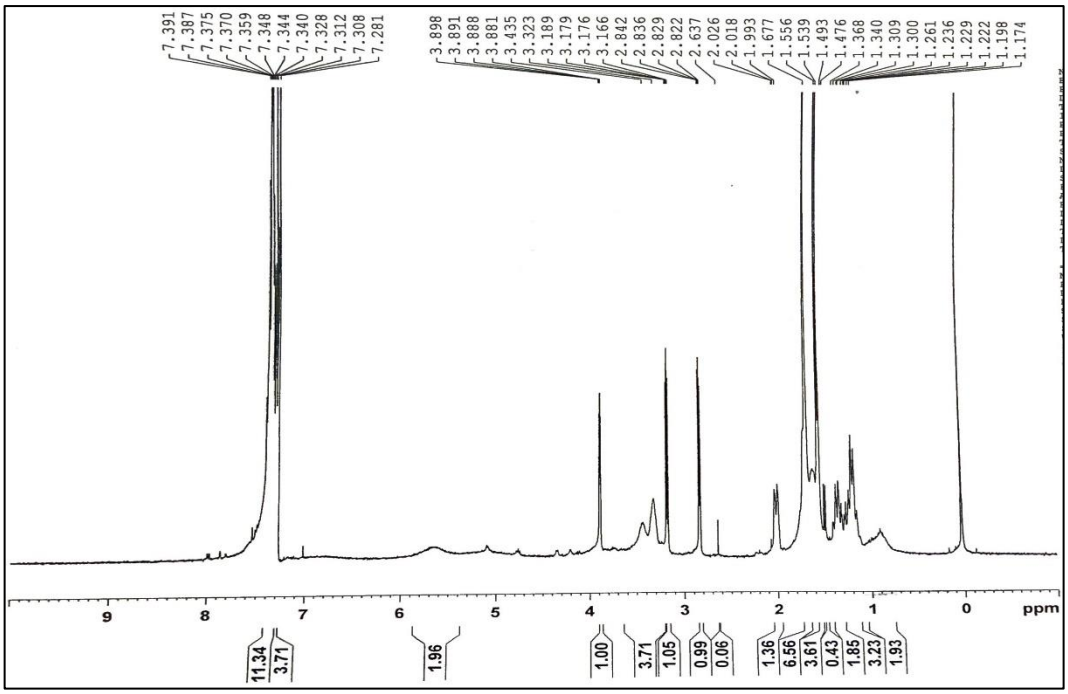
^{1}H NMR spectrum of (*R*, *R*)-**58** + **66**



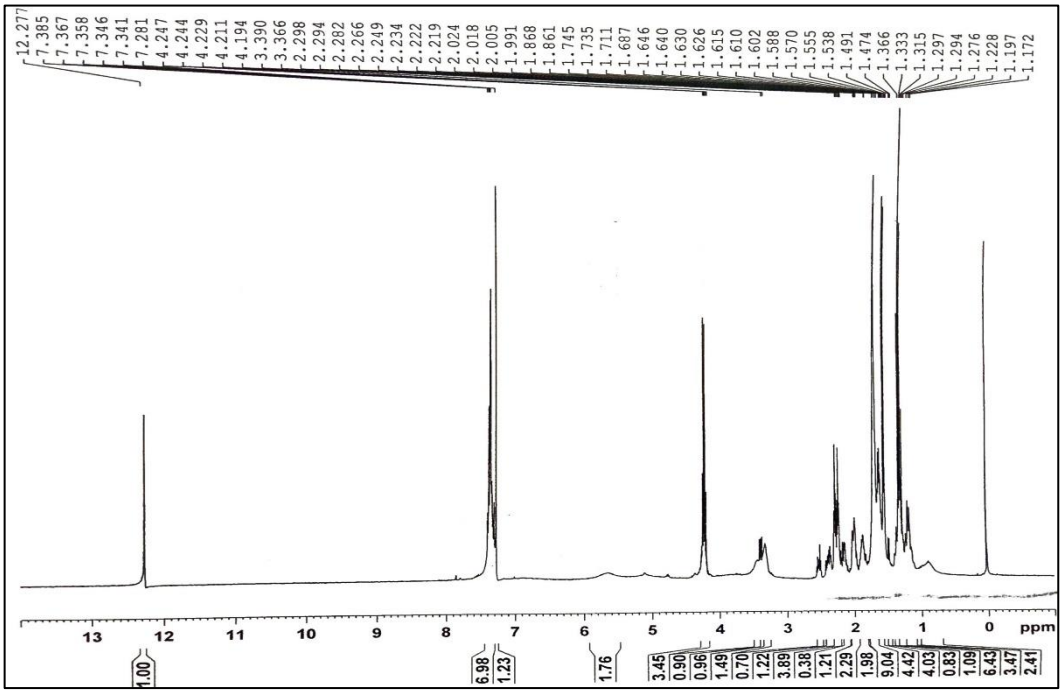
^{1}H NMR spectrum of (*R*, *R*)-**58** + **67**



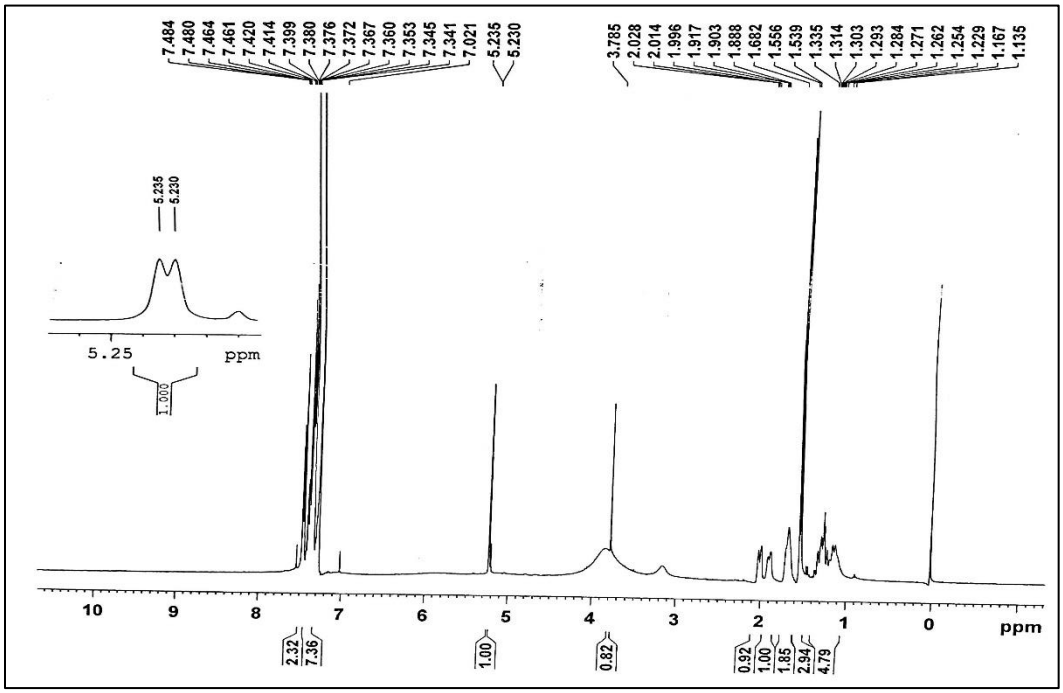
^{1}H NMR spectrum of (*R*, *R*)-**58** + **68**



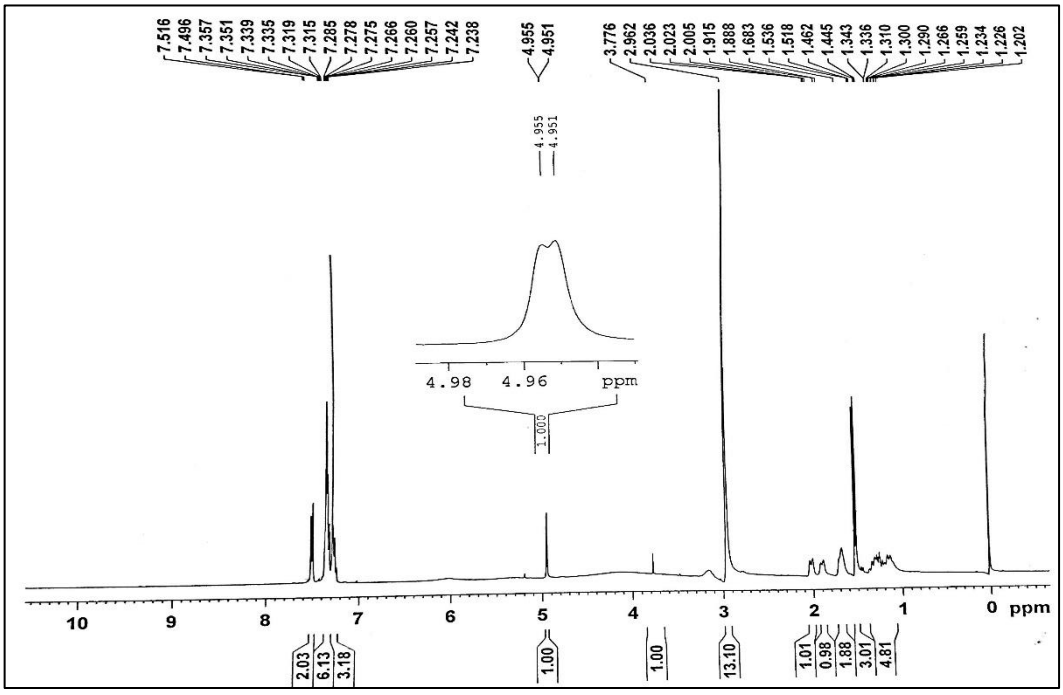
^{1}H NMR spectrum of (*R*, *R*)-**58** + **70**



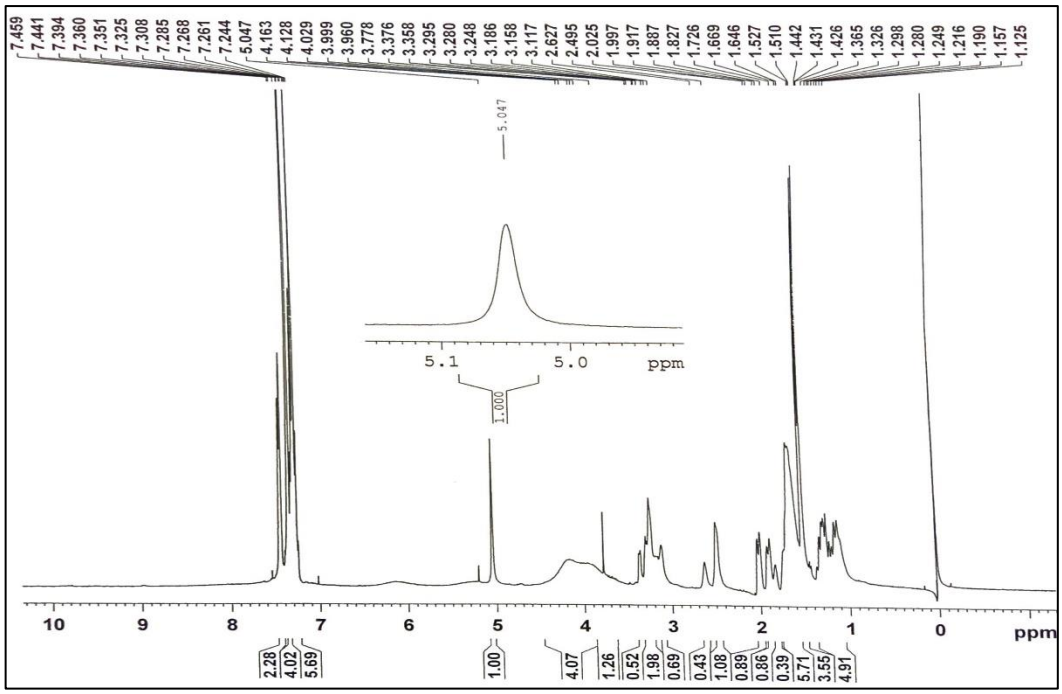
^{1}H NMR spectrum of (*R*, *R*)-**58** + **71**



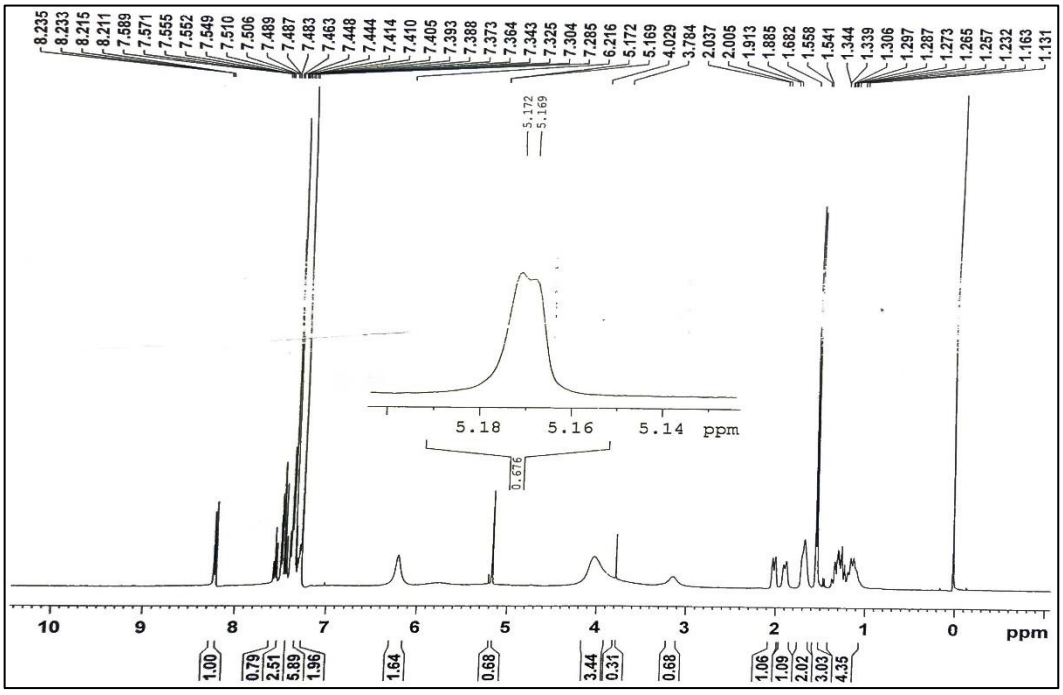
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA



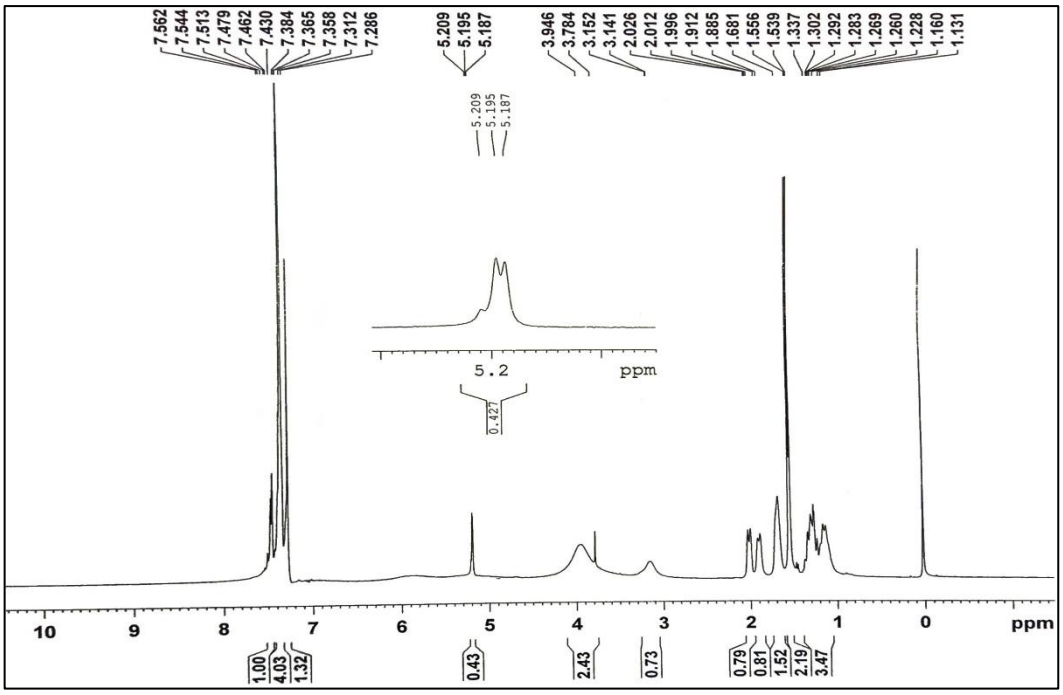
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA + DABCO



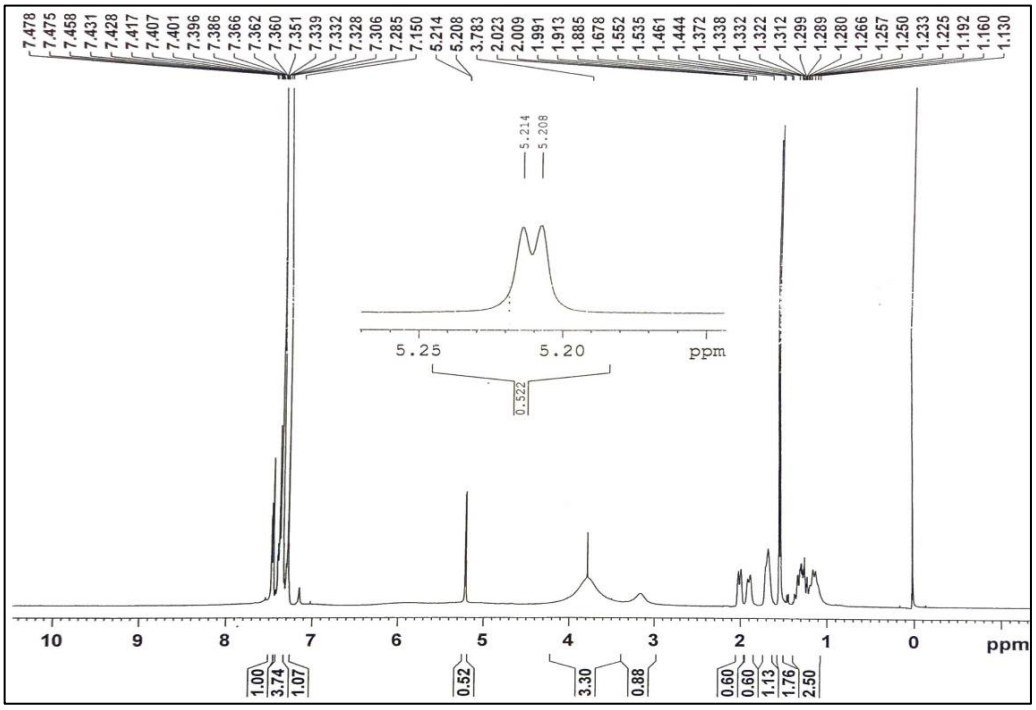
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA + DBU



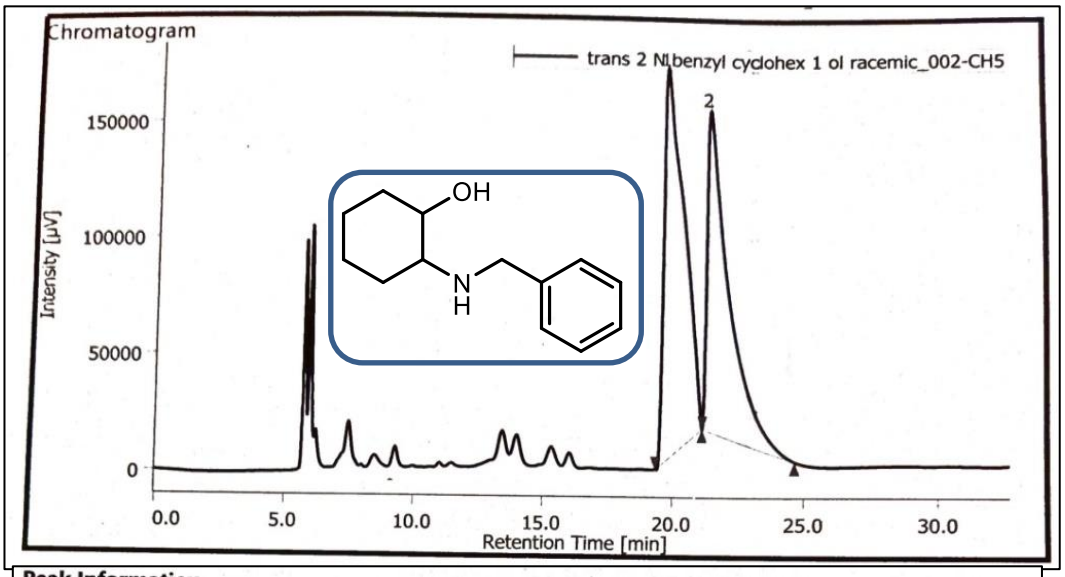
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA + Benzguanine



^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA + 3 amino triazole



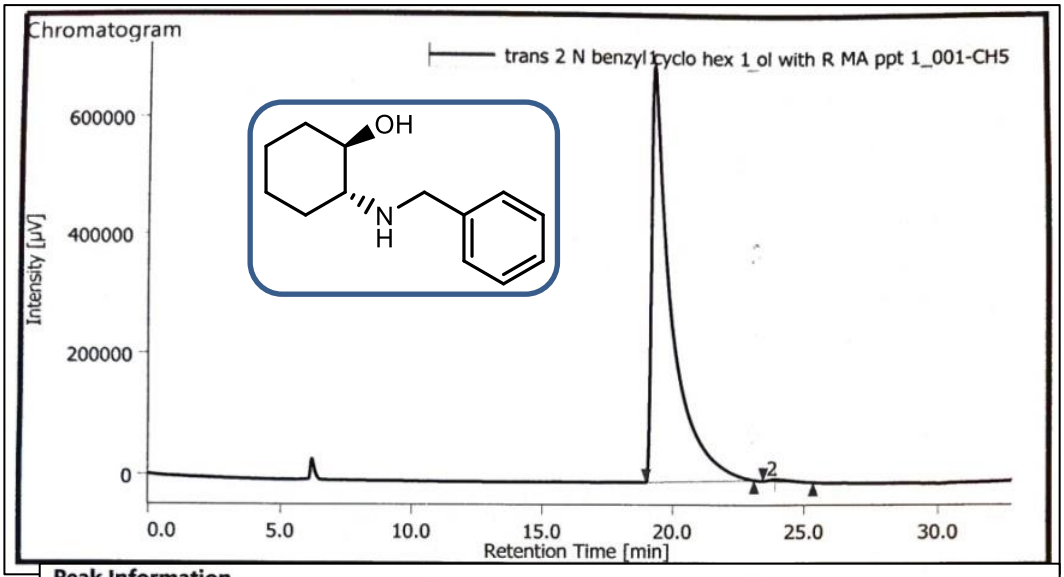
^{1}H NMR spectrum of (*R*, *R*, *R*)-**56** + MA + 2 amino benzimmidazole



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	19.690	8916341	170151	53.076	55.116	N/A	2587	1.181	3.612	
2	Unknown	5	21.360	7882712	138563	46.924	44.884	N/A	4402	N/A	5.825	

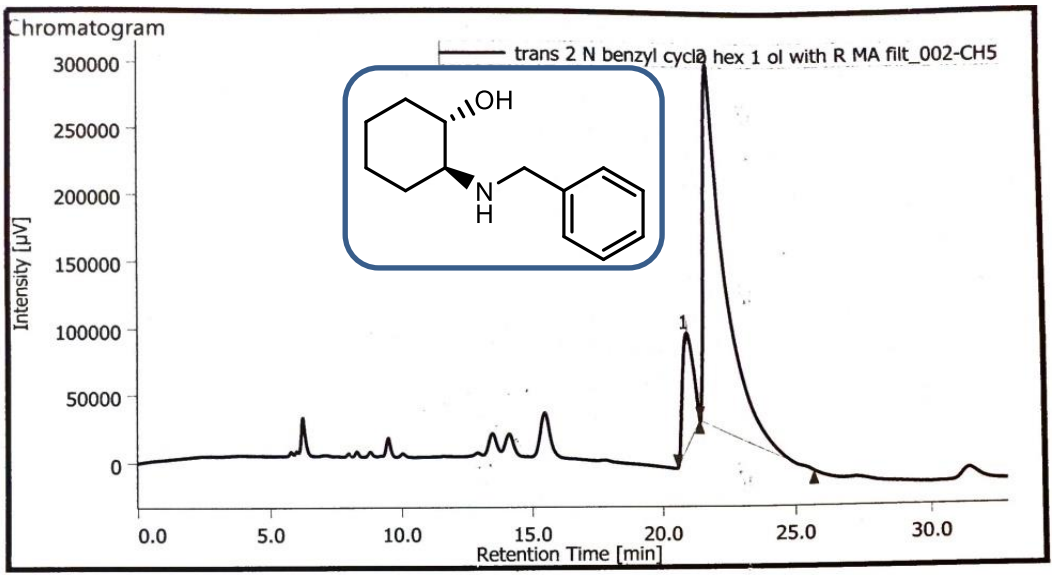
HPLC chromatogram of Racemic 2-(benzylamino)cyclohexan-1-ol **48**



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	19.260	35818115	701099	99.463	99.523	N/A	5463	3.529	5.938	
2	Unknown	5	23.887	193276	3357	0.537	0.477	N/A	3626	N/A	2.069	

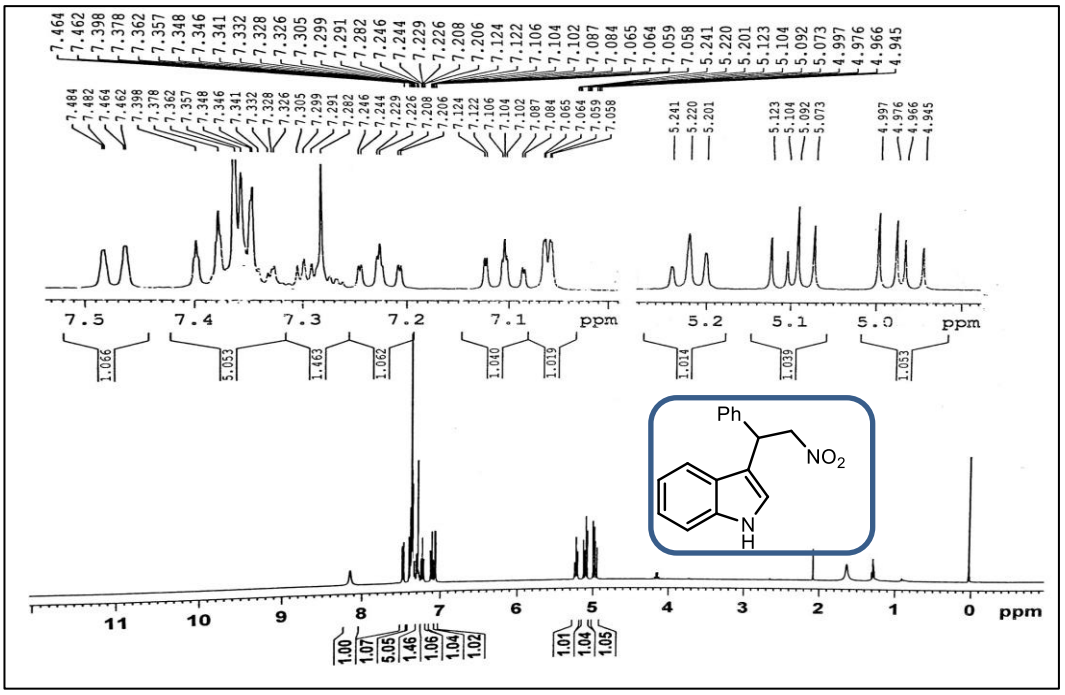
HPLC chromatogram of (1R,2R)-2-(benzylamino)cyclohexan-1-ol **48**



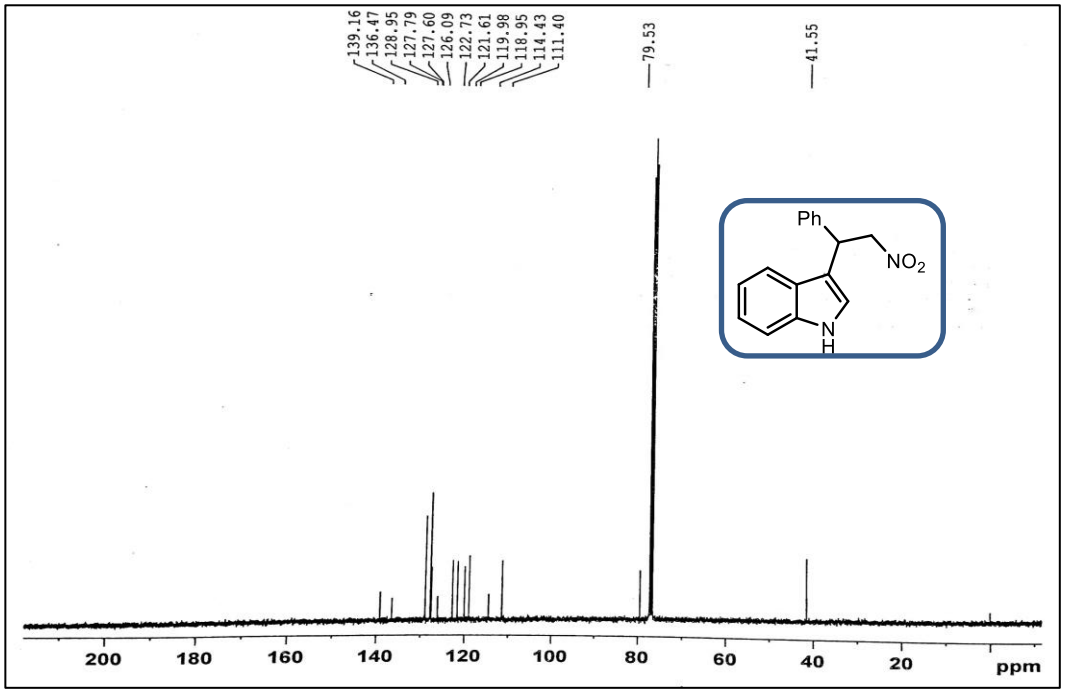
Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	20.853	2389156	87105	14.156	24.270	N/A	10999	0.805	1.483	
2	Unknown	5	21.647	14488486	271789	85.844	75.730	N/A	5387	N/A	5.478	

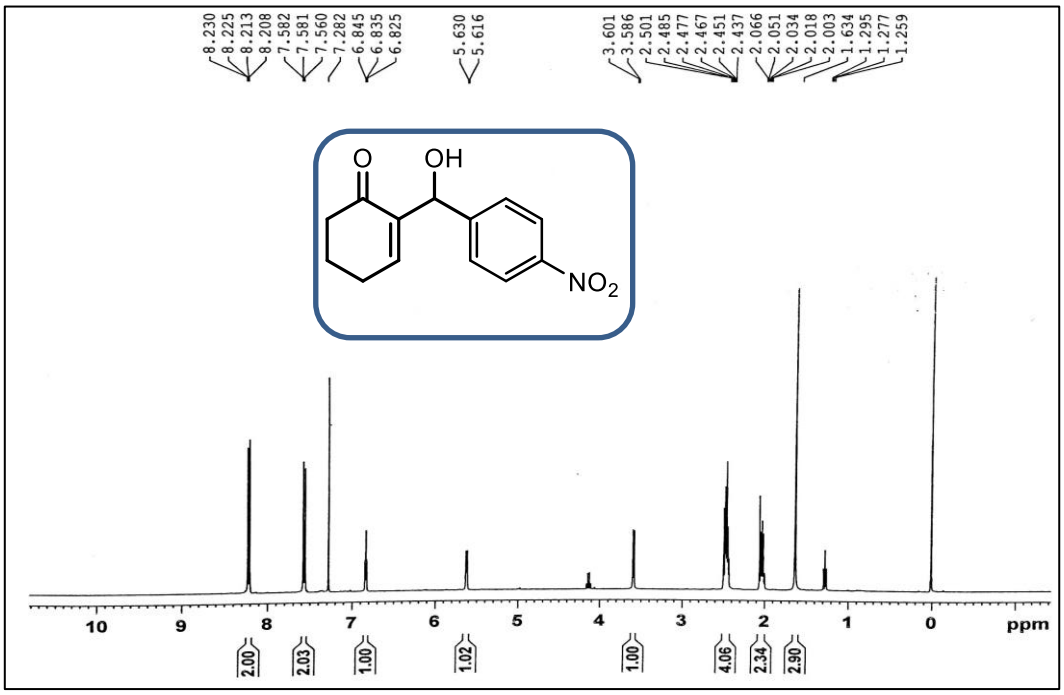
HPLC chromatogram of (1S,2S)-2-(benzylamino)cyclohexan-1-ol **48**



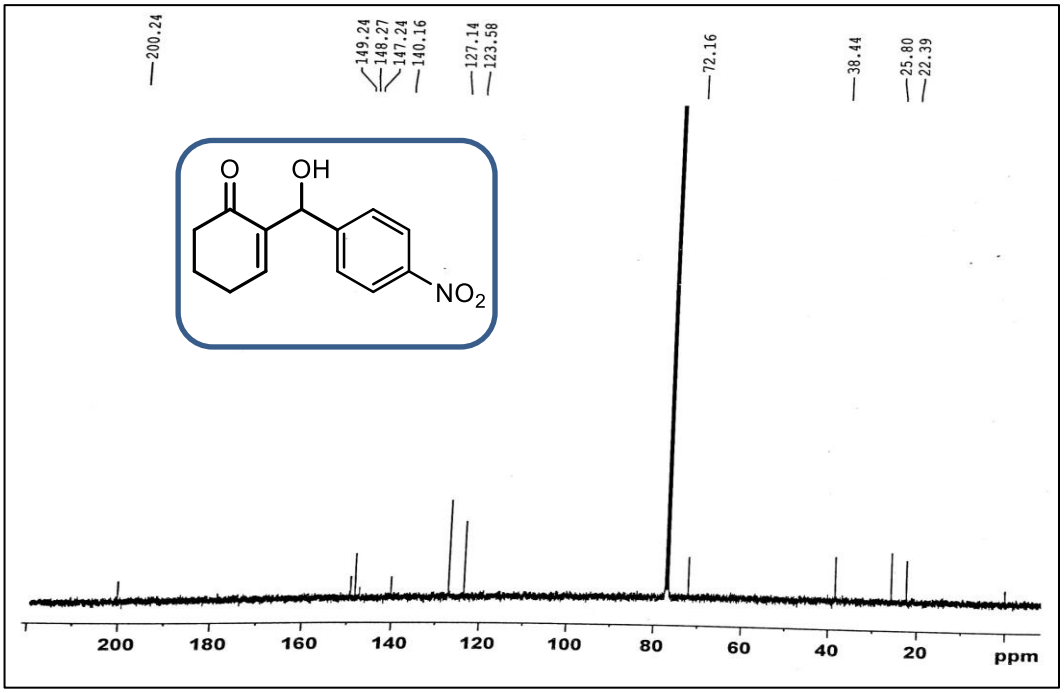
^{1}H NMR of 3-(2-nitro-1-phenylethyl)-1H-indole **61**



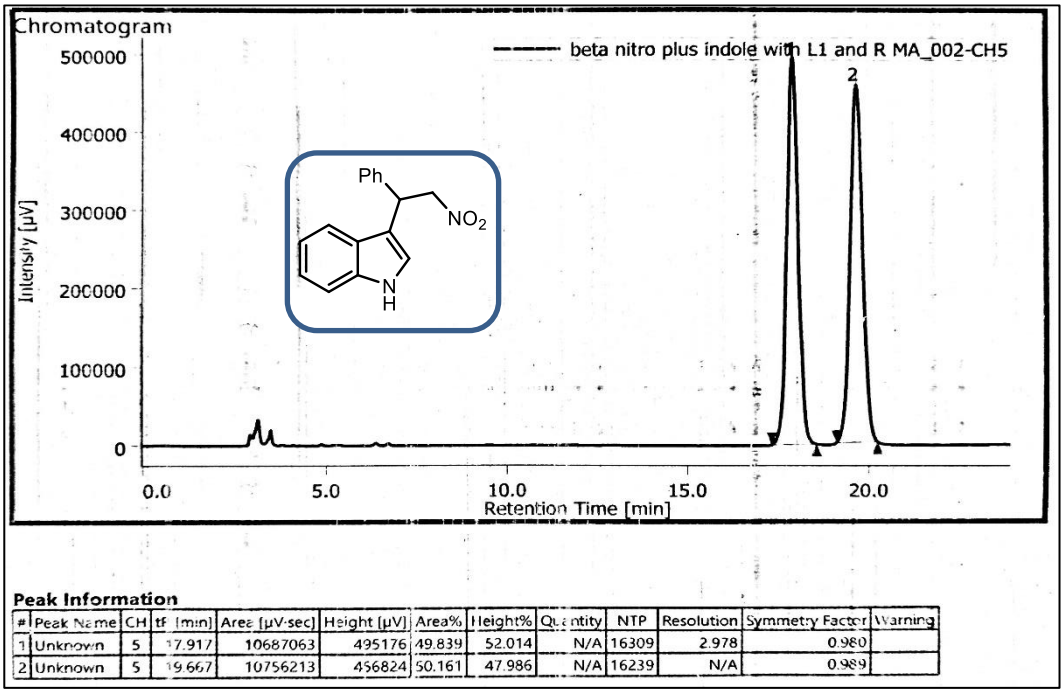
^{13}C NMR of 3-(2-nitro-1-phenylethyl)-1H-indole **61**



^{1}H NMR of 2-(hydroxy(4-nitrophenyl)methyl)cyclohex-2-en-1-one **64**



^{13}C NMR of 2-(hydroxy(4-nitrophenyl)methyl)cyclohex-2-en-1-one **64**

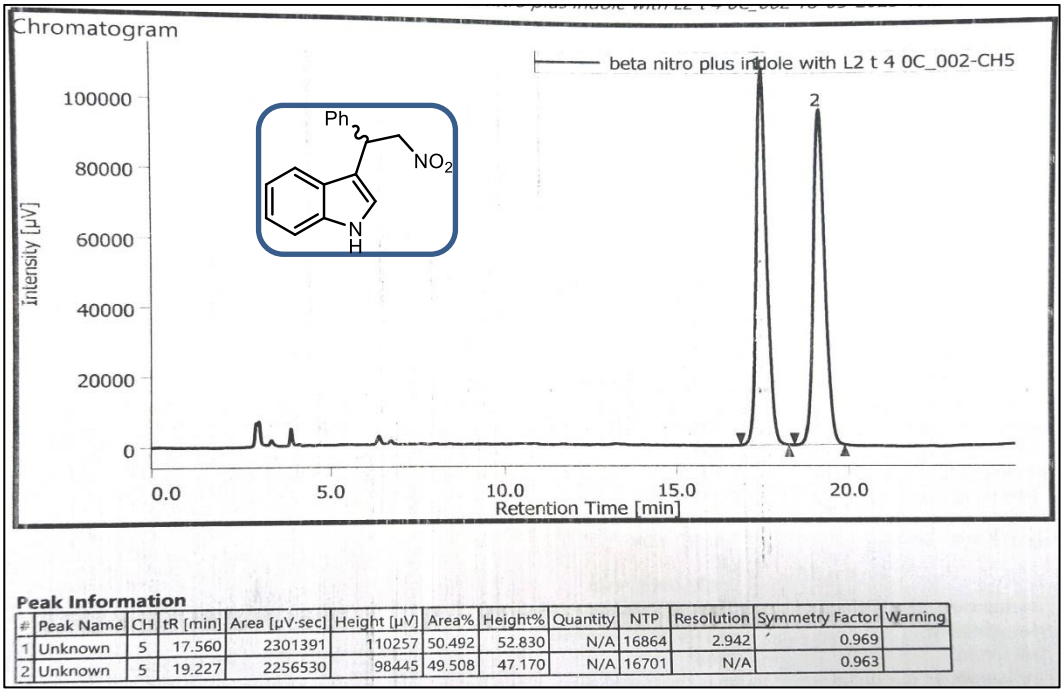


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10687063	495176	49.839	52.014	N/A	16309	2.978	0.980	
2	Unknown	5	19.667	10756213	456824	50.161	47.986	N/A	16239	N/A	0.989	

HPLC chromatogram of racemic 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 1)

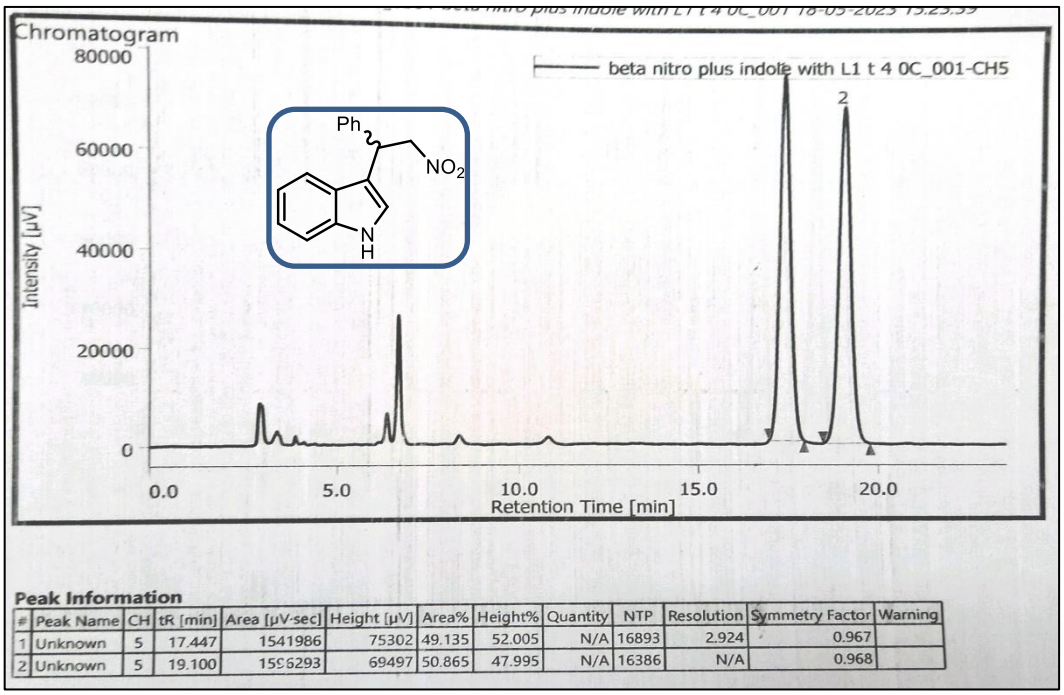


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.560	2301391	110257	50.492	52.830	N/A	16864	2.942	0.969	
2	Unknown	5	19.227	2256530	98445	49.508	47.170	N/A	16701	N/A	0.963	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 2)

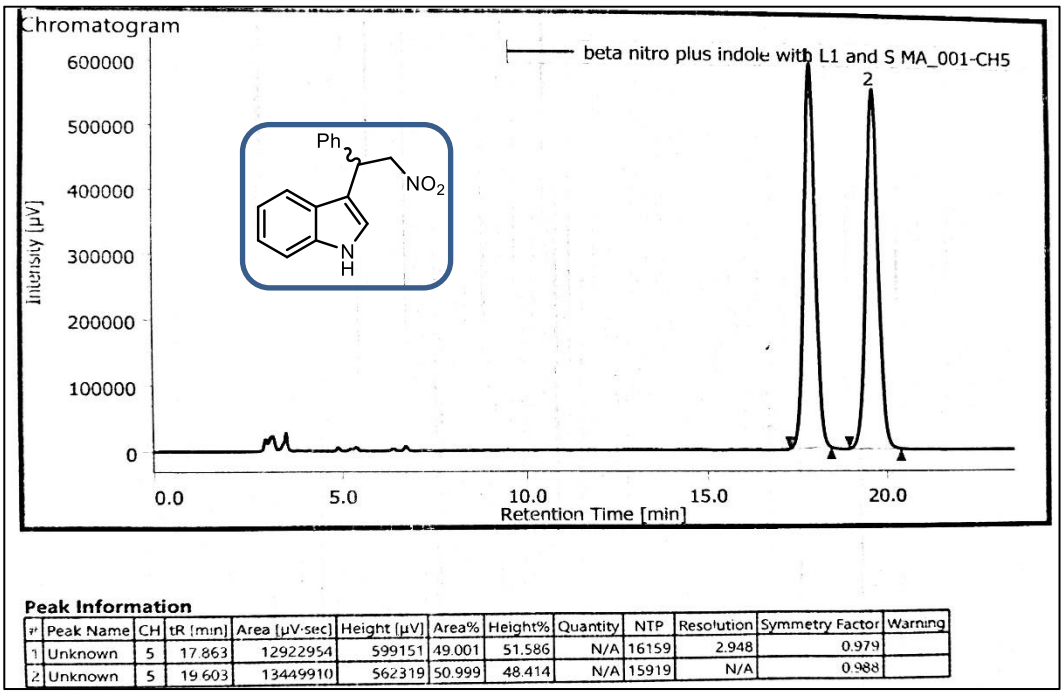


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.447	1541986	75302	49.135	52.005	N/A	16893	2.924	0.967	
2	Unknown	5	19.100	1596293	69497	50.865	47.995	N/A	16386	N/A	0.968	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 3)

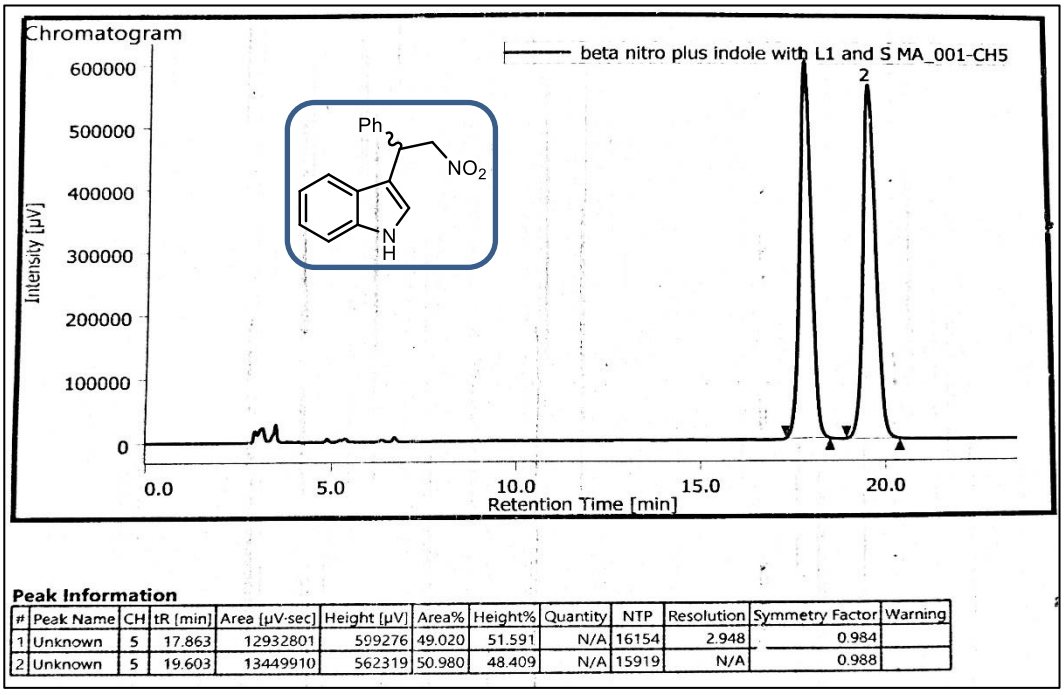


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.863	12922954	599151	49.001	51.586	N/A	16159	2.948	0.979	
2	Unknown	5	19.603	13449910	562319	50.999	48.414	N/A	15919	N/A	0.988	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 4)

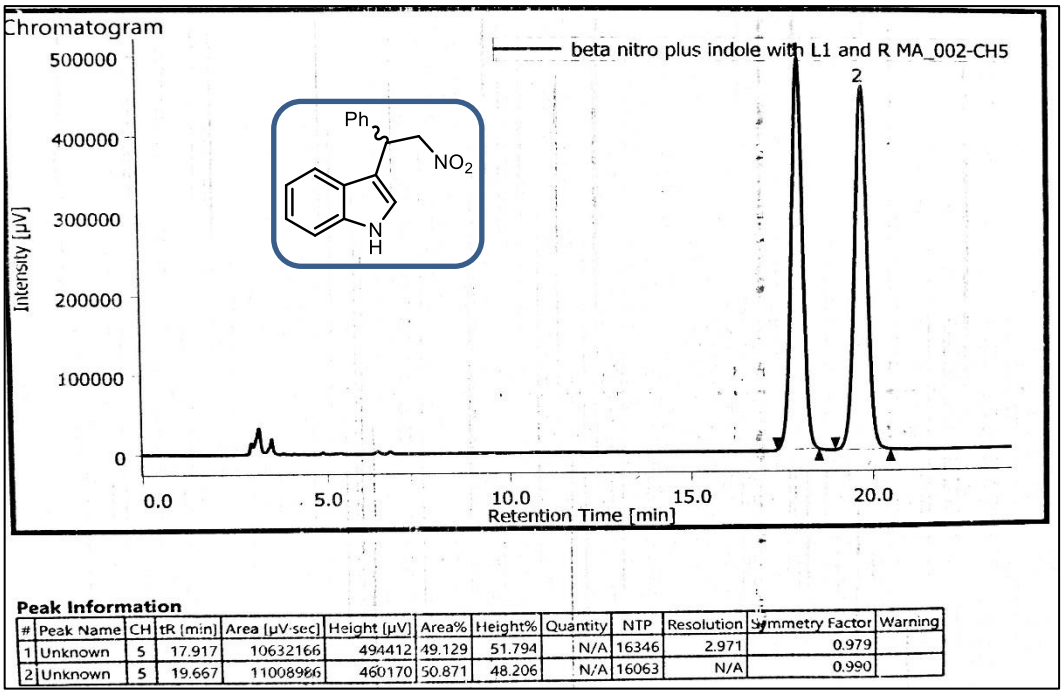


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.863	12932801	599276	49.020	51.591	N/A	16154	2.948	0.984	
2	Unknown	5	19.603	13449910	562319	50.980	48.409	N/A	15919	N/A	0.988	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 5)

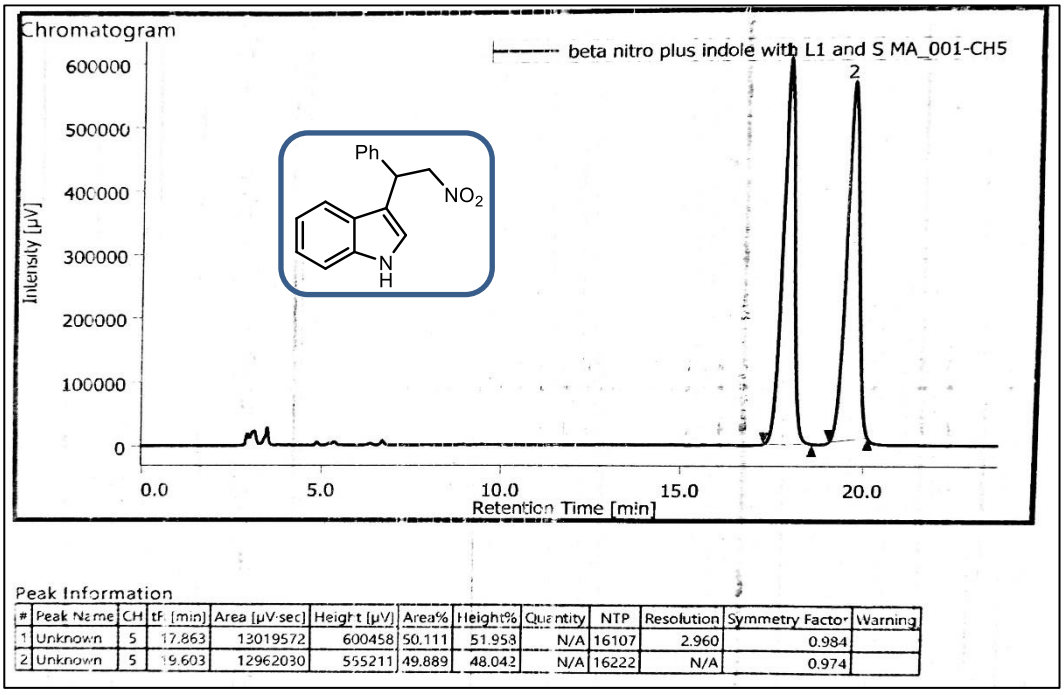


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10632166	494412	49.129	51.794	N/A	16346	2.971	0.979	
2	Unknown	5	19.667	11008966	460170	50.871	48.206	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 1, Entry 6)

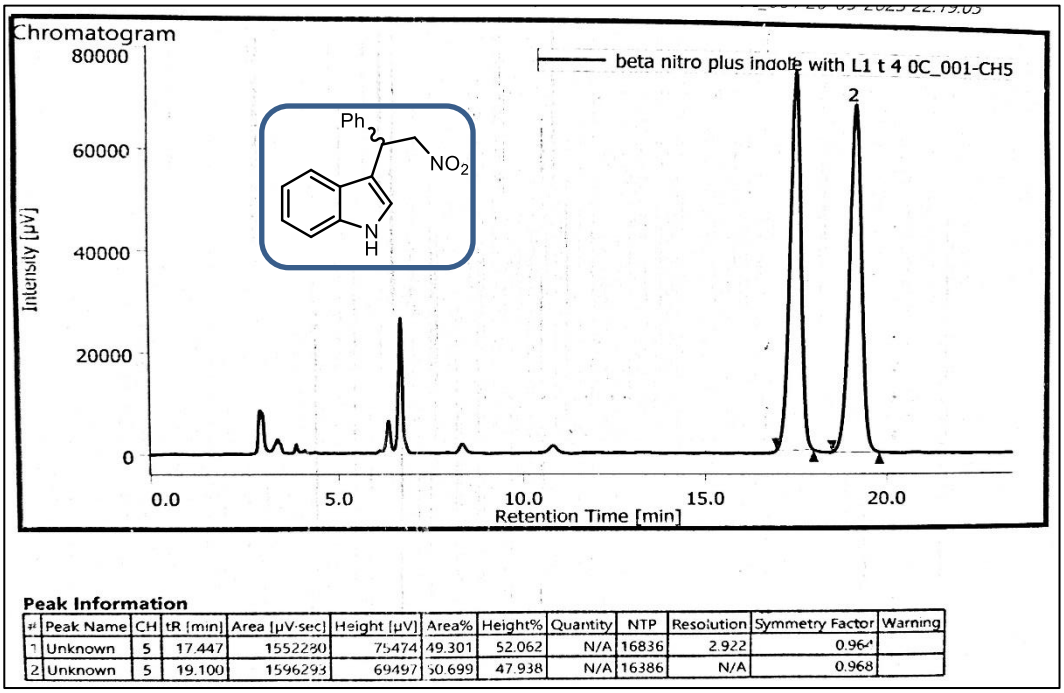


Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.863	13019572	600458	50.111	51.958	N/A	16107	2.960	0.984	
2	Unknown	5	19.603	12962030	555211	49.889	48.042	N/A	16222	N/A	0.974	

HPLC chromatogram of racemic 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 1)

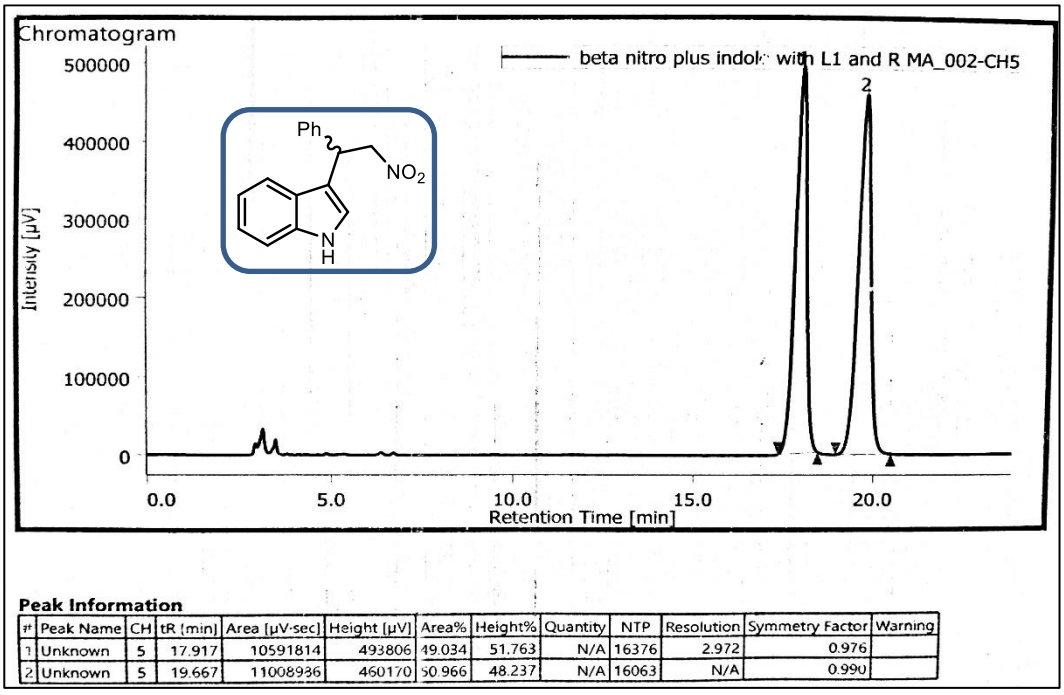


Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.447	1552280	75474	49.301	52.062	N/A	16836	2.922	0.964	
2	Unknown	5	19.100	1596293	69497	50.699	47.938	N/A	16386	N/A	0.968	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 2)

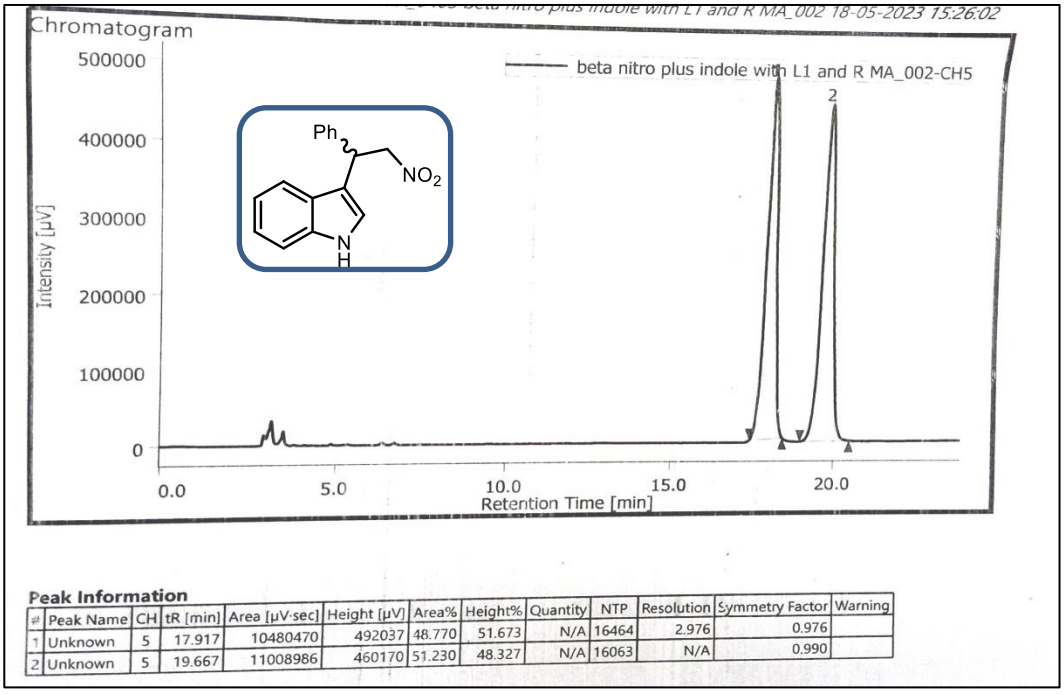


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10591814	493806	49.034	51.763	N/A	16376	2.972	0.976	
2	Unknown	5	19.667	11008986	460170	50.966	48.237	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 3)

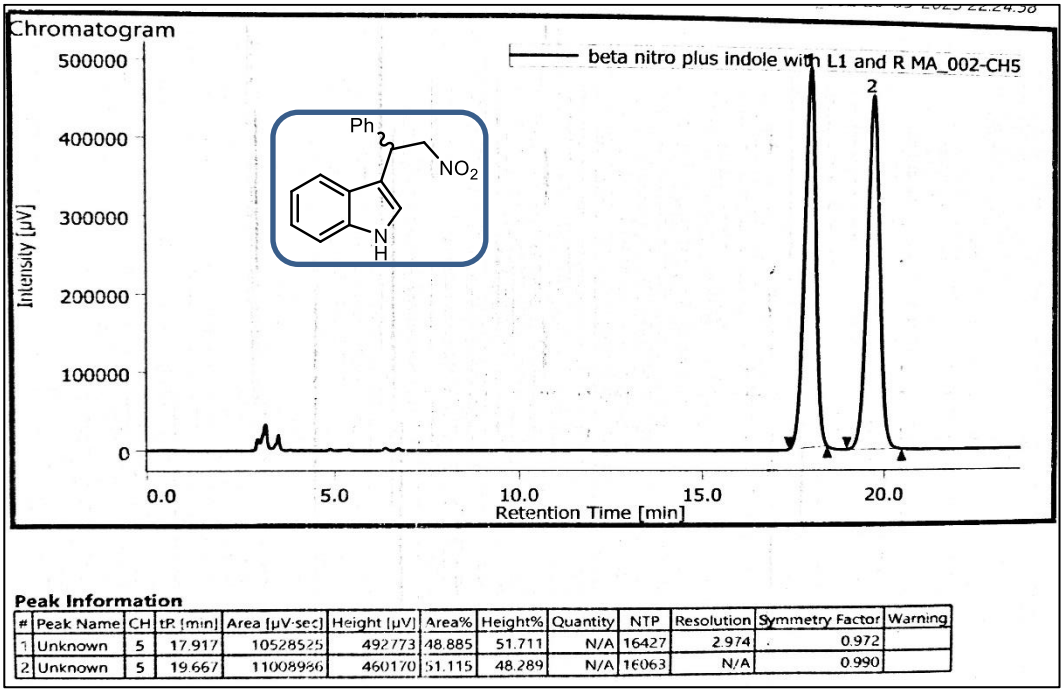


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10480470	492037	48.770	51.673	N/A	16464	2.976	0.976	
2	Unknown	5	19.667	11008986	460170	51.230	48.327	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 4)

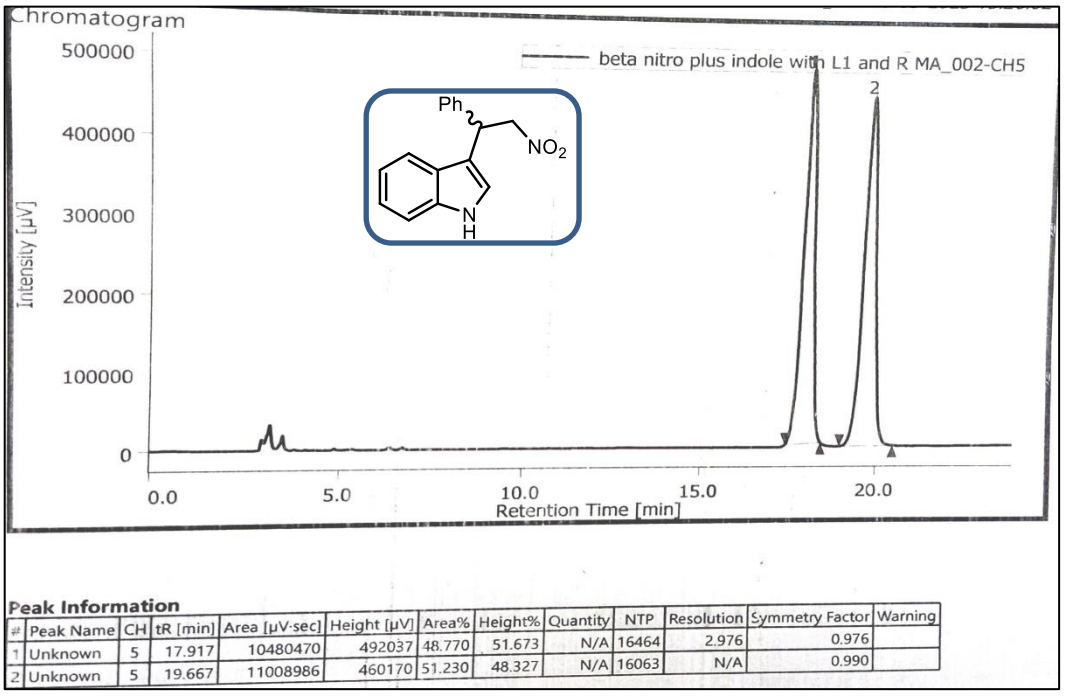


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10528525	492773	48.885	51.711	N/A	16427	2.974	0.972	
2	Unknown	5	19.667	11008986	460170	51.115	48.289	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 5)

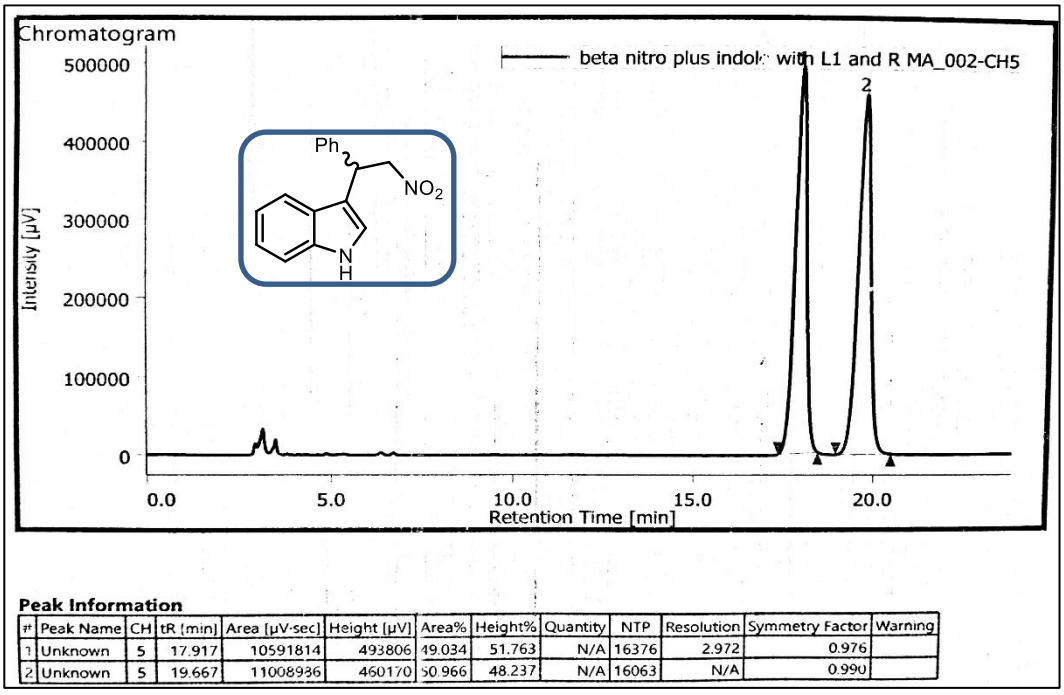


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10480470	492037	48.770	51.673	N/A	16464	2.976	0.976	
2	Unknown	5	19.667	11008986	460170	51.230	48.327	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 2, Entry 6)

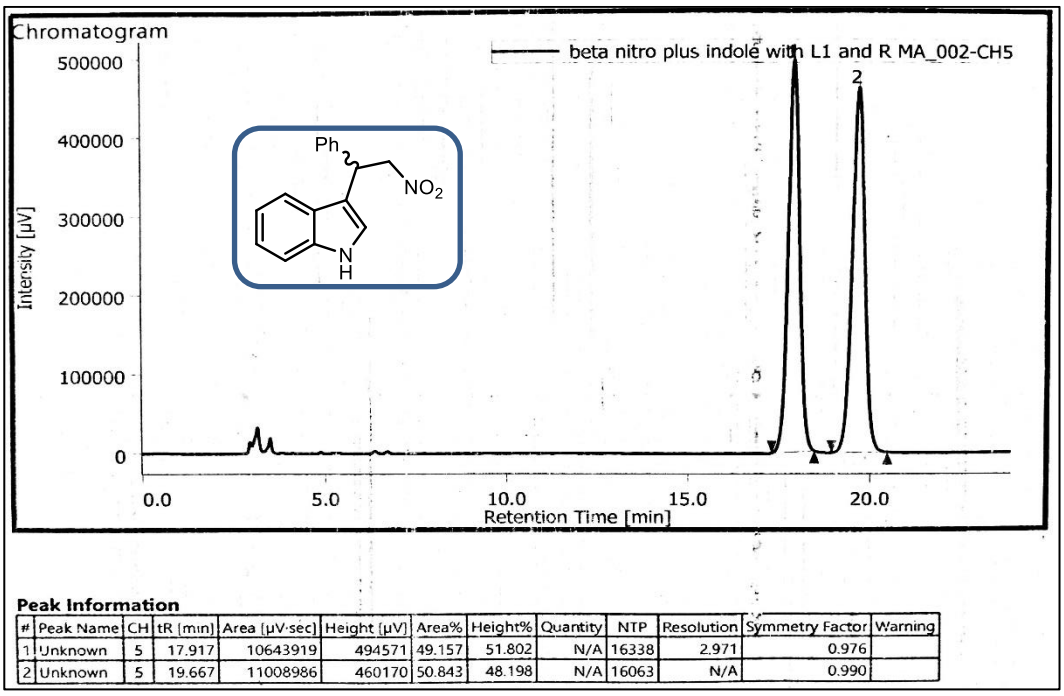


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10591814	493806	49.034	51.763	N/A	16376	2.972	0.976	
2	Unknown	5	19.667	11008986	460170	50.966	48.237	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 3, Entry 1)

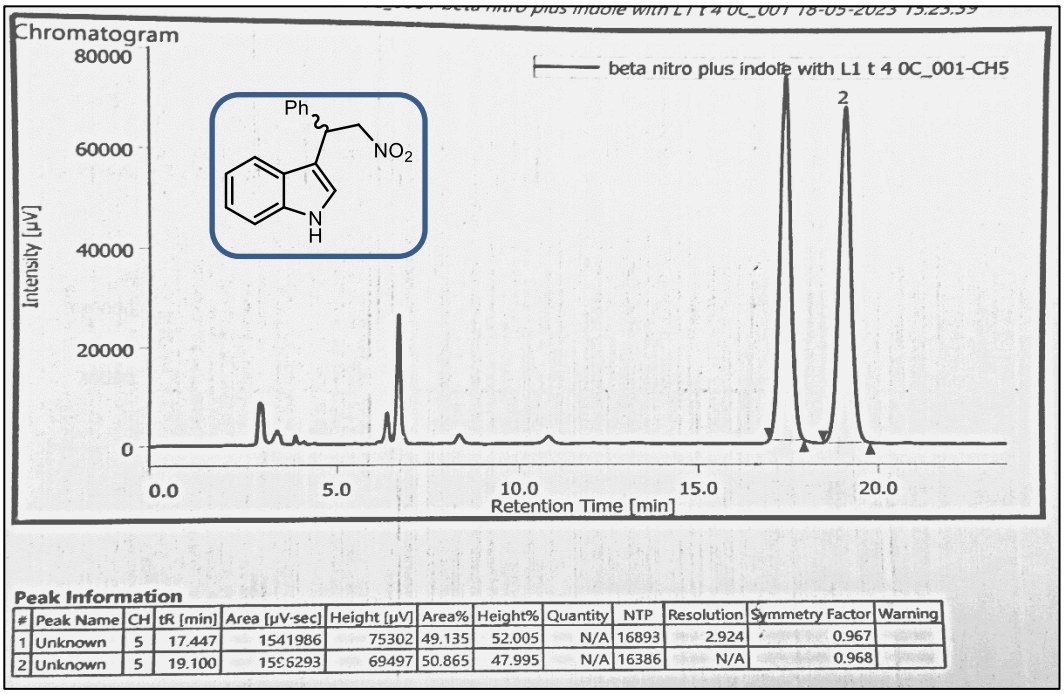


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.917	10643919	494571	49.157	51.802	N/A	16338	2.971	0.976	
2	Unknown	5	19.667	11008986	460170	50.843	48.198	N/A	16063	N/A	0.990	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 3, Entry 2)

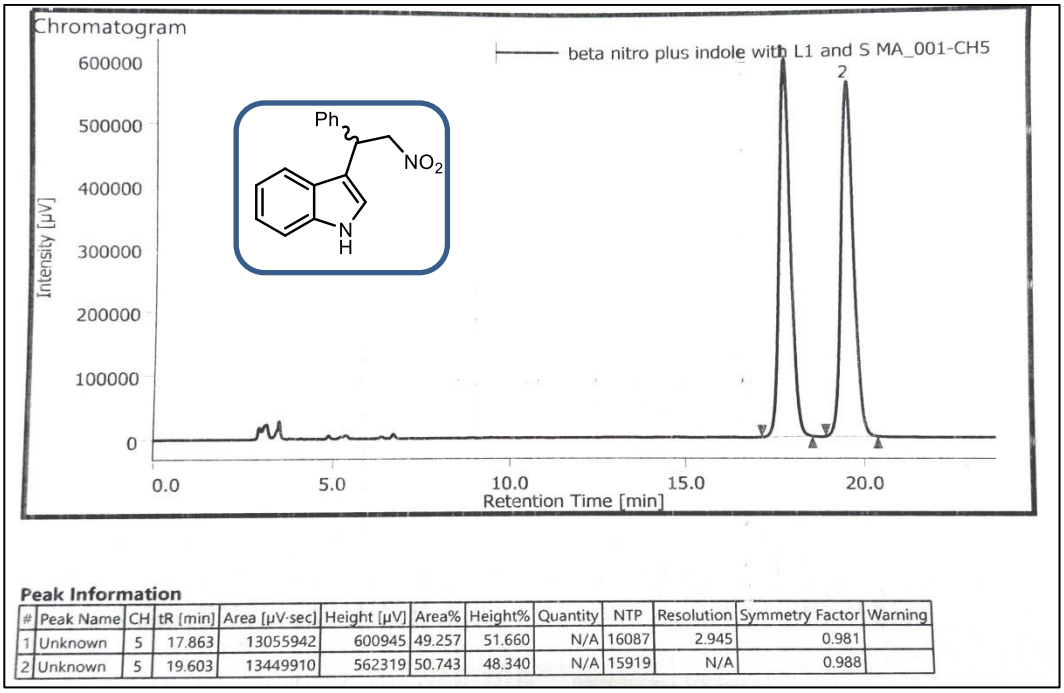


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.447	1541986	75302	49.135	52.005	N/A	16893	2.924	0.967	
2	Unknown	5	19.100	1596293	69497	50.865	47.995	N/A	16386	N/A	0.968	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 3, Entry 3)

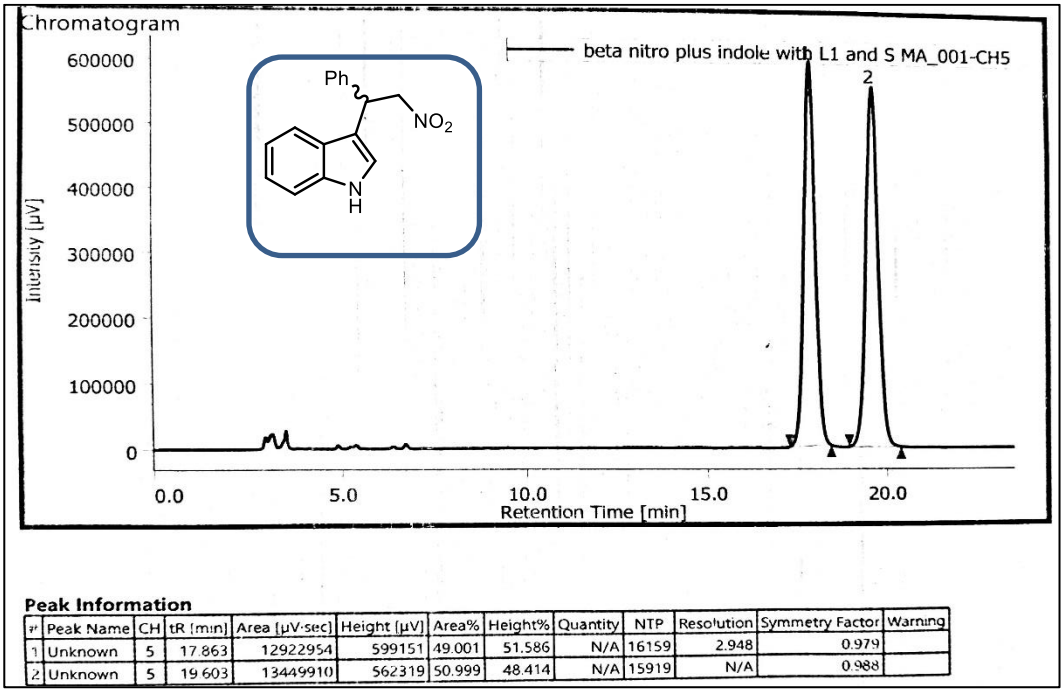


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.863	13055942	600945	49.257	51.660	N/A	16087	2.945	0.981	
2	Unknown	5	19.603	13449910	562319	50.743	48.340	N/A	15919	N/A	0.988	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

(Table 3, Entry 4)

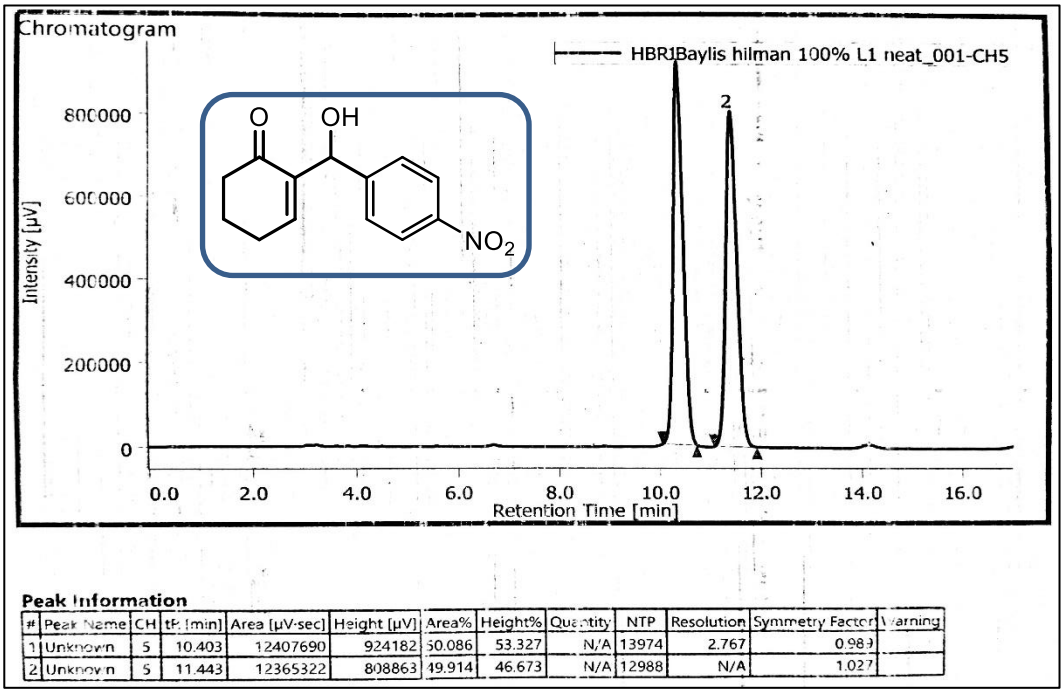


Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	17.863	12922954	599151	49.001	51.586	N/A	16159	2.948	0.979	
2	Unknown	5	19.603	13449910	562319	50.999	48.414	N/A	15919	N/A	0.988	

HPLC chromatogram of 3-(2-nitro-1-phenylethyl)-1H-indole **61**

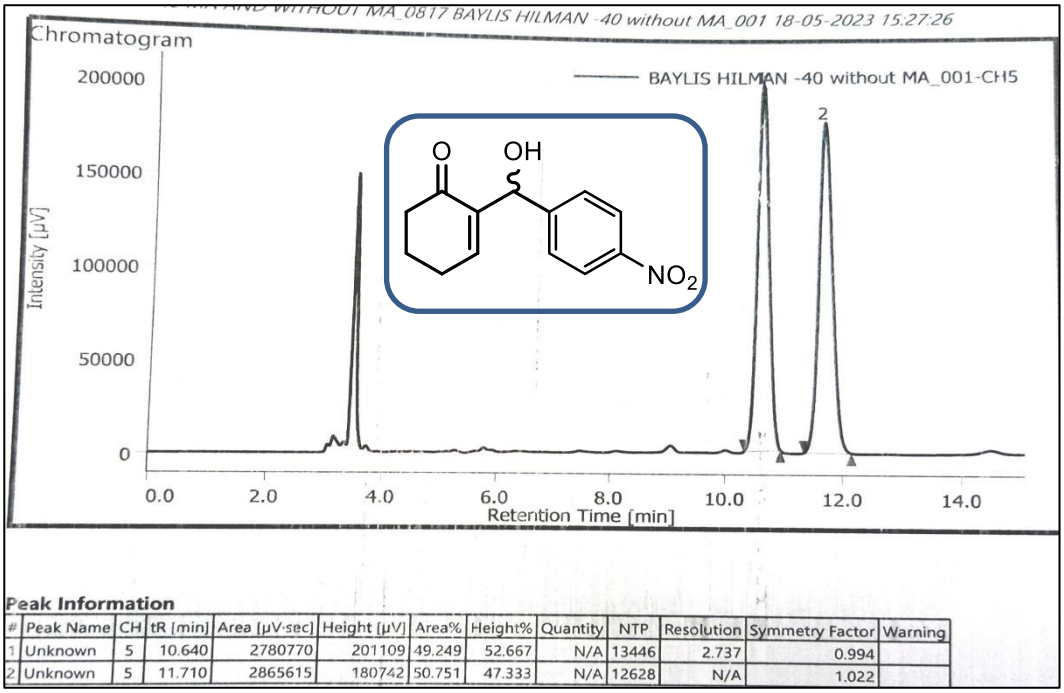
(Table 3, Entry 5)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.403	12407690	924182	50.086	53.327	N/A	13974	2.767	0.989	
2	Unknown	5	11.443	12365322	808863	49.914	46.673	N/A	12988	N/A	1.027	

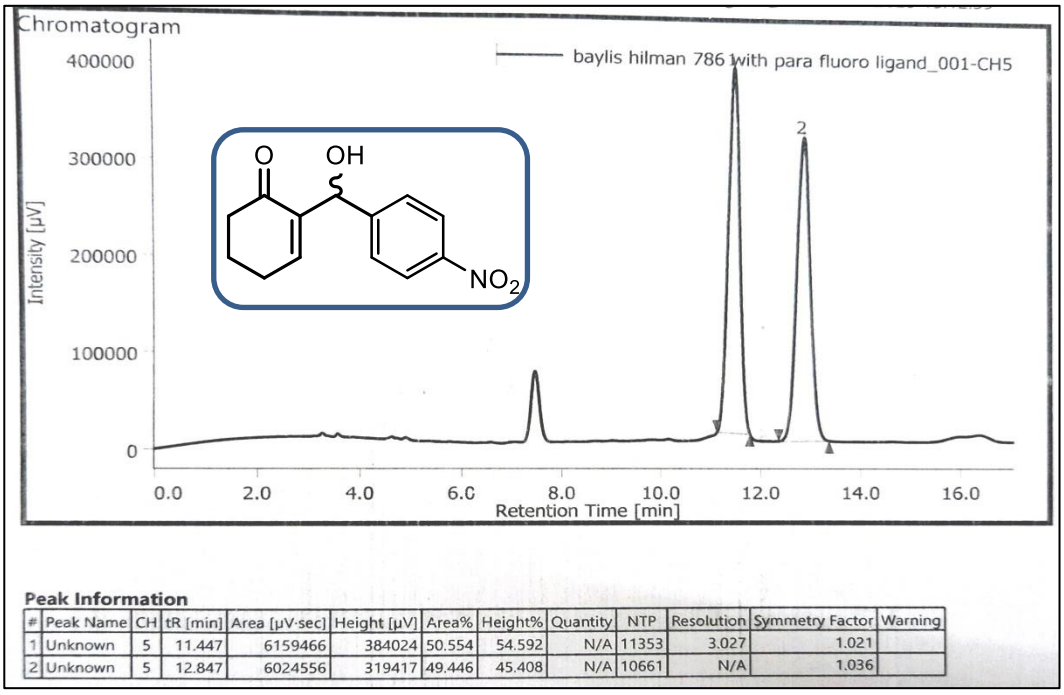
HPLC chromatogram racemic of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 1)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.640	2780770	201109	49.249	52.667	N/A	13446	2.737	0.994	
2	Unknown	5	11.710	2865615	180742	50.751	47.333	N/A	12628	N/A	1.022	

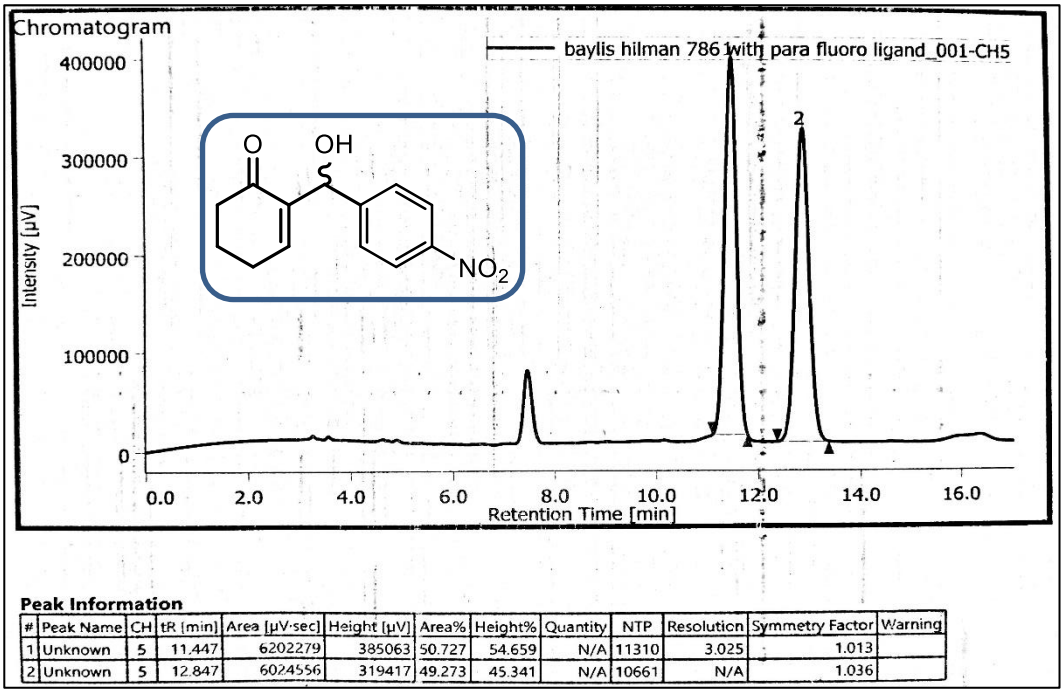
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 2)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6159466	384024	50.554	54.592	N/A	11353	3.027	1.021	
2	Unknown	5	12.847	6024556	319417	49.446	45.408	N/A	10661	N/A	1.036	

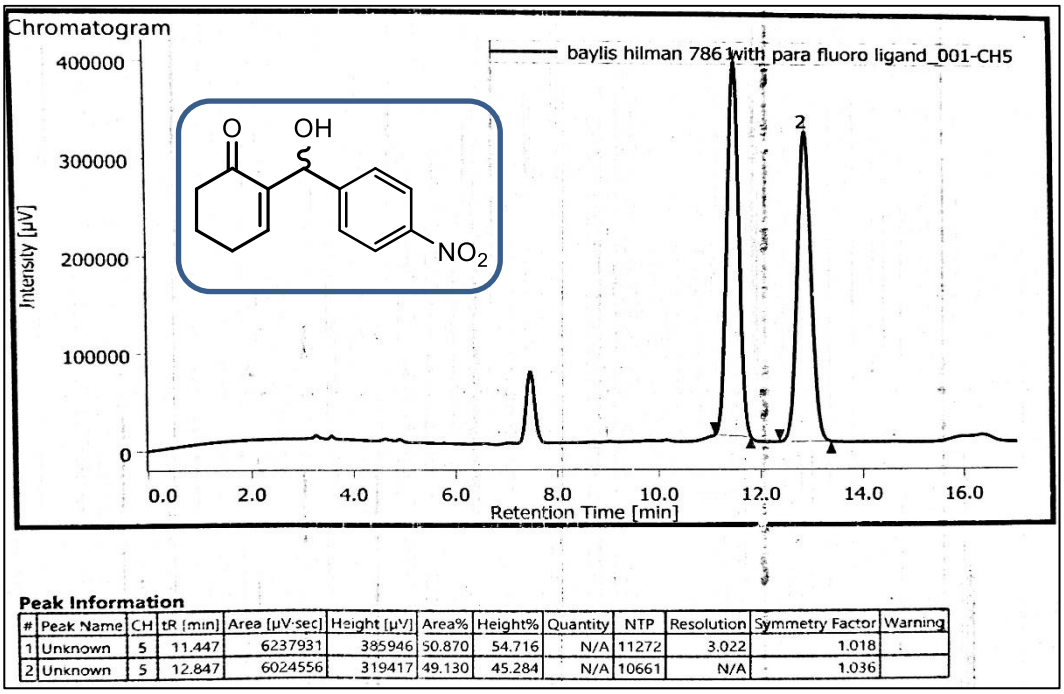
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 3)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6202279	385063	50.727	54.659	N/A	11310	3.025	1.013	
2	Unknown	5	12.847	6024556	319417	49.273	45.341	N/A	10661	N/A	1.036	

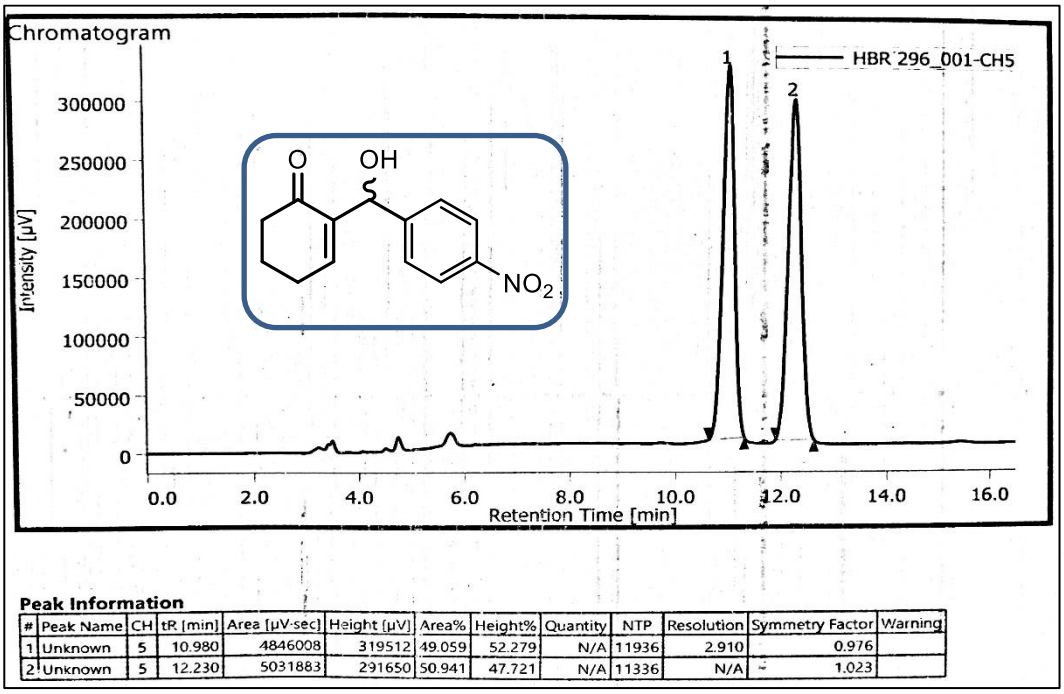
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 4)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6237931	385946	50.870	54.716	N/A	11272	3.022	1.018	
2	Unknown	5	12.847	6024556	319417	49.130	45.284	N/A	10661	N/A	1.036	

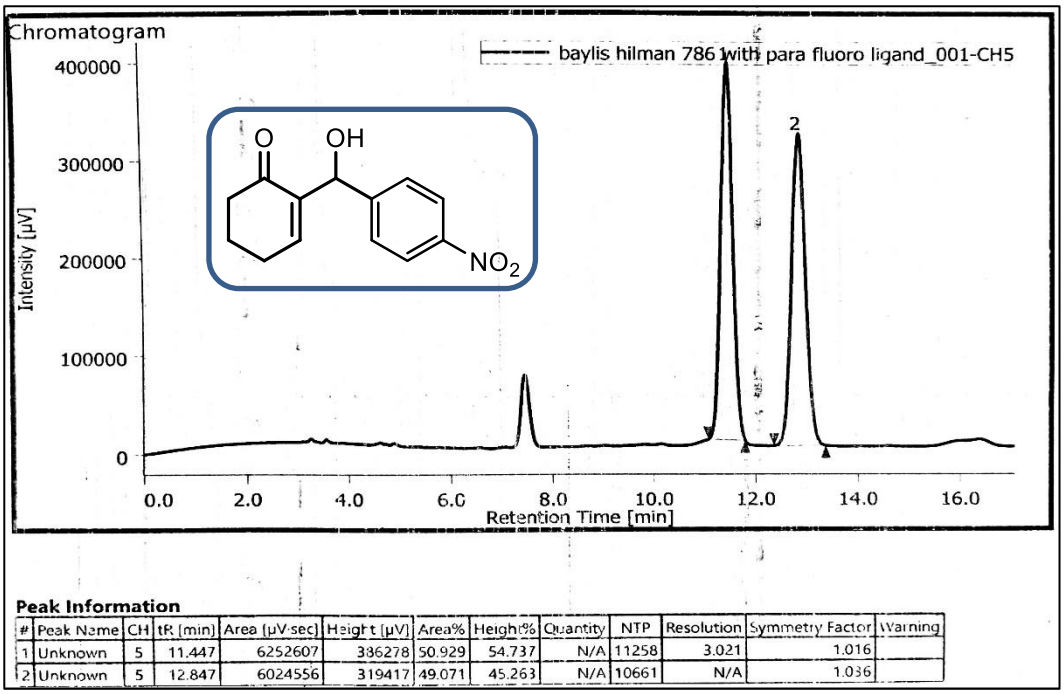
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 5)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.980	4846008	319512	49.059	52.279	N/A	11936	2.910	0.976	
2	Unknown	5	12.230	5031883	291650	50.941	47.721	N/A	11336	N/A	1.023	

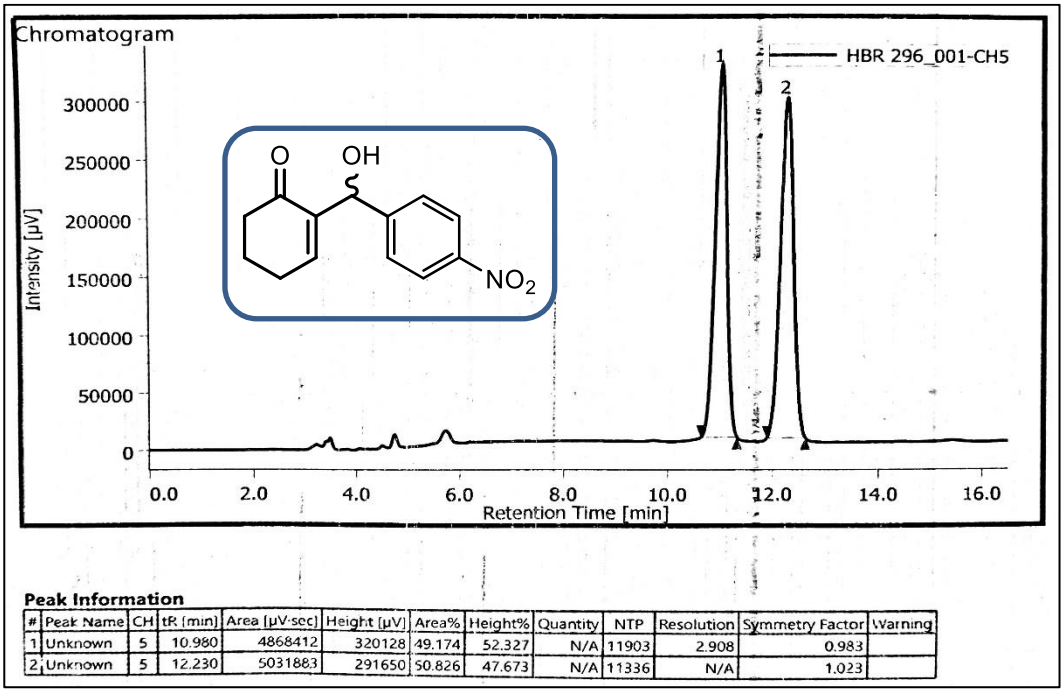
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 4, Entry 6)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6252607	386278	50.929	54.737	N/A	11258	3.021	1.016	
2	Unknown	5	12.847	6024556	319417	49.071	45.263	N/A	10661	N/A	1.036	

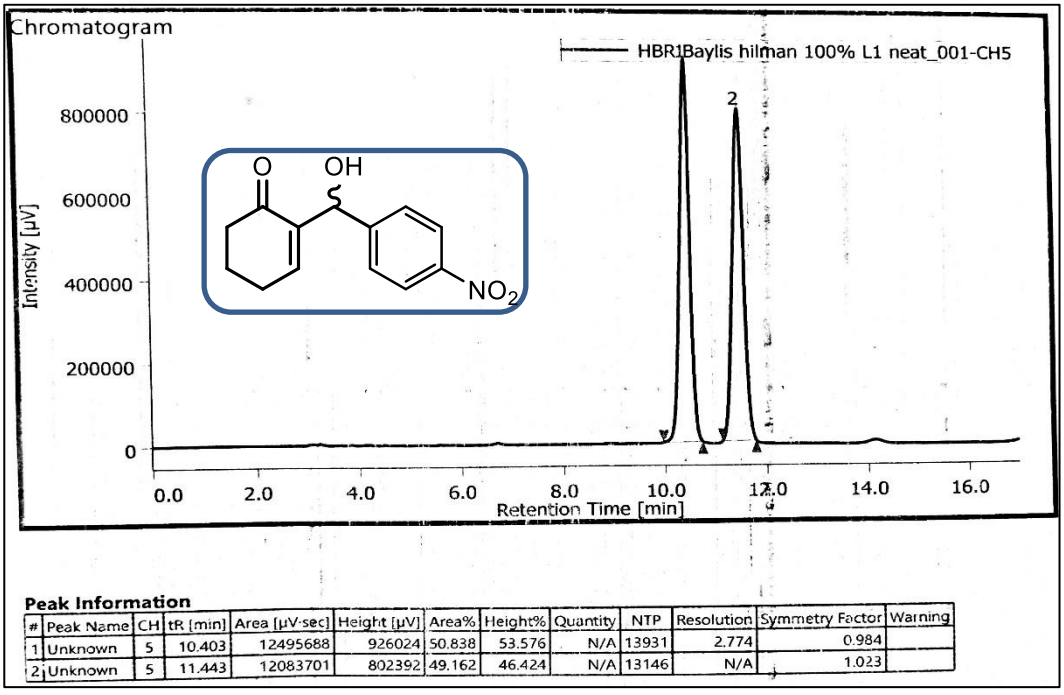
HPLC chromatogram of racemic 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 2, Entry 1)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.980	4868412	320128	49.174	52.327	N/A	11903	2.908	0.983	
2	Unknown	5	12.230	5031883	291650	50.826	47.673	N/A	11336	N/A	1.023	

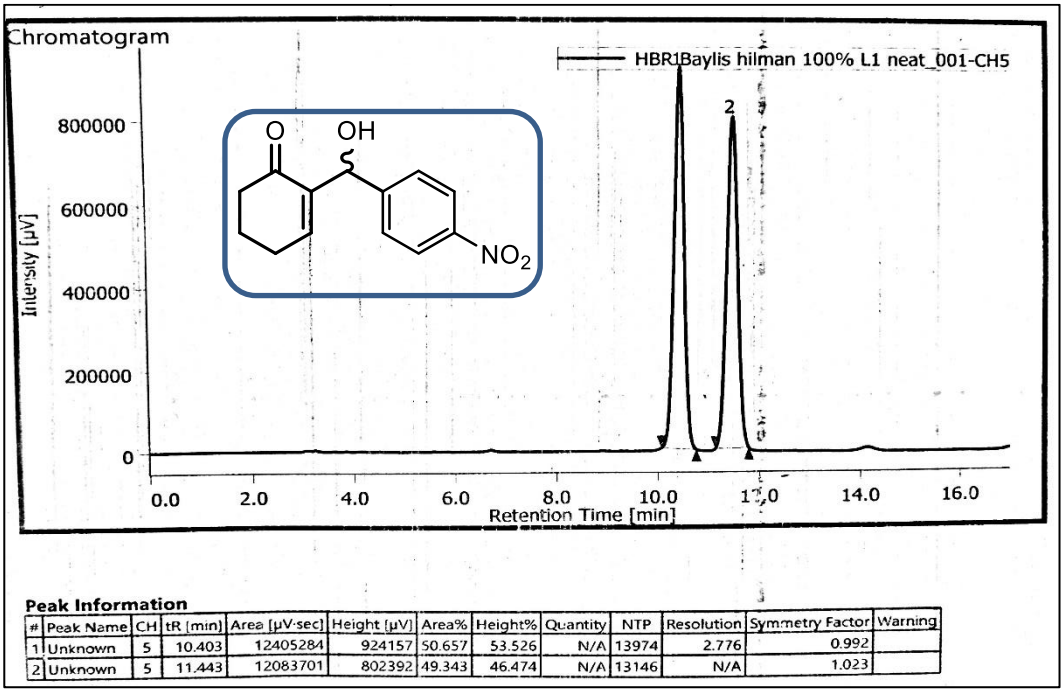
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 2, Entry 2)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.403	12495688	926024	50.838	53.576	N/A	13931	2.774	0.984	
2	Unknown	5	11.443	12083701	802392	49.162	46.424	N/A	13146	N/A	1.023	

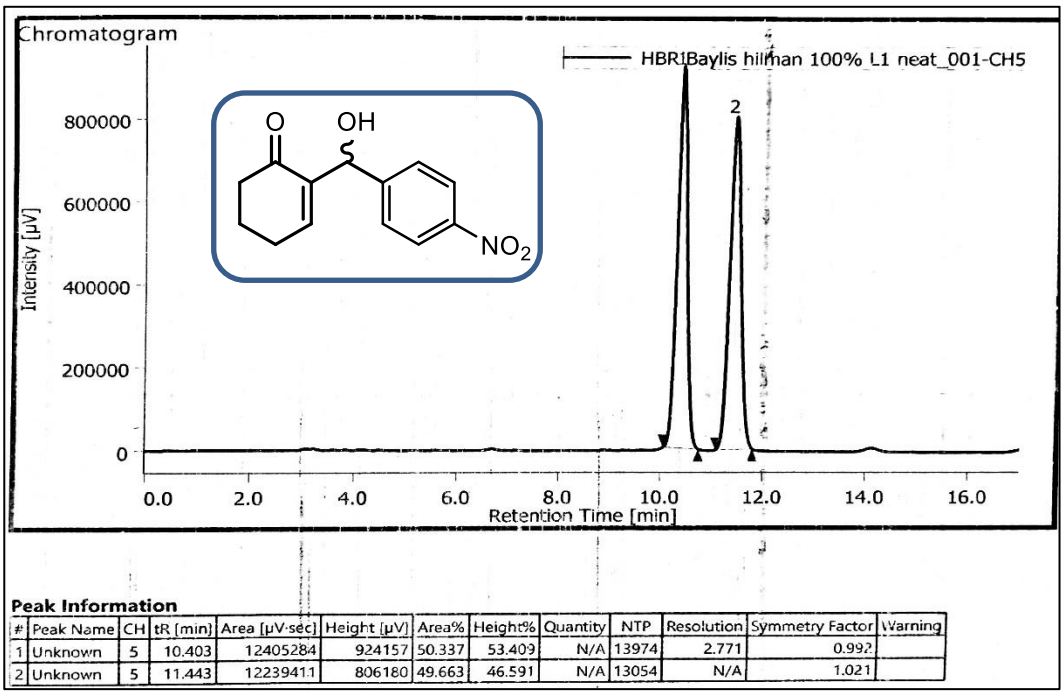
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 2, Entry 3)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.403	12405284	924157	50.657	53.526	N/A	13974	2.776	0.992	
2	Unknown	5	11.443	12083701	802392	49.343	46.474	N/A	13146	N/A	1.023	

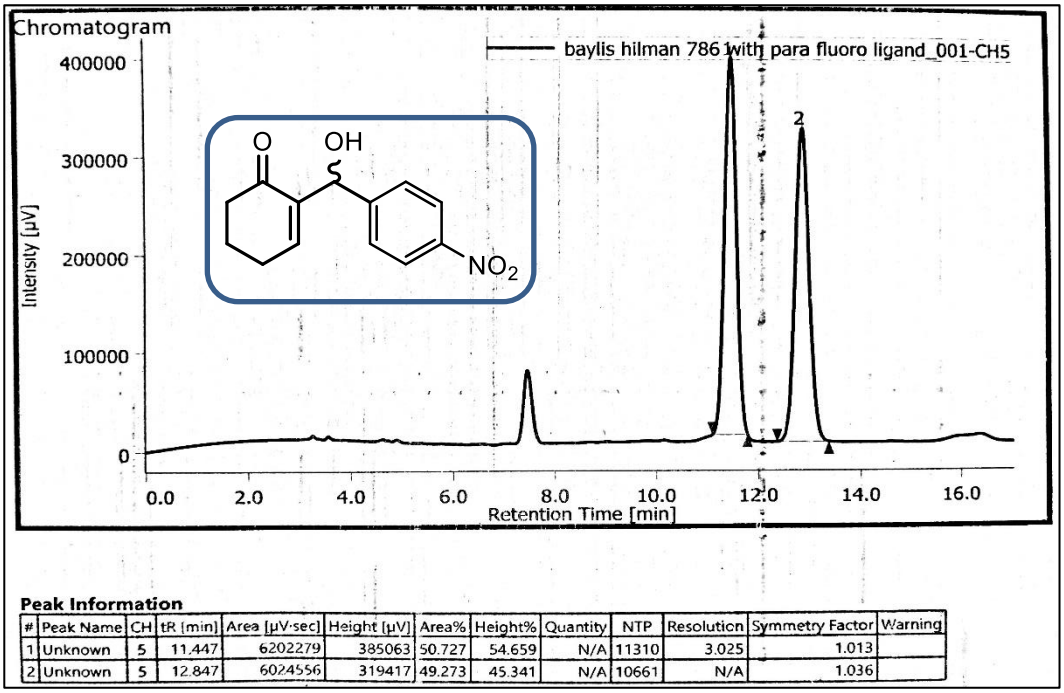
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 2, Entry 4)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.403	12405284	924157	50.337	53.409	N/A	13974	2.771	0.992	
2	Unknown	5	11.443	12239411	806180	49.663	46.591	N/A	13054	N/A	1.021	

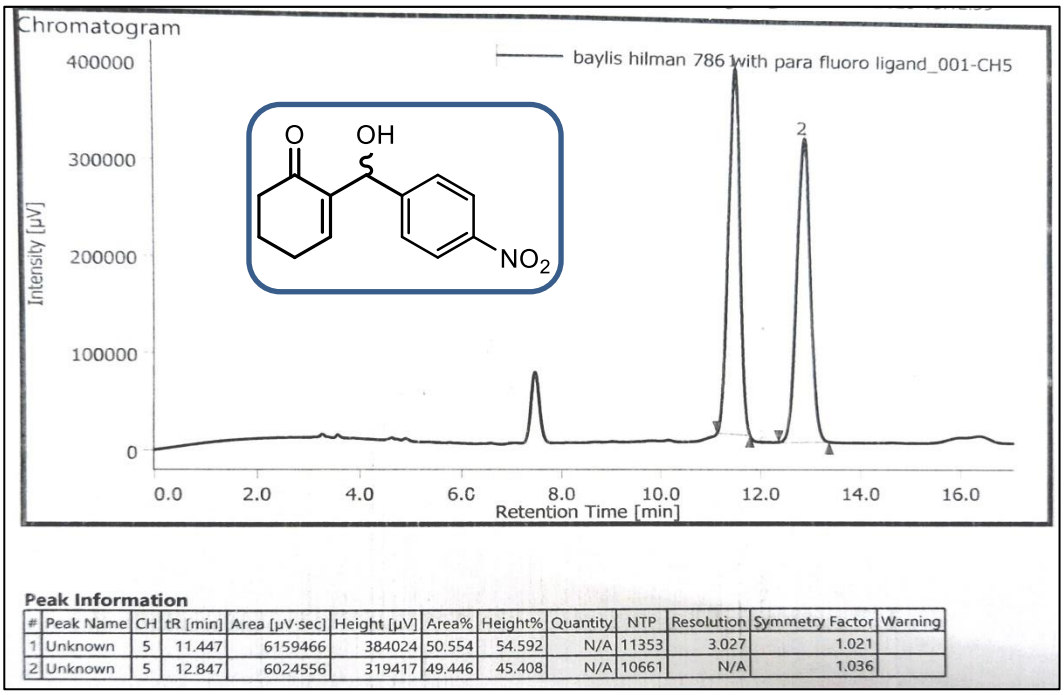
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 2, Entry 5)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6202279	385063	50.727	54.659	N/A	11310	3.025	1.013	
2	Unknown	5	12.847	6024556	319417	49.273	45.341	N/A	10661	N/A	1.036	

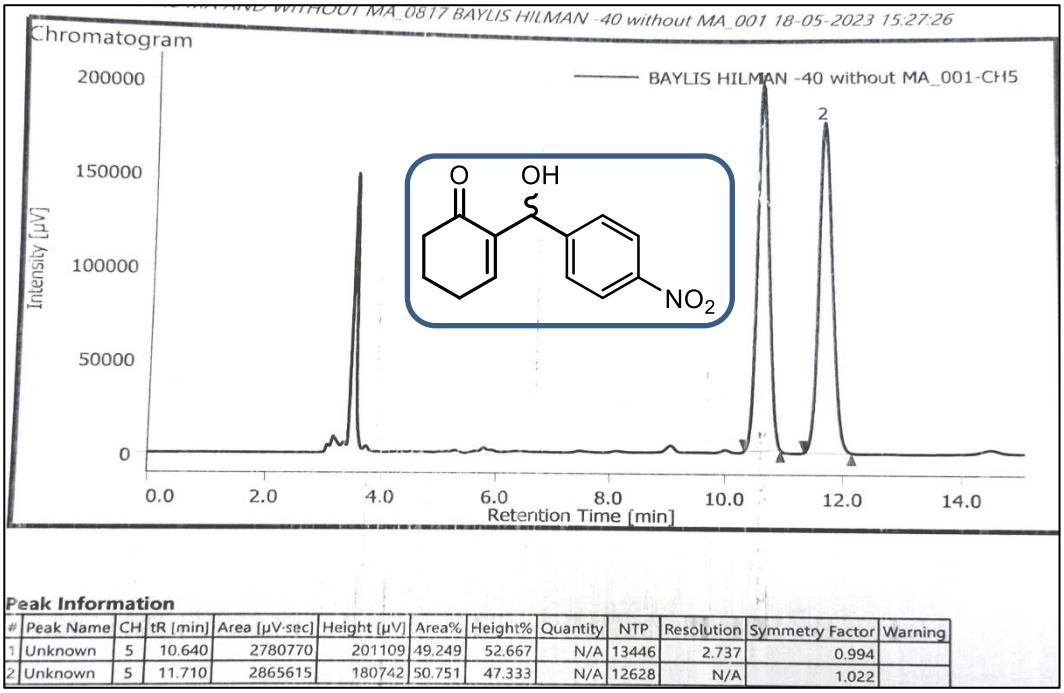
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 1)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6159466	384024	50.554	54.592	N/A	11353	3.027	1.021	
2	Unknown	5	12.847	6024556	319417	49.446	45.408	N/A	10661	N/A	1.036	

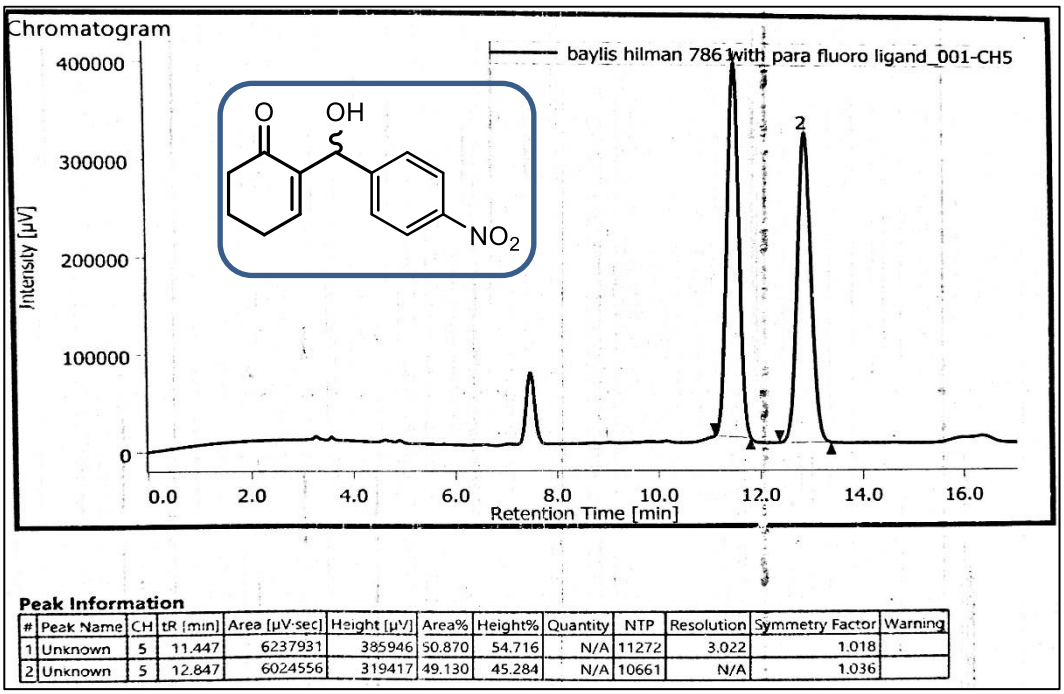
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 2)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	10.640	2780770	201109	49.249	52.667	N/A	13446	2.737	0.994	
2	Unknown	5	11.710	2865615	180742	50.751	47.333	N/A	12628	N/A	1.022	

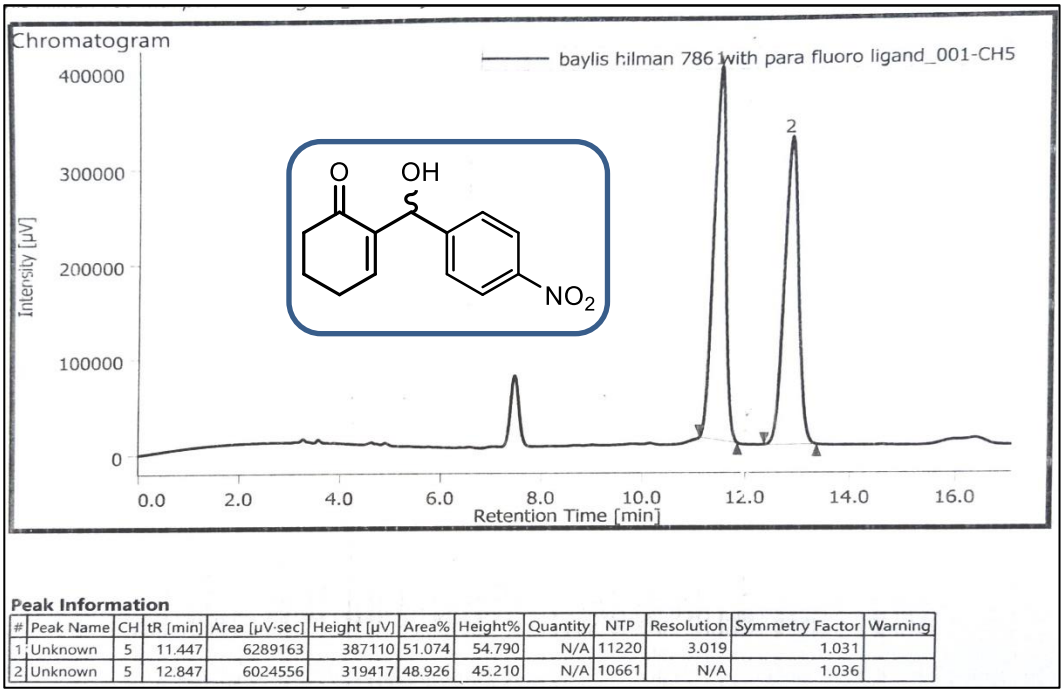
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 3)



Peak Information

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6237931	385946	50.870	54.716	N/A	11272	3.022	1.018	
2	Unknown	5	12.847	6024556	319417	49.130	45.284	N/A	10661	N/A	1.036	

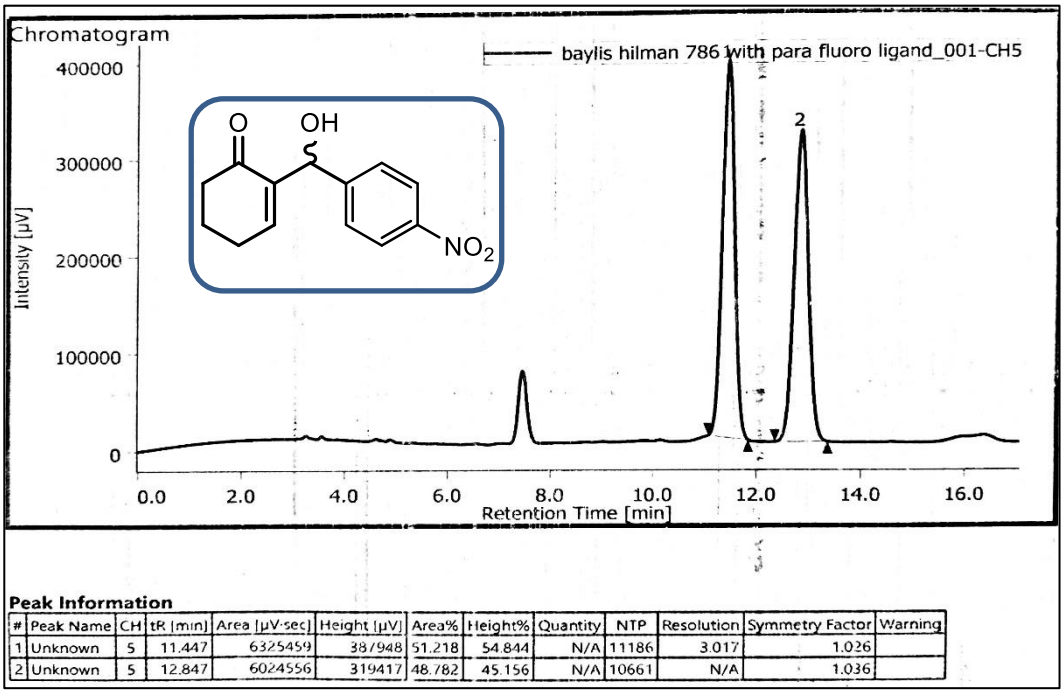
HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 4)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6289163	387110	51.074	54.790	N/A	11220	3.019	1.031	
2	Unknown	5	12.847	6024556	319417	48.926	45.210	N/A	10661	N/A	1.036	

HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 5)



Peak Information

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	11.447	6325459	387948	51.218	54.844	N/A	11186	3.017	1.026	
2	Unknown	5	12.847	6024556	319417	48.782	45.156	N/A	10661	N/A	1.036	

HPLC chromatogram of 2-(hydroxy(4-nitrophenyl)methyl) cyclohex-2-en-1-one **64** (Table 3, Entry 6)

4.6 References

1 (a) Berkessel, A.; Groger, H. (eds.) *Asymmetric Organocatalysis.* Wiley-VCH: Weinheim, **2005**. (b) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520–1543. (c) Doyle, A. G.; Jacobsen, E. N. *Chem., Rev.* **2007**, *107*, 5713−5743. (d) Pihko, P. M. (ed.) *Hydrogen Bonding in Organic Synthesis.* Wiley-VCH:Weinheim, **2009.**

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