Chapter 4

Study of miscellaneous atropisomeric molecules

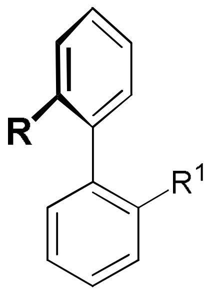
4.1 Introduction

As discussed in the earlier chapters, the biphenyl moiety containing molecules are capable of forming atropisomers. Atropisomeric biaryls are axially chiral compounds with a long history of providing significantly effective chiral ligands for asymmetric synthesis.[1] They are the major structural components of various biologically active natural products, such as vancomycin, knipholone, korupensamines and michellamines.[2] Typically, the enantiomerically enriched atropisomeric ligands are obtained by kinetic resolution, however their asymmetric synthesis remains a major challenge.[3] Recently developed strategies include dynamic kinetic resolution,[4] dynamic thermodynamic resolution,[5] resolutions based on sulfoxide chemistry,[5, 6] and atropselective transition-metal-catalysed coupling.[7] Enzymatic desymmetrisation is an appealing method for asymmetric synthesis.[8,9]

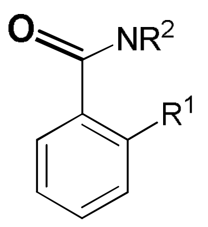
The main aim of the present work is to synthesize, characterize and study the behaviour of new axially chiral molecules. The isomers which arise due to the restriction of rotation about a single bond are referred as atropisomers. Many types of atropisomeric compounds are known in the literature (see in chapter 1), mainly the rotation about the two kinds of bond leads to this isomerism.[10]

i. σ bond between aromatic sp^2 carbon and another aromatic sp^2 carbon

ii. σ bond between aromatic sp^2 carbon and carbonyl sp^2 carbon group.



Ar sp^2 **C** - Ar sp^2 **C**



Ar sp^2 **C** - carbonyl sp^2 **C**

4.2 Results and Discussion

This is divided into two parts.

Part I

4.2.1 Synthesis of biphenyl-based ligand: application in copper- mediated chemoselective Michael reaction

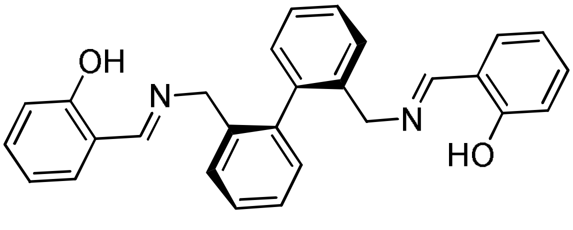
Michael reaction of active methylene compounds with α,β-unsaturated ketone is one of the most powerful and well studied carbon-carbon bond forming reactions of modern chemistry.[11] Similarly the Michael reaction with other heteroatom nucleophiles with activated π-system is extensively utilized for making carbon-heteroatom bonds.[12] This reaction is extensively studied under various conditions such as in presence of ionic liquids,[13] aqueous,[14] micellar,[15] presence of base[16] and DNA,[17] Lewis acids,[18]other acidic reagents[19]etc. with considerable success. The Michael reaction of conjugated systems with amines as nucleophiles, aza-Michael reaction, is quite common method to synthesize important derivatives of β-amino ketones, esters and acids. Similarly, the reaction with sulfur nucleophile, thia-Michael reaction is widely employed in biosynthesis and for the synthesis of bioactive compounds[20] and for the protection of a double bond.[21]

Many homogeneous catalyst systems are developed for promoting the Michael reaction.[22] The homogeneous complexes of different ligands with metal salts of vanadium,[23] copper,[24] nickel,[25] cobalt,[26] iron,[27] boron,[28] zinc,[29] ruthenium,[30] palladium[31]etc. have been investigated for variants of Michael reaction. Some of these catalysts work equally well with different types of nucleophiles towards reactive conjugated substrates. The crucial aspect for a useful catalyst system is the possibility of achieving a certain degree of selectivity in favor of one type of reaction. For Michael reaction the addition of amine nucleophile to α,β-unsaturated ketones is favored in most of the homogeneous catalysts. The heterogeneous catalyst of Li-X-type zeolite was found to be selective for sulfur nucleophile compared to the oxygen nucleophile for the Michael reaction.[32] The thia-Michael reaction is also frequently studied and several efficient catalysts are developed.[33]However, the availability of catalyst systems for chemoselective Michael reaction is limited.

In this part we present synthesis of a new atropisomeric bis-Schiff base ligand and the preliminary applications in copper catalyzed Michael reaction of α,β-unsaturated ketones. There are two references available for the structurally similar ligands in the literature.[34a] In one of the references its cobalt complex is explored as a catalyst for the addition of diethyl zinc to aldehydes.[34b]

Results and Discussion

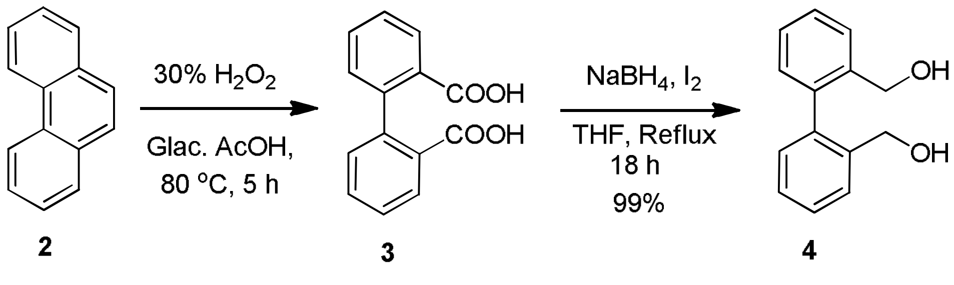
The design of new ligands is a crucial aspect for developing homogeneous catalyst systems. The structure of new atropisomeric biphenyl based ligand 2,2'-((1*E*,1'*E*)-(([1,1'-biphenyl]-2,2'-diylbis(methylene))bis(azanylylidene))bis(methanylylidene))diphenol **1** is given in Figure-1. The design of the ligand is made in such a manner that one of the Schiff base units is arranged perpendicular to the other phenyl ring of biphenyl moiety. This arrangement is expected to influence the catalytic process as one side of the metal complex should be blocked by the other π-ring.



1

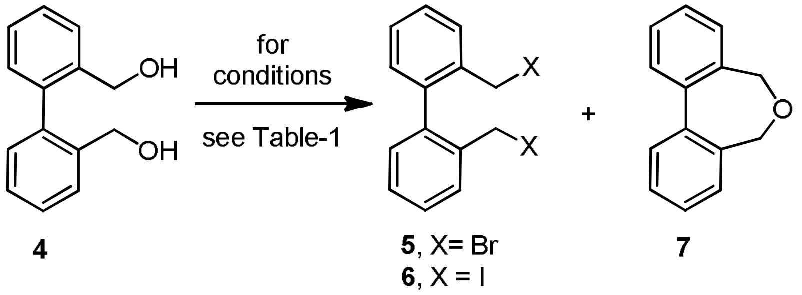
Figure-1: The new atropisomeric ligand for the present study.

With this aim initially phenanthrene **2** is oxidized to 2,2'-biphenyldicarboxylic acid **3** by the known procedure.[35] The diacid **3** is then reduced by improved procedure with $NaBH_4$ - I_2[36] to yield the [1,1'-biphenyl]-2,2'-diyldimethanol **4** in good conversion (99 %).[37]



Scheme 1

The diol **4** shows a broad signal in ^{1}H-NMR for the Ar-CH_2-OH indicating that the *gem* hydrogen atoms are unequal because the molecule has a slow rotation about the Ar - Ar bond. The EI-mass spectrum of the molecule **4** showing the molecular ion peak at 214 $[M]^{\cdot+}$and further stable fragmentations of cleavage of $[\text{-OH}]^{\bullet+}$ at *m/z* 197, and the base peak observed at *m/z* 167. The IR spectrum showed a peak at 3355 cm^{-1} for -OH. The diol **4** is the starting material for connecting various functional groups and hence –OH needs to be converted to more reactive halides or –OTs groups. With this idea compound **4** is treated under different conditions usually applied for substitution of hydroxyl group to halide moiety and the results are summarized in Table-1.



Scheme 2

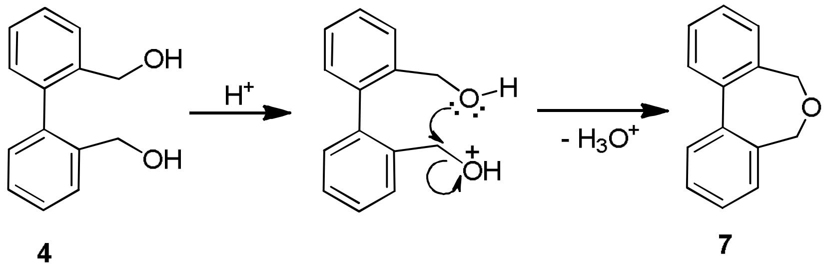
The diol **4** is converted to corresponding dibromo compound 2,2'-bis(bromomethyl)-1,1'-biphenyl **5**[38] in excellent conversion, yield and selectivity (entry-1, Table-1). Other conditions were not very selective and with the anticipated dibromo **5** a considerable amount of cyclized product 5,7-dihydrodibenzo[*c*,*e*]oxepine **7** was observed. The formation of ether **7** was found to be dominant in acidic conditions (entry-2 to 4, Table-1).

Table-1: Conditions developed for conversion of diol **4** to dihalides **5**/**6** or ether **7**.

Sr. No.	**Reaction Condition**	**Isolated Yield (%)[a]**		**Total Yield (%)[b]**
		5 or **6**	7	
1	PPh_3 (2.1 eq.), Br_2 (2.2 eq.) acetonitrile, r.t.	88 (X = Br)	--	88
2	48% aq. HBr (2.5 eq.) dioxane, 60 °C	26 (X = Br)	38	64
3	NaBr (2.5 eq.), H_2SO_4 (cat. 0.1 eq.) dioxane, 60 °C	9 (X = Br)	42	51
4	NaBr (2.5 eq.), H_2SO_4 (2.2 eq.) dioxane, 60 °C	50 (X = Br)	39	89
5	H_2SO_4 (0.1 eq.) dioxane, 60 °C	--	90	90
6	NaCl (2.5 eq.), H_2SO_4 (2.2 eq.) dioxane, 60 °C	--	76	76
7	NaI (2.5 eq.), H_2SO_4 (2.2 eq.) dioxane, 60 °C	17 (X = I)	51	68

[a]Isolated. [b]Combined isolated yield.

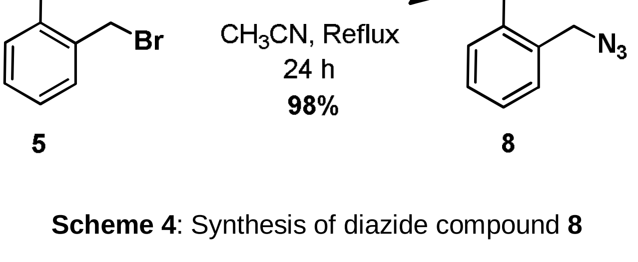
The possible mechanism of acid catalyzed cyclization is outlined in Scheme-3. In order to test this, a reaction was run with just the catalytic quantity of concentrated sulfuric acid in the absence of NaBr wherein just the cyclized ether **7** was isolated in good yield (entry 5, Table-1). The H-NMR analysis of **7** clearly showed a singlet peak for the Ar-$\underline{CH_2}$-O protons. The EI-mass spectrum of the molecule **7** showing the molecular ion peak at 196 $[M]^{\cdot+}$. The IR spectrum showed a weak peak at 3066 cm^{-1} for Ar-H stretching and 1238-1198 cm^{-1} for -C-O- stretching frequency.



Scheme 3

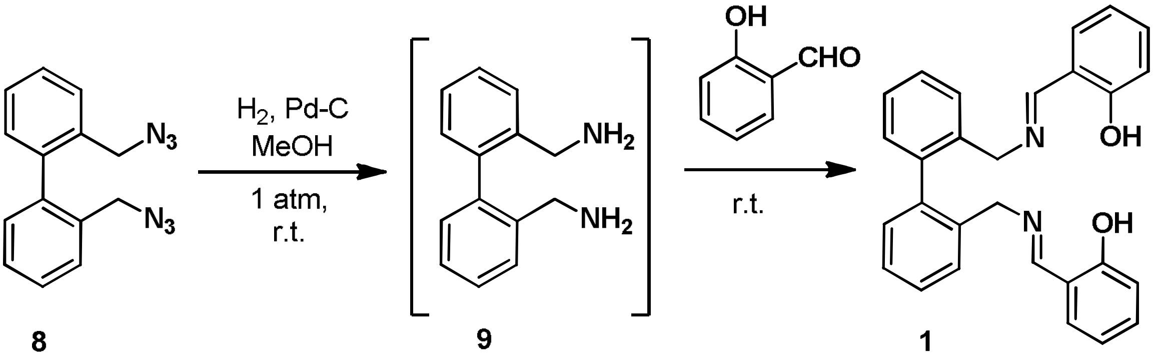
Other attempts to make corresponding dichloro- and diiodo- derivatives met with limited success (entries 6 & 7, Table-1) where mostly same cyclization was observed. On the other hand the ring opening reaction of ether **7** with NaI-$AlCl_3$ to furnish diiodo compound **6** was successful (98% Y). The H-NMR analysis of **5** and **6** clearly showed an AB splitting pattern for the Ar-CH_2-Br protons. This suggests that the barrier of rotation is even higher for these two molecules.

The dibromo compound **5** was then converted to the 2,2'-bis(azidomethyl)-1,1'-biphenyl **8** by simply heating with sodium azide. The H-NMR spectrum of diazide **8** clearly showed an AB splitting pattern for the Ar-$\underline{CH_2}$-N_3 protons. The EI-mass spectrum of the molecule **8** showing the molecular ion peak at 264 $[M]^{\cdot+}$ and further stable fragmentations of cleavage of $[-N_3]^{\cdot+}$ at *m/z* 208, and the base peak observed $[2 X -N_3]^{\cdot+}$ at *m/z* 180. IR spectrum showed a peak at 2097 cm^{-1} characteristic for the azide group ($-N_3$).



Scheme 4: Synthesis of diazide compound **8**

In the next step we have synthesized target atropisomeric bis-Schiff base compound **1**. Accordingly, the diazide was converted to diamine **9**, which, without purification was immediately subjected to the Schiff base formation with excess of salicylaldehyde at ambient conditions. The Schiff base **1** was separated as yellow crystals from the reaction mixture, which was filtered and recrystallized in ethyl acetate to get pure material. The Ar-CH_2-N shows the expected splitting pattern in H-NMR clearly indicating the unequal nature of geminal dihydrogens and the atropisomerism in **1**. The EI-mass spectrum of the molecule **1** shows the molecular ion $[M]^{\cdot+}$ peak at 420 *m/z* and the base peak observed the further stable fragmentations of cleavage of $[-C_7H_6NO]^{\cdot+}$ at 300 *m/z*. The IR spectrum of compound **1** showed -OH stretching frequency at 3649 cm^{-1}, for imine –C=N stretching at 1670 cm^{-1}, for aromatic -C=C- stretching at 1636 $cm.^{-1}$



Scheme 5: Synthesis of atropisomeric bis Schiff base compound **1**

The H-NMR analysis of the four molecules, i.e. the diol **4**, the dibromo **5**, the diazide **8** and the bis-Schiff base **1** with respect to the Ar-CH_2-X part is presented in Figure 2. The splitting pattern clearly shows that the atropisomer is not very stable in case of diol and the barrier of rotation is quite low. The two isomers are in equilibrium and hence the signals are broad. On the other hand the dibromo, diazide and bis-Schiff base compounds are quite stable isomers and the the high rotational barrier.

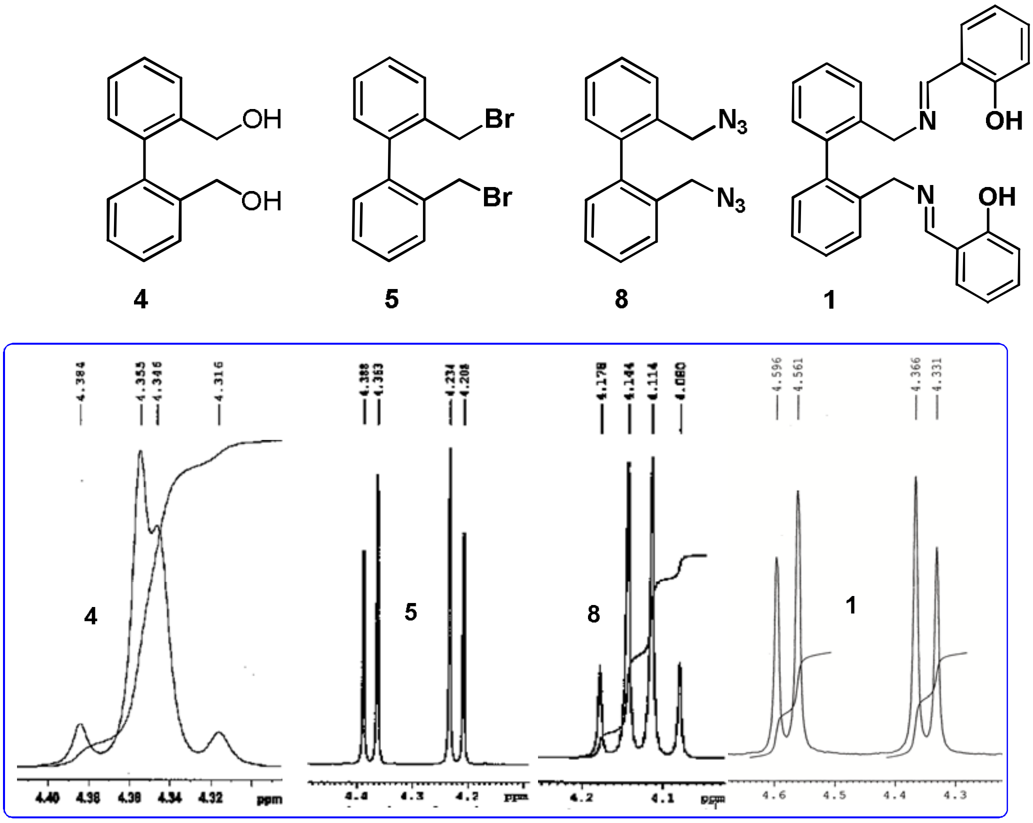
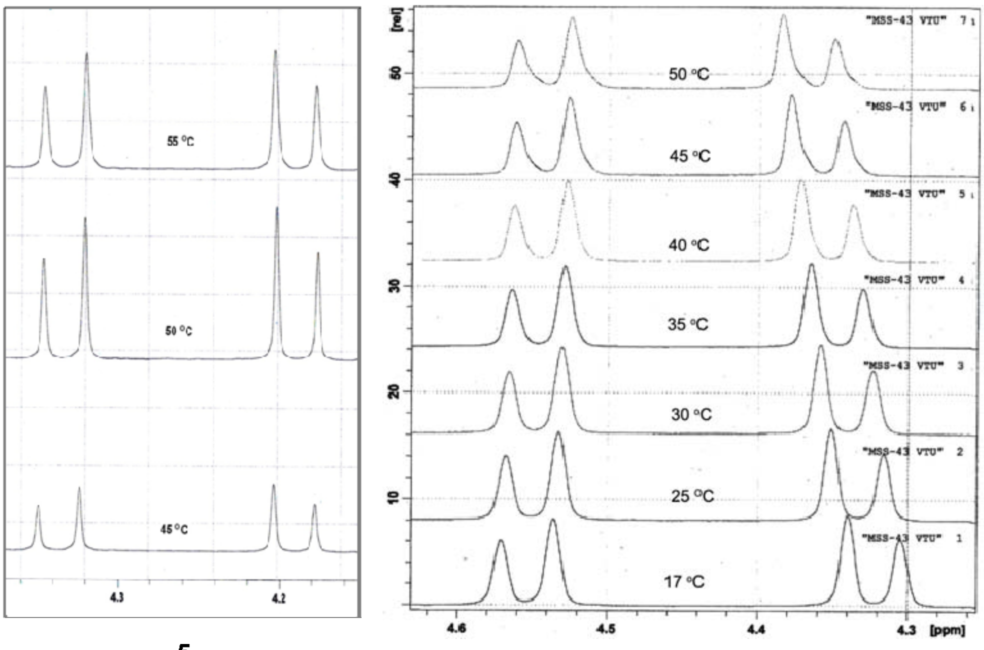


Figure 2

The stability of the conformation of dibromo compound **5** and bis-Schiff base compound **1** was studied by the variable temperature ^{1}H-NMR analysis, we found that the AB-type methylene (-CH_2) proton signals do not merge with each other, even at higher temperature (up to 55 °C) (Figure 3).

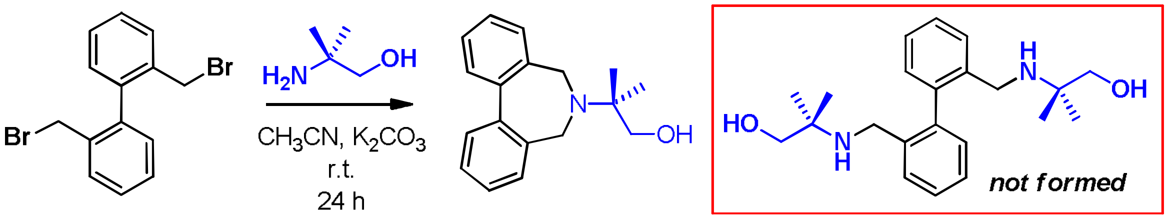


5 1

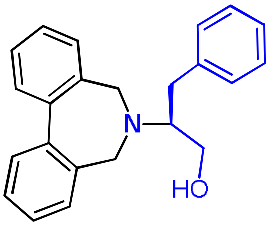
Figure 3: The Ar – CH_2 – X splitting pattern in VT -NMR

Results of the ^{1}H-NMR analysis of four molecules, such as diol **4**, dibromo **5**, diazide **8** and bis-Schiff base **1** compounds specific to the Ar-CH_2-X part have been represented in Figure-2. The splitting pattern clearly indicated that the atropisomer was not very stable in case of diol **4** and the barrier of rotation was quite low. The two isomers were in equilibrium and hence the signals obtained were broad. On the other hand dibromo **5** and diazide **8** may be quite stable isomers and the splitting is confirming the high rotational barrier. The stability of the dibromo and bis-Schiff base compounds were checked by variable temperature (VT) H-NMR analysis, and the VT-NMR results revealed that both compounds were stable at higher temperature (up to 50 °C). Therefore, resolutions of these compounds were studied by different methods.

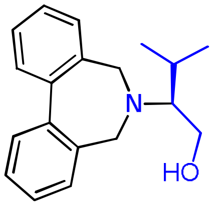
In order to separate the isomers, the enantiomeric dibromo **5** should be converted to another diastereomeric molecule for attempting physical separation. With this intension we plan to convert **5** to another chiral diamine by its nucleophilic reaction with a suitable chiral amine. Reaction of the dibromo **5** with 2-amino-2-methylpropan-1-ol (2.2 eq.) furnished many products as observed on TLC. The prominent of them was isolated and established to be a cyclized compound **10**. Same type of reaction was then performed on **5** with different chiral amino alcohols such as phenylalaninol (to give **11**) and with valinol (to give **12**), iso-lucinol (to give **13**) etc.



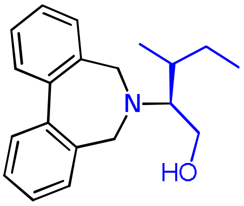
5 **10** **(89%)**



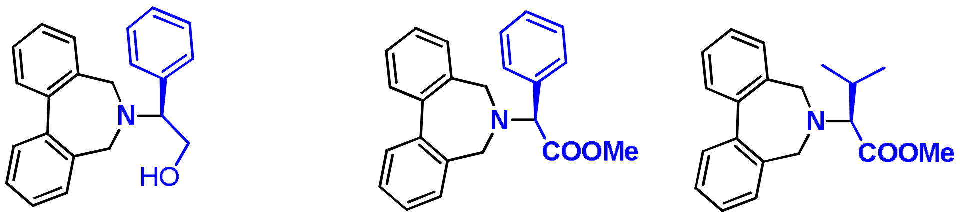
11 **(85%)**



12 **(49%)**



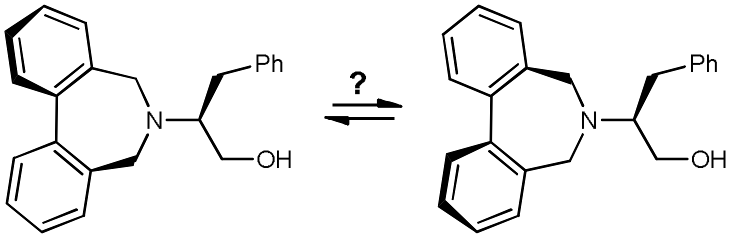
13 **(69%)**



14 (66%) **15** (98%) **16** (93%)

Scheme 6

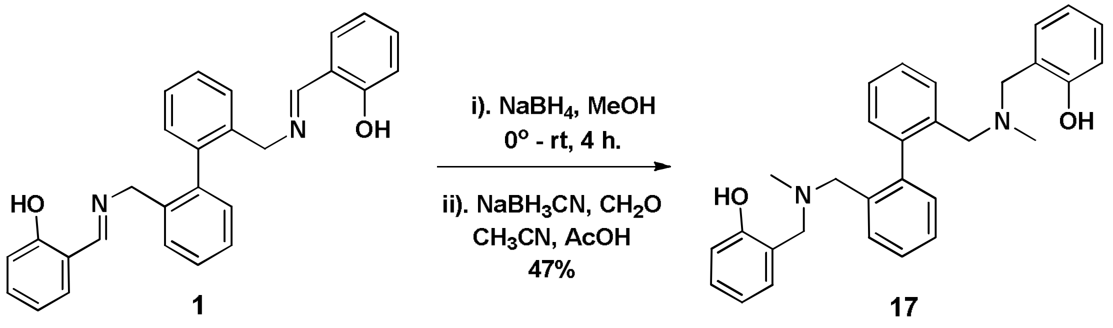
The comparison of the H-NMR analysis of the above compounds clearly showed that the two protons of cyclic system Ar-CH_2-N in **10**, being enantiotopic were quite similar and appeared as a sharp singlet while for **11, 12, 13, 14, 15,** and **16** showed AB splitting pattern, as in these cases they are diastereotopic in nature. This is because of the presence of the chiral center of amino group which induces torsion (*P* or *M* type) on the flexible biphenyl probe. This transfer of central-to-axial chirality in conformationally flexible biphenyl systems is known in literature.[10e,f] The two atropisomers of compounds such as **11** is presented as **11a** and **11b** (Figure 4). At this stage the presence of these isomers at ambient temperature in solution state is not clearly established.



11 a **11 b**

Figure 4

Another method that we tried for the resolution through salt formation leading to diastereomeric salts. With this purpose we converted compound **1** to teriary amine **17** by reduction or reductive alkylation conditions (Scheme 7). Our further attempts to separate them by fractional crystallization using chiral acids as resolving agents were unsuccessful. In this case we could not succeed to separate the two isomers, probably because of low barrier of isomerization for both the compounds.



Scheme 7

Application of biphenyl based ligand 1:

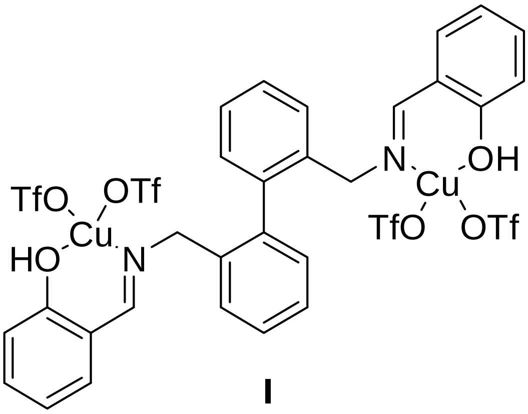
In the mean while we believe that the ligand **1** can complex with metal ion and can furnish effective catalyst systems. With this concept the copper catalysis for promoting Michael reaction was investigated with the ligand **1** and $Cu(OTf)_2$ as the metal source.The role of copper catalysts for promoting Michael reaction has been previously established[24f] hence in the present study we chose this catalyst system. Reaction of chalcone **18** as the π-conjugated substrate, acetyl acetone as the active methylene compound was investigated with the ligand **1** and $Cu(OTf)_2$ as the metal source. It was interesting to note that best result was obtained when two equivalent metal salt was employed with respect to the bidentate ligand **1**. Neither the reverse ratio nor equal ratio of copper and ligand was effective. Absence of copper and ligand did not provide any product under the present condition of carbon-carbon bond forming Michael reaction (Table 2). Efforts to accelerate the reaction by elevating temperature also did not see any improvement in the results. The other copper metal salts ($Cu(OAc)_2•H_2O$, $CuCl_2•H_2O$ and CuI) were ineffective under the optimized reaction conditions (entry 2, Table 2).

Table 2: Optimization of reaction parameters for Michael reaction.

No	Ratio[a]			Conditions	Isolated yield/%
	Acetyl acetone (eq.)	$Cu(OTf)_2$ (mol %)	Ligand **1** (mol %)		
1	1.0	10	5.5	r.t., 6 d	35
2	1.5	10	5.5	r.t., 6 d	67.6
3	1.5	10	10	r.t., 6 d	*trace*
4	1.5	5.5	10	r.t., 6 d	*trace*
5	1.5	0	0	r.t., 6 d	NR[b]
6	1.5	10	0	r.t., 6 d	*trace*
7	1.5	10	5.5	75 °C, 30 h	21
8	2.0	10	5.5	r.t., 6 d	37

[a] ForPhCOCH=CHPh**18** (1.0 eq.), in 1,2-dichloroethane; [b] No reaction.

The structure of the active catalyst of the complex of ligand **1** and $Cu(OTf)_2$ can have the possible structure **I** (Figure 5). Based on our observation of best conversion, the possible structure may be complex **I** formed by ratio of ligand to $Cu(OTf)_2$ of 1:2 (entry 2, Table 2).



I

Ligand - Cu ratio = 1 : 2

Figure 5: Possible compositions of complex of ligand **1** and Cu(OTf)$_2$.

The ESI mass spectrum of complex **I** showed [M+4Na] peak at 1236 *m/z*, endorsing the above structure (Figure 6). Its IR spectrum showed strong stretching peak for sulfones at 1263, 1171 cm^{-1}.

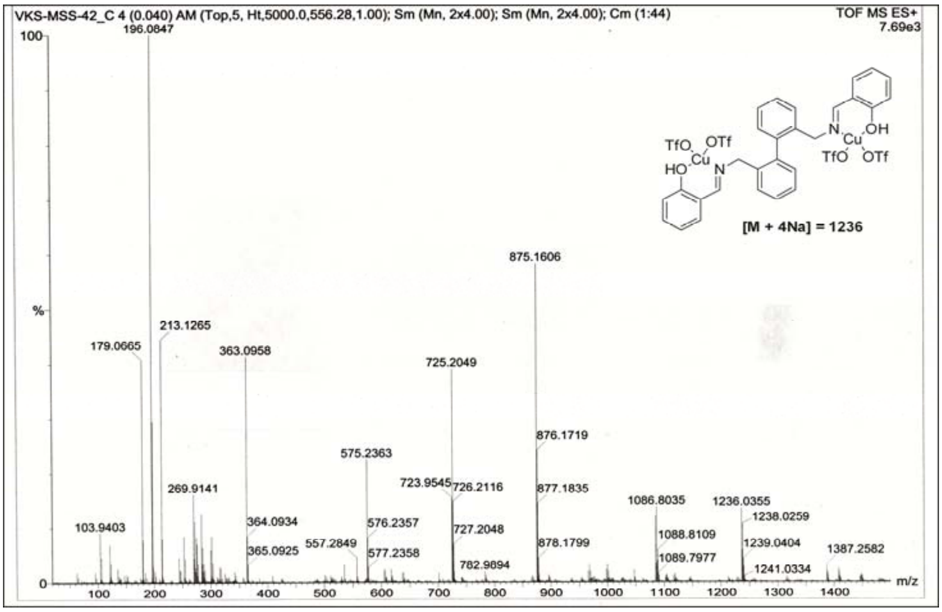
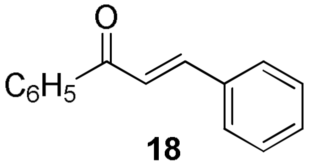
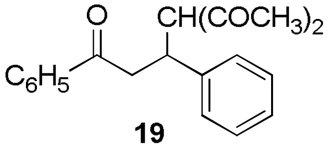
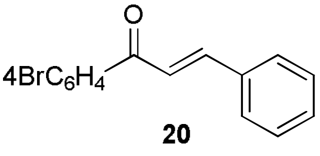
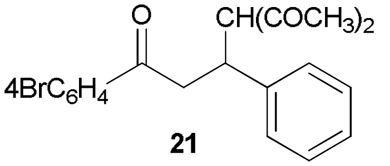
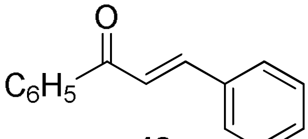
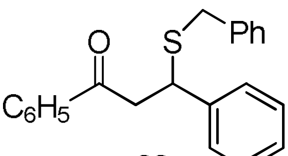
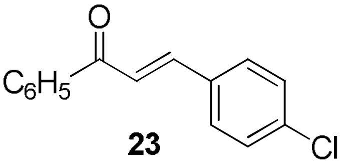
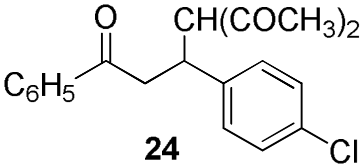
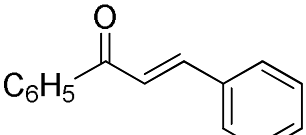
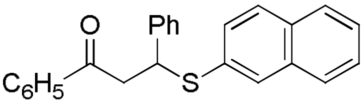
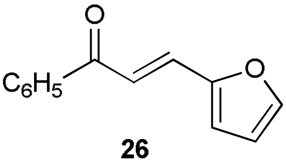
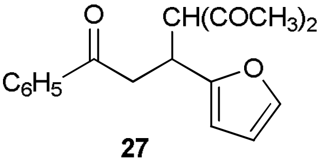
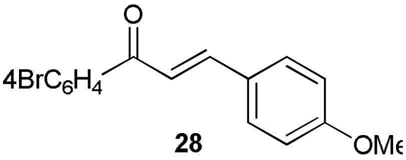
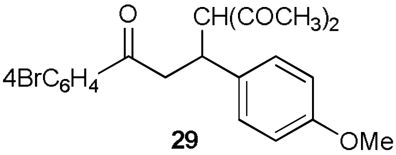
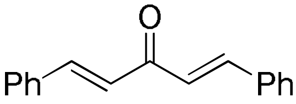
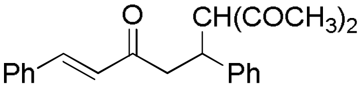
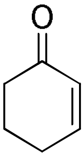
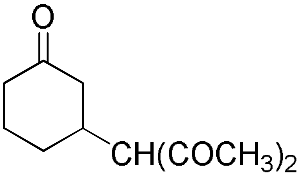
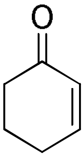
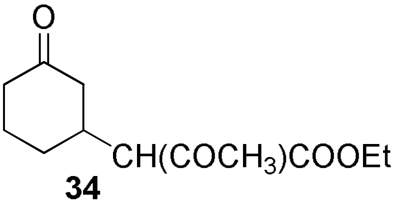


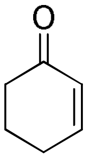
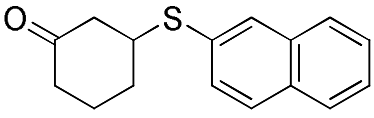
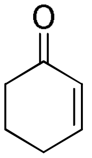
Figure 6: ESI mass of complex **I**

Having established mild and neutral condition for Michael reaction a number of other α,β-unsaturated ketones were subjected to the same condition to test the generality (Table 3). The reaction with other active methylene compounds like $CH_2(CN)_2$ and $CH_2(COOCH_3)_2$ with **18** under identical conditions was not as effective and only a trace amount of the desired product was detected.

Table 3: Examples of Michael reaction with the present catalysts system.[a]

No	α,β-Unsaturated ketone	Product	Yield[b]/%
1	 **18**	 **19**	67
2	 **20**	 **21**	54

3	 **18**	 **22**	89
4	 **23**	 **24**	65
5	 **18**	 **25**	40
6	 **26**	 **27**	47
7	 **28**	 **29**	54
8	 **30**	 **31**	81
9	 **32**	 **33**	82
10	 **32**	 **34**	83

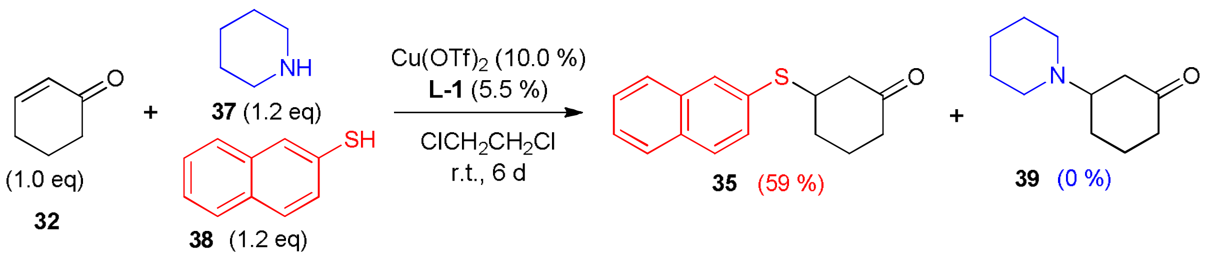
11	 **32**	 **35**	81
12	 **32**	 **36**	84

---

[a]With acetyl acetone (1.5 eq.), 1,2-dichoroethane, $Cu(OTf)_2$ (10.0 mol %), L-**1** (5.5 mol %), r.t., 6 d; [b]Isolated.

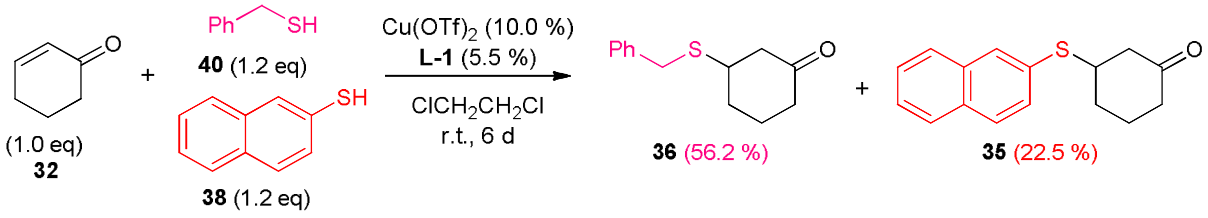
The results of the present neutral and mild Michael reaction are encouraging and hence were further studied from the point-of-view of chemoselectivity. It was interesting to observe negligible conversions in oxa- and aza-Michael reaction with phenol and amines. Reaction of cyclohexenone**32** with β-naphthol did not furnish oxa-Michael product but gave BINOL (36%Y) by copper catalyzed oxidation reaction.[39] Similarly reaction with amino nucleophiles as Michael donors such as piperidine, aniline, imidazole did not furnish 1,4-addition products. On the other hand reaction with soft nucleophile such as thiols gave the desired thia-Michael reaction products in good yields.

Reaction of cyclohexenone **32** with 2-naphthalenethiol **38** (1.5 eq.) furnished the thia-Michael product **35** in good yield (81%) under the standard condition. The chemoselectivity of the system was then further investigated with different combinations. In the first reaction cyclohexenone was exposed to the established conditions with piperidine and 2-naphthalenethiol and the products were carefully analyzed. The aza-Michael product **39** was not detected while the thia-Michael product **35** was isolated, though in lesser yield (Scheme 8).This observation of chemoselectivity in favor of thia-Michael over aza-Michael is noted previously for copper catalyst.[12a] The H-NMR of **35** showed seven aromatic protons at aromatic region (7.91-7.47 ppm), one of the hydrogens shows meta coupling (J = 1.2 Hz). Cyclohexane hydrogens show multiple splitting between δ1.74-2.75 ppm. The mass spectrum showed molecular ion peak at 258 m/z.



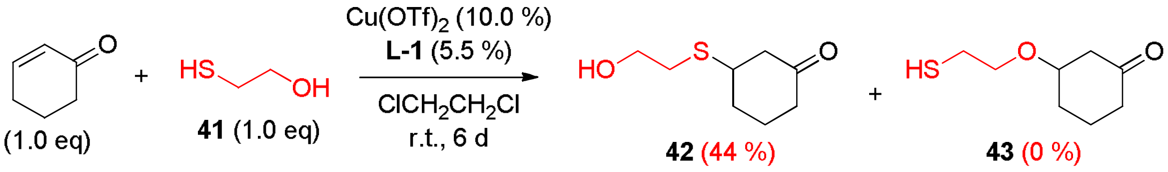
Scheme 8: Selective thia-Michael reaction of **32**

In the next experiment the comparison between aromatic and aliphatic thiols was examined (Scheme 9). Reaction of the benzyl mercaptan **40** was slightly favoured because of more nucleophilic sulfhydryl sulfur atom and the corresponding product **36** was formed in excess compared to the product of weaker nucleophilic aromatic thiol. This observation is slightly different than the recently reported example for ionic liquid mediated Michael reaction for **38** and **40** with cyclohexenone.[13d] In the study weaker nucleophilic but stronger acidic **38** gave faster product **39** in the thia-Michael reaction. Reaction of **32** with only aryl alkyl thiol **40** (1.5 eq.) gave product **36** in good yield (84 %).The H-NMR of **36** showed five aromatic protons at δ 7.33-7.22 ppm, the Ar$\underline{CH_2}$S protons shows at δ3.76 singlet, C$\underline{H}$S proton showed at δ 2.92 ppm with multiple splitting and the rest of the cyclohexane hydrogens show multiple splitting between δ 1.65-2.69 ppm. The mass spectrum showed expected molecular ion peak at 220 m/z.



Scheme 9: Selectivity towards R-SH compared to Ar-SH.

Reaction of 2-mercaptoethanol **41** with cyclohexene selectively gave thia-Michael product **42** (Scheme 10), while **43** was not detected. Such observation of selectivity are in accordance with other reported catalytic systems.[33,34j] The isolated yield of the experiments carried out to test chemoselectivity, were lower because only 1.0 or 1.2 equivalent reagents were utilized to assess the selectivity and no attempts were made to optimize the conditions. The H-NMR of **42** showed C$\underline{H_2}$O protons showed multiple splitting at δ 3.76 ppm, for C$\underline{H_2}$S protons multiple splitting at δ 3.21 ppm and rest off cyclohexane hydrogens showed multiple splitting between δ 1.71-2.79 ppm. The mass spectrum showed expected molecular ion peak at 173 *m/z*.



Scheme 10: Selectivity between thiol and alcohol.

An atropisomeric ligand attached to biphenyl unit was synthesized and screened in copper mediated Michael reaction. The catalyst system works well with carbon or sulfur nucleophiles as Michael donors and cyclohexenone *or* chalcones as the acceptors under mild and neutral reaction conditions in chemoselective manner.

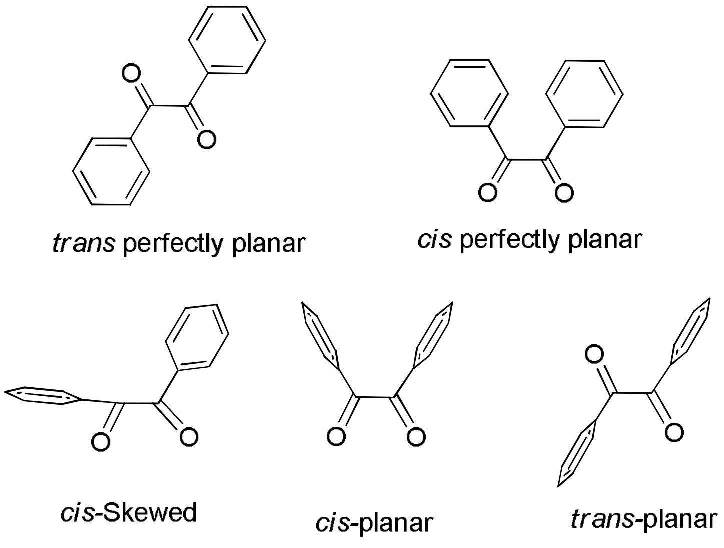
Conclusion

The new ligand **1** is easy to make and is effective in copper catalyzed Michael reaction. Further the homogeneous catalysts system is capable of assisting Michael reaction in *chemoselective* manner for the useful carbon-carbon (**C-C**) and carbon-sulfur (**C-S**) bond forming Michael reaction.

Part II

4.2.2 Chiral axis of benzil [sp^2 (CO) - (CO) sp^2 type atropisomers]

Benzil, a 1,2-diketo compound structurally contains the planes of two benzoyl groups which are nearly orthogonal with sp^2 carbon atoms. Structural, spectroscopic and photophysical properties of benzyl are the areas of interest for the extensive research. The presence of the dihedral angle (Scheme 11), between the two symmetric halves, each containing the C_6H_5–C=O group provides structural flexibility to the compounds which for the further research. This flexibility is probably due to not-so-high energy barrier of the rotation around the central single bond between the two C=O groups.[40] Benzil serves as a subject for many investigations on the conformations occurring both in the ground state (S^0) as well as in the excited singlet (S^1) and triplet (T^1) states [40 d,e]


trans perfectly planar

cis perfectly planar

cis-Skewed

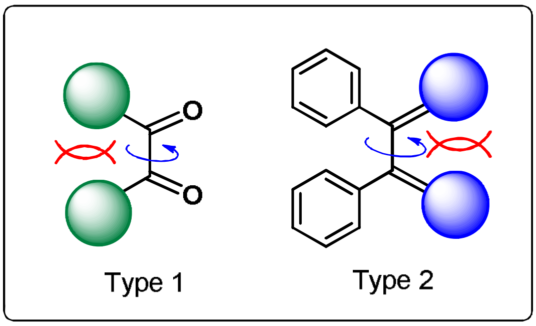
cis-planar

trans-planar

Scheme 11: Physical properties of benzil

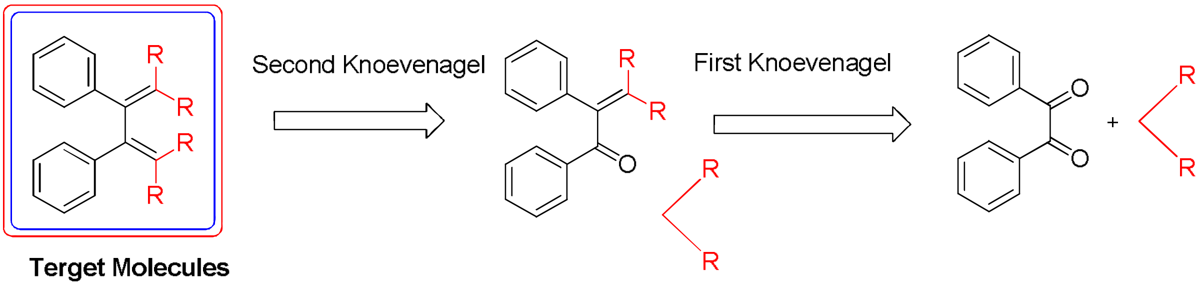
Benzil is known to react with various nucleophilic species like hydroxide to undergo benzilic acid rearrangement,[41] diphenyl acetone to give tetraphenyl cyclopentadienone,[42] with primary amines to form mono imines,[43] etc. Benzils are also known to form other heterocyclic compounds when treated with nucleophilic reagents under specific conditions.[44]

The C-C bond of the 1, 2-diketo shows restricted rotation when the bulky groups are attached on the carbonyl carbons (type 1) or in place of the carbonyl oxygen (type 2) as showed as below.



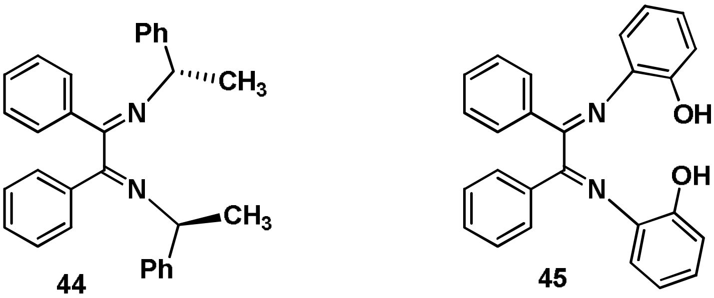
We plan to increase the bulk by incorporating different functional group on chiral axis of benzyl without disturbing of sp^2 hybridization (type 2). For the synthesis of type 2 molecules first we chose Knoevenagel reaction on benzil with molecule containing active methylene group. For the synthesis of target molecule we proposed retrosynthetic scheme see the below.

Retro synthetic scheme:



Scheme 12

The reaction of benzil with primary chiral amine gives monoamine and diimines. A bis-imine **44** prepared from benzil with two equivalents of chiral 1° amines is used as a ligand for Mo-catalyzed reactions[45] and another one prepared from aminophenols **45** is used in catalytic oxidation reactions.[46] However, the authors of these works do not focus on atropisomeric nature of the benzil axis.

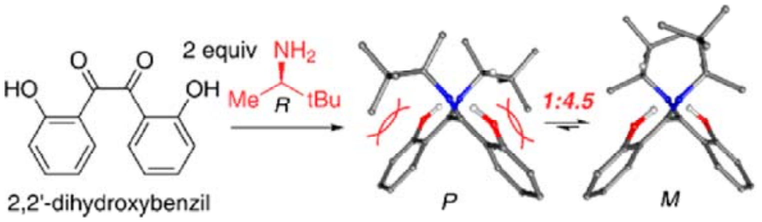


44

45

Scheme 13: Observed products from earlier literature

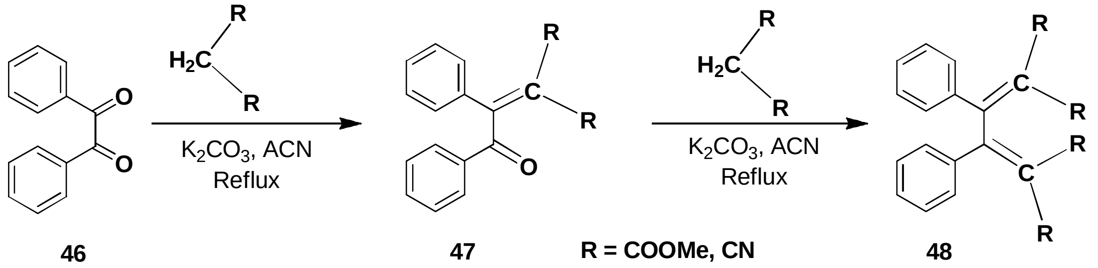
While planning and executing some of our earlier research, a relevant paper was published by Kim and co-authors (in 2014) reporting on generating an axial chirality in 2,2 –dihydroxybenzil,[47] in this reaction (Scheme 14) 2,2 –dihydroxybenzil combines with 2 equivalent of primary amine to form a diimine of which axial chirality is controlled by steric strain with moderate (1.4:1) to good (4.7:1) stereoselectivity.



Scheme 14

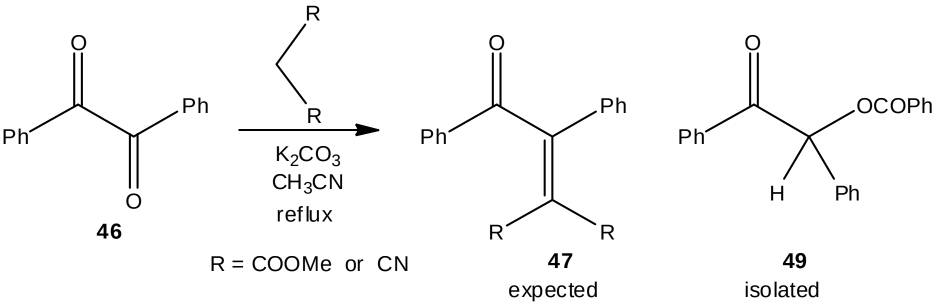
However, before the above report we have carried out some experiments in this direction. We utilized the classical Knoevenagel reaction of aldehydes and ketones with molecules containing active methylene group, like Z-CH_2-Z where Z is electron withdrawing group, to rendering a conjugated systems.[48] As a part of our target molecule we were keen to carry out Knoevenagel condensation on 1,2-diketo compounds like benzil **46** to prepare mono substituted conjugated system **47**.

Proposed scheme with dimethylmalonate or malononitrile: We expect double Knoevenagel condensation on benzil to follow stepwise formation of bis-imine.



Scheme 15

However, a number of attempts in our laboratory to carry out the above conversion could not furnish the desired compound **47**. Initially, the reaction of benzil and dimethylmalonate was conducted in dry acetonitrile in presence of potassium carbonate to facilitate the anion formation. Two new products were detected in the reaction mixture, but on separation and analysis none of them matched with the expected compound **47**. One of the less polar products was isolated and identified to be 2-oxo-1,2-diphenylethyl benzoate (benzoyl benzoin), **49** by spectroscopic analysis and also by comparison of melting point with that of the reported one[49] (Scheme 16). Interestingly, the same product **49** was formed when reaction of benzil was carried out with malononitrile. It was noteworthy to observe complete absence of this product when neither dimethylmalonate nor malononitrile was used and **46** was heated only with K_2CO_3 in acetonitrile.



Scheme 16: Attempted Knoevenagel reaction of benzil

The structure of **49** was established by spectroscopic methods. The H-NMR of the compound **49** showed one singlet signal for COC<u>H</u>OCO proton at δ 7.12 ppm and the ^{13}C-NMR indicating two carbonyl signals (δ 199 & 166) and for aliphatic carbon signal at δ 77 ppm. The correlation of the methine (C<u>H</u>) proton of compound **49** was also established by the ^{1}H-^{13}C correlation 2D NMR experiment HSQCGP as shown below (Figure 7). In the ^{1}H-^{13}C correlation spectrum the carbon at δ 77 ppm correlates with the proton at δ 7.12 ppm.

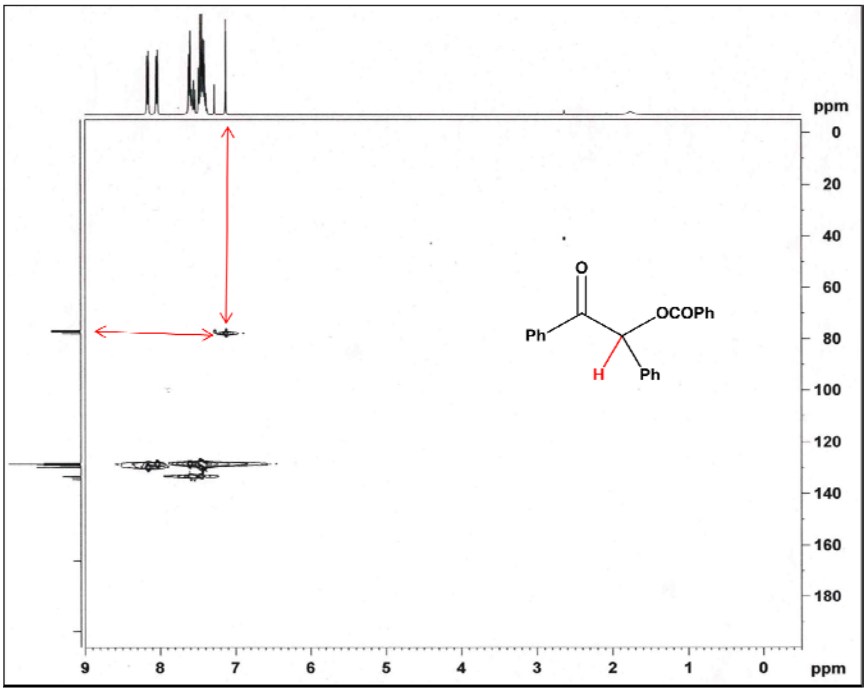


Figure 7:^{1}H-^{13}C Correlation (HSQCGP) spectrum of the compound **49**

The IR spectrum of the compound **49** showed for Ar-H stretching at 3070 cm^{-1}, for C-H at 2952cm^{-1} for -C=O stretching at 1734, 1695 cm^{-1} (–PhCO, OCOPh respectively), and for aromatic -C=C- stretching at 1594 cm^{-1}.

The EI-mass spectrum of the compound **49** showed the *m/z* 316 $[M]^{\cdot+}$ and further signals due to fragmentations of $[-COPh]^{\cdot+}$ at *m/z* 211, and the base peak at *m/z* 105 for the $[Ph\text{-}CH\text{-}O]^{\cdot+}$

The structure of **49** was conclusively established by single crystal X-ray analysis as shown in the Figure 8.

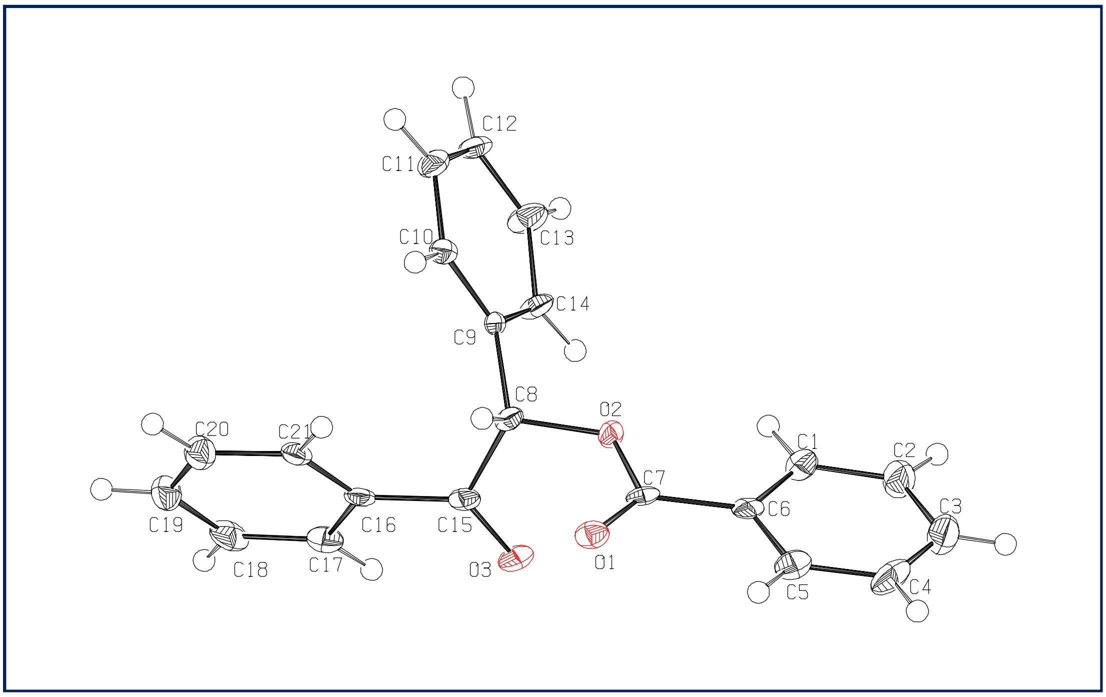
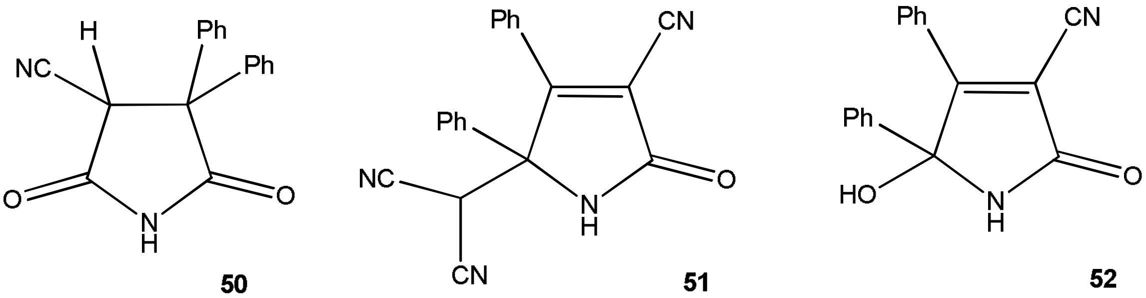


Figure 8: ORTEP diagram of the organic compound **49** with atom numbering scheme (50% probability factor for the thermal ellipsoids

Reaction of benzil with malononitrile is first reported by Junek *et al.*[50] to observe the formation of 2-benzoyl-2-phenyl-ethylene-1,1-dicarbonitrile (**47**; R=CN) and 2,5-dioxo-4,4-diphenyl-pyrrolidine-3-carbonitrile **50**. This reaction was reinvestigated by Ducker and Gunter[51] and have proposed formation of two other heterocyclic products, 4’-cyano-5’-oxo-2’,3’-diphenyl-3’-pyrrolin-2’-ylmalononitrile **51** and 5-hydroxy-2-oxo-4,5-diphenyl-3-pyrrolin-3-carbonitrile **52** (Scheme-17).



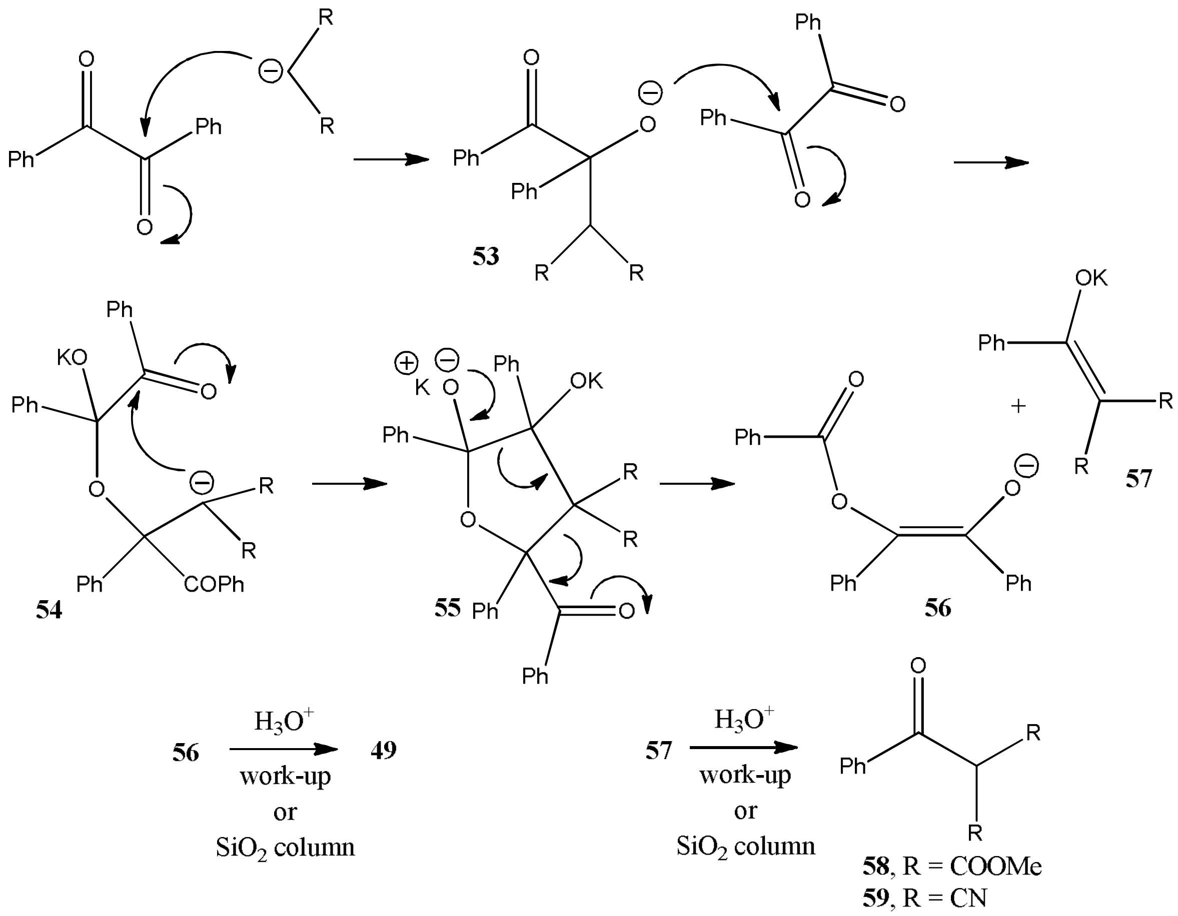
50 **51** **52**

ref. 50a ref. 51 ref. 51

Scheme-17: Observed unusual products for similar systems from the literature

The same product **49** is reported to have formed when benzil is treated with cyanide ion in presence of benzaldehyde and the key step in the mechanism involves 1,2 C-O shift.[49a] Such a possibility can be ruled out in the present case as the reaction does not have cyanide ion neither benzaldehyde. Another reaction of benzil with cyanide ion is reported to be following a different mechanistic pathway.[52]

The proposed mechanism of formation of product **49** from benzil is outlined in Scheme-3. The fact that the reaction does not proceed in the absence of either a base or dimethylmalonate or malononitrile clearly indicate that the reaction starts by nucleophilic attack of the anion of active methylene to one of the carbonyls of benzil. The intermediate **53** may further attach to another benzil molecule to form intermediate **54**, which can undergo intramolecularnucleophilic attack on the second carbonyl of the second benzil molecule to give a tetrahydrofuran intermediate **55**. Intramolecular ring opening of this highly substituted intermediate **9** is quite possible to give stabilized species **56** and **57**, which during work up can give **49** and **58**/**59** as products, respectively. Product **58** is isolated (43 % Y) and its structure was confirmed by spectral analysis (Mass and ^{1}H-NMR) when dimethylmalonate was used with benzil. The ^{1}H-NMR of the compound **58** showed a singlet at δ 3.81 ppm for methyl protons -COO$\underline{CH_3}$, and one singlet at δ 5.34 ppm for $\underline{CH}(COOCH_3)_2$.The EI-mass spectrum of the compound **58** showed the *m/z* 236 $[M]^{\cdot+}$ and the base peak at *m/z* 235 for the $[-H]^{\cdot+}$ and further signals due to fragmentations of $[-(CH3)_2]^{\cdot+}$ at *m/z* 205, $[-(O)_2]^{\cdot+}$at *m/z* 175 and $[-C(CO)_2]^{\cdot+}$ at *m/z* 105.



Scheme-3: Suggested mechanism to explain formation of **49** from benzil **46**.

Our attempts to carry out identical reaction with camphorquinone and phenanthraquinone with dimethylmalonate did not result in similar reaction and products from usual mono-Knovenagel condensation were detected.

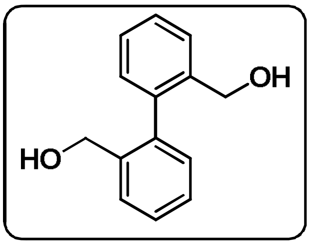
Conclusion

An unexpected product, 2-oxo-1,2-diphenylethyl benzoate (benzoyl benzoin), was isolated during the attempted Knoevenagel reaction of benzil and dimethylmalonate (or malononitrile) in presence of potassium carbonate. The product was confirmed by spectral analysis as well as by single crystal studies and a mechanism is proposed to explain its formation.

4.3 Experimental Procedures

Reagents were purchased from Sigma-Aldrich Chemicals Limited, SD Fine, Qualigens Limited etc. Thin Layer Chromatography was performed on Merck 60 F_{254} Aluminium coated plates. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography using silica gel (60-120 mesh). All the products were characterized by H-NMR, IR, Mass spectroscopy and by comparison of m.p. with the reported values. ^{1}H NMR spectra were recorded on Bruker Avance 400 Spectrometer and were run in $CDCl_3$. Mass spectra were recorded on Thermo-Fischer DSQ II GCMS instrument. IR spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pallets. Melting points were recorded in Thiele's tube using paraffin oil and are uncorrected.

2,2'-Bis(hydroxymethyl)biphenyl (**4**):



To a 1000 mL two neck round bottom flask, fitted with magnetic stir bar and a reflux condenser was added sodium borohydride (7.404 g, 0.198 mol), dry THF (200 mL), diacid **3** (10.0 g, 0.041 mol) in one portion. The flask was cooled in an ice bath. To this a solution of iodine (21.95 g, 0.087 mol) in dry THF (100 mL) was poured in via an addition funnel slowly over 45 min resulting in vigorous evolution of hydrogen. After the addition of iodine was complete the flask was heated to reflux (18 h), cooled to room temperature and methanol (30 mL) was added cautiously until the mixture become clear. After stirring (30 min), the solvent was removed, leaving a white paste which was dissolved in KOH solution (20 % aq. 200 mL). The resultant solution was stirred (4 h) and extracted with ethyl acetate (3 x 250 mL). The organic layer was dried over sodium sulfate and concentrated in vacuum, affording a white solid (8.77 g, 99 %).

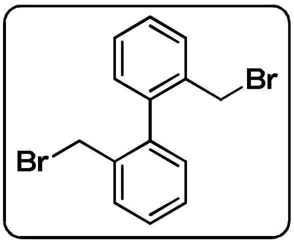
M. p. = 110 - 112 ^{o}C (Lit.[53] 110.5 - 111.5 ^{o}C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.49 (dd, J = 6.4 and 1.2 Hz, 2H), 7.44-7.39 (td, J = 6.0 and 1.6 Hz, 2H), 7.38-7.34 (td, J = 6.0 and 1.6 Hz, 2H), 7.18-7.16 (dd, J = 6.0 and J = 1.2 Hz, 2H), 4.35 (broad s, 4H), 3.07 (s, 2H).

Mass (EI^+) m/z (%): 198 (6), 197 (40), 196 (9), 195 (10), 181 (2), 180 (2), 179 (11), 168 (14), 167 (100), 165 (1).

IR (KBr): υ 3355, 3064, 2918, 1479, 1448, 1428, 1423, 1339, 1250, 1194, 1104, 1034, 998, 774, 755, 654 cm.$^{-1}$

2,2’-Bis(bromomethyl)biphenyl (**5**):



To an oven dried two neck round bottom flask triphenyl phoshine (25.76 g, 0.098 mol) and acetonitrile (100 mL) was added and cooled in an ice bath. To this stirred mixture bromine (5.29 mL, 0.103 mol) was slowly added (30 min). After addition, the yellow slurry was formed to which the diol **4** (10.0 g, 0.047 mol) was added in one portion the yellow slurry changed to a clear solution, after 10 min again the yellow slurry was formed. The whole reaction mixture was stirred (15 h) at room temperature. Then solvent was removed at reduced pressure and the resulting product was washed with water (2 × 250 mL) and extracted with ethyl acetate (2 × 250 mL). The organic layer was dried over sodium sulfate and concentrated in vacuum. The crude product was purified by column chromatography on silica gel using petroleum ether as eluent to give 2,2$'$–bis(bromomethyl)biphenyl **5** (13.98 g, 88%) as colorless prisms.

M. p. = 86-88 °C (Lit.[54] 87-89 °C)
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.56 (dd, *J* = 7.6 and 1.6 Hz, 2H), 7.47-7.43 (td, *J* = 7.6 and 1.6 Hz, 2H), 7.42-7.38 (td, *J* = 7.6 and 1.6 Hz, 2H), 7.31-7.28 (dd, *J* = 7.6 and 1.6 Hz, 2H), 4.39-4.36 (d, *J* = 10 Hz, 2H), 4.23-4.21 (d, *J* = 10 Hz, 2H).

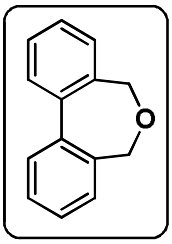
Mass (EI^+) m/z (%) 348 (20), 346 (36), 344 (48), 342 (23), 314 (20), 312 (60), 311 (12), 310 (100), 310 (10), 308 (79), 306 (22), 279 (19), 274 (76), 272 (51), 241 (24), 239 (34), 236 (18), 61 (12), 57 (9).

IR (KBr): υ 3064, 3025, 1972, 1558, 1479, 1434, 1272, 1219, 1158, 1135, 1006, 953, 805, 772, 606, 537cm^{-1}

2,2'-bis(iodomethyl)-1,1'-biphenyl (**6**)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.57 (dd, *J* = 7.6 and 1.6 Hz, 2H), 7.56-7.34 (m, 4H), 7.27-7.25 (m, 2H), 4.39-4.37 (d, *J* = 9.6 Hz, 2H), 4.14-4.12 (d, *J* = 9.6 Hz, 2H).

6,7-Dihydro-5*H*-dibenz[*c*,*e*]oxepine (7):



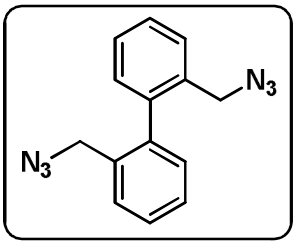
M. p. = 68 - 70 °C (Lit.[54] 71.5 – 72.0 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.58 (m, 2H), 7.55-7.51 (m, 2H), 7.48-7.42 (m, 4H), 4.39 (s, 4H).

Mass (EI^+) m/z (%): 196 (28), 195 (27), 167 (26), 166 (16), 164 (44), 152 (13), 148 (11), 121 (10), 94 (20), 83 (12), 80 (53), 71 (12), 68 (100), 68 (15), 66 (22), 56 (20), 54 (19).

IR (KBr): υ 3066, 3018, 2965, 2913, 2855, 1483, 1458, 1442, 1377, 1198, 1073, 1044, 991, 902, 890, 786, 757, 602, 501 cm^{-1}

2,2'-Bis(azidomethyl)biphenyl (8)



A solution of dibromo **5** (7.0 g, 0.177 mol), sodium azide (3.35 g, 0.044 mol) in acetonitrile (30 mL) was refluxed for 24 h. The mixture was cooled to room temperature and solvent was removed at high vacuum, the crude product was quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 250 mL) and then dried with anhydrous sodium sulfate. The organic solvent was evaporated under reduced pressure to give a pale yellow liquid as crude product, which was purified by column chromatography on silica gel using petroleum ether as eluent to give diazide **8** (5.35 g, 98%) as a colorless oil.

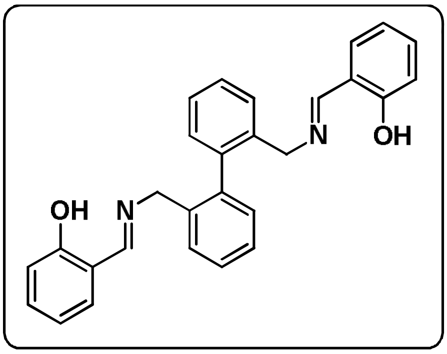
Colorless oil.[55]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.41 (m, 6H), 7.26-7.24 (m, 2H), 4.18-4.14 (d, J = 13.6 Hz, 2H), 4.11-4.08 (d, J = 13.6 Hz, 2H).

Mass (EI^+) m/z (%) 207 (7), 195 (10), 194 (12), 193 (20), 192 (17), 181 (15), 180 (100), 179 (20), 178 (15), 167 (11), 166 (18), 165 (36), 164 (8), 153 (12), 52 (38), 151 (17), 77 (9), 76 (8), 63 (8), 51 (7).

IR (Neat): υ 3063, 3023, 2941, 2877, 2097, 1598, 1477, 1446, 1344, 1256, 1193, 1007, 886, 759 cm^{-1}

2,2'-{(1*E*,1'*E*)-(([1,1'-biphenyl]-2,2'diylbis(methylene))bis(azanylylidene)) bis(methanylylid- ene)}diphenol (**1**):



A solution of diazide **8** (2.0 g, 0.007 mol) in ethanol (20 mL) was hydrogenated (H_2 balloon) in presence of palladium/carbon (10 % Pd, 0.2 g) for 15 h with stirring at room temperature. After the reaction was complete (tlc), the catalyst was removed by filtration through Celite and wash with ethanol (2 X 5 mL). The filtered solution was concentrated to its half volume on rotary evaporator. To this salicylaldehyde (2.02 mL, 0.018 mol) was added and the mixture stirred at room temperature. After about 1h, slowly yellow slurry was formed and the reaction was continuing (15 h). The yellow precipitates were filtered through sintered funnel and wash with cold ethanol (2 x 5 mL), further purified by recrystallization from methanol to get yellow crystals of **1** (2.08 g, 65%).

Mp. = 128-130 $^{\circ}$C.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 13.33 (s, 2H), 7.78 (s, 2H), 7.44-7.36 (m, 6H), 7.31-7.26 (m, 2H), 7.24-7.22 (d, *J* = 6.8 Hz, 2H), 7.06-7.04 (dd, *J* = 7.6 and 1.2 Hz, 2H), 6.95-6.93 (d, *J* = 8.4 Hz, 2H), 6.85-6.82 (m, 2H), 4.59-4.56 (d, *J* = 14.0 Hz, 2H), 4.36-4.33 (d, *J* = 14.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 165.76, 160.95, 139.79, 135.87, 132.30, 131.48, 129.88, 128.99, 128.18, 127.43, 118.67, 118.58, 116.89, 61.61.

Mass (EI^+) m/z (%) 301 (4), 300 (21), 299 (92), 298 (6), 286 (3), 180 (16), 179 (90), 178 (100), 177 (7), 175 (7), 166 (9), 165 (30), 152 (5), 134 (3), 122 (6), 121 (35), 119 (4), 106 (10), 77 (5).

IR (KBr): υ 3649, 3060, 3017, 2884, 1670, 1636, 1582, 1500, 1472, 1462, 1441, 1375, 1333, 1279, 1210, 1159, 1119, 1058, 1030, 995, 959, 943, 895, 876, 847, 757, 722, 655 cm^{-1}

Anal. Calcd. for $C_{28}H_{24}N_2O_2$: C, 79.98; H, 5.75; N, 6.66. Found: C, 79.68; H, 5.67; N, 6.77.

Standard procedure for resolution of diol (±)-**4**

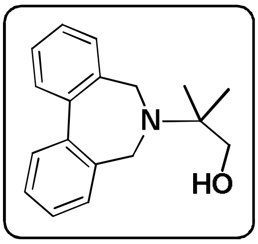
To a solution of diol (±)-**3** (0.25 g, 1.17 mmol) in dry THF (10 mL) SRL made immobilized granular steapsin lipase enzyme (0.25 g) and vinyl acetate (0.15 g, 1.75 mmol) were added and reaction mixture was stirred for 48 h at 8–9 °C. The reaction was followed by TLC (48 h). The material was filtered and the filtrate was concentrated in vacuo. Separation was carried out by columnchromatography over silica gel using light petroleum ether and ethyl acetate (80-20) as the eluent. The mono-acetate **4b** was isolated with a 0.11 g, 37%) and diol **4a** with a 0.10 g, 35%).

Spectral data for **4a**: [compound **4**]

Spectral data for **4b**:

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.57-7.55 (dd, *J* = 7.6 and 0.8 Hz, 2H), 7.48-7.46 (m, 1H), 7.43-7.30 (m, 4H), 7.21-7.18 (dd, *J* = 6.8 and 2 Hz, 1H), 7.14-7.12 (dd, *J* = 7.2 and 1.2 Hz, 1H), 4.90-4.82 (d, *J* = 12.4Hz, 2H), 4.45-4.35 (d, *J* = 12.4Hz, 2H), 2.06 (broad singlet, 1H), 1.98 (s, 3H).

2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-2-methylpropan-1-ol (**10**)

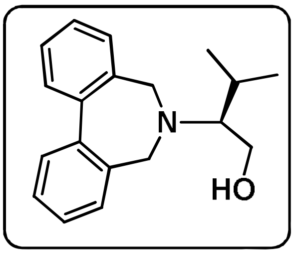


^{1}H NMR (400 MHz, CDCl$_3$): δ 7.53-7.51 (m, 2H), 7.48-7.37 (m, 6H), 3.61 (s, 4H), 3.51 (s, 2H), 2.91 (s, 1H), 1.23 (s, 6H).

Mass (EI$^+$) m/z (%): 268 (3), 266 (2), 237 (17), 236 (100), 180 (6), 179 (30).

IR (KBr): υ 3420, 3061, 3018, 2975, 2943, 1480, 1451, 1440, 1371, 1188, 1063, 1054, 991, 890 cm^{-1}

(*S*)-2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-3-methylbutan-1-ol (**12**)

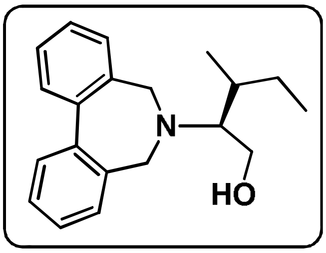


IR (KBr): υ 3422, 3052, 3015, 2972, 2932, 2869, 1463, 1367, 1088, 1039, 923, 876 cm.$^{-1}$

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.53-7.47 (m, 2H), 7.46-7.37 (m, 6H), 3.76-3.72 (m, 1H), 3.70-3.64 (dd, *J* = 12.8 Hz, 4H), 3.49-3.45 (m, 1H), 3.19 (s, 1H), 2.70-2.65 (m, 1H), 2.06-1.94(m, 1H), 0.94-0.92 (d, *J* = 6.8 Hz, 3H), 0.92-0.90 (d, *J* = 5.6 Hz, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): 140.90, 135.53, 129.60, 128.13, 128.00, 127.82, 71.83, 59.71, 52.40, 29.02, 22.92, 19.46.

(2*S*,3*R*)-2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-3-methylpentan-1-ol (13)

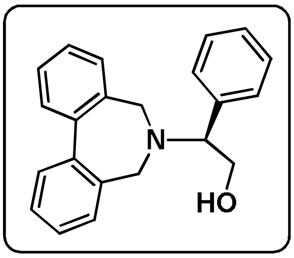


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.49 (m, 2H), 7.46-7.42 (m, 2H), 7.39-7.36 (m, 4H), 3.70-3.67 (m, 1H), 3.66-3.59 (m, 4H), 3.53-3.48 (m, 1H), 2.80-2.75 (m, 1H), 1.85-1.74(m, 1H), 1.44-1.34 (m, 1H), 1.21-1.1.10 (m, 1H), 0.88-0.83 (m, 6H)

Mass (EI^+) m/z (%): 295 (2), 279 (10), 265 (44), 264 (88), 237 (100), 178 (70), 177 (79).

IR (KBr): υ 3426, 3062, 3020, 2960, 2929, 2875, 1479, 1453, 1377, 1074, 1046, 923 cm^{-1}

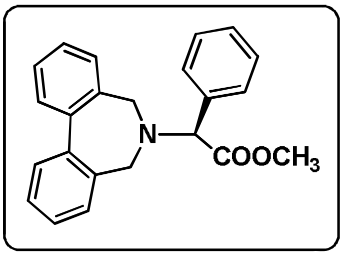
(*S*)-2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-2-phenylethanol (14)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49-7.37 (m, 8H), 7.35-7.29 (m, 3H), 7.23-7.19 (m, 2H), 4.02-3.98 (dd, *J* = 11.2 & 5.6, 1H), 3.92-3.89 (dd, *J* = 11.2 & 4.8, 1H), 3.72-3.69 (t, J = 4.8 Hz, 1H), 3.59-3.56 (d, *J* = 12.4 Hz, 2H), 3.39-3.36 (d, *J* = 12.4 Hz, 2H), 2.23 (s, broad 1H)

Mass (EI^+) m/z (%): 314 (2), 285 (57), 284 (57), 283 (76), 283 (55), 194 (6), 180 (11), 179 (65), 178 (100).

(*S*)-methyl 2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-2-phenylacetate (15)



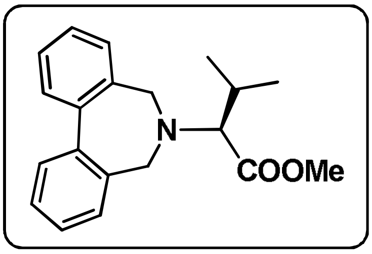
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62-7.59 (m, 2H), 7.51-7.49 (m, 2H), 7.47-7.34 (m, 7H), 7.28-7.26 (m, 2H), 4.25 (s, 1H), 3.73 (s, 3H), 3.45-3.42 (d, *J* = 12.8 Hz, 2H), 3.31-3.28 (d, *J* = 12.4 Hz, 2H), 1.69 (s, 1H)

^{13}C NMR (100 MHz, $CDCl_3$): 172.36, 141.13, 136.51, 133.95, 130.01, 129.11, 128.83, 128.66, 128.22, 127.68, 127.56, 71.87, 53.19, 52.38

Mass (EI^+) m/z (%): 343 (7), 285 (45), 284 (58), 283 (100), 193 (48), 178 (49), 177 (81).

IR (KBr): υ 3065, 3020, 2961,1724, 1442, 1370, 1290, 1173, 1064, 890,701 cm^{-1}

(*S*)-methyl 2-(1H-dibenzo[c,e]azepin-2(3H)-yl)-3-methylbutanoate (16)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.48 (m, 2H), 7.45-7.33 (m, 6H), 3.66-3.63 (d, *J* = 12.8 Hz, 1H), 3.56 (s, 3H), 3.57-3.54 (d, *J* = 12.8 Hz, 1H), 3.08-3.06 (d, *J* = 9.6 Hz, 1H), 2.27-2.18 (m, 1H), 1.28 (s, 1H), 1.09-1.08 (d, *J* = 6.4 Hz, 3H), 0.99-0.97 (d, *J* = 6.8 Hz, 3H)

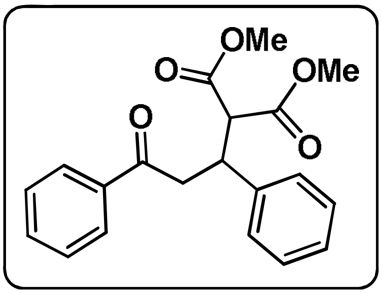
IR (KBr): υ 3063, 3021, 2957, 2868, 1728, 1447, 1367, 1241, 1193, 1147, 1076, 1007, 843, 721 cm^{-1}

2,2'-((([1,1'-biphenyl]-2,2'-diylbis(methylene))bis(methylazanediyl))bis(methylene)) diphenol (17)

A round bottom flask (50 mL capacity) was charged with **1** (1.0 g, 8.25 mmol) in dry methanol (5 mL) and stirred (10 min.). To this solution sodium brorohydride (0.874 g, 8.25 mmol) was added. The stirring was continued at ambient temperature and completion of reaction was checked by TLC to give secondary amine compound, which was (without purification) converted to tertiary amine **17** by reduction with sodiumcyanoborohydride (0.259 g, 4.13 mmol) and formaldehyde solution. After the completion of the reaction (monitored by tlc) the mixture was poured in ice cold water. The aqueous layer was extracted with ethyl acetate (3 X 100 mL). The combined extract was washed with water (2 X 100 mL) and dried over Na_2SO_4. The solution was evaporated to obtain crude product. The crude product was purified by column chromatography over silica gel using light petroleum ether:ethyl acetate as eluent to get final compound **17** as solid.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.58-7.56 (m, 2H), 7.48-7.44 (m, 2H), 7.38-7.34 (m, 2H), 7.18-7.15 (m, 2H), 6.91-6.89 (dd, *J* = 7.6 &1.6 Hz, 2H), 6.85-6.84 (dd, *J* = 8 & 1.2 Hz, 2H), 6.76-6.75 (dt, *J* = 7.2 & 1.2 Hz, 2H), 3.65-3.62 (d, *J* = 14.0 Hz, 2H), 3.53-3.50 (d, *J* = 14.0 Hz, 2H), 3.45-3.42 (d, *J* = 13.2 Hz, 2H), 3.19-3.16 (d, *J* = 13.2 Hz, 2H), 2.06 (s, 6H)

4-Acetyl-1,3-diphenylhexane-1,5-dione (**19**) [Table 3, entry 1]:



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (17 mg, 0.048 mmol, 10.0 mol %) and the Ligand **1** (11 mg, 0.026 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.48 mmol, 1.0 eq.), acety acetone (0.07 g ,0.72 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**9**) (0.10 g, 67%).

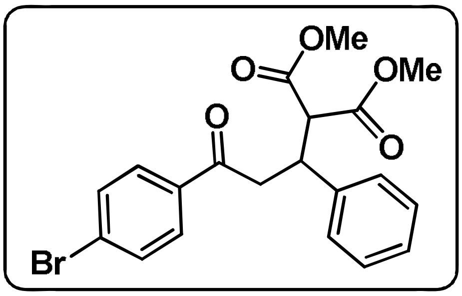
M. p. = 144-146 °C (Lit.[18g] 146-147 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H), 7.55-7.50 (m, 1H), 7.43-7.39 (m, 2H), 7.26-7.21 (m, 4H), 7.19-7.17 (m, 1H), 4.34-4.31 (d, *J* = 11.2 Hz, 1H), 4.26-4.19 (m, 1H), 3.36-3.29 (dd, *J* = 16.4 and 9.2 Hz, 1H), 3.22-3.17 (dd, *J* = 16.4 and 4 Hz, 1H), 2.29 (s, 3H), 1.89 (s, 3H).

Mass (EI^+) m/z (%) 266 (4), 264 (47), 248 (5), 247 (27), 246 (13), 209 (5), 208 (5), 147 (5), 146 (11), 130 (6), 119 (6), 114 (5), 106 (5), 104 (100), 102 (8), 90 (4), 78 (4), 76 (43), 68 (5).

IR (KBr): υ 3085, 3060, 3028, 2938, 2916, 1693, 1595, 1496, 1449, 1411, 1262, 1242, 1209, 1187, 1154, 1074, 1004, 982, 948, 919, 746, 700, 688 cm^{-1}

4-Acetyl-1-(4-bromophenyl)-3-phenylhexane-1,5-dione (**21)** [Table 3, entry 2].



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (12.5 mg, 0.035 mmol, 10.0 mol %) and the Ligand **1** (8.1 mg, 0.019 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate 4-acetyl-1-(4-bromophenyl)-3- phenylhexane-1,5-dione (0.10 g, 0.35 mmol, 1.0 eq.), acetyl acetone (0.05 g, 0.52 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**21**) (0.07 g, 54%).

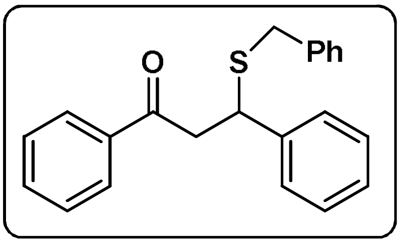
M. p. = 136-138 °C (Lit.[56] 129 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.67 (m, 2H), 7.57-7.52 (m, 2H), 7.26-7.23 (m, 2H), 7.21-7.17 (m, 3H), 4.32-4.29 (d, *J* = 10.8 Hz, 1H), 4.21-4.15 (m, 1H), 3.28-3.22 (dd, *J* = 16.4 and 8.8 Hz, 1H), 3.19-3.15 (dd, *J* = 16.4 and 4.4 Hz, 1H), 2.28 (s, 3H), 1.89 (s, 3H).

Mass (EI^+) m/z (%): 345 (22), 344 (21), 342 (41), 327 (26), 326 (25), 188 (5), 184 (100), 182 (94), 157 (5), 156 (14), 154 (20), 146 (20), 144 (6), 130 (7), 104 (5), 102 (7), 75 (7).

IR (KBr): υ 3062, 2949, 1692, 1586, 1495, 1454, 1399, 1357, 1260, 1242, 1208, 1154, 1073, 1009, 981, 816, 760, 772, 703 cm^{-1}

3-(Benzylthio)-1,3-diphenylpropan-1-one (**22**), [Table 3, entry 3]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (17.4 mg, 0.048 mmol, 10.0 mol %) and the Ligand **1** (11.1 mg, 0.026 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.48 mmol, 1.0 eq.), benzyl mercaptan (0.089 g, 0.72 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a white solid (**22**) (0.142 g, 89%).

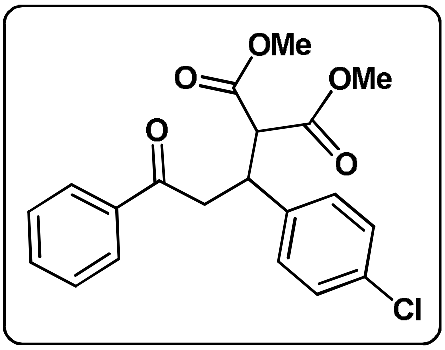
M. p. = 68-70 °C (Lit.[57] 70-72 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.84 (m, 2H), 7.55-7.53 (m, 1H), 7.43-7.37 (m, 4H), 7.33-7.20 (m, 8H), 4.47-4.45 (dd, *J* = 7.6 Hz, 1H), 3.58-3.44 (m, 4H).

Mass (EI^+) m/z (%): 331 (10), 242 (12), 241 (64), 240 (60), 209 (100), 120 (12), 105 (60), 90 (60), 77 (69).

IR (KBr): υ 3058, 3021, 2891, 1680, 1595, 1491, 1447, 1369, 1343, 1225, 1074, 980, 922, 725 cm^{-1}

4-Acetyl-3-(4-chlorophenyl)-1-phenylhexane-1,5-dione (**24**) (Table 3, entry 4):



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (14.9 mg, 0.041 mmol, 10.0 mol %) and the Ligand **1** (9.5 mg, 0.023 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate (E)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (0.10 g, 0.41 mmol, 1.0 eq.), acetyl acetone (0.06 g, 0.62 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**14**) (0.09 g, 65%).

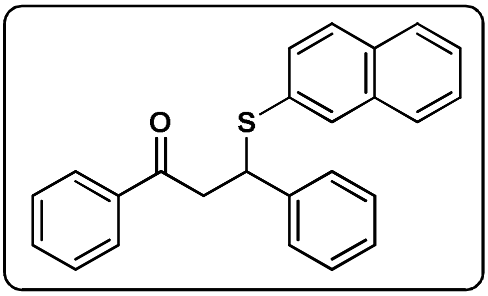
M. p. = 138-140 °C (Lit.[56] 141 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H), 7.57-7.52 (tt, *J* =7.2 and 1.2 Hz, 1H), 7.44-7.41 (m, 2H), 7.23-7.21 (m, 2H), 7.19-7.16 (m, 2H), 4.29-4.27 (d, *J* = 11.2 Hz, 1H), 4.25-4.19 (m, 1H), 3.33-3.26 (dd, *J* = 16.4 and 8.8 Hz, 1H), 3.21-3.16 (dd, *J* = 16.4 and 3.6 Hz, 1H), 2.28 (s, 3H), 1.92 (s, 3H).

Mass (EI^+) m/z (%) 301 (5), 300 (7), 299 (17), 298 (11), 283 (5), 282 (7), 280 (25), 18 (5), 119 (5), 106 (5), 104 (100), 78 (3), 76 (34).

IR (KBr): υ 3069, 2909, 1693, 1581, 1493, 1449, 1413, 1363, 1242, 1209, 1192, 1149, 1092, 1013, 953, 919, 823, 789, 750, 687, 594, 532 cm^{-1}

3-(naphthalen-2-ylthio)-1,3-diphenylpropan-1-one (**25**) [Table 3, entry 5]



In an oven dried round bottom flask (10 mL capacity) placed copper(II) trifluomethane sulfonate (17.4 mg, 0.048 mmol, 10.0 mol %) and the Ligand **1** (11.1 mg, 0.026 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.48 mmol, 1.0 eq.), 2-naphthalithiol (0.115 g, 0.72 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 90:10) as eluent to obtain a solid (**25**) (0.07 g, 40%).

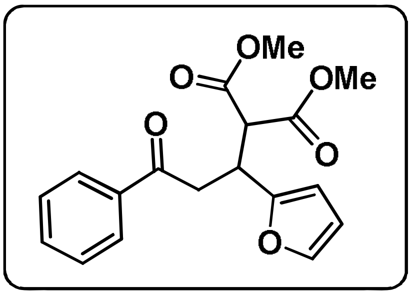
M. p. = 46-48 °C (Lit.[57])

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.86 (m, 2H), 7.79-7.76 (m, 2H), 7.72-7.68 (m, 2H), 7.55-7.51 (m, 1H), 7.46-7.37 (m, 7H) 7.28-7.24 (m, 2H) 7.21-7.19 (m, 1H) 5.10-5.07 (dd, *J* = 6 Hz, 1H) 3.73-3.65 (d, *J* = 17.2 and 8 Hz, 1H), 3.65-3.59 (d, *J* = 17.2 and 6.4 Hz, 1H).

Mass (EI^+) m/z (%): 369 (29), 368 (43), 367 (100), 208 (69), 158 (46), 114 (71), 104 (67), 76 (52).

IR (KBr): υ 3054, 3024, 1673, 1593, 1497, 1448, 1362, 1335, 1228, 1077, 983, 864, 817, 746, 713, 690 cm^{-1}

4-acetyl-3-(furan-2-yl)-1-phenylhexane-1,5-dione (**27**) [Table 3, entry 6]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (18.3 mg, 0.05 mmol, 10.0 mol %) and the Ligand **1** (11.6 mg, 0.027 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.51 mmol, 1.0 eq.), acetyl acetone (0.07 g, 0.76 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 90:30) as eluent to obtain a solid (**27**) (0.07 g, 47%).

Yield = 47 % (0.70 g).

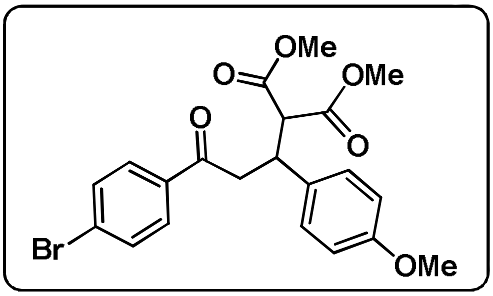
M. p. = 96-98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (m, 2H), 7.55 (m, 1H), 7.44 (m, 2H), 7.27 (1H), 6.22 (dd, *J* = 3.2 and 3.2 Hz, 1H), 6.07 (d, *J* = 3.2 Hz, 1H), 4.34 (m, 2H), 3.46 (m, 1H), 3.21 (m, 1H), 2.25 (s, 3H), 2.04 (s, 3H).

Mass (EI$^+$) m/z (%) 256.26 (28), 255.47 (49), 254.92 (37), 254.27 (64), 238.25 (13), 236.86 (100), 212.86 (21), 148.62 (8), 136.80 (18), 120.78 (16), 106.13 (24), 105.24 (64), 104.32 (66), 94.08 (10), 80.93 (8),78.17 (7), 76.87 (87), 68.85 (14), 64.92 (13), 50.90 (9).

IR (KBr): υ 3126, 3069, 2910, 1696, 1678, 1597, 1505, 1449, 1410, 1361, 1239, 1201, 1154, 1072, 1015, 961, 912, 815, 763, 735, 690 cm^{-1}

4-acetyl-1-(4-bromophenyl)-3-(4-methoxyphenyl)hexane-1,5-dione (**29**)[Table 3, entry 7]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethane sulfonate (7028 mg, 0.017 mmol, 10.0 mol %) and the Ligand **1** (11.4 mg, 0.032 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate chalcone (0.10 g, 0.32 mmol, 1.0 eq.), acetyl acetone (0.05 g, 0.47 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 90:30) as eluent to obtain a solid (**29**) (0.07 g, 54%).

Yield = 54 % (0.71 g).

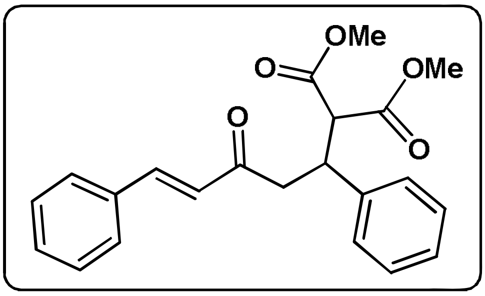
M. p. = 72-76 °C.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.70 (m, 2H), 7.56 (m, 2H), 7.11 (m, 2H), 6.77 (m, 2H), 4.26 (d, *J* = 10.8 Hz, 1H), 4.16-4.09 (m, 1H), 3.74 (s, 3H), 3.23-3.12 (m, 2H), 2.27 (s, 3H), 1.89 (s, 3H).

Mass (EI$^+$) m/z (%) 376.31 (8), 375.19 (25), 374.51 (17), 373.96 (18), 372.59 (57), 357.30 (17), 356.75 (11), 356.07 (25), 354.59 (46), 184.89 (100), 184.11 (40), 183.08 (63),182.32 (76), 160.79 (14), 156.96 (15), 156.21 (8), 155.21 (7), 154.48 (15), 133.20 (18), 103.70 (13), 90.85 (9).

IR (KBr): υ 3003, 2955, 2850, 1691, 1611, 1585, 1514, 1464, 1399, 1359, 1256, 1184, 1072, 1034, 1008, 845, 825, 733 cm^{-1}

(E)-3-Acetyl-4,8-diphenyloct-7-ene-2,6-dione (**31**) [Table 3, entry 8]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (15.5 mg, 0.043 mmol, 10.0 mol %) and the Ligand **1** (9.87 mg, 0.024 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate (1E,4E)-1,5-diphenylpenta-1,4-dien-3-one (0.10 g, 0.43 mmol, 1.0 eq.), acetyl acetone (0.064 g, 0.64 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a white solid (**31**) (0.115 g, 81%).

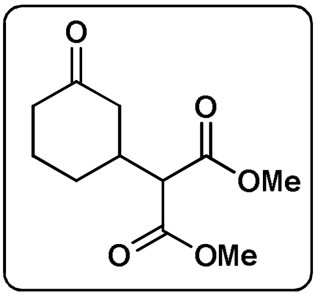
M. p. = 138-140 °C (Lit.[58] 139-141 °C).

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.48-7.46 (m, 2H), 7.44-7.40 (d, *J* = 16.4 Hz, 1H), 7.39-7.37 (m, 3H), 7.25-7.22 (m, 4H), 7.21-7.16 (m, 1H), 6.58-6.54 (d, *J* = 16.4 Hz, 1H), 4.32-4.29 (d, *J* = 11.2 Hz, 1H), 4.17-4.11 (m, 1H), 3.03-2.96 (dd, *J* = 15.6 and 9.2 Hz, 1H), 2.92-2.87 (dd, *J* = 15.6 and 4 Hz, 1H), 2.29 (s, 3H). 1.89 (s, 3H)..

Mass (EI$^+$) m/z (%): 315 (25), 290 (86), 273 (35), 272 (90), 144 (42), 131 (58), 130 (64), 102 (100).

IR (KBr): υ 3031, 2891, 1693, 1655, 1495, 1450, 1356, 1261, 1201, 1085, 975, 748, 703cm^{-1}

3-(2,4-Dioxopentan-3-yl)cyclohexanone (**33**) [Table 3, entry 9].



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10 g, 1.04 mmol, 1.0 eq.), acetyl acetone (0.17 g, 1.56 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a yellow solid (**33**) (0.167 g, 82%).

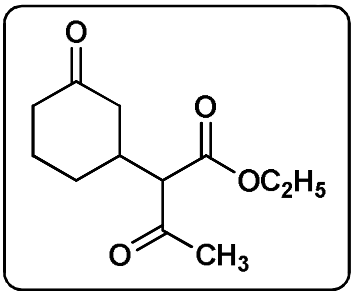
M. p. = 52-54 °C (Lit.[59] 53-54 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66-3.63 (d, *J* = 10 Hz, 1H), 2.74-2.64 (m, 1H), 2.4-2.39 (m, 1H), 2.34-2.22 (m, 2H), 2.19 (s, 3H), 2.17 (s, 3H), 2.09-2.01 (m, 2H), 1.81 (m, 1H), 1.77-1.66 (m, 1H), 1.43-1.33 (m, 1H).

Mass (EI$^+$) m/z (%) 152 (53), 111 (18), 110 (16), 107 (10), 99 (7), 96 (100), 95 (10), 84 (15), 83 (11), 82 (13), 68 (18), 67 (13), 66 (7), 54 (17).

IR (KBr): ν 2956, 2873, 2848, 1711, 1427, 1361, 1327, 1264, 1218, 1154, 1063, 1041, 975, 947, 906, 868, 832, 778, 757, 674, 627, 600, 565, 505 cm^{-1}

Ethyl 3-oxo-2-(3-oxocyclohexyl)butanoate (**34**) [Table 3, entry 10]



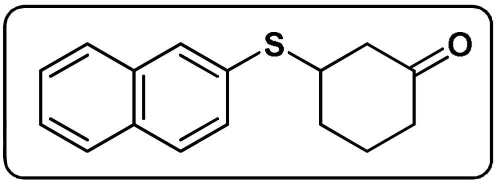
In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10 g, 1.04 mmol, 1.0 eq.), ethyl aceto aceteate (0.203 g, 1.56 mmol, 1.5 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 70:30) as eluent to obtain a colorless oil (**34**) [60] (0.198 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25-4.18 (m, 3H, CH_2-CH_3 and CH-CO protons merged) 3.76-3.75 (d, *J* = 6.4 Hz, 1H), 3.46-3.38 (m, 2H), 2.61-2.58 (m, 2H), 2.43-2.35 (m, 4H), 2.31-2.22 (m, 8H), 2.19-1.26 (m, 15H).

Mass (EI$^+$) m/z (%) 226 (M$^+$) (5), 182 (16), 152 (29), 129 (39), 109 (14), 96 (100), 95 (38), 80 (32).

IR (KBr): υ 2942, 2870, 1734, 1714, 1448, 1424, 1360, 1252, 1227, 1156, 1097, 1024, 869cm.$^{-1}$

3-(Naphthalen-3-ylthio)cyclohexanone (**35**) [Table 3, entry 11]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethane sulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), naphthalene-2-thiol (0.20 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a white solid (**35**) (0.158 g, 81 %).

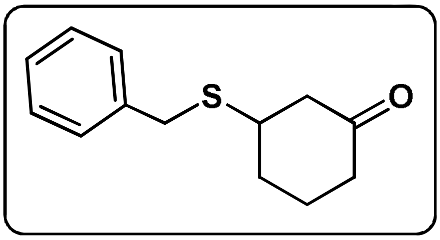
M. p. = 46-48 °C. (lit.[57] 48 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.91 (d, *J* = 1.2 Hz, 1H), 7.83-7.78 (m, 3H), 7.53-7.47 (m, 3H), 3.55-3.54 (m, 1H), 2.76-2.71 (m, 1H), 2.46-2.42 (m, 1H), 2.39-2.26 (m, 2H), 2.24-2.13 (m, 2H), 1.80-1.73 (m, 2H).

Mass (EI^+) m/z (%) 258 (12), 257 (42), 256 (43), 255. (73), 255 (71), 162 (10), 161 (25), 160 (40), 159 (73), 159 (70), 157 (22), 148 (10), 128 (17), 127 (15), 125 (13), 116 (11), 114 (100), 96 (57), 68 (97), 54 (23).

IR (KBr): υ 3050, 2934, 2912, 1712, 1595, 1496, 1444, 1313, 1278, 1218, 969, 864, 817, 747 cm^{-1}

3-(Benzylthio)cyclohexanone (**36**) [Table 3, entry 12]



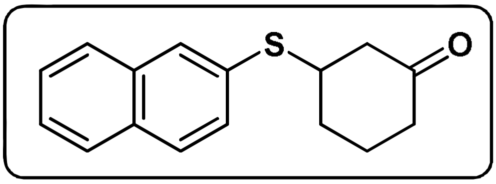
In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), and benzyl mercaptan (0.16 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a yellow liquid (**36**)[57] (0.127 g, 84 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.29 (m, 4H), 7.29-7.2 (m, 1H), 3.76-3.74 (ab, q, *J* = 13.6 Hz, and 2 Hz), 2.96-2.89 (m, 1H), 2.70-2.66 (m, 1H), 2.41-2.29 (m, 3H), 2.10 (m, 2H), 1.72-1.65 (m, 2H).

Mass (EI^+) m/z (%) 219 (48), 129 (17), 127 (30), 124 (12), 122 (100), 100 (13), 98 (10), 97 (46), 96 (47), 95 (9), 92 (23), 91 (58), 90 (39), 88 (9), 76 (9), 68 (38), 66 (13), 64 (30), 54 (15).

IR (Neat): υ 3060, 3027, 2942, 2867, 1712, 1601, 1494, 1452, 1421, 1341, 1314, 1283, 1222, 1175, 1069, 1030, 972, 879, 766, 704 cm^{-1}

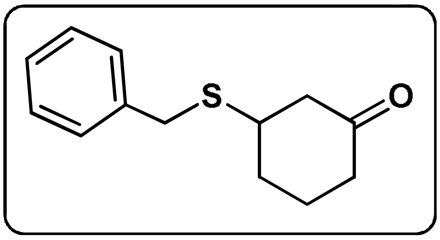
3-(Naphthalen-3-ylthio)cyclohexanone (**35**) [Scheme 9]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethane sulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), naphthalene-2-thiol (0.20 g, 1.25 mmol, 1.2 eq.) and piperidine (0.11 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a white solid (**35**) (0.158 g, 59 %).

Spectral data for **35**: [see Table 3, entry 11]

3-(Benzylthio)cyclohexanone (**36**) [Scheme 10]

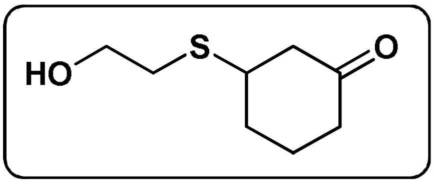


In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred (15 min). to this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), naphthalene-2-thiol (0.20 g, 1.25 mmol, 1.2 eq.) and benzyl mercaptan (0.16 g, 1.25 mmol, 1.2 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using light petroleum ether:ethyl acetate (100:0 to 80:20) as eluent to obtain a yellow liquid (**36**)[57] (0.127 g, 56.2 %) and a white solid (**35**) (0.06 g, 22.5 %).

Spectral data for **35**: [see Table 3, entry 11]

Spectral data for **36**: [see Table 3, entry 12]

3-(2-Hydroxyethylthio)cyclohexanone (**42**) [Scheme 11]



In an oven dried round bottom flask (10 mL capacity) placed copper(II)trifluomethanesulfonate (37.6 mg, 0.10 mmol, 10.0 mol %) and the Ligand **1** (24.0 mg, 0.057 mmol, 5.5 mol%) in 1,2–dichloroethane (2 mL) stirred for 15 min. To this mixture the appropriate cyclohex-2-enone (0.10, 1.04 mmol, 1.0 eq.), 2–mercapto ethanol (0.08 g, 1.04 mmol, 1 eq.) was added and resulting mixture was stirred at room temperature (6 d). After the completion of reaction (as monitored by TLC) the material was loaded on silica gel column for chromatographic separation using petroleum ether:ethyl acetate (100:0 to 60:40) as eluent to obtain a pale yellow oil (**42**)[61] (0.08 g, 44 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.76-3.73 (t, J = 6 Hz, and 2 Hz), 3.11 (m, 1H), 2.78 (t, J = 6 Hz, and 2 Hz), 2.73 (m, 1H), 2.43-2.34 (m, 3H), 2.15 (m, 3H), 1.74 (m, 2H).

Mass (EI$^+$) m/z (%) 173 (18), 155 (16), 143 (100), 98 (11), 97 (98), 96 (42), 95 (85), 78 (11), 73 (10), 69 (59), 68 (80), 67 (29), 54 (67).

IR (Neat): υ 3407, 2943, 2869, 1706, 1446, 1418, 1343, 1315, 1283, 1223, 1175, 1046, 1013, 972, 879 cm^{-1}

***General reaction condition*:**

Benzil (0.25 g, 1.19 mmol) was dissolved in acetonitrile (10 mL) in a two neck round bottom flask attached with water condenser. To this mixture K_2CO_3 (0.411 g, 2.98 mmol) was added and stirred for few minutes at room temperature and dimethylmalonate (0.157 mg, 1.19 mmol) was drop wise added. The reaction mixture was stirred at reflux temperature for 72 h. The reaction mixture was cooled to room temperature and the solvent was removed in vacuum, the residue was taken in saturated aqueous NH_4Cl, extracted with ethyl acetate (3 x 25 mL). The organic layer was washed with dilute aqueous NaOH (2x25 mL) and the ethyl acetate layer was dried on anhydrous sodium sulfate, and evaporated in vacuum. The crude white solid was purified over silica gel column (petroleum ether/ethyl acetate 95:5) to obtain pure compound **3** (0.175 g, 47 %Y) and further purified by recrystallization from acetonitrile. The aqueous NaOH layer was combined and acidified with cold dilute HCl, and extracted with ethyl acetate (3 x 25 mL), dried over anhydrous sodium sulfate, concentrated in vacuum to obtained a pale yellow liquid as crude product, purified over silica gel column (petroleum ether /ethyl acetate 90:10) to obtain pure compound **12**, as colorless liquid (0.12 g, 43% Y).

2-Oxo-1,2-diphenylethyl benzoate (benzoyl benzoin) (**49**)

Mp. = 130-132 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17-8.14 (2H, m), 8.05-8.02 (2H, m), 7.62-7.54 (4H, m), 7.49-7.39 (7H, m), 7.12 (1H, s).

^{13}C NMR (100 MHz $CDCl_3$): δ193.7, 166.1, 134.66, 133.7, 133.6, 133.4, 130.0, 129.4, 129.2, 128.9, 128.7, 128.5, 77.9.

Mass (EI$^+$): m/z (%) 316.07, 211.02 (17%), 106.01 (9%), 104.96 (100%), 77.01 (36%).

IR: ν cm^{-1}(KBr): 3070 (C-H Stretch aromatic), 2952 (C-H Stretch aliphatic), 1714 (Ar-COO), 1695 (Ar-CO), 1597, 1451, 1353, 1314, 1281, 1247, 1174, 1118, 1068, 1029, 956, 853, 758, 702, 590.

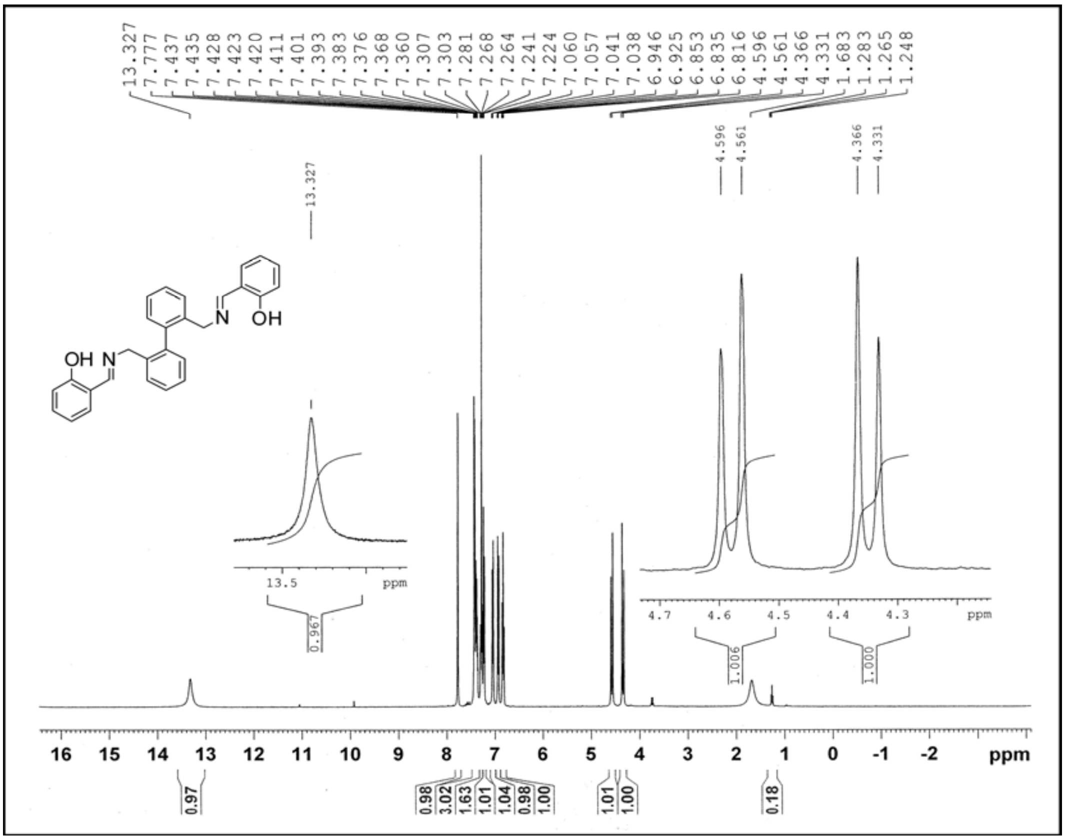
2-Benzoyl dimethylmalonate (**58**)

Colorless oil.

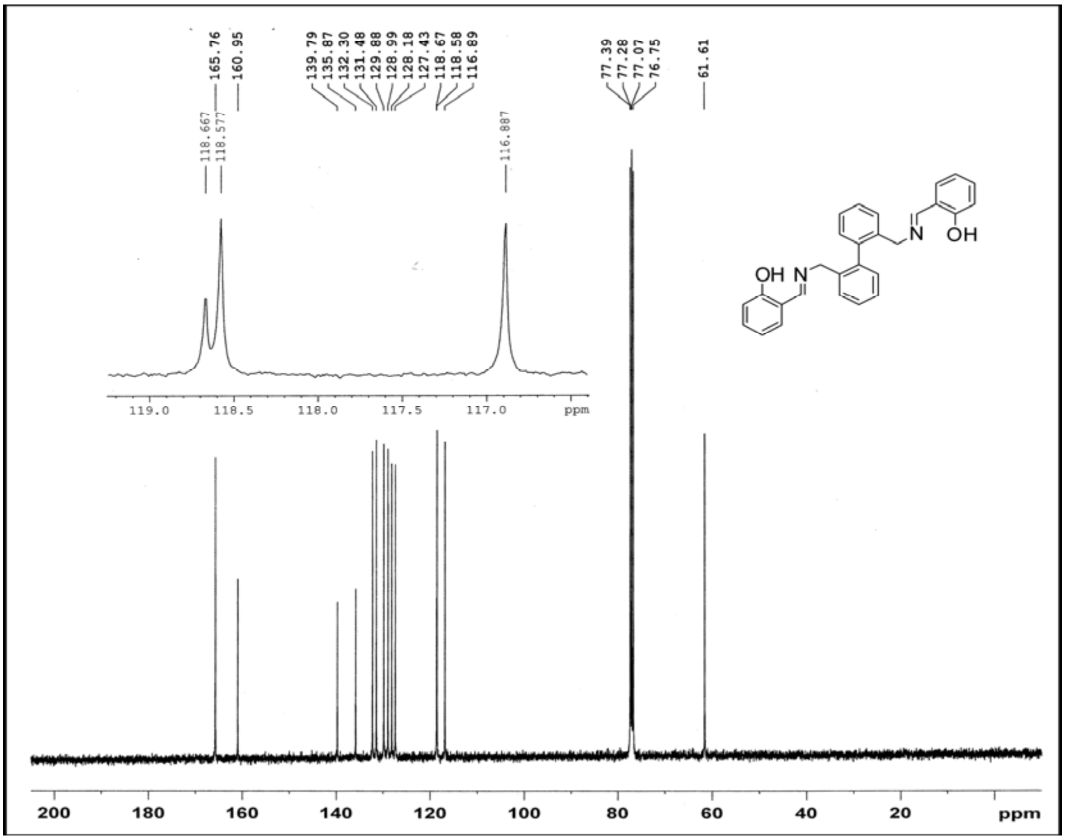
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.89 (2H, m), 7.65-7.60 (1H, m), 7.52-7.46 (2H, m), 5.36 (1H, s), 3.81 (6H, s).

Mass (EI$^+$): m/z (%) 237.2 (M+1), 236.3 (46%), 235.4 (100%), 205.1 (24%), 175.8 (23%), 106.1 (49%), 105.3 (72%), 104.3 (87%), 77.3 (49%), 76.5 (66%), 78.1 (11%), 58.9 (13%).

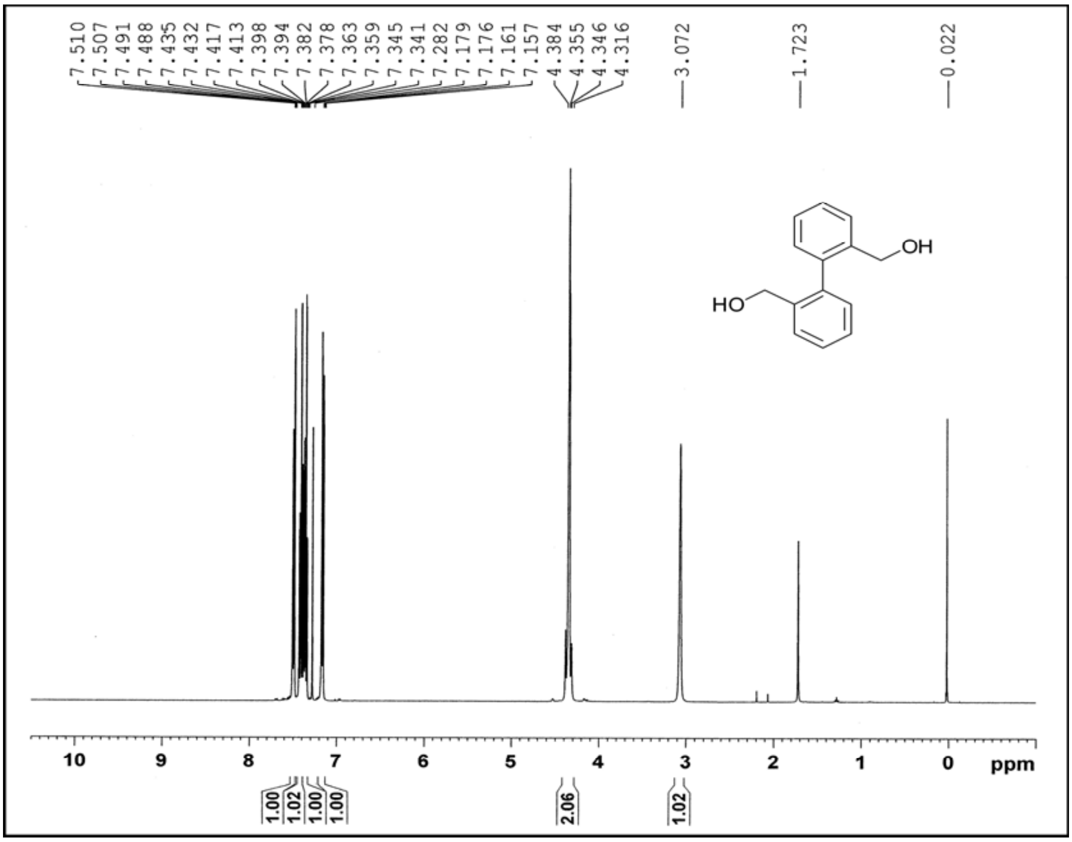
4.4 Spectral Data



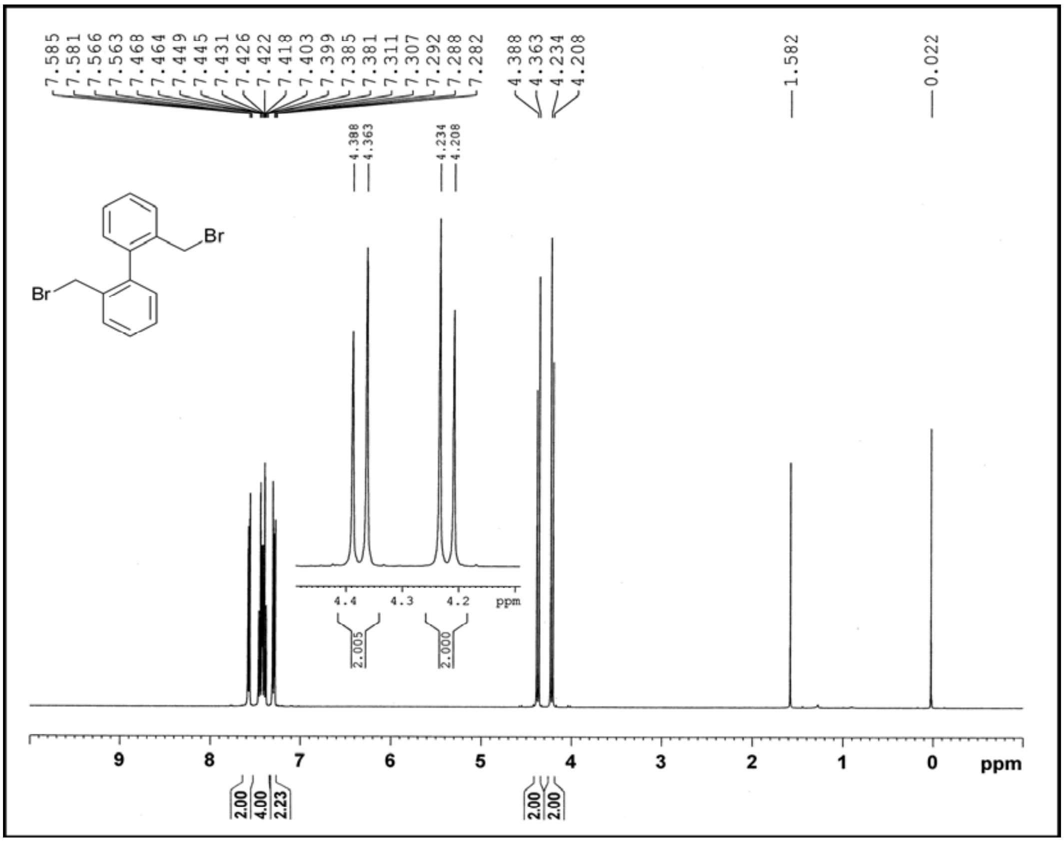
^{1}H-NMR Spectrum of Compound 1 in $CDCl_3$ (400 MHz)



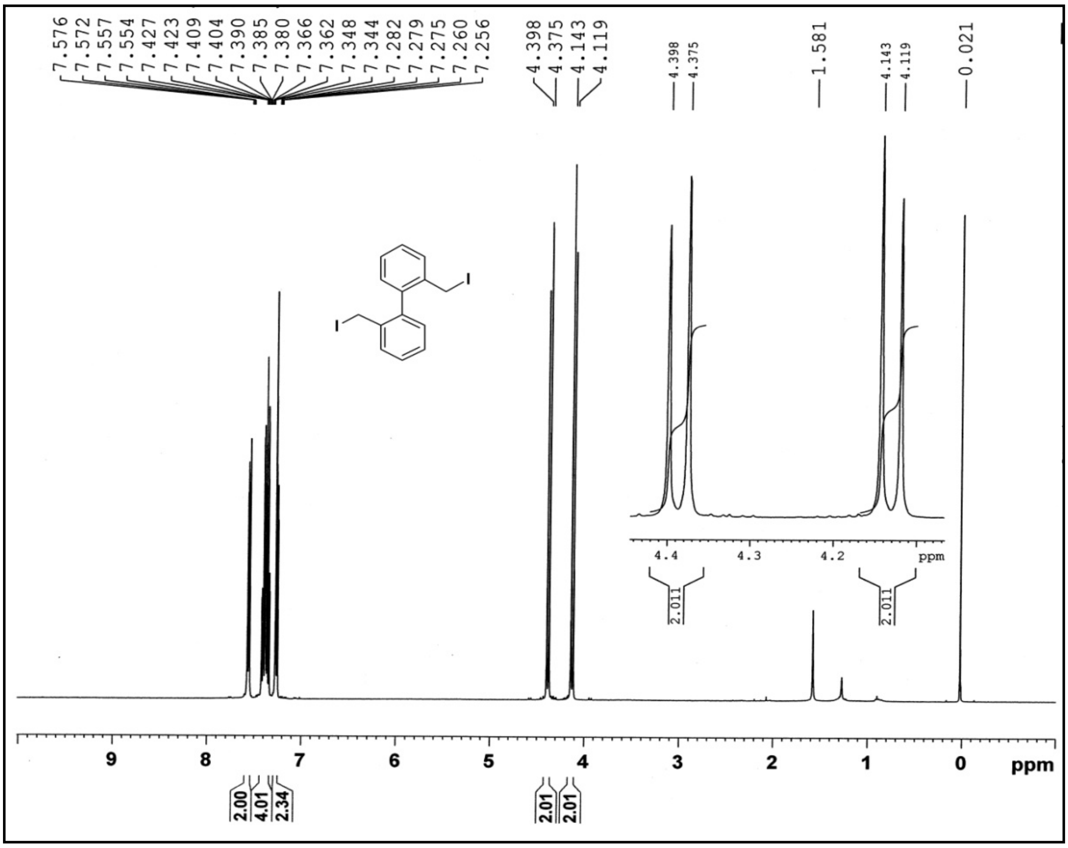
^{13}C-NMR Spectrum of Compound 1 in $CDCl_3$ (100 MHz)



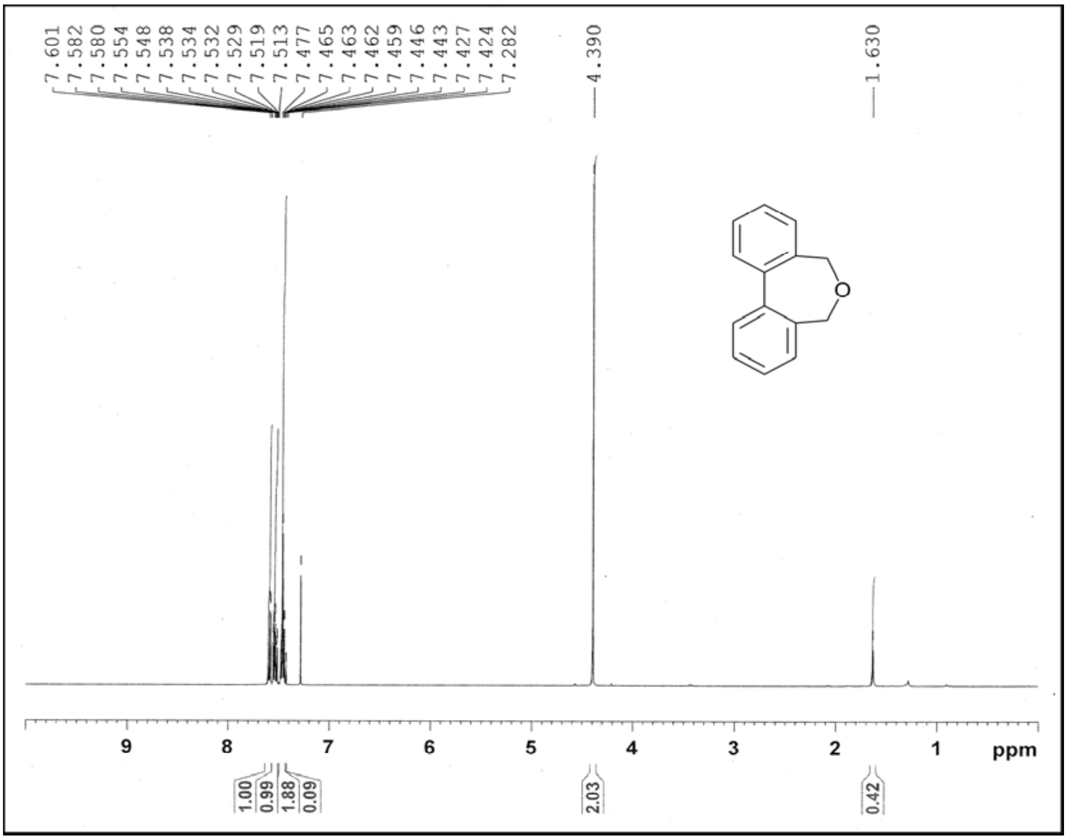
^{1}H-NMR Spectrum of Compound 4 in $CDCl_3$ (400 MHz)



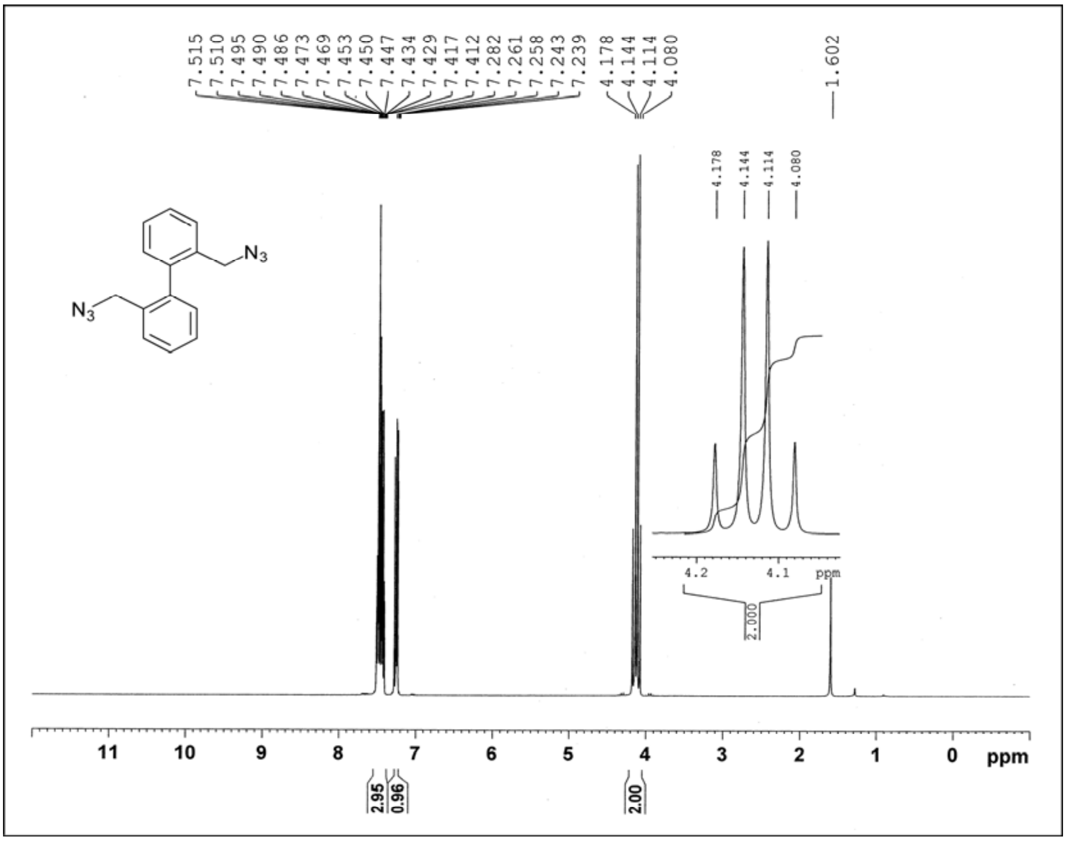
^{1}H-NMR Spectrum of Compound 5 in $CDCl_3$ (400 MHz)



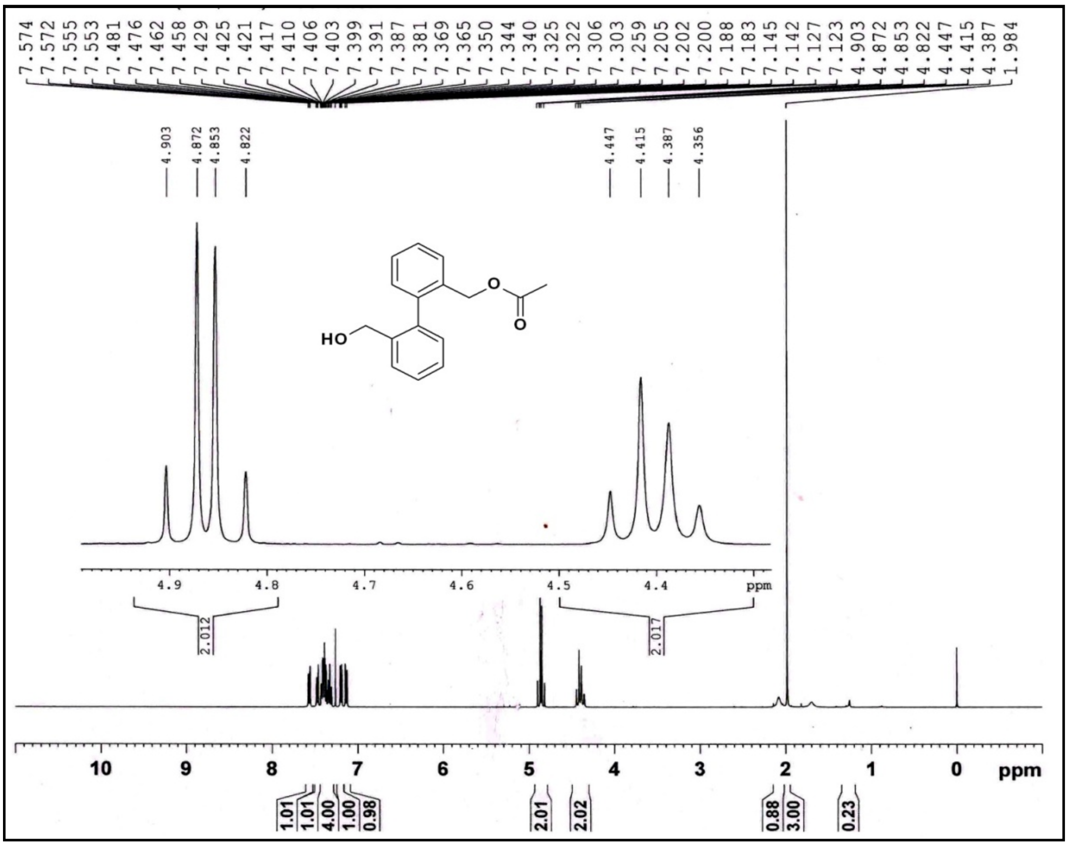
^{1}H-NMR Spectrum of Compound 6 in $CDCl_3$ (400 MHz)



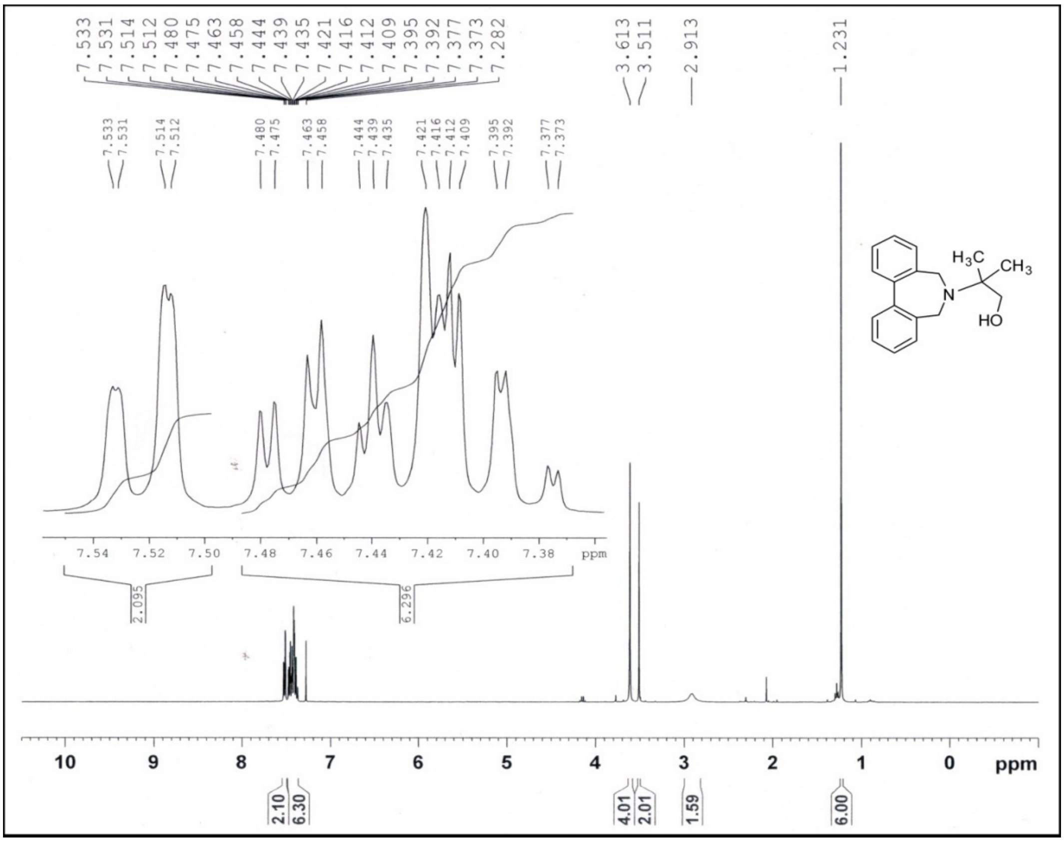
^{1}H-NMR Spectrum of Compound 7 in $CDCl_3$ (400 MHz)



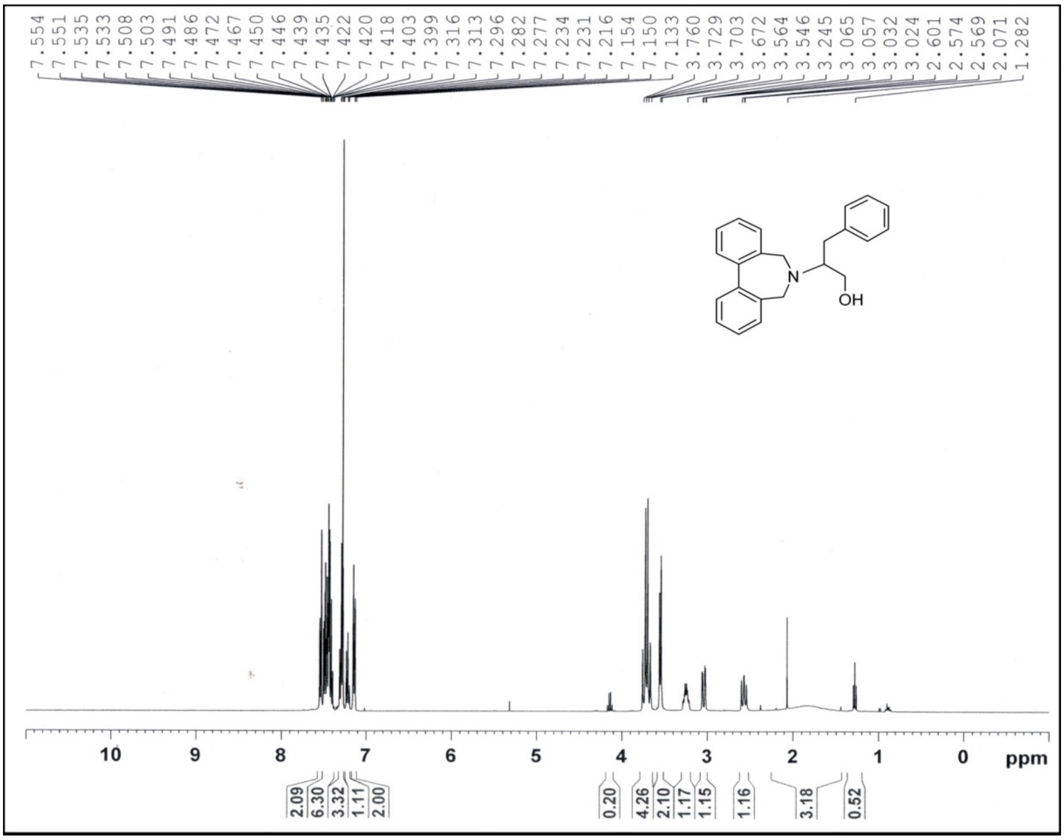
^{1}H-NMR Spectrum of Compound 8 in $CDCl_3$ (400 MHz)



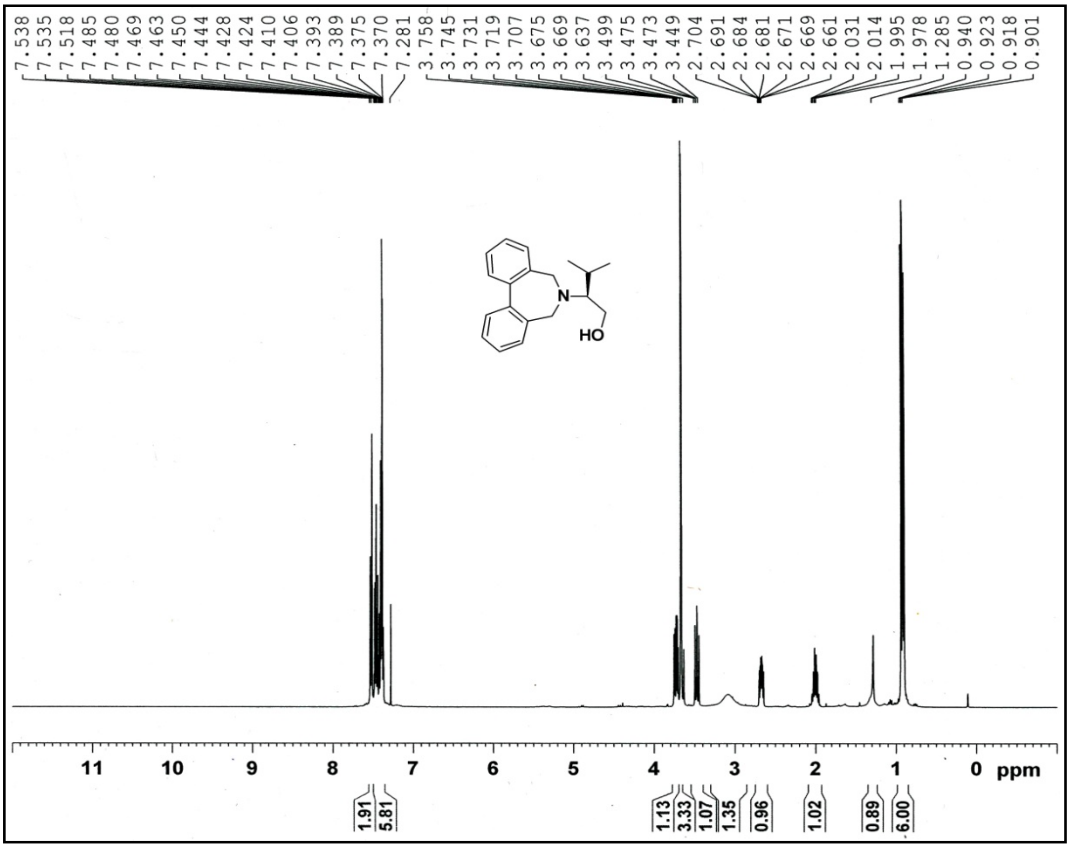
^{1}H-NMR Spectrum of Compound 4b in $CDCl_3$ (400 MHz)



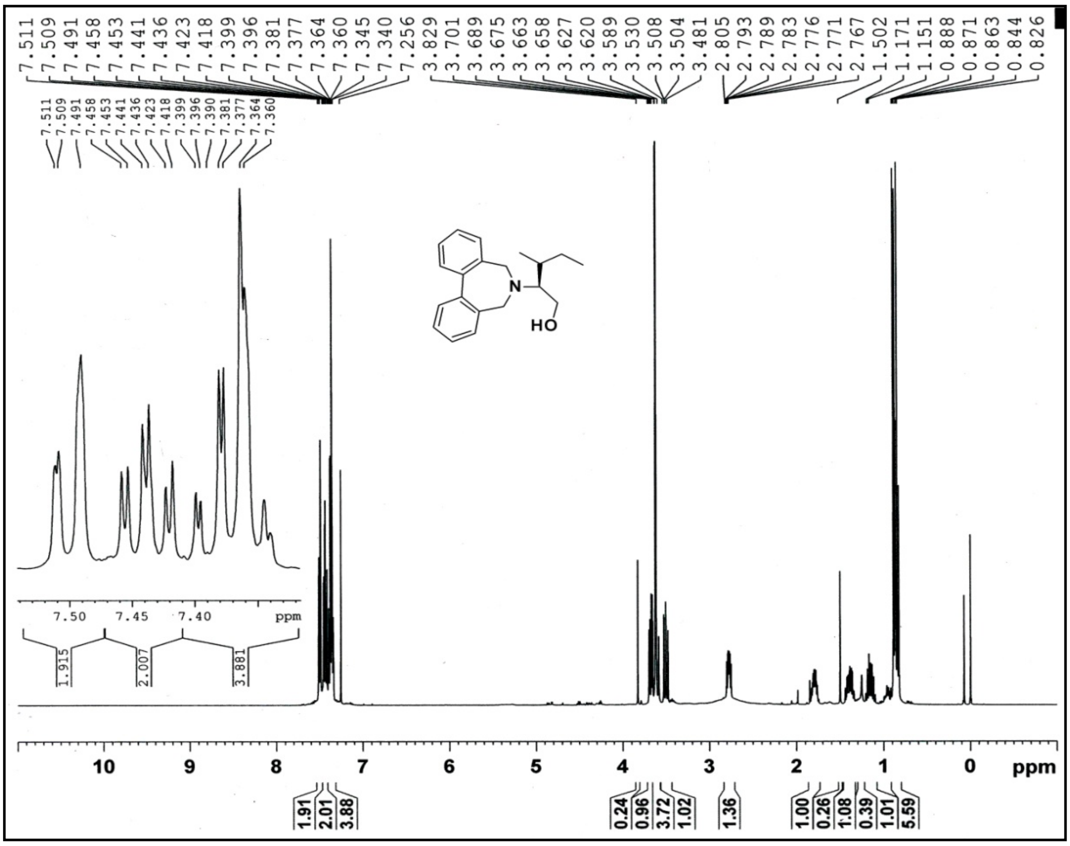
^{1}H-NMR Spectrum of Compound 10 in $CDCl_3$ (400 MHz)



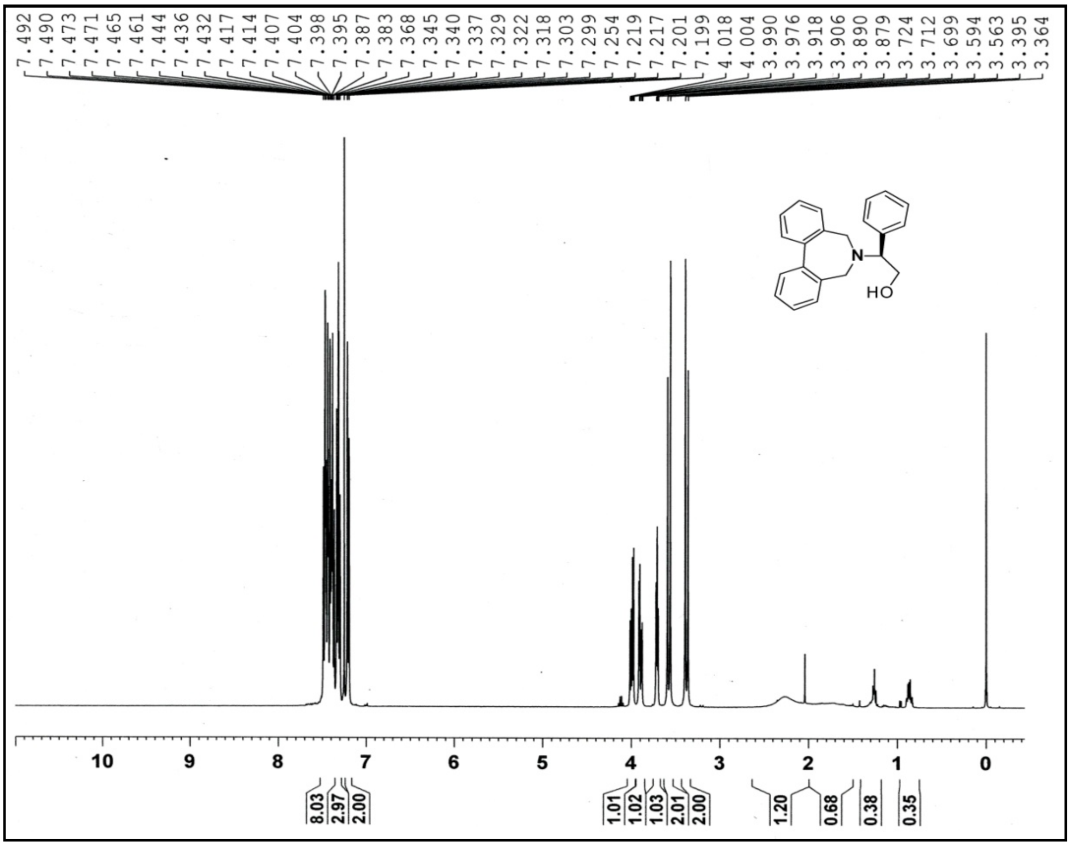
^{1}H-NMR Spectrum of Compound 11 in $CDCl_3$ (400 MHz)



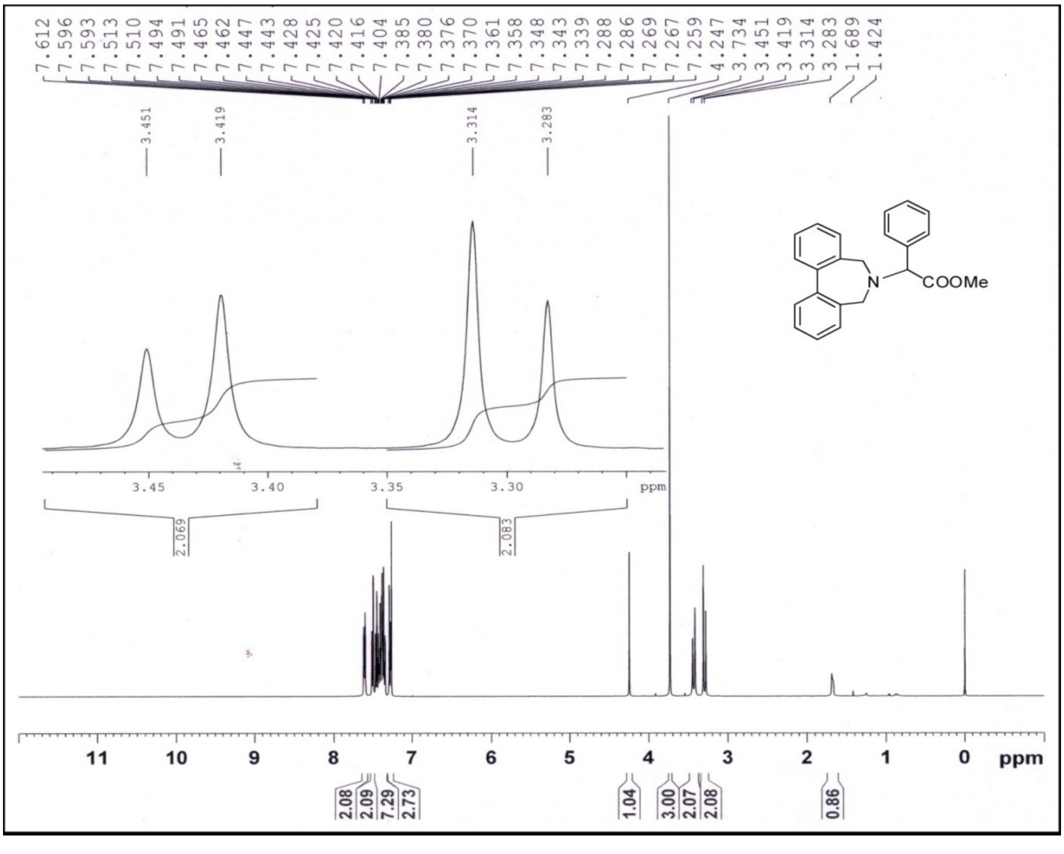
^{1}H-NMR Spectrum of Compound 12 in $CDCl_3$ (400 MHz)



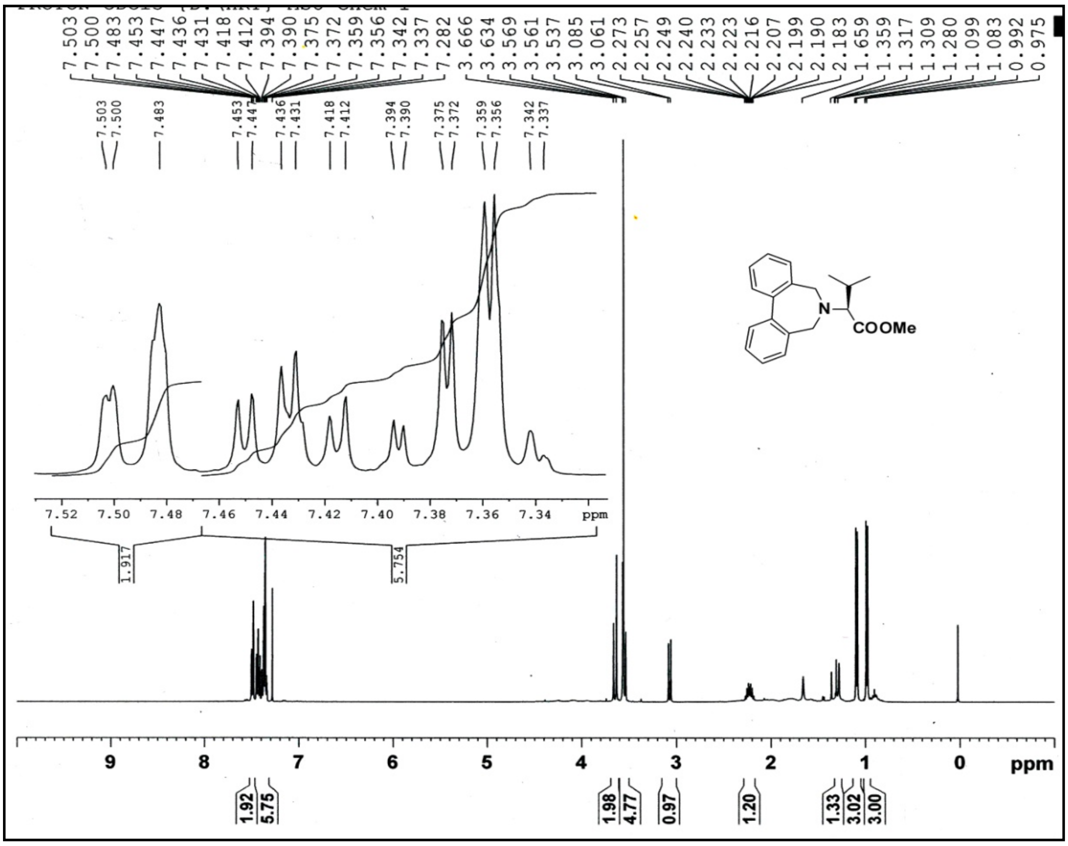
^{1}H-NMR Spectrum of Compound 13 in $CDCl_3$ (400 MHz)



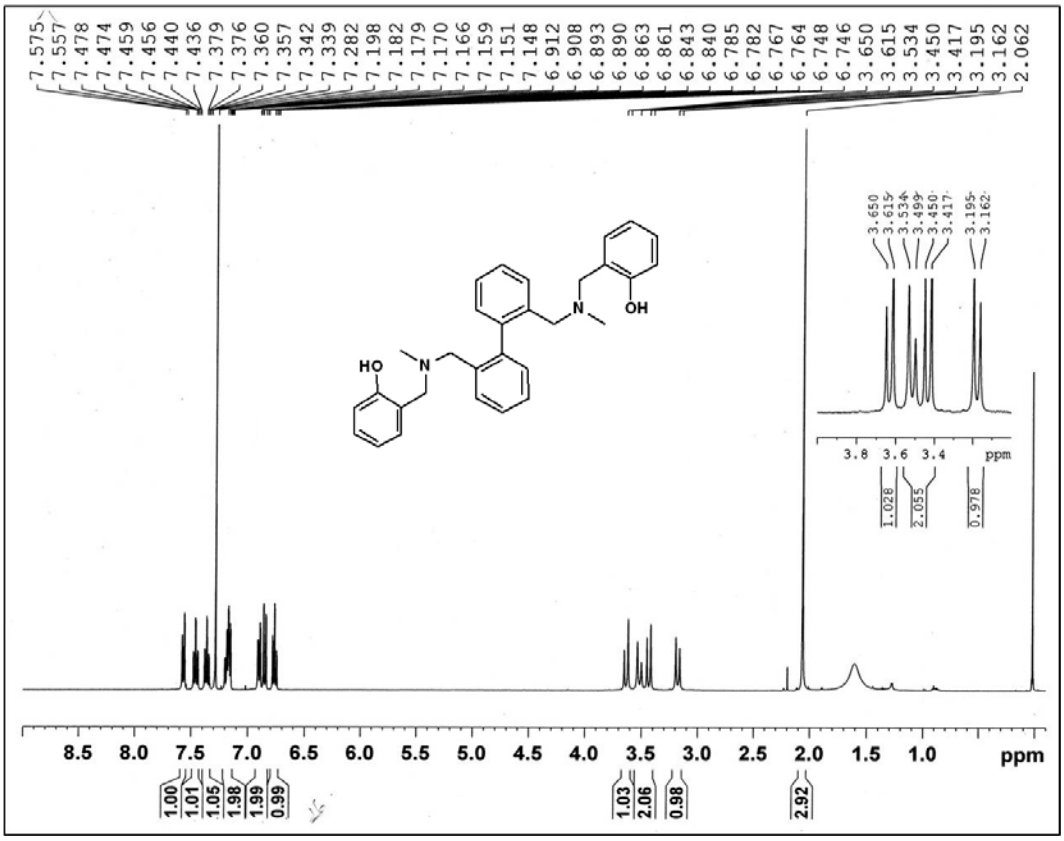
^{1}H-NMR Spectrum of Compound 14 in CDCl$_3$ (400 MHz)



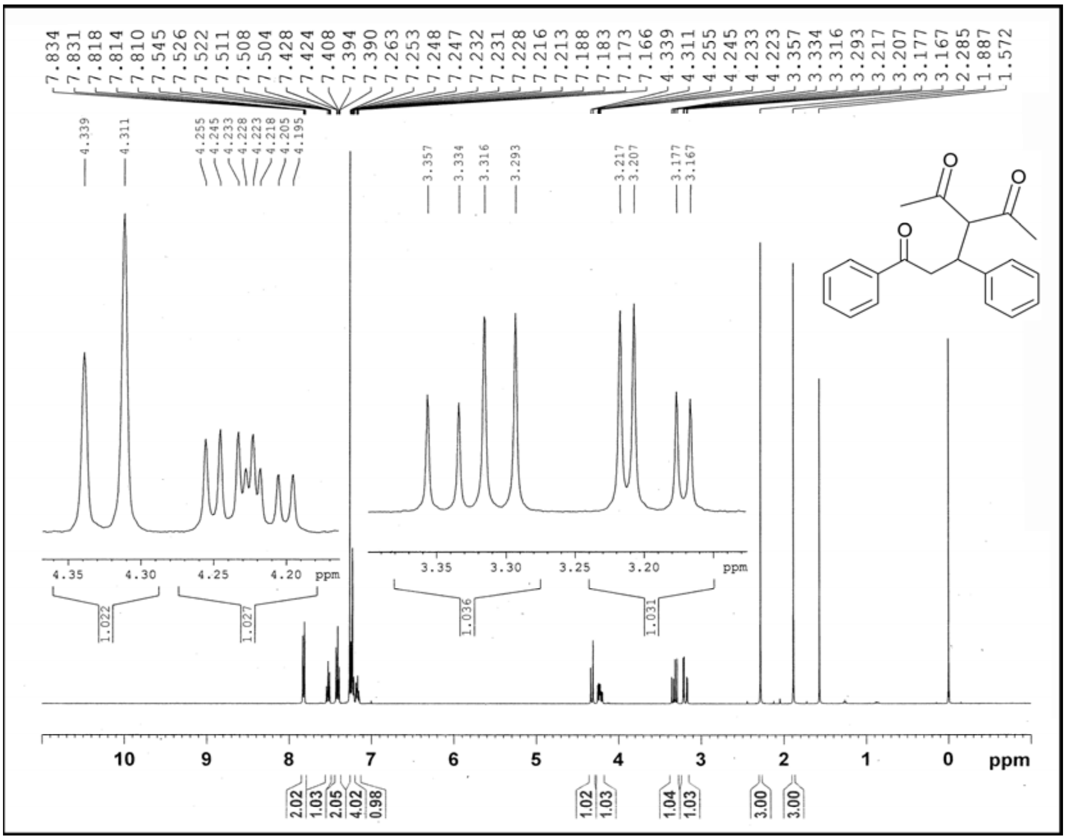
^{1}H-NMR Spectrum of Compound 15 in $CDCl_3$ (400 MHz)



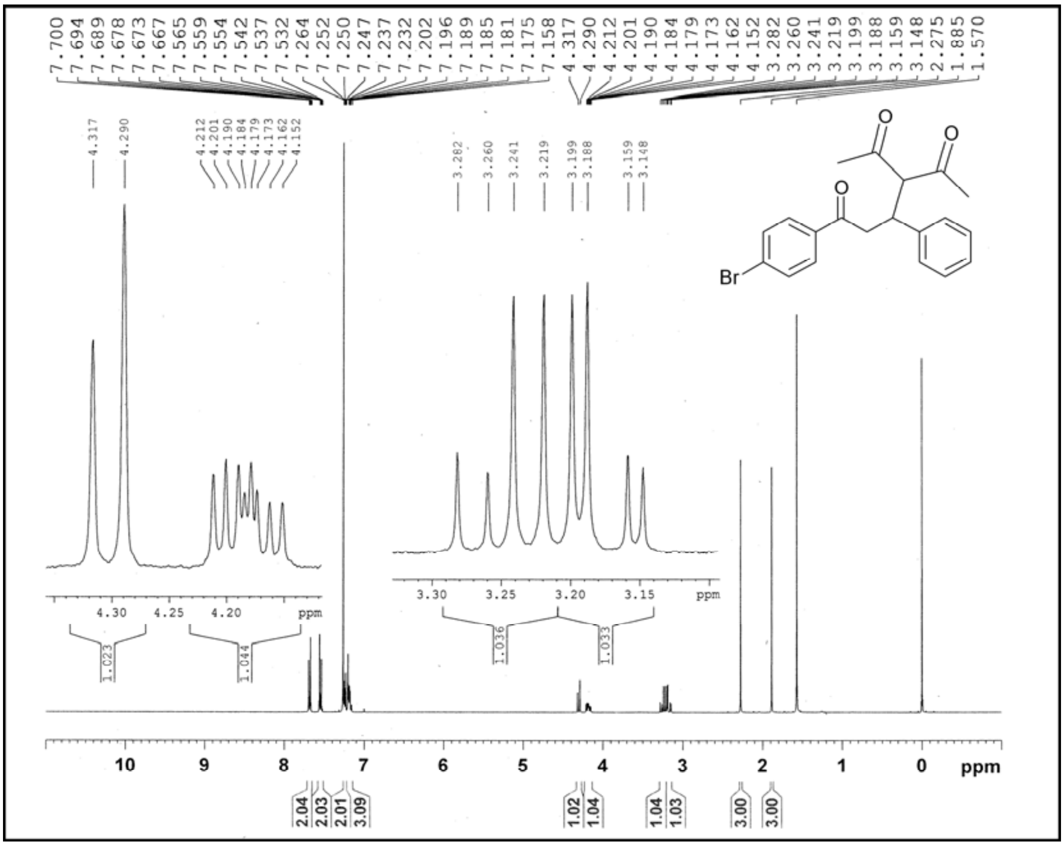
^{1}H-NMR Spectrum of Compound 16 in $CDCl_3$ (400 MHz)



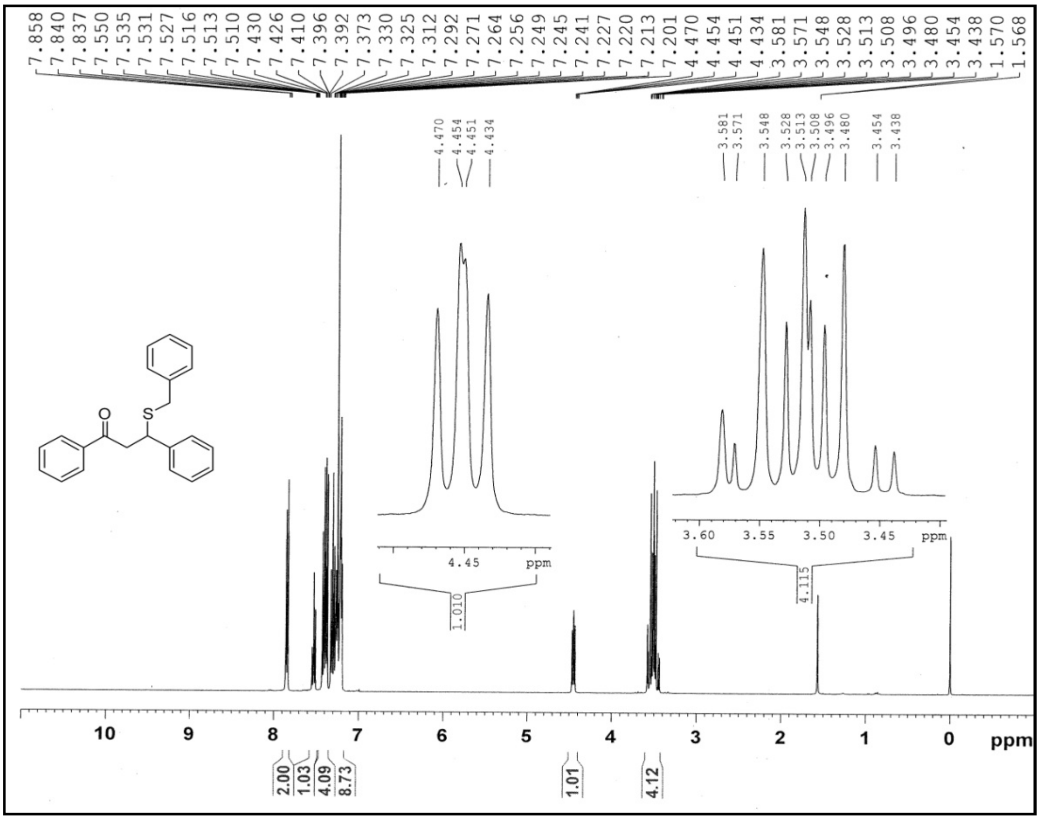
^{1}H-NMR Spectrum of Compound 17 in $CDCl_3$ (400 MHz)



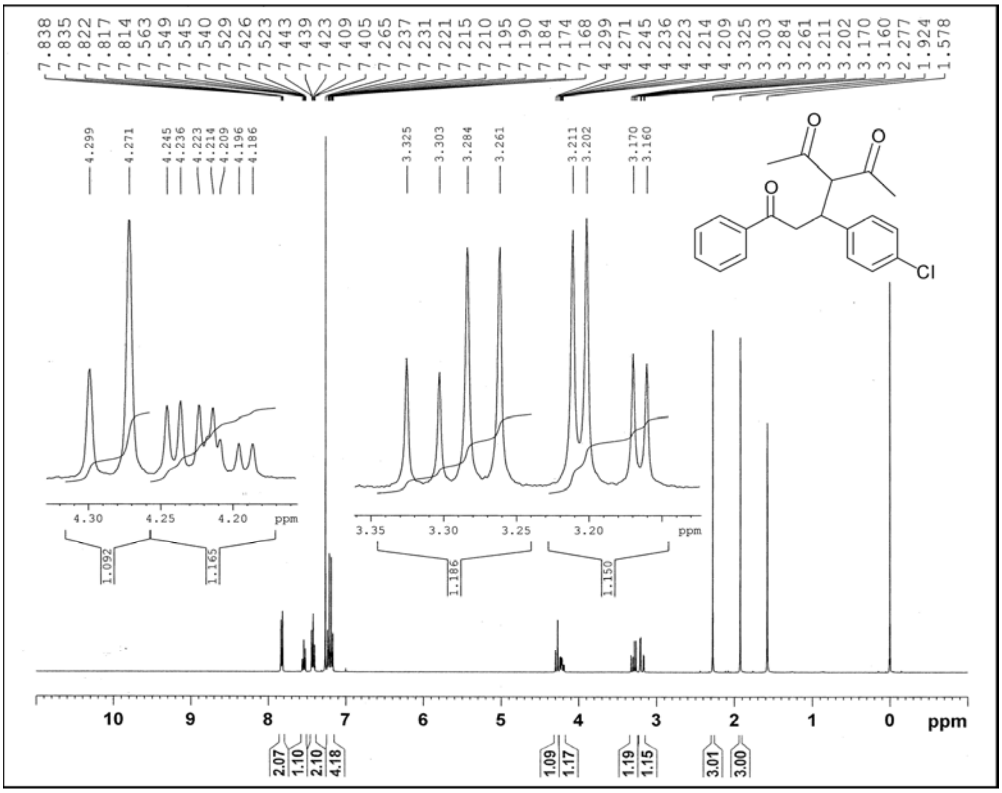
^{1}H-NMR Spectrum of Compound 19 in $CDCl_3$ (400 MHz)



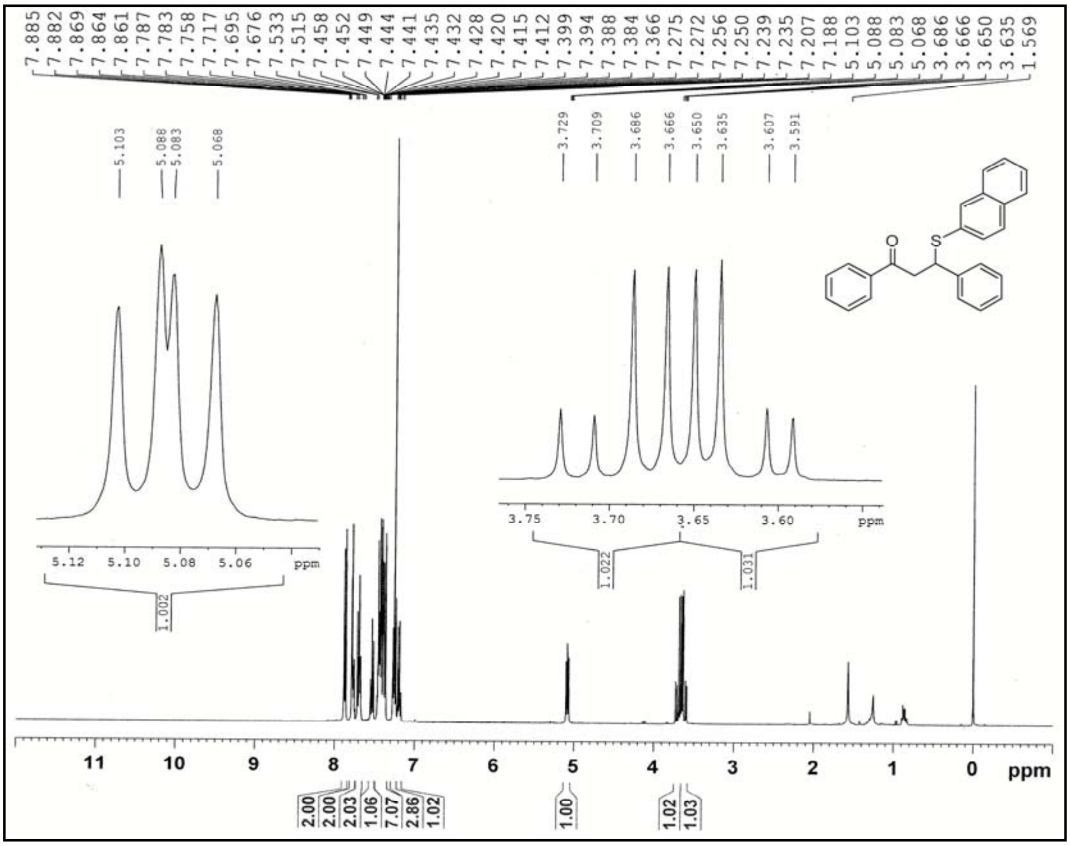
^{1}H-NMR Spectrum of Compound 21 in $CDCl_3$ (400 MHz)



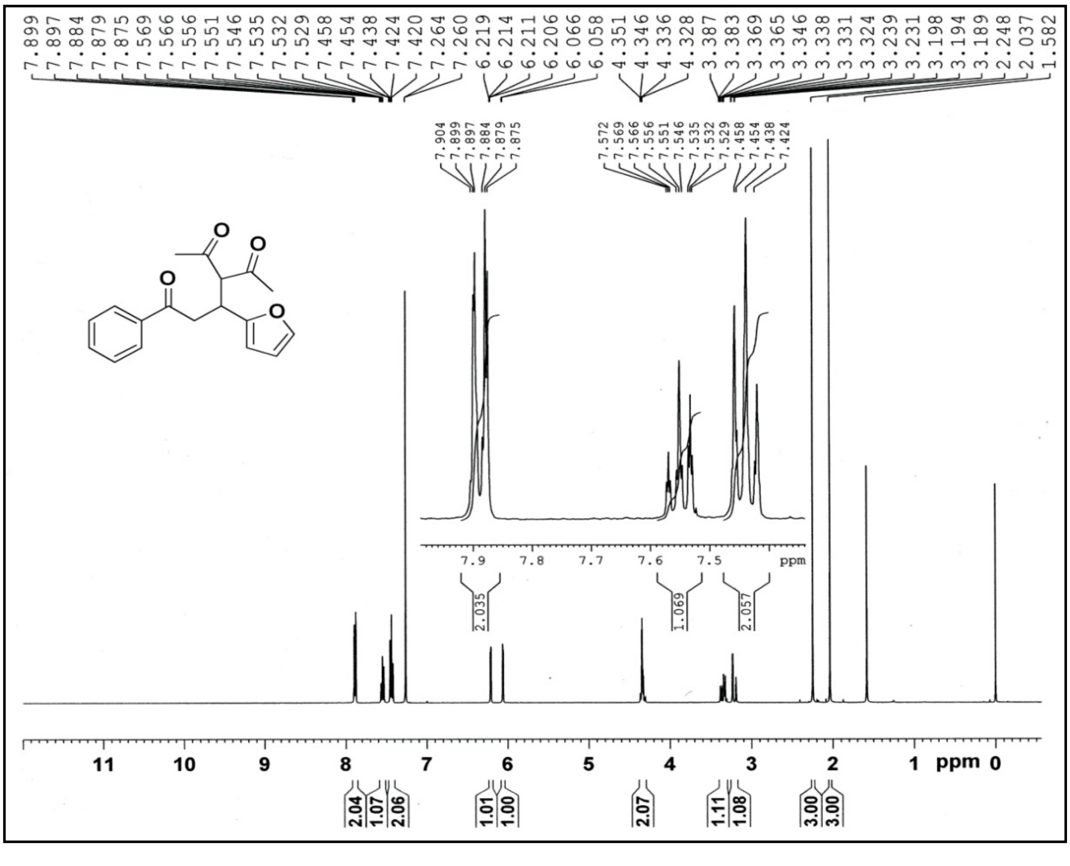
^{1}H-NMR Spectrum of Compound 22 in $CDCl_3$ (400 MHz)



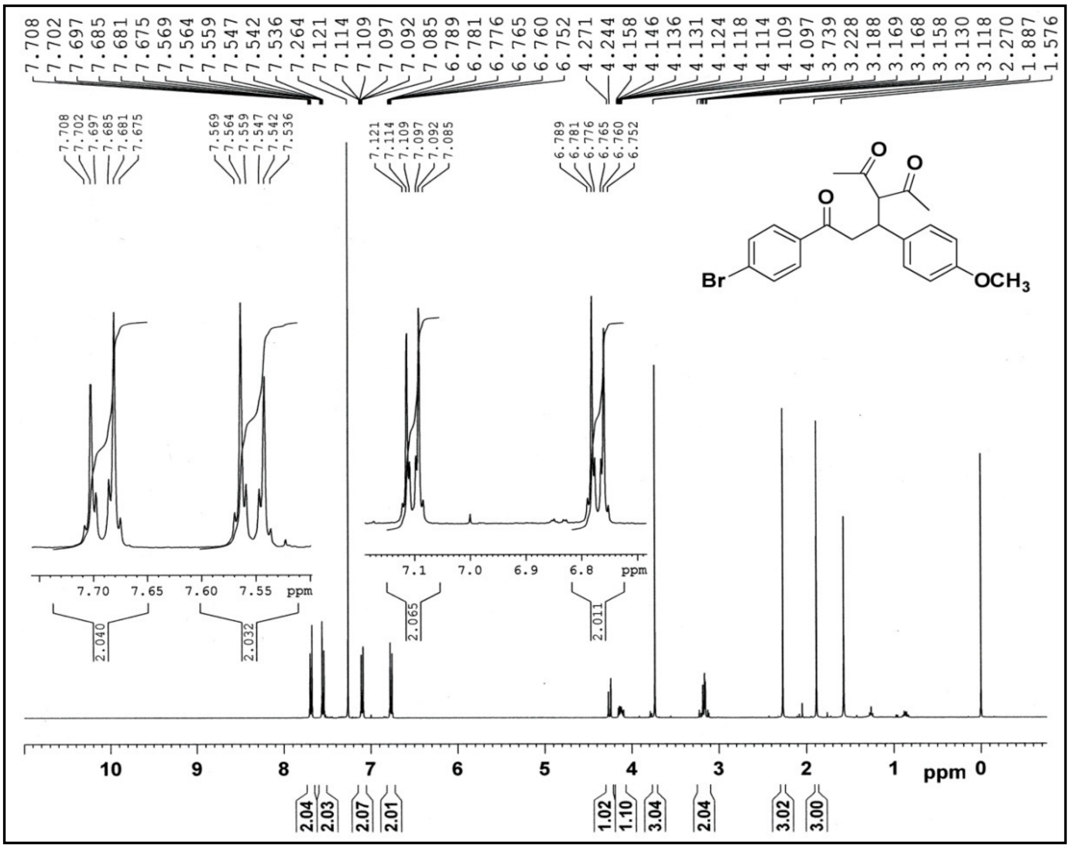
^{1}H-NMR Spectrum of Compound 24 in $CDCl_3$ (400 MHz)



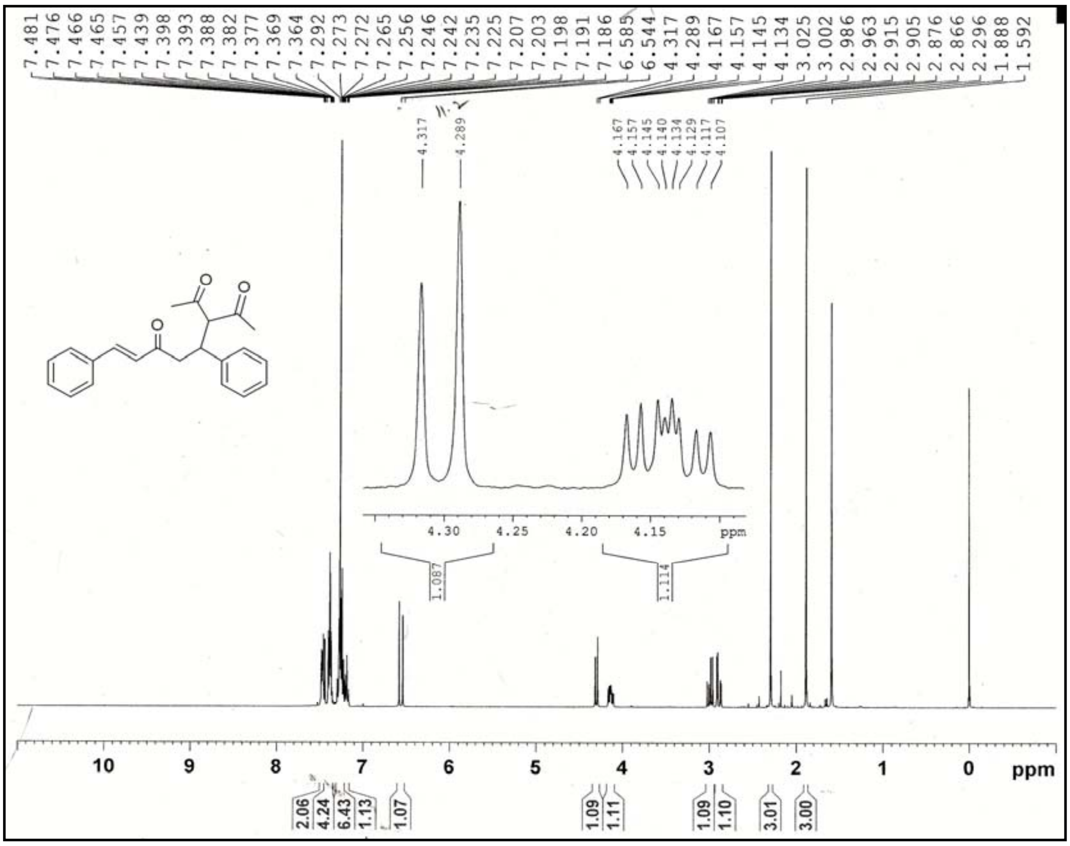
^{1}H-NMR Spectrum of Compound 25 in $CDCl_3$ (400 MHz)



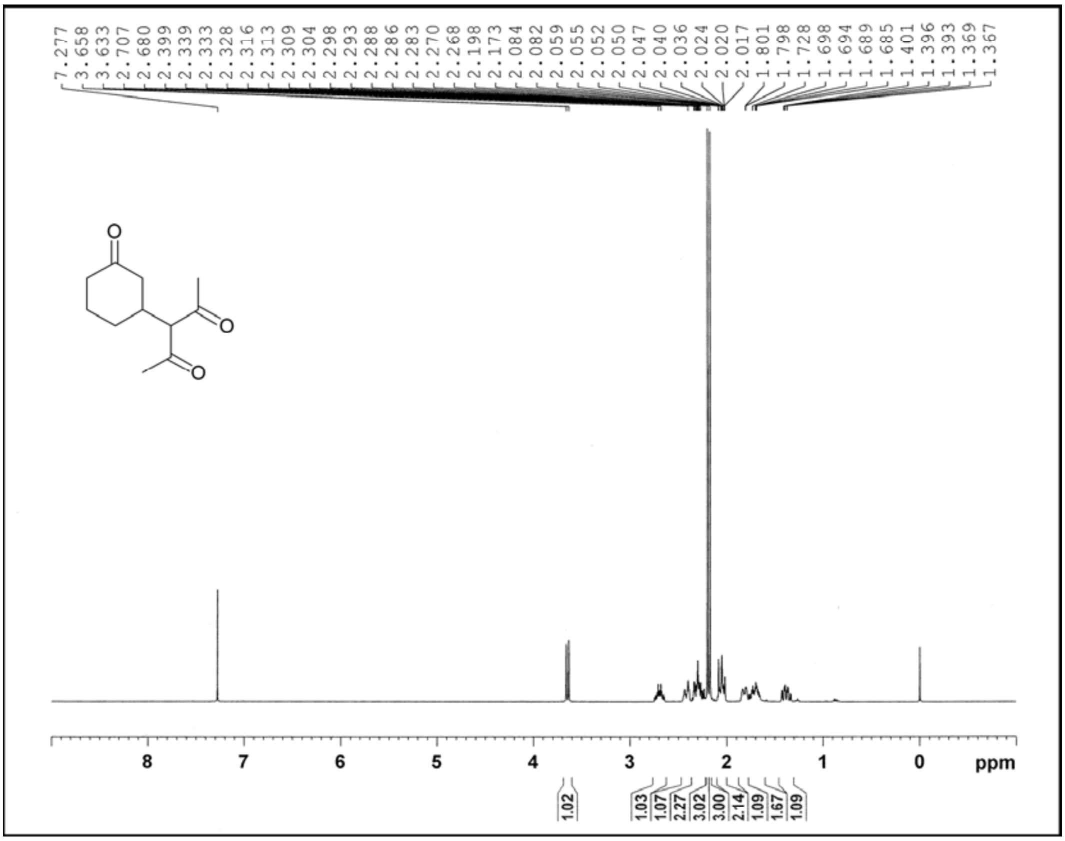
^{1}H-NMR Spectrum of Compound 27 in $CDCl_3$ (400 MHz)



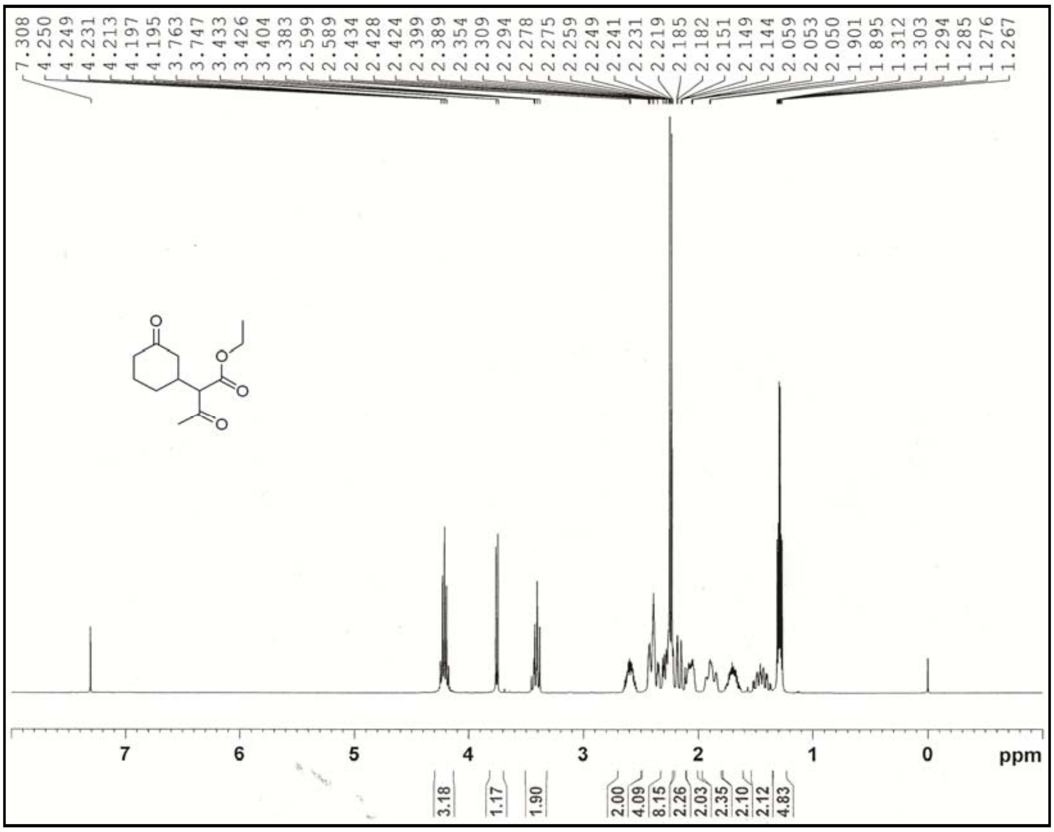
^{1}H-NMR Spectrum of Compound 29 in CDCl$_3$ (400 MHz)



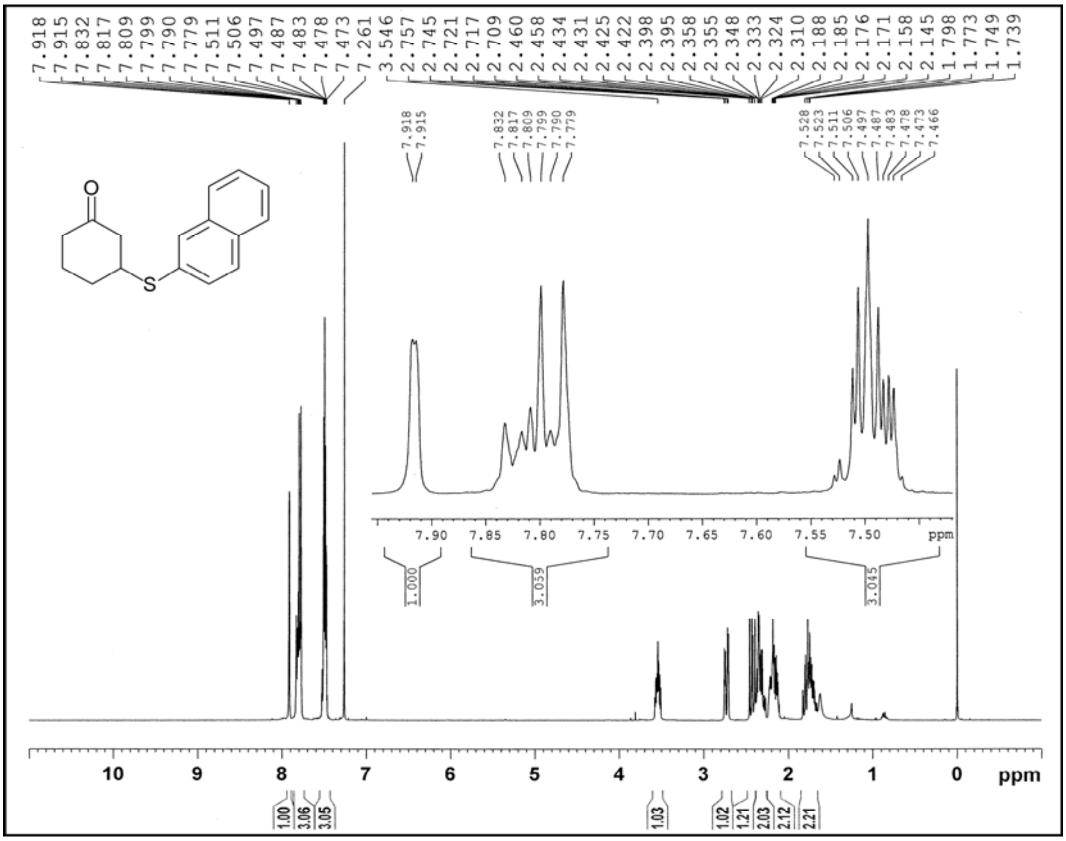
^{1}H-NMR Spectrum of Compound 31in CDCl$_3$ (400 MHz)



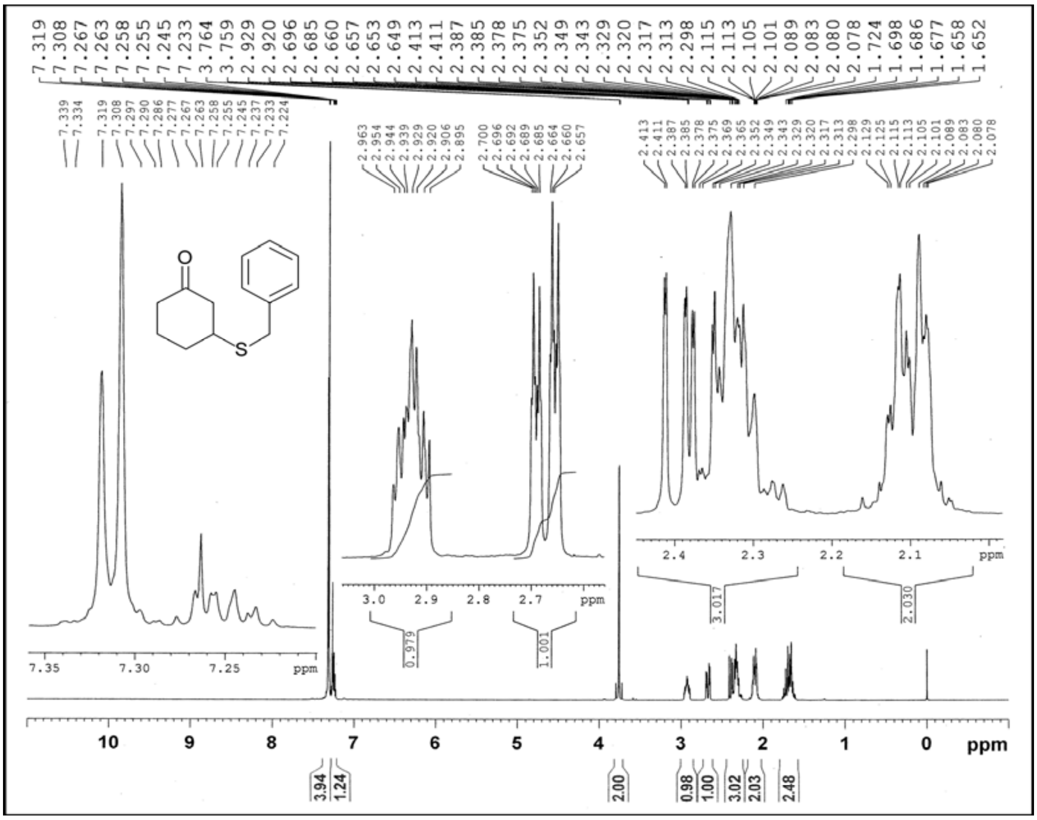
^{1}H-NMR Spectrum of Compound 33 in $CDCl_3$ (400 MHz)



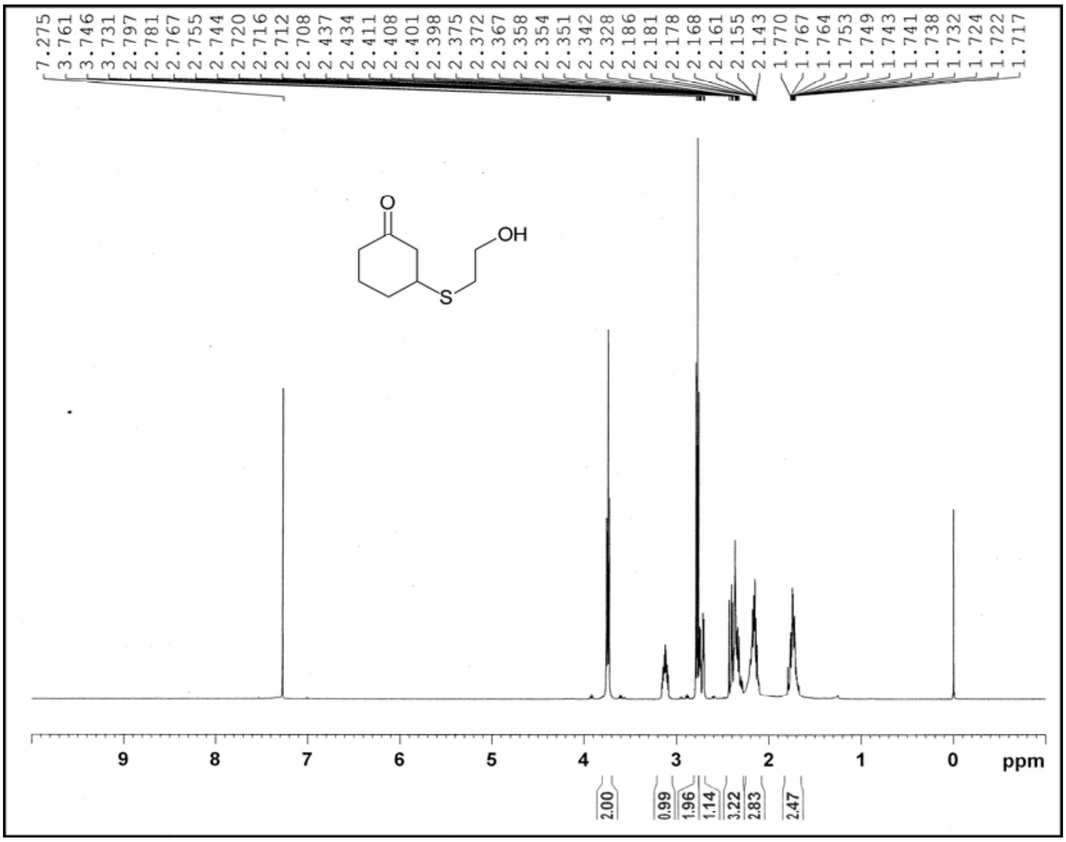
^{1}H-NMR Spectrum of Compound 34 in $CDCl_3$ (400 MHz)



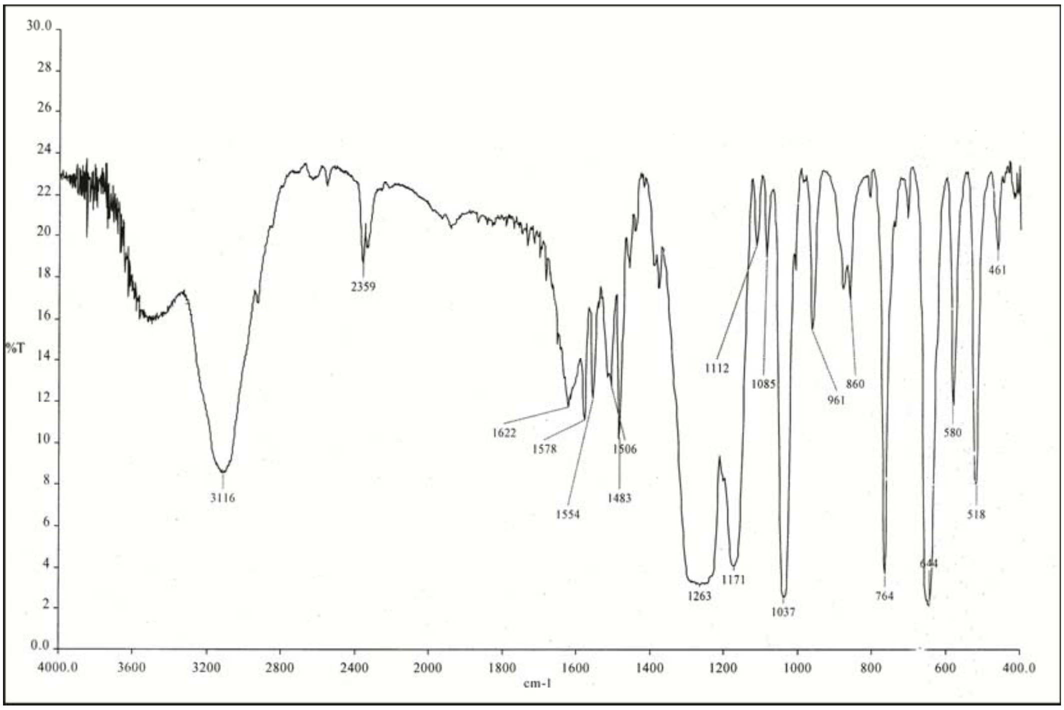
^{1}H-NMR Spectrum of Compound 35 in $CDCl_3$ (400 MHz)



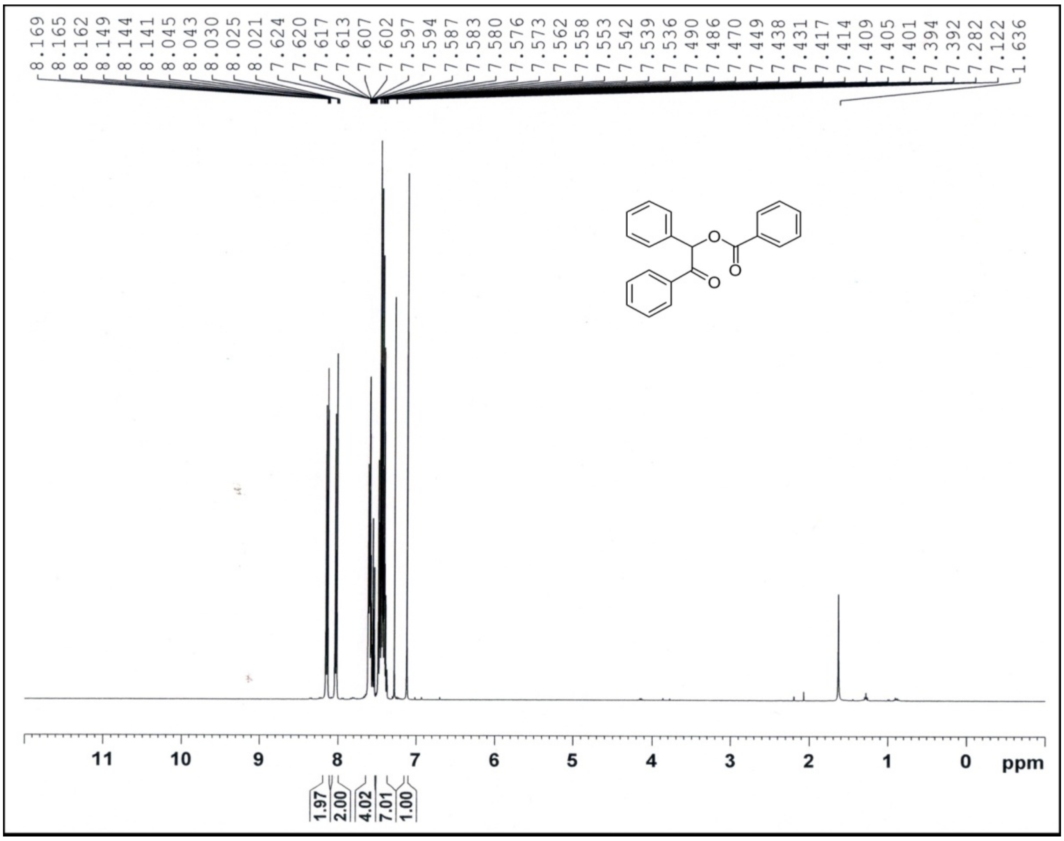
^{1}H-NMR Spectrum of Compound 36 in $CDCl_3$ (400 MHz)



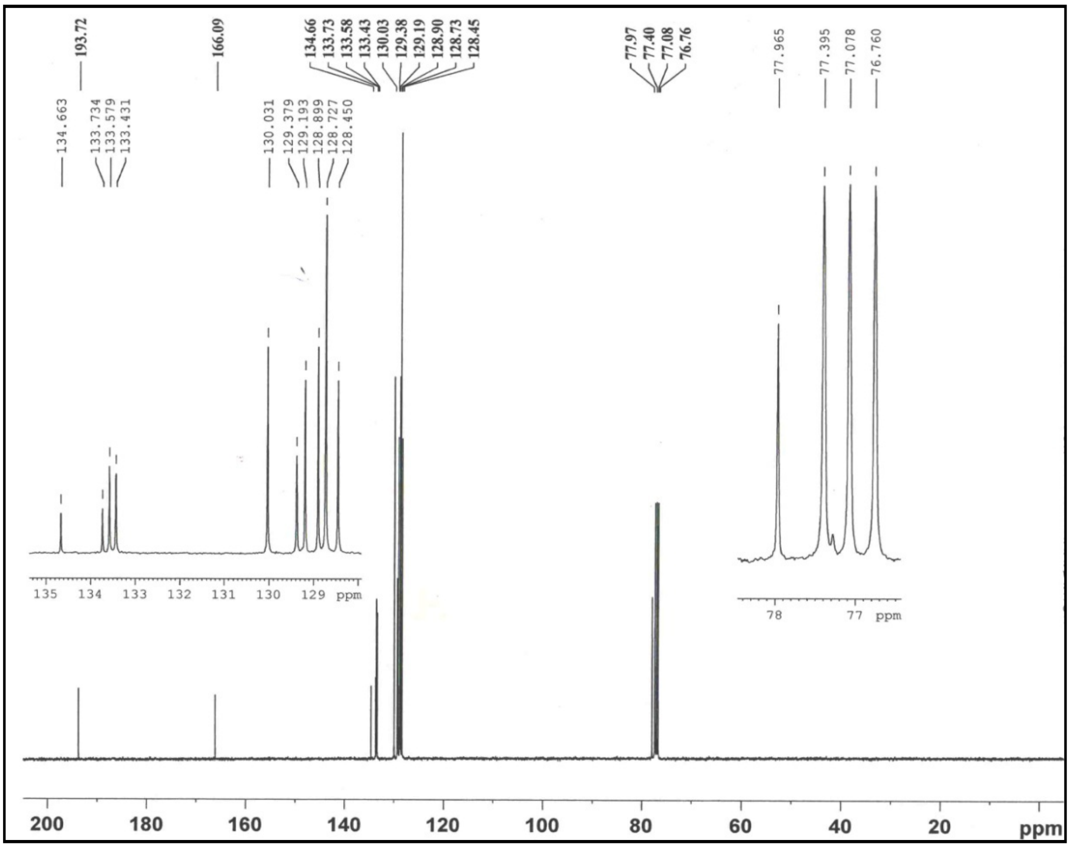
^{1}H-NMR Spectrum of Compound 42 in CDCl$_3$ (400 MHz)



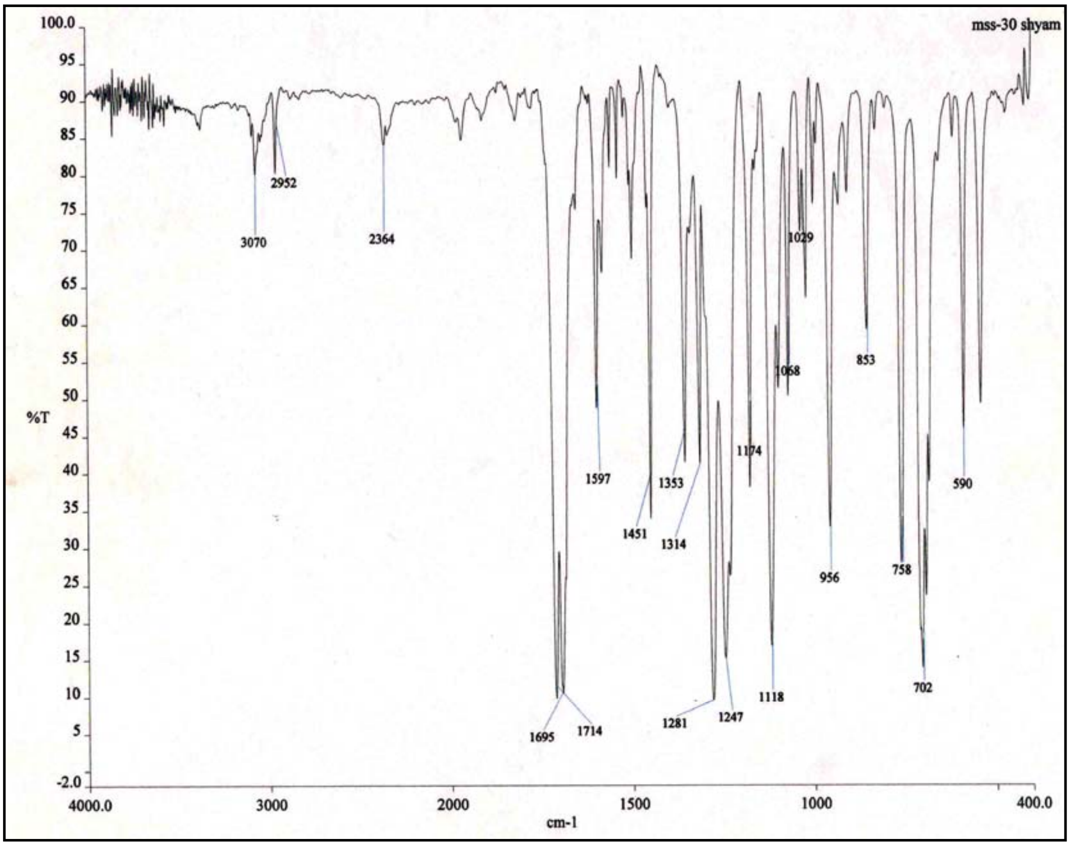
IR spectrum of complex I with ligand 1 and Cu(OTf)$_2$



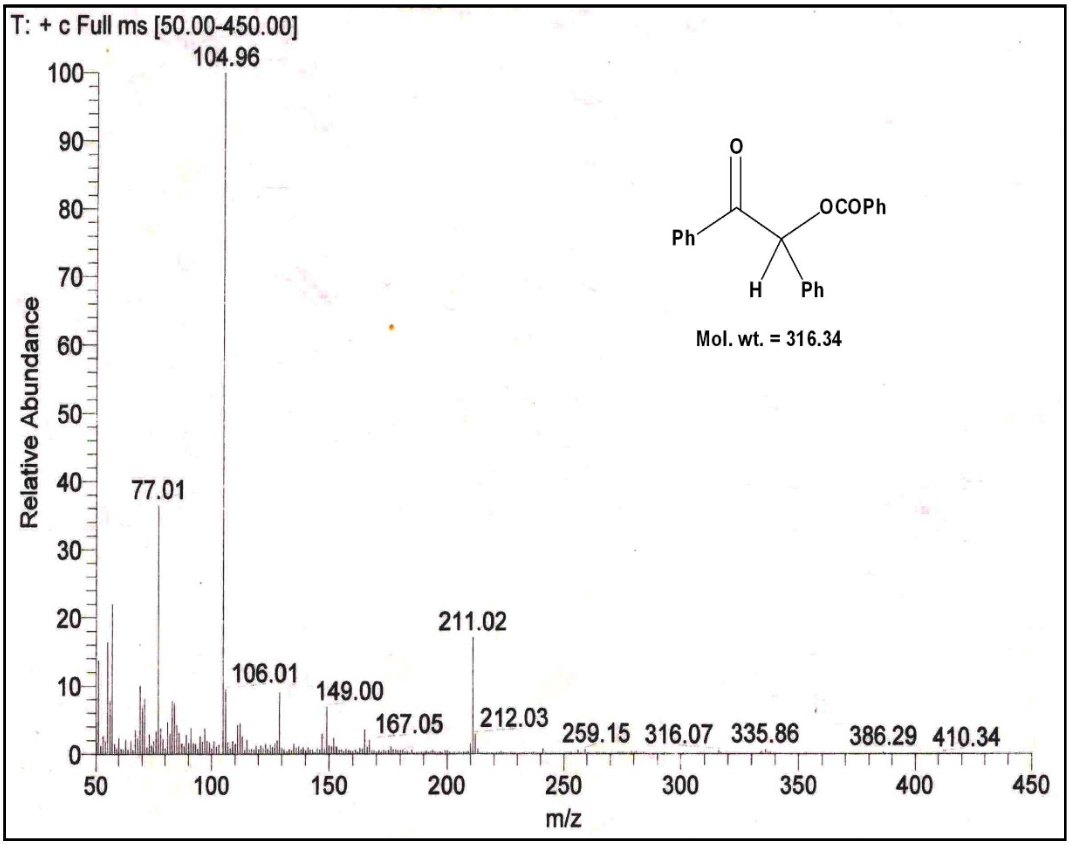
^{1}H-NMR Spectrum of Compound 49 in CDCl$_3$ (400 MHz)



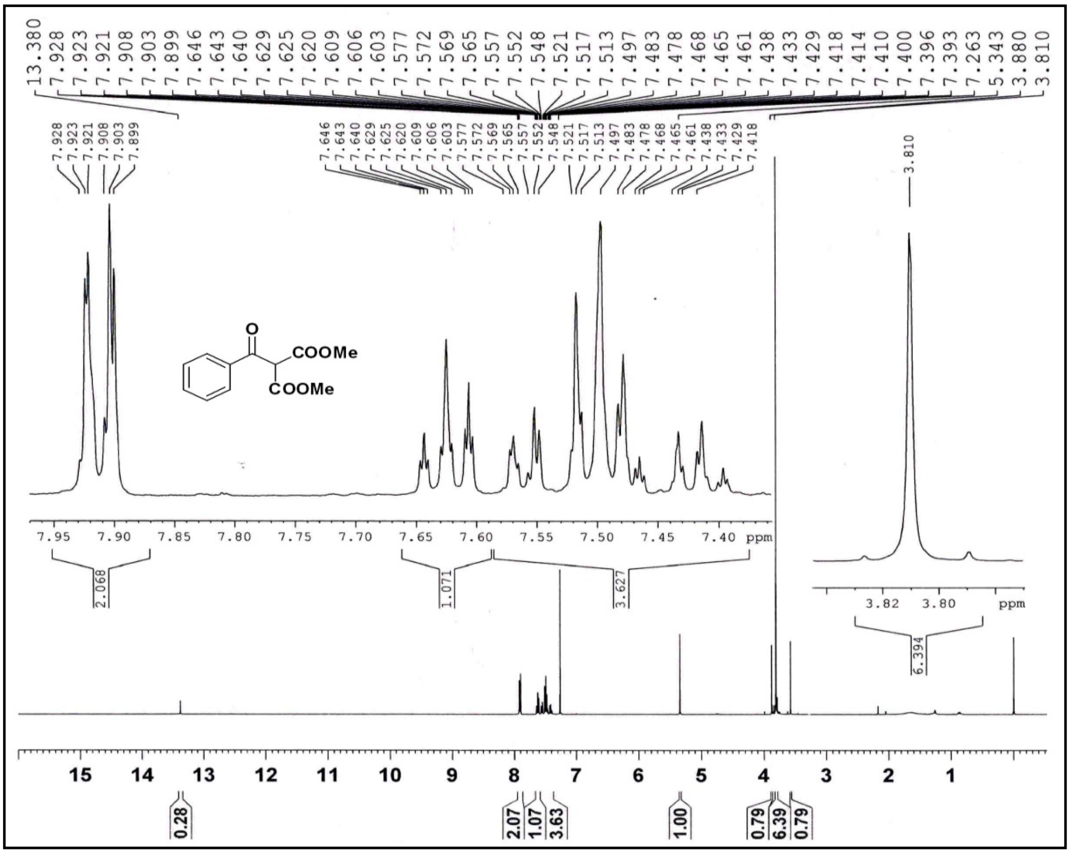
^{13}C-NMR Spectrum of Compound 49 in CDCl$_3$ (100 MHz)



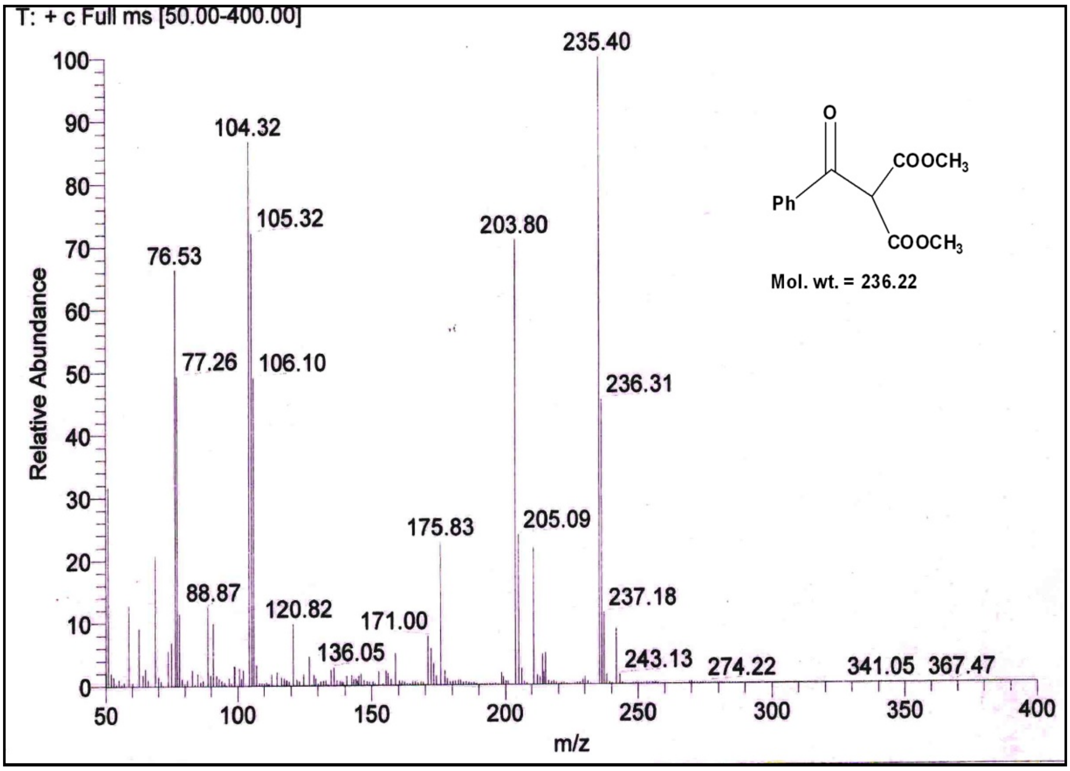
IR spectrum of **49**



Mass chromatogram of 49



^{1}H-NMR Spectrum of Compound 58 in $CDCl_3$ (400 MHz)



Mass chromatogram of **58**

4.5 References

1. (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994.** (c) McCarthy, M.; Guiry, P. J. *Tetrahedron* **2001**, *57*, 3809. (d) Tang, W.; Zhang, Z. *Chem. Rev.* **2003**, *103*, 3029. (e) Johnson, N. B.; Lennon, I. C.; Moran, P. H.; Ramsden, J. A. *Acc. Chem. Res.* **2007**, *40*, 1291.
2. (a) Lloyd-Williams, P.; Giralt, E. *Chem. Soc. Rev.* **2001**, *30*, 145. (b) Kozlowski, M. C.; Morgan, B. J.; Linton, E. C. *Chem. Soc. Rev.* **2009**, *38*, 3193. (c) Clayden, J.; Moran, W. J.; Edwards, P. J.; LaPlante, S. R. *Angew. Chem.* **2009**, *121*, 6516*; Angew. Chem. Int. Ed.* **2009**, *48*, 6398. (d) Bringmann, G.; Gulder, T.; Gulder, T. A. M.; Breuning, M. *Chem. Rev.* **2011**, *111*, 563. (e) Fu, X.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 8820.
3. (a) Hassan, J.; vignon, M. S.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Bringmann, G.; Price Mortimer, A. J.; Keller, P. A.; Gresser, M. J.; Garner, J.; Breuning, M. *Angew. Chem.* **2005**, *117*, 5518; *Angew. Chem. Int. Ed.* **2005**, *44*, 5384.
4. (a) Gustafson, J. L.; Lim, D.; Miller, S.J. *Science*, **2010**, *328*, 1251. (b) Bracegirdle, A.; Clayden, J.; Lai, L.W. *Beilstein J. Org. Chem.* **2008**, *4*, 47. (c) Bringmann, G.; Menche, D. *Acc. Chem. Res.* **2001**, *34*, 615.
5. (a) Leroux, F. R.; Berthelot, A.; Bonnafoux, L.; Panossian, A.; Colobert, F. *Chem. Eur. J.* **2012**, *18*, 14232. (b) Clayden, J.; Fletcher, S. P.; McDouall, J. J. W.; Rowbottom, S. G. M. *J. Am. Chem. Soc.* **2009**, *131*, 5331. (c) Clayden, J.; Fletcher, S. P.; Rowbottom, S. J. M.; Helliwell, M. *Org. Lett.* **2009**, *11*, 2313.
6. (a) Clayden, J.; Kubinski, P.M.; Sammiceli, F.; Helliwell, M.; Diorazio, L. *Tetrahedron* **1994**, *50*, 4387. (b) Clayden, J.; Mitjans, D.; Youssef, L.H. *J. Am. Chem. Soc.* **2002**, *124*, 5266. (c) Thaler, T.; Geittner, F.; Knochel, P. *Synlett* **2007**, 2655.
7. (a) Baudoin, O. *Eur. J. Org. Chem.* **2005**, 4223. (b) Lipshutz, B.; Kayser, F.; Liu, Z. P. *Angew. Chem.* **1994**, *106*, 1962; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1842. (c) Cammidge, A. N.; Cr_py, K. V. L. *Chem. Commun.* **2000**, 1723. (d) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051. (e) Zhou, Y.; Wang, S.; Wu, W.; Li, Q.; He, Y.; Zhuang, Y.; Li, L.; Pang, J.; Zhou, Z.; Qiu, L. *Org. Lett.* **2013**, *15*, 5508 and reference 2e).

8. (a) Urdiales, E. G.; Alfonso, I.; Gotor, V. *Chem. Rev.* **2005**, *105*, 313. (b) Hudlicky, T.; Reed, J. W. *Chem. Soc. Rev.* **2009**, *38*, 3117.
9. (a) Okuyama, K.; Shingubara, K.; Tsujiyama, S.; Suzuki, K.; Matsumoto, T. *Synlett* **2009**, 941. (b) Matsumoto, T.; Konegawa, T.; Nakamura, T.; Suzuki, K. *Synlett* **2002**, 122.
10. (a) Clayden, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 949. (b) Clayden, J. *Synlett* **1998**, *1998*, 810. (c) Clayden, J. *Organic Synthesis Highlights IV*; Wiley-VCH Verlag GmbH: Weinheim, Germany, **2000**, 48. (d) Clayden, J. *Chem. Commun.* **2004**, 127. (e) Campolo, D.; Gastaldi, S.; Roussel, C.; Bertrand, M. P.; Nechab, M. *Chem. Soc. Rev.* **2013**, *42*, 8434. (f) Clayden, J.; Vassiliou, N. *Org. Biomol. Chem.* **2006**, *4*, 2667. (g) Caroline, A. C.; Richard, S. M.; Silvain, L. P.; Robin, G. P.; Timothy, W. W. *Org. Biomol. Chem.* **2011**, *9*, 1831.
11. Perlmutter, P. in *Conjugate addition reactions in organic synthesis*, Pergamon Press, New York, **1992**.
12. (a) Khatik, G. L.; Sharma, G.; Kumar, R.; Chakraborti, A. K. *Tetrahedron* **2007**, *63*, 1200. (b) Chaudhary, M. K.; Hussain, S. *J. Mol. Catal. A: Chem.* **2007**, *269*, 214. (c) Kumar, A.; Ahmad, I.; Sudershan Rao, M. *J. Sulfur Chem.* **2009**, *30*, 570. *and references cited therein*.
13. (a) Bhosale, R. S.; Suryawanshi, P. A.; Ingle, S. A.; Lokhande, M. N.; More, S. P.; Mane, S. B.; Bhosale, S. V.; Pawar, R. P. *Synlett* **2006**, 933. (b) Verma, A. K.; Attri, P.; Chopra, V.; Tiwari, R. K.; Chandra, R. *Monatsh. Chem.* **2008**, *139*, 1041. (c) Ying, A.-G.; Liu, L.; Wu, G.-F.; Chen, G.; Chen, X.-Z.; Ye, W.-D. *Tetrahedron Lett.* **2009**, *50*, 1653. (d) Han, F.; Yang, L.; Li, Z.; Xia, C. *Org. Biomol. Chem.* **2012**, *10*, 346 *and the references cited therein*.
14. (a) Narasimhulu Naidu, B.; Sorenson, M.E.; Connolly, T.P.; Ueda, Y. *J. Org. Chem.* **2003**, *68*, 10098. (b) Yadav, J. S.; Swamy, T.; Reddy, B. V. S.; Rao, D. K. *J. Mol. Catal. A: Chem.* **2007**, *274*, 116. (c) Marjani, K.; Khalesi, M.; Ashouri, A.; Jalali, A.; Ziyaei-Halimehjani, A. *Synth. Commun.* **2011**, *41*, 451. (d) Soleimani, E.; Khodaei, M. M.; Batooie, N.; Baghbanzadeh, M. *Green Chem.* **2011**, *13*, 566. (e) Bandyopadhyay, D.; Mukherjee, S.; Turrubiartes, L. C.; Banik, B. K. *Ultrasonics Sonochem.* **2012**, *19*, 969.

15. (a) Mori, Y.; Kakumoto, K.; Manabe, K.; Kobayashi, S. *Tetrahedron Lett.* **2000**, *41*, 3107. (b) Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. *Adv. Synth. Cat.* **2005**, *347*, 655. (c) Jafari, A. A.; Moradgholi, F.; Tamaddon, F. *J. Iran. Chem. Soc.* **2009**, *6*, 588.
16. (a) Oare, D. A.; Heathcock, C. H. *Top. in Stereochem.* **1989**, *19*, 227. (b) Torii, S.; Hayashi, N.; Kuroboshi, M. *Synlett* **1998**, 599. (c) Bull, S. D.; Davies, S. G.; Delgado-Ballester, S.; Fenton, G.; Kelly, P. M.; Smith, A. D. *Synlett* **2000**, 1257. (d) Bensa, D.; Rodriguez, J. *Synth. Commun.* **2004**, *34*, 1515. (e) Iwamura, I.; Gotoh, Y.; Hashimoto, T.; Sakurai, R. *Tetrahedron Lett.* **2005**, *46*, 6275. (f) Choudary, B. M.; Rajasekhar, C. V.; Gopi Krishna, G.; Rajendra Reddy, K. *Synth. Commun.* **2007**, *37*, 91. (g) Yeom, C.-F.; Kim, M. J.; Kim, B. M. *Tetrahedron*, **2007**, *63*, 904.
17. Coquière, D.; Feringa, B. L.; Roelfes, G. *Angew. Chem., Int. Ed.* **2007**, 46, 9308.
18. (a) Christoffers, J. *Chem. Commun.* **1997**, 943. (b) Zhuang, W.; Hazell, R. G.; Jorgensen, K. A. *Chem. Commun.* **2001**, 1240. (c) Fadini, L.; Togni, A. *Chem. Commun.* **2003**, 30. (d) Sani, M.; Briche, L.; Chiva, G.; Fustero, S.; Piera, J.; Volonterio, A.; Zanda, M. *Angew. Chem., Int. Ed.* **2003**, *22*, 2060. (e) Azizi, N.; Saidi, M.R. *Tetrahedron* **2004**, *60*, 383. (f) Ding, R.; Katebzadeh, K.; Roman, L.; Bergquist, K.-E.; Lindström, U.M. *J. Org. Chem.* **2006**, *71*, 352. (g) Patel, A. L.; Talele, H. R.; Rama, H.; Bedekar, A.V. *Synth. Commun.* **2009**, *39*, 3016.
19. (a) Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur. J. Org. Chem.* **2006**, 2226. (b) Polshettiwar, V.; Varma, R.S. *Tetrahedron Lett.* **2007**, *48*, 8735 *and references cited therein.*
20. (a) Fluharty, A.L. *The chemistry of thiol group*; Patai, S. Ed.; Wiley Interscience: New York, 1974, Part-2, p. 589. (b) Fujita, E.; Nagao, Y. *Bioorg. Chem.* **1977**, *6*, 287. (c) Kumar, A.; Salunke, R.V.; Rane, R. A.; Dike, S.Y. *J. Chem. Soc., Chem. Commun.* **1991**, 485. (d) Sani, M.; Candiani, G.; Pecker, F.; Malpezzi, L.; Zanda, M. *Tetrahedron Lett.* **2005**, *46*, 2393.
21. Trost, B. M.; Keeley, D. E. *J. Org. Chem.* **1975**, *40*, 2013.
22. *Some examples of homogeneous catalyst systems for Michael reaction with different nucleophiles:* (a) Srivastava, N.; Banik, B. K. *J. Org. Chem.* **2003**, *68*, 2109. (b) Wabnitz, T. C.; Spencer, J. B. *Org. Lett.* **2003**, *5*, 2141. (c) Stewart, I. C.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 8696. (d) Wabnitz, T. C.; Yu, J.-Q.; Spencer, J.B. *Chem. –Eur. J.* **2004**, *10*, 484. (e) Xu, L.-W.; Xia, C.-G. *Tetrahedron Lett.* **2004**, *45*, 4507. (f) Ménand, M.; Dalla, V. *Synlett* **2005**, 95. (g) Bernal, P.;

Tamariz, J. *Tetrahedron Lett.* **2006**, *47*, 2905. (h) Hussain, S.; Bharadwaj, S.; Chaudhuri, M. K.; Kalita, H. *Eur. J. Org. Chem.* **2007**, 374.

23. *Vanadium:* (a) Lin, Y.-D.; Kao, J.-Q.; Chen, C.-T. *Org. Lett.* **2007**, *9*, 5195. (b) Chen, C.-T.; Lin, Y.-D.; Liu, C.-Y. *Tetrahedron* **2009**, *65*, 10470.
24. *Copper:* (a) Howells, P. N.; Kenney, J. W.; Nelson, J. H.; Henry, R. A. *Inorg. Chem.* **1976**, *15*, 124. (b) Eckberg, R. P.; Henry, R. A.; Cary, L. W.; Nelson, J. H. *Inorg. Chem.* **1977**, *16*, 2977. (c) Marigo, M.; Juhl, K.; Jorgensen, K. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 1367. (d) Yadav, J. S.; Reddy, B. V. S.; Baishya, G.; Narsaiah, A.V. *Chem. Lett.* **2005**, *34*, 102. (e) Palomo, C.; Oiarbide, M.; Garcia, J. M.; Bañuelos, P.; Odriozola, J. M.; Razkin, J.; Linden, A. *Org. Lett.* **2008**, *10*, 2637. (f) Pérez, E.; Moreno-Mañas, M.; Sebastián, R. M.; Vallribera, A.; Jutand, A. *Eur. J. Inorg. Chem.* **2010**, 1013.
25. *Nickel:* (a) Clariana, J.; Gálvez, N.; Marchi, C.; Moreno-Mañas, M.; Vallribera, A.; Molins, E.; *Tetrahedron*, **1999**, *55*, 7331. (b) Meseguer, M.; Moreno-Mañas, M.; Vallribera, A. *Tetrahedron Lett.* **2000**, *41*, 4093. (c) Shepherd, N. E.; Tanabe, H.; Xu, Y.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 3666.
26. *Cobalt:* (a) Christoffers, J.; Mann, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 2752. (b) Baik, T.-G.; Luiz, A.L.; Wang, L.-C.; Krische, M.J. *J. Am. Chem. Soc.* **2001**, *123*, 5112.
27. *Iron:* (a) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686. (b) Nagano, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 1297. (c) Lee, W.-Z.; Wang, T.-L.; Chang, H.-C.; Chen, Y.-T.; Kuo, T.-S. *Organometallics* **2012**, *31*, 4106. (d) Alt, I.; Rohse, P.; Plietker, B. *ACS Catalysis* **2013**, *3*, 3002-3005.
28. *Boron:* (a) Harada, T.; Iwai, H.; Takatsuki, H.; Fujita, K.; Kubo, M.; Oku, A. *Org. Lett.* **2001**, *3*, 2101. (b) Li, D. R.; Falck, J. R. *J. Am. Chem. Soc.* **2008**, *130*, 46.
29. *Zinc:* Ray, S. R.; Singh, P. K.; Singh, V. K. *Org. Lett.* **2011**, *13*, 5812.
30. *Ruthenium:* (a) Watanabe, M.; Murata, K.; Ikariya, T. *J. Am. Chem. Soc.* **2003**, *125*, 7508. (b) Santoro, F.; Althaus, M.; Bonaccorsi, C.; Gischig, S.; Mezzetti, A. *Organometallics* **2008**, *27*, 3866.
31. *Palladium:* Hamashima, Y.; Hotta, D.; Sodeoka, M. *J. Am. Chem. Soc.* **2002**, *124*, 11240.
32. Shinde, P. D.; Mahajan, V. A.; Borate, H. B.; Tillu, V. H.; Bal, R.; Chandwadkar, A.; Wakharkar, R. D. *J. Mol. Catal. A: Chem.* **2004**, *216*, 115.

33. (a) Hiemstra, H.; Wiberg, H. *J. Am. Chem. Soc.* **1981**, *103*, 417. (b) Suzuki, K.; Ikewata, A.; Mukaiyama, T. *Bull. Soc. Chem. Jpn.* **1982**, *55*, 3277. (c) Yamashita, H.; Mukaiyama, T. *Chem. Lett.* **1985**, 363. (d) Nishimura, K.; Ono, M.; Nagaoka, Y.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 12974. (e) Emori, E.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 4043. (f) Mujahid Alam, M.; Varala, R.; Adapa, S. R. *Tetrahedron Lett.* **2003**, *44*, 5115. (g) Sharma, G.; Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2008**, *49*, 4272. (h) Chu, C.-M.; Gao, S.; Sastry, M. N. V.; Kuo, C.-W. ; Lu,C.; Liu, J.-T.; Yao, C.-F. *Tetrahedron* **2007**, *63*, 1863. (i) Sharma, G.; Kumar, R.; Chakraborti, A. K. *J. Mol. Cat. A: Chem.* **2007**, *263*, 143. (j) Lanari, D.; Ballini, R.; Bonollo, S.; Palmieri, A.; Pizzo, F.; Vaccaro, L. *Green Chem.* **2011**, *13*, 3181.
34. (a) Shi, M.; Itoh, N.; Masaki, Y. *J. Chem. Res. (S)* **1996**, 352. (b) Keller, F.; Rippert, A.J. *Helv. Chim. Acta* **1999**, *82*, 125.
35. *Vogel's textbook of practical organic chemistry*, 5th Ed.; **1989**, p. 1061.
36. McKennon, M.J.; Meyers, A.I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568.
37. Casarini, D.; Lunazzi, L.; Mancinelli, M.; Mazzanti, A.; Rosini, C. *J. Org. Chem.* **2007**, *72*, 7667.
38. (a) Dutot, L.; Wright, K.; Wakselman, M.; Mazaleyrat, J.-P.; Peggion, C.; De Zotti, M.; Formaggio, F.; Toniolo, C. *Tetrahedron Lett.* **2008**, *49*, 3475. (b) Aillaud, I.; Wright, K.; Collin, J.; Schulz, E.; Mazaleyrat, J.-P. *Tetrahedron*: *Asymmetry* **2008**, *19*, 82. (c) Upadhye, K.; Prakashareddy, J.; Pedireddi, V.R. *J. Mol. Struct.* **2009**, *937*, 81.
39. Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857.
40. (a) Morantz, D. J.; Wright, A. J. C. *J. Chem. Phys.* **1971**, *54*, 692. (b) Arnett, J. F.; McGlynn, S. P., *J. Phys. Chem.* **1975**, *79*, 626. (c) Asano, K.; Aita, S.; Azumi, T., *J. Phys. Chem.* **1984**, *88*, 5538. (d) Brown, C. J.; Sadanaga, R., *Acta. Crystallogr.* **1965**, *18*, 158. (e) Cumper, C. W. N.; Thurston, A. P., *J. Chem. Soc. Perkin Trans. II,* **1972,** 106. (f) Fessenden, R. W.; Carton, P. M.; Shimamori, H.; Scaiano, J. C., *J. Phys. Chem.*, **1982**, *86*, 3803.
41. Liebig, J. *Annalen der Chemie.* **1838**, *25*, 1.
42. Johnson, J.R.; Grummitt, J.R., *Org. Synth. Coll. Vol. 2*, **1943**, *23*, 805.
43. (a) Garcia-Ruano, J. L.; Henao, M.A.; Molina, D.; Pérez-Ossorio, R.; Plumet, J. *Tetrahedron Lett.* , **1979**, *33*, 3123. (b) Haro, R.; Jimenez-Tebar, A.; Pérez-Ossorio,

R.; Plumet, J. *Tetrahedron Lett.* **1979**, *33*, 1355. (c) Nomura, K.; Oshima, K.; Matsubara, S. *Tetrahedron Lett.* **2004**, *45*, 5957. (d) Krishnan, G. R.; Sreekumar, K. *Eur. J. Org. Chem.* **2008**, 4763.

44. (a) Singh, S.B.; Mehrotra, K. N. *Can. J. Chem.* **1982**, *60*, 1901. (b) Mehrotra, K. N.; Singh, I. S.; Roy, J. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2399. (c) Charrier, J.-D.; Landreau, C.; Deniaud, D.; Reliquet, F.; Reliquet, A.; Meslin, J. C. *Tetrahedron* **2001**, *57*, 4195.
45. Gago, S.; Rodríguez-Borges, J. E.; Teixeira, C.; Santos, A. M.; Zhao, J.; Pillinger, M.; Nunes, C. D.; Petrovski, Z.; Santos, T. M.; Kühn, F. E.; Romão, C. C.; Gonçalves, I. S. *J. Mol. Catal. A: Chem.* **2005**, *236*, 1.
46. Salavati-Niasari, M.; Mirsattari, S.N. *J. Mol. Catal. A: Chem.* **2007**, *268*, 50.
47. Min-Seob, S.; Ansoo, L.; Hyunwoo, K. *Org. Lett.* **2014**, *16*, 2950.
48. Jones G. *Org. React.* **1967**, *15*, 204.
49. (a) Kuebrich, J.P.; Schowen, R.L. *J. Am. Chem. Soc.* **1971**, *93*, 1220. (b) Celebi, N.; Yildiz, N.; Demir, A.S.; Calimli, A. *J. Supercritical Fluids* **2007**, *41*, 386.
50. (a) Junek, H.; Hornischer, B.; Hambock, H. *Monatsh. Chem.* **1969**, *100*, 503. (b) Junek, H.; Hambock, H.; Hornischer, B. *Monatsh. Chem.* **1969**, *100*, 699.
51. Ducker, J. W.; Gunter, M. J. *Aust. J. Chem.* **1974**, *27*, 2229.
52. Trisler, J. C.; Frye, J. L. *J. Org. Chem.* **1965**, *30*, 306.
53. Wenheimer, A. J.; Kantor, S. W.; Hauser, C. R. *J. Org. Chem.* **1953**, *18*, 801.
54. Yamato, T.; Sakaue, N.; Fujita, K. *Organic Preparations and Procedures INT.*, **1998**, *30*, 331.
55. Alajarin, M.; Bonillo, B.; Sanchez-Andrada, P.; Vidal, A.; Bautista, D. *J. Org. Chem.* **2007**, *72*, 5863.
56. Bapat, U. R.; Manjrekar, P. P.; Hosangadi, B. D. *Ind. J. Chem. B,* **1989**, *28B*, 810.
57. Sharma, G.; Kumar, R.; Chakraborti, A. K., *Tetrahedron Letters 49*, **2008**, 4272.
58. See reference 18g
59. Corsico, C. A.; Giouanni, D.; Pierpaolo, R.; Gianfranco, T. *Gazz. Chem. Ital.* **1984**, *114*, 417.
60. Bartoli, G.; Bosco, M.; Bellucci, M. C.; Marcantoni, E.; Sambri, L.; Torregiani, E., *Eur. J. Org. Chem.* **1999**, 617.
61. (a) Han, F.; Yang, L.; Li, Z.; Xia, C. *Org. Biomol. Chem.* **2012**, *10*, 346. (b) Alt, I.; Rohse, P.; Plietker, B. *ACS Catalysis* **2013**, *3*, 3002.