

**Zinc Catalyzed Hydroamination of Carbodiimides/Isocyanate Leading
to Guanidines/Urea Derivatives Formation**

and

**Lanthanides Mediated Oxidative Cross Coupling of Benzyl Alcohols and
Various Amines to form corresponding Imines**

A Project Report

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MASTER OF SCIENCE

By

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Under the supervision of

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INDIA

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Declaration

I hereby declare that the matter embodied in this report is the result of investigation carried out by me in the Department of Chemistry, Indian Institute of Technology Hyderabad under the supervision of **Dr. Tarun K. Panda**

In keeping with general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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This thesis entitled **“Zinc Catalyzed Hydroamination of Carbodiimides/Isocyanate Leading to Guanidines/Urea Derivatives Formation and Lanthanides Mediated Oxidative Cross Coupling of Benzyl Alcohols and Various Amines to form corresponding Imines”** by Mitali Sachdeva is approved for the degree of Master of Science from IIT Hyderabad.



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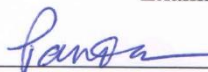
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Dedicated to
My beloved parents
and
my respected teachers

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Abstract

In the chapter 1, we report the highly chemo-selective catalytic addition of N–H bonds from various aromatic amines to carbodiimides and isocyanates using (Ar-BIAO)ZnCl₂ complexes [Ar-BIAO = *N*-(aryl)imino-acenaphthenone, Ar = 2,6-Me₂C₆H₃ (**1**), 2,4,6 Me₃C₆H₂ (**2**), 2,6-^{*i*}Pr₂C₆H₃ (**3**)] as the pre-catalyst to prepare guanidines and urea derivatives in 55-90% yield. The complex **3** showed higher catalytic activity than analogous complexes **1** and **2** under similar reaction conditions. The catalytic addition of N–H bonds into heterocumulenes displays a broad substrate scope. The amines having electron donating groups underwent higher conversion than the amines having electron withdrawing groups to afford corresponding guanidine or urea derivative. A possible mechanism involving penta-coordinated zinc transition state for the catalytic reaction is presented.

In the chapter 2, we have presented a new and efficient approach towards the oxidative cross coupling of alcohols and amines to form corresponding imines using lanthanide salts as the catalysts. The reaction went smoothly to afford the various substituted imines from the reaction of benzyl alcohols with ample variety of amines in good to excellent yields.

Chapter-1

Zinc Catalyzed Hydroamination of Carbodiimides/Isocyanate Leading to Guanidines/Urea Derivatives Formation

1. Introduction

Guanidine, $\text{HN}=\text{C}(\text{NH}_2)_2$ is a vital 'CN₃' core containing molecule having broad range of fascinating properties since it was first synthesized by oxidative degradation of guanine by Strecker in 1861.^[1-2] The substituted guanidine derivatives $\text{R}_1\text{N}=\text{C}(\text{NR}_2\text{R}_3)\text{NHR}_4$ have received considerable recognition due to their variable electronic and steric effects. It is well known that guanidine derivatives are an important class of N-containing compounds and are of significant importance due to their characteristic applications in numerous fields. First, they function as building blocks in several pharmaceuticals, natural products, sweeteners, explosives, agrochemicals, etc.^[3-8] In particular, they act as very efficient pharmacophores in the field of medicinal chemistry because of their ability to interact with functional groups present in various receptors or enzymes through hydrogen bonds and electrostatic interactions.^[9] Moreover, guanidine is a substructure of many important molecules having biological activity and have found wide spectrum of activity such as antibacterial, anti-inflammatory, antidiabetic, antihistaminic and cardiovascular activity.^[10] Second, guanidine derivatives are used extensively in organic chemistry as organic bases owing to the resonance stabilization of their conjugated acids which catalyze various types of organic reactions. Third, they are widely used as good supporting ligands in organometallic and coordination chemistry and stabilize different metal complexes (Figure 1).^[11] Urea derivatives play significant role in organic, medicinal, supramolecular and material chemistry.^[12] They are important structural motifs found in

biologically active compounds, agricultural pesticides, dyes or cellulose fibers, and antioxidants in gasoline (Figure 2).^[13]

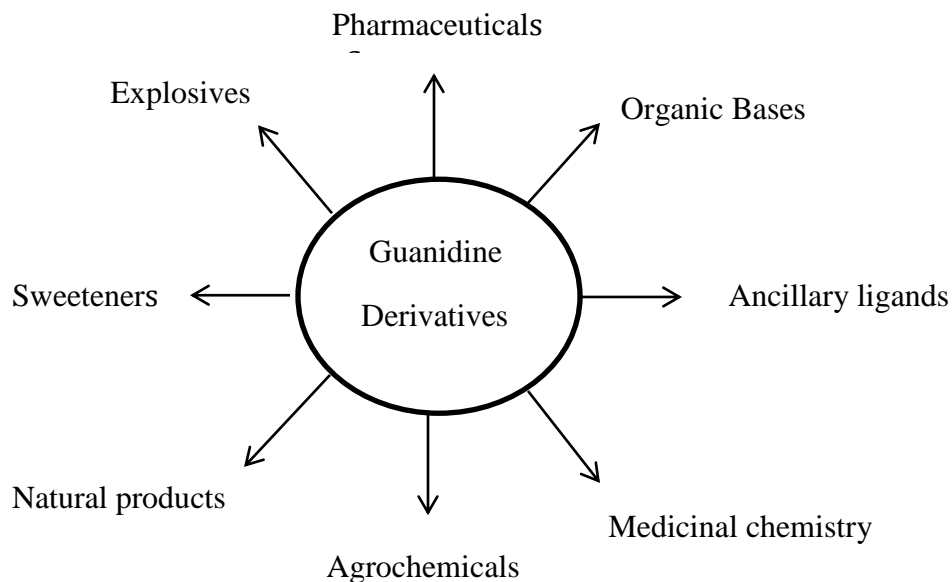


Figure 1: Applications of Guanidines derivatives for various products.

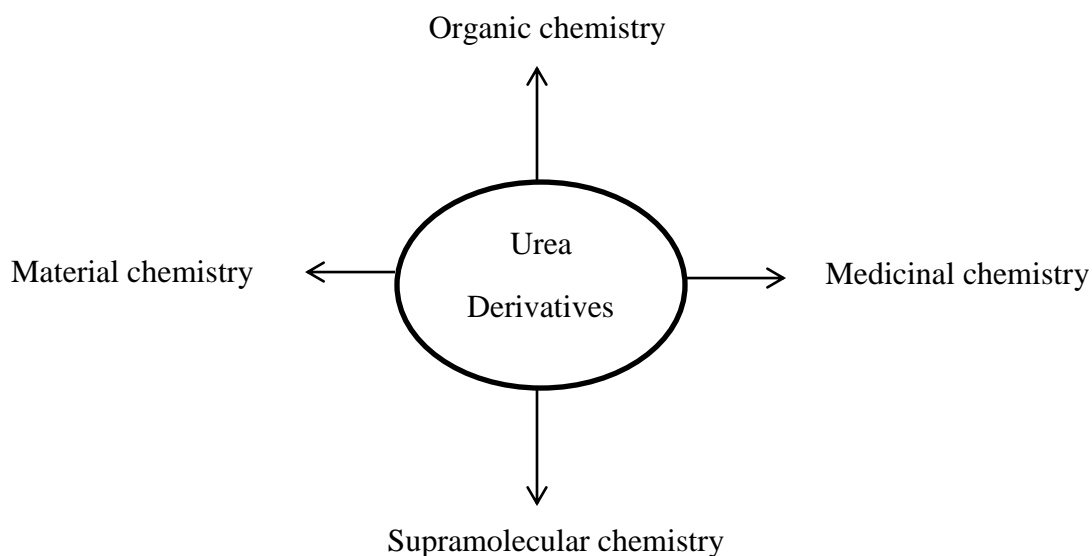


Figure 2: Applications of urea derivatives in various areas.

The synthesis of guanidines has been widely investigated by numerous methods and many synthetic strategies have been explored. Among the direct methods for the synthesis of

guanidines, the catalytic guanylation reaction of amines with carbodiimides ($\text{RN}=\text{C}=\text{NR}$) which is also known as catalytic addition of an amine N-H bond to the C=N double bond of carbodiimides or hydroamination of carbodiimides is the most relevant, straightforward and atom economical route via C-N bond formation to prepare substituted guanidines. In a similar manner, the addition of N-H bond to the isocyanates by utilizing a suitable catalyst produces corresponding urea derivatives.^[14] Although various synthetic methodologies including oxidative carbonylation of amines^[15] have been developed, the catalytic addition of amine N-H bond to an isocyanate is limited to a very few metal complexes. This is in sharp contrast to the preparation of guanidines where a broad range of metal complexes are known to act as suitable and efficient catalysts. Although, the uncatalyzed direct guanylation reaction of aromatic amines and secondary amines with carbodiimides cannot be achieved even under harsh reaction conditions.^[16] Therefore, much effort has been devoted to develop active catalysts for the catalytic hydroamination reaction of carbodiimides with aromatic, heterocyclic and secondary amines for the synthesis of guanidines. In 2003, Richeson et.al reported the first catalytic guanylation of primary aromatic amines with unactivated carbodiimides using titanium imido complexes.^[17] Further, Hou and coworkers achieved catalytic addition of both primary and secondary amines to carbodiimides through nucleophilic addition mechanism of a metal-nitrogen single bond to a carbodiimide by rare earth metal alkyl complex in 2006.^[18,19] Other catalytic systems such as vanadium imido,^[20] half sandwich lanthanide alkyls,^[21] lanthanide amides and aryloxides,^[22] $\text{LiN}(\text{SiMe}_3)_2$ ^[23], titanocarborane amide^[24] and commercially available alkyl metals ZnEt_2 ,^[25] MgBu_2 ,^[25] LiBu ,^[25] AlR_3 ,^[26] and $\text{Zn}(\text{OTf})_2$ ^[27] were explored to be the efficient, cheap and versatile catalysts with a broad scope of amines including primary aromatic amines

and aliphatic secondary amines. Recently, convenient iron catalyst, $\text{Fe}(\text{OAc})_2$ ^[28] and $\text{Yb}(\text{OTf})_3$ ^[29] were reported with excellent functional group tolerance and wide scope.

2. Aim of the project

The direct guanylation reaction of primary aliphatic amines with carbodiimides can be performed under rather harsh conditions without catalyst but hydroamination reaction of aromatic and secondary amines to carbodiimides and isocyanates cannot be achieved without catalyst even under harsh reaction conditions owing to their decreased nucleophilicity. In recent years, there has been a significant progress on the development of various catalytic systems. However, most of the catalytic systems are sensitive to air and the synthetic methodologies are very tedious. Hence, there is an increasing demand to explore simple and efficient catalysts for the chemical transformation that will allow for the further advancement of guanidine and urea chemistry.

Following our interest in developing new catalytic systems, we decided to explore the catalytic activity of some systems for the efficient addition of amines to carbodiimides and isocyanates leading to formation of guanidine and urea derivatives.

3. Scope of work

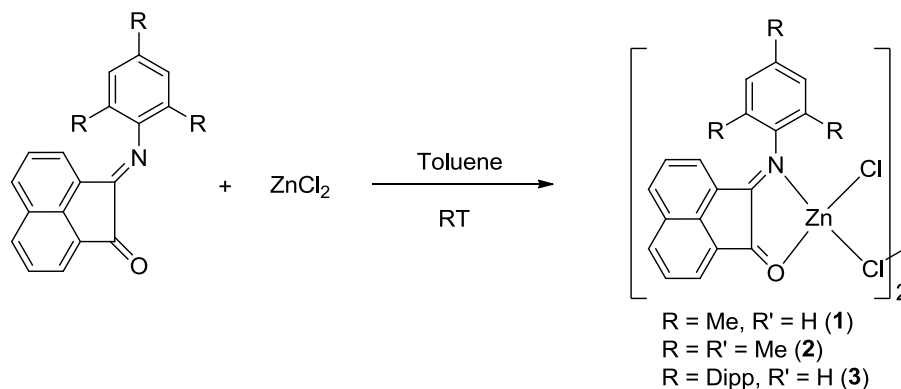
Over the past decades, catalytic guanylation reactions of amines with carbodiimides have attracted increasing attention as it has an atom economy of 100% and is a waste free process. An early trial was carried out by tetrabutylammonium fluoride (TBAF) supported guanylation of some aromatic amines with activated N,N'-diarylsubstituted carbodiimides.^[30] However, such a catalytic process was hardly explored until Richeson et. al reported the first example of the transition metal catalyzed guanylation of aromatic amines with carbodiimides.^[31] Titanium complexes undergo this kind of reaction but in this catalytic system, secondary amines could not be utilized because the regeneration of Ti=N imido species is required. The guanylation of aromatic amines catalyzed by simple metal amides $MN(SiMe_3)_2.(THF)_2$ ($M = Li, Na, K$) has been reported.^[32] This was followed by Hill and co-workers using almost similar Group 2 metal catalysts $M[N(SiMe_3)_2]_2.(THF)_2$ ($M = Ca, Sr, Ba$).^[33] Later, Hou et. al reported the catalytic guanylation reaction of both aromatic and secondary amines using a half sandwiched rare earth metal alkyl complex in 2006.^[34] In this process, the regeneration of Ln-N amido species met the needs for secondary amines. Thereafter, the catalytic guanylation reaction become an attractive area for the atom economical preparation of guanidines. In the past 10 years, the reaction has covered more than 40 types of compounds acting as suitable catalysts for the synthesis of approximately 260 guanidines. Very recently, Carrilo-Hermosilla and co-workers developed the reaction mediated by $MgBn_2.(THF)_2$ or Mg_nBu_2 .^[35] Similarly, commercially available catalysts such as $ZnEt_2$ and $n-BuLi$ have also been explored as cheap, versatile and efficient catalysts for the reaction. Recently, aluminum alkyl reagents such as $AlEt_3$, $AlEt_2Cl$, and $AlMe_3$ have been employed as efficient precatalysts for this reaction.^[36] Similarly, the hydroamination of the highly activated C=O bond in isocyanates yielding ureas can proceed under forced and harsh

conditions without catalyst. However, a catalyst like $M[N(\text{SiMe}_3)_2]_2 \cdot (\text{THF})_2$ ($M = \text{Ca}, \text{Sr}, \text{Ba}$)^[37] or $\text{LiN}(\text{SiMe}_3)_2$ is required for less nucleophilic amines.

In the context of the information outlined above, we present a new approach towards the formation of guanidine and urea derivatives using zinc metal complexes with BIAO ligands as catalysts. These catalysts are air-stable, cheaper and easy to synthesize.

4. Results and Discussions

4.1 Synthesis of zinc (II) complexes with *N*-(aryl) imino-acenaphthenone (Ar-BIAO) ligands



Scheme 1.1: Synthesis of zinc catalysts 1-3.³⁸

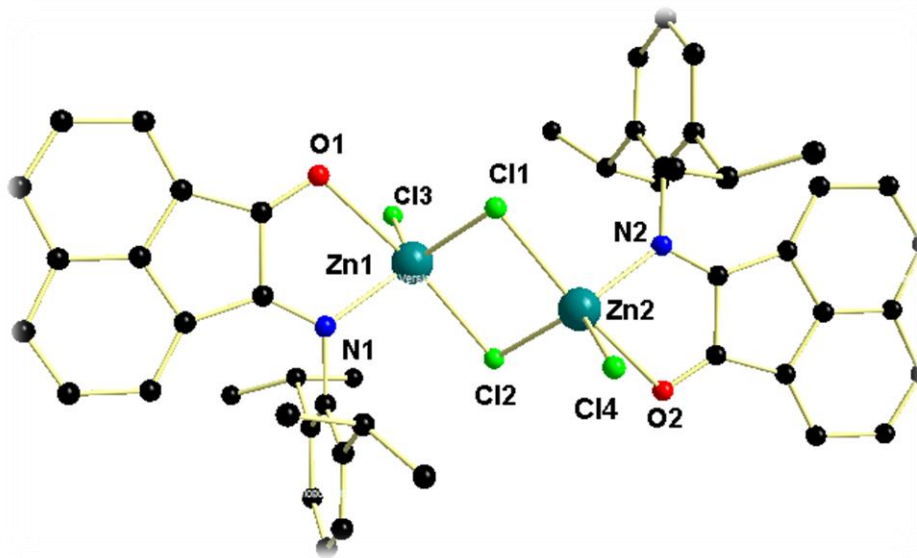
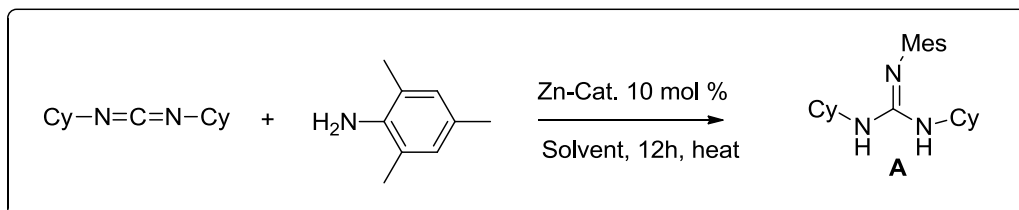


Figure 1.1: The molecular structure of zinc catalyst **3**.

The synthesis and structural details of various zinc complexes with bi-dentate *N*-(aryl)imino-acenapthenone (Ar-BIAO) ligand have been reported in our group where Ar-BIAO ligand contains conjugated exocyclic carbonyl and imine groups (Scheme 1.1 and Figure 1.1).^[38] We have observed from their molecular structures that a bidentate ligation from the Ar-BIAO ligands occur in each case through lone pairs of nitrogen and oxygen atoms and by changing the steric crowding on the Ar-BIAO ligand, the nuclearity of the zinc complexes can be changed. In continuation with this project we found that these zinc complexes are extremely active as pre-catalyst for the guanylation reaction among the carbodiimides and amines. In this chapter, we describe the reactivity of zinc complexes as pre-catalyst for a number of amines with different carbodiimides and isocyanates to achieve various guanidine and urea derivatives.

4.2 Synthesis of guanidine and urea derivatives

In this study, we described the catalytic addition of N–H bonds from various amines to N,N'-dicyclohexylcarbodiimides and isocyanates with zinc complexes **1-3** as the pre-catalyst. Catalytic experiments were carried out using 10 mol% of zinc complex and equimolar amounts of either carbodiimides or isocyanate and amines which were added to a solution of the catalyst with suitable solvent under an inert atmosphere. Initially we employed mesitylamine (2,3,4-Me₃C₃H₂NH₂) and N,N'-dicyclohexylcarbodiimide (DCC) as model substrates to explore and optimize their catalytic reaction. When 10 mol% of zinc catalyst **1** was employed as Lewis acid catalyst at 90 °C, we were pleased to find that the desired guanidine product **A** was obtained in good yield (Table 1, entry 1). Then, other zinc catalysts were examined as Lewis acids in the reaction. The experimental results indicated among these three zinc complexes **1-3**, complex **3** exhibited best catalytic activity to the desired guanidine **A** in 81% yield (Table 1, compare entry 3 with entries 1-2). When a zinc bromide complex **2*** (MesBIAOZnBr₂)³⁹ was used as pre-catalyst, only 76% yield was isolated (Table 1, entry 7). We also examine the solvent effect into the reaction and observed that toluene could be the better combination than tetrahydrofuran and methylene dichloride (Table 1, entries 3-5). It should be noted when only zinc dichloride was used as catalyst, no product was detected (Table 1, entry 6). Further raising the temperature from 90 °C to 110 °C was not beneficial to the reaction as no increase in yield was observed (Table 1, entry 8). The aliphatic amines are not suitable for this catalytic reaction due to lower boiling point of most of the aliphatic amines.

Table 1. Optimization of catalytic reaction between DCC and mesityl amine.

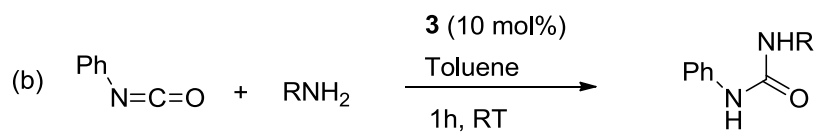
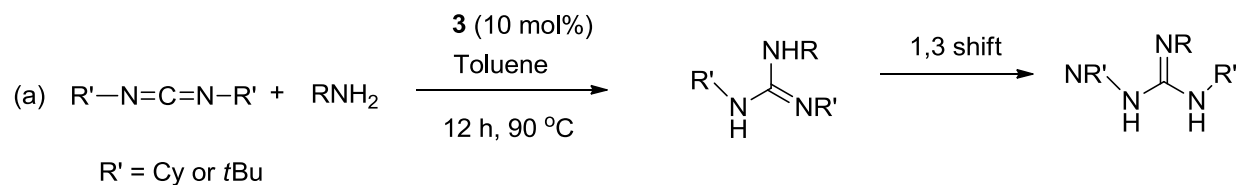
Entry	Amine	Carbodiimide	Catalyst	Solvent	Time (h)	T (°C)	Yield (%) ^a
1	Mesityl amine	DCC	1	Toluene	12	90	75
2	Mesityl amine	DCC	2	Toluene	12	90	78
3	Mesityl amine	DCC	3	Toluene	12	90	81
4	Mesityl amine	DCC	3	THF	12	60	70
5	Mesityl amine	DCC	3	CH ₂ Cl ₂	12	25	65
6	Mesityl amine	DCC	ZnCl₂	Toluene	12	90	0
7	Mesityl amine	DCC	2*	Toluene	12	90	76
8	Mesityl amine	DCC	3	Toluene	12	110	81

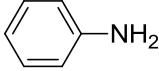
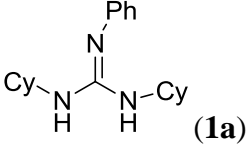
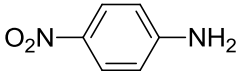
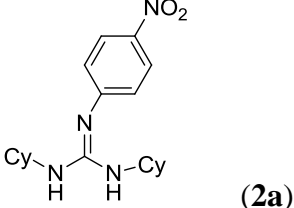
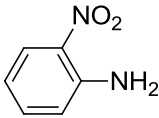
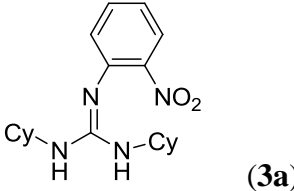
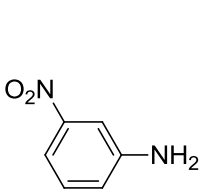
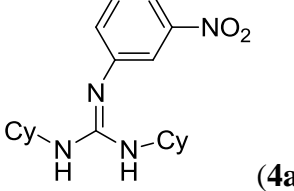
^aIsolated yields

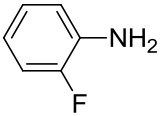
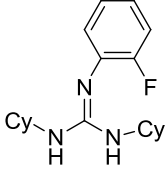
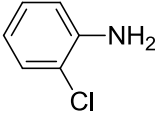
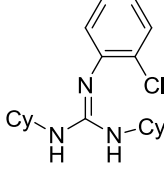
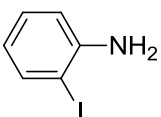
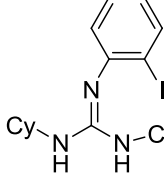
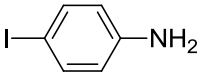
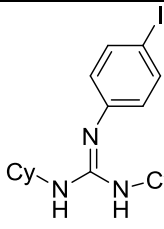
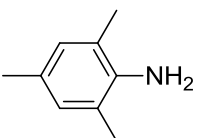
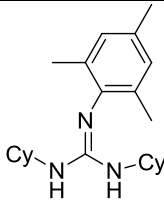
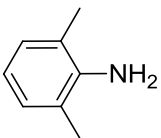
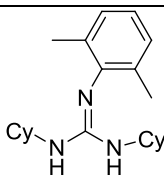
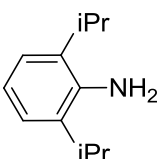
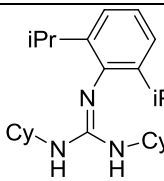
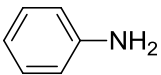
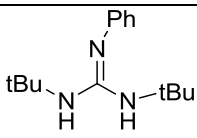
After screening reaction conditions, it can be concluded that the optimized reaction should be performed under the catalysis of 10 mol% complex **3** at 90 °C using toluene as the solvent. The reaction mixture in each case was kept under stirring at elevated temperature for guanidine and at room temperature for urea for 1 h, and the respective guanidine or urea products were isolated. The isolated products were analysed through ¹H and ¹³C NMR spectroscopy and yield were calculated after isolation of pure products (Table 2). Under optimized condition we found that a series of amines had also undergone the N-H addition reaction smoothly with two different carbodiimides to give corresponding guanidine derivatives in moderate yield. The reaction of unsubstituted aniline with DCC gave 95% yield (Table 2, entry 1). The anilines having nitro

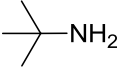
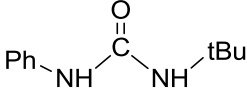

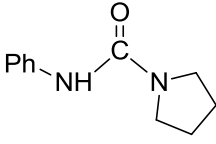
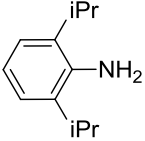
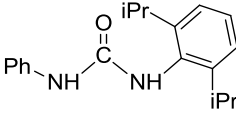
group in *ortho*-, or in *para*- position were tested for the N-H addition reaction and the yield of 85% and 75% of the respective guanidines were observed (Table 2, entries 2 and 3); however substantial decrease in the yield (53%) could be noticed when *m*- nitro aniline was used as the substrate due to greater extent of deactivating nature of the nitro group at *m*- position of the aniline. However, the aniline moieties were further deactivated when a halide group (F, Cl, I) was attached to the phenyl ring as 55-57% yield of respective urea derivative were obtained (Table 2, entries 5-8). The mesityl and 2,6-dimethyl aniline having electron donating effect from the methyl groups were observed having no significant increase in the yield (Table 2, entries 9-10). However, no guanylation product was observed when DippNH₂ was used as the amine substrate probably due to enhanced steric hindrance of DippNH₂ which restricted the approach of the bulky carbodiimide (DCC) towards itself (Table 2, entry 11). When we reacted N,N'-di-*tert*-butylcarbodiimide with aniline we obtained corresponding guanidine in good yield 75% (entry 13). To extend the scope of the reaction we treated phenyl isocyanate with *tert*-butylamine and pyrrolidine under room temperature using the zinc pre-catalyst **3**. In both the cases we obtained excellent yield to produce corresponding urea derivatives (Table 2, entry 14 and 15). However the DippNH₂ gave slightly reduced yield of the respective urea due to bulky size of the aniline moiety. Thus we observed that, zinc pre-catalyst **3** can smoothly catalyse the guanylation reaction of a number of anilines with DCC at slightly elevated temperature; however the reaction with phenyl isocyanate with amines required a room temperature only.

Table 2 Catalytic formation of guanidine and urea derivatives using **3** as pre-catalyst.^a



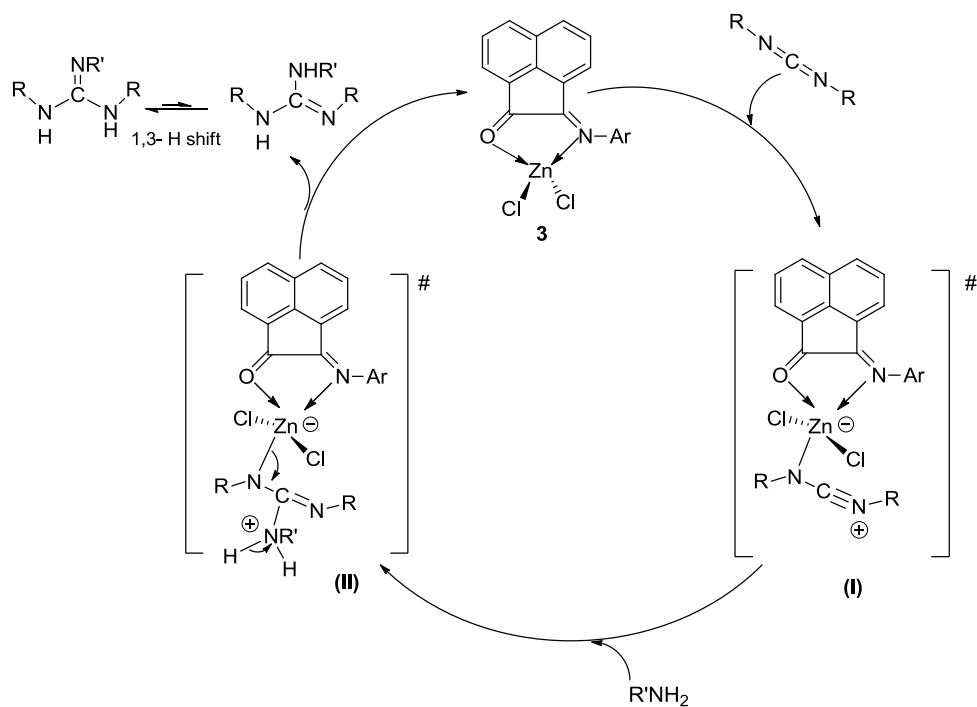
Entry	Amine	Carbodiimide/ Isocyanate	Product	Yield (%) ^b
1		CyN=C=NCy	 (1a)	95
2		CyN=C=NCy	 (2a)	85
3		CyN=C=NCy	 (3a)	75
4		CyN=C=NCy	 (4a)	53

5		$\text{CyN}=\text{C}=\text{NCy}$	 (5a)	57
6		$\text{CyN}=\text{C}=\text{NCy}$	 (6a)	53
7		$\text{CyN}=\text{C}=\text{NCy}$	 (7a)	57
8		$\text{CyN}=\text{C}=\text{NCy}$	 (8a)	55
9		$\text{CyN}=\text{C}=\text{NCy}$	 (9a)	81
10		$\text{CyN}=\text{C}=\text{NCy}$	 (10a)	52
11		$\text{CyN}=\text{C}=\text{NCy}$	 (11a)	0
12		$\text{tBuN}=\text{C}=\text{NtBu}$	 (12a)	75

13		PhN=C=O ^c	 (13a)	88
14		PhN=C=O ^c	 (14a)	95
15		PhN=C=O ^c	 (15a)	79

^aAll reactions were performed in toluene solvent; reaction time 12 hours at 90°C temperature; compounds were isolated and purified by washing with *n*-hexane. All compounds were characterized by ¹H and ¹³C NMR spectroscopy using CDCl₃ as NMR solvent. ^bYields are calculated from isolated pure products. ^cRoom temperature.

A possible mechanism for zinc complex **3** catalyzed guanylation of amines to carbodiimides is proposed in Scheme 2. In the first step, carbodiimido nitrogen should react with zinc complex **3** which is a Lewis acid catalyst through the nitrogen's lone pair to generate a penta-coordinated zinc(II) intermediate **I** where zinc ion can bear the negative charge over it and the second nitrogen of the carbodiimido moiety possess positive charge. The nucleophilic addition of an amine to **I** would afford another penta-coordinated zinc intermediate **II**. Finally, intramolecular proton transfer of **II** readily led to regenerate pre-catalyst **3** and release the free guanidine. Similar mechanistic cycles are known in literature.^[39]



Scheme 2. Most plausible mechanism for the catalytic addition of N-H bond to carbodiimide using zinc pre-catalyst **3**.

5. Conclusion

In summary, we have presented the highly chemo-selective catalytic addition of N-H bonds from various aromatic amines to carbodiimides and isocyanate using a zinc pre-catalyst supported by *N*-(aryl)imino-acenaphthenone ligand. The complex **3** was proved as efficient pre-catalyst for the conversion of aromatic amines to corresponding guanidines via guanylation reaction with carbodiimides at elevated temperature in 55-95% yield. Complex **3** was also potent catalyst for the conversion of isocyanate to corresponding urea in excellent yield when amines were reacted with isocyanate at room temperature. A possible mechanism involving five coordinated zinc intermediate was proposed for guanylation reaction.

6. Experimental section

6.1 General Information

All manipulations of air-sensitive materials were performed under inert atmosphere and in flame-dried Schlenk-type glassware, either on a dual manifold Schlenk line interfaced with a high vacuum (10^{-4} Torr) line, or in an argon-filled MBRAUN glovebox. Hydrocarbon solvents (toluene and *n*-hexane) were distilled under nitrogen from LiAlH_4 and stored in the glove box. ^1H NMR (400 MHz) and $^{13}\text{C}\{^1\text{H}\}$ (100 MHz), spectra were recorded on a BRUKER AVANCE III-400 spectrometer. All amines, *N,N'*-di-cyclohexylcarbodiimide, *N,N'*-di-*tert*-butylcarbodiimide and phenylisocyanate were purchased from either Sigma Aldrich or Alfa Aesar. Amines were distilled over CaH_2 prior to use. Zinc complexes **1-3** were synthesized according to the published procedure.^[38] NMR solvent (CDCl_3) was purchased from Alfa Aesar and distilled over molecular sieves.

6.2 General Procedure for the preparation of zinc (II) complexes with *N*-(aryl) imino-acenaphthenone (Ar-BIAO) ligands^[38]

In a dry degassed Schlenk tube, *N*-(aryl) imino-acenaphthenone (Ar-BIAO) ligand (0.37 mmol) was taken and about 6 mL of CH_2Cl_2 was added onto it. To this solution mixture, anhydrous ZnCl_2 (50 mg, 0.37 mmol) was added. The reaction mixture was stirred for 6 h at ambient temperature. This reaction mixture was filtered using cannula filtration. The colour of the filtrate was deep orange in colour. The CH_2Cl_2 was evaporated under *vacuo* resulting in a concentrated clear solution which was subjected to crystallization at -40°C . Single crystals of light orange colour were obtained after second re-crystallization.

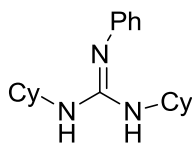
Spectral data for complex **3** [ZnCl₂(Dipp-BIAO)]₂

Yield: 140 mg (80%). FT-IR (selected frequency): $\nu = 3063, 2962, 2926, 1729$ (C=O), 1651(C=N), 1588, 1434, 1273, 779, 728 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): $\delta = 8.31$ (t, 2H, An *H*), 8.11 (d, 1H, An *H*), 7.91 (t, 1H, An *H*), 7.48 (t, 1H, An *H*), 7.34(m, 1H, Ar *H*) 7.27 (d, 2H, Ar *H*), 6.65 (d, 1H, An *H*), 2.90 (sept, 2H, CH(CH₃)₂), 1.19, (d, 6H, CH(CH₃)₂), 0.76 (d, 6H, CH(CH₃)₂); ¹³C{¹H} NMR (100 MHz, CDCl₃, selected resonances): $\delta = 189.32$ (C=O), 161.61 (C=N), 137.2, 133.8, 131.0, 129.9, 128.3, 127.7, 126.7, 124.7, 123.9, 123.7, 123.6, 27.6 (CH(CH₃)₂), 23.4, 23.0 (CH(CH₃)₂).

6.3 General Procedure for the guanylation of amines with carbodiimides.

A solution of primary or secondary amine (0.99 mmol) in toluene (1.0 mL) was added drop wise into the reaction mix of carbodiimide (0.99 mmol) and DippBIAOZnCl₂ (**3**) (0.276 mmol) to a 25 mL dry Schlenk flask inside the glovebox. The dark red reaction mixture was stirred for 12 h at 90°C temperature. Solvent was evaporated under *vacuo*, and a solid residue was obtained, which was washed with hexane (5 mL). White solid compound obtained in each case. The conversion of amines was calculated from isolated pure products.

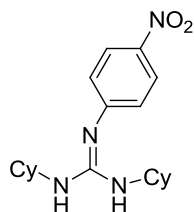
6.3.1 N-phenyl-N',N''-dicyclohexylguanidine (**1a**):



Yield: 280 mg, 95%. ¹H NMR (400 MHz, CDCl₃): δ 7.27-7.24 (m, 2H, Ar-*H*), 7.03-6.95 (m, 1H, Ar-*H*), 6.92-6.90 (d, 2H, Ar-*H*), 3.40 (br, 2H, NH), 1.98-1.13 (m, 22H, CH and CH₂ of cyclohexyl) ppm. ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5,

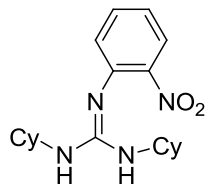
125.5, 122.9, (Ar-C), 50.5(CH), 33.7 (CH₂), 25.6 (CH₂), 24.8(CH₂). FT-IR (selected frequencies): $\nu = 3271$ (N-H), 3062 (aromatic C-H), 2927 (sp³ C-H), 2852 (sp³ C-H), 1550 (aromatic C-C), 1447 (C-H bend), 1346 (C=N), 889, 862, 837, 795, 738 (aromatic C-H oop)cm⁻¹. HRMS (ESI): m/z found 345.2898, calcd for C₂₂H₃₅N₃ (M+H)⁺ requires 345.2246.

6.3.2 N-*p*-nitrophenyl-N',N''-dicyclohexylguanidine (2a):



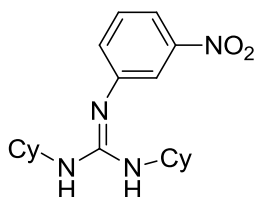
Yield: 289.5 mg, 85%. ¹H NMR (400 MHz, CDCl₃): δ 8.11-8.09 (m, 2H, Ar-H), 6.92-6.90 (d, 2H, Ar-H), 3.43 (br, 2H, NH), 2.00-1.15 (m, 22H, CH and CH₂ of cyclohexyl) ppm. ¹³C {¹H} NMR (100 MHz, CDCl₃): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5, 125.5, 122.9, (Ar-C), 50.5(CH), 33.7 (CH₂), 25.6 (CH₂), 24.8(CH₂). FT-IR (selected frequencies): $\nu = 3368$ (N-H), 2929 (sp³ C-H), 2853 (sp³ C-H), 1566 (aromatic C-C), 1449 (C-H bend), 1302 (C=N), 1105, 854, 734, 701 (aromatic C-H oop) cm⁻¹. HRMS (ESI): m/z found 345.2266, calcd for C₁₉H₂₈N₄O₂ (M+H)⁺ requires 345.2246.

6.3.3 N-*o*-nitrophenyl-N',N''-dicyclohexylguanidine (3a):



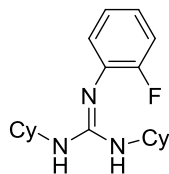
Yield: 256 mg, 75%. ^1H NMR (400 MHz, CDCl_3): δ 8.13-7.92 (m, 2H, Ar-H), 7.34-7.15 (m, 2H, Ar-H), 3.33 (br, 2H, NH), 1.90-1.14 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5, 125.5, 122.9, (Ar-C), 50.5(CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2). FT-IR (selected frequencies): ν = 3292 (N-H), 2930 (sp^3 C-H), 2854 (sp^3 C-H), 1587 (aromatic C-C), 1448 (C-H bend), 1344 (C=N), 891, 839, 781, 738 (aromatic C-H oop) cm^{-1} . HRMS (ESI): m/z found 345.2266, calcd for $\text{C}_{19}\text{H}_{28}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$ requires 345.2246.

6.3.4 N-*m*-nitrophenyl-N',N''-dicyclohexylguanidine (**4a**):



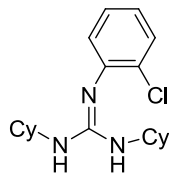
Yield: 181 mg, 53%. ^1H NMR (400 MHz, CDCl_3): δ 7.07-7.05 (m, 2H, Ar-H), 6.88-6.82 (m, 2H, Ar-H), 3.35 (br, 2H, NH), 1.96-1.02 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5, 125.5, 122.9, (Ar-C), 50.5(CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2). FT-IR (selected frequencies): ν = 3292 (N-H), 2930 (sp^3 C-H), 2854 (sp^3 C-H), 1587 (aromatic C-C), 1448 (C-H bend), 1344 (C=N), 891, 839, 781, 738 (aromatic C-H oop) cm^{-1} . HRMS (ESI): m/z found 345.2266, calcd for $\text{C}_{19}\text{H}_{28}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$ requires 345.2246.

6.3.5 N-*o*-fluorophenyl-N',N''-dicyclohexylguanidine (**5a**):



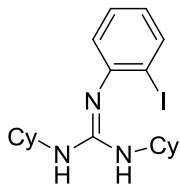
Yield: 179 mg, 57%. ^1H NMR (400 MHz, CDCl_3): δ 7.03-6.99 (m, 1H, Ar-*H*), 6.94-6.92 (m, 1H, Ar-*H*), 6.90-6.87 (m, 2H, Ar-*H*), 3.44 (br, 2H, NH), 2.02-1.06 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 160.3(CF), 154.53 (C=N), 127.8, 126.3, 124.5, 122.2, 116.0 (Ar-C), 50.3(CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2) IR(neat, cm^{-1}): ν = 3277 (N-H), 3059 (aromatic C-H), 2927 (sp^3 C-H), 2852 (sp^3 C-H), 1582 (aromatic C-C), 1448 (C-H bend), 1350 (C=N), 891, 836, 758, 698 (aromatic C-H oop) cm^{-1} . HRMS (ESI): m/z found 318.2327, calcd for $\text{C}_{19}\text{H}_{28}\text{N}_3\text{F}$ (M+H) $^+$ requires 318.2301. .

6.3.6 N-*o*-chlorophenyl-N',N''-dicyclohexylguanidine (**6a**):



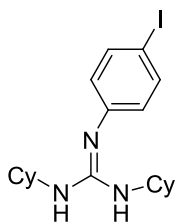
Yield: 175 mg, 53%. ^1H NMR (400MHz, CDCl_3): δ 7.22-7.18 (m, 1H, Ar-*H*), 7.07-7.03 (m, 1H, Ar-*H*), 6.77-6.75 (m, 1H, Ar-*H*), 6.70-6.66 (m, 1H, Ar-*H*), 3.35 (br, 2H, NH), 1.96-1.12 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5, 125.5, 122.9, (Ar-C), 50.5 (CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2). IR(neat, cm^{-1}): ν = 3281 (N-H), 3056 (aromatic C-H), 2926 (sp^3 C-H), 2852 (sp^3 C-H), 1574 (aromatic C-C), 1470 (C-H bend), 1348 (C=N), 1058, 889, 803, 739 (aromatic C-H oop) cm^{-1} . HRMS (ESI): m/z found 334.2036, calcd for $\text{C}_{19}\text{H}_{28}\text{ClN}_3$ (M+H) $^+$ requires 335.1942.

6.3.7 N-*o*-iodophenyl-N',N''-dicyclohexylguanidine (**7a**):



Yield: 240 mg, 57%. ^1H NMR (400 MHz, CDCl_3): δ =7.86-7.78 (m, 1H, Ar-*H*), 7.46-7.40 (m, 1H, Ar-*H*), 7.38-7.31 (m, 1H, Ar-*H*), 6.95-6.81(m, 1H, Ar-*H*), 3.37 (br, 2H, NH), 1.96-1.16 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 160.3(CF), 154.53 (C=N), 127.8, 126.3, 124.5, 122.2, 116.0 (Ar-C), 50.3(CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2). FT-IR (selected frequencies): ν = 3272 (N-H), 2928 ($\text{sp}^3\text{C-H}$), 2853 ($\text{sp}^3\text{C-H}$), 1569 (C-C aromatic), 1456 (C-H bend), 1354 (C=N), 1019, 887, 802, 735 (C-H oop bending) cm^{-1} . HRMS (ESI): m/z found 426.1382, calcd for $\text{C}_{19}\text{H}_{28}\text{IN}_3$ ($\text{M}+\text{H}$) $^+$ requires 426.1361.

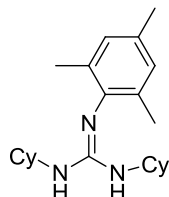
6.3.8 N-*p*-iodophenyl-N',N''-dicyclohexylguanidine (**8a**):



Yield: 232 mg, 55%. ^1H NMR (400 MHz, CDCl_3): δ =7.85-7.79 (m, 2H, Ar-*H*), 7.41-7.34 (m, 2H, Ar-*H*), 3.37 (br, 2H, NH), 1.96-1.16 (m, 22H, CH and CH_2 of cyclohexyl) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.8 (C=N), 150.2, 129.9, 128.5, 127.5, 125.5, 122.9 (Ar-C), 50.5(CH), 33.7 (CH_2), 25.6 (CH_2), 24.8(CH_2). FT-IR (selected frequencies): ν = 3275 (N-H),

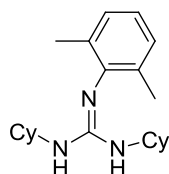
3055 (aromatic C-H), 2928 (sp^3 C-H), 2853 (sp^3 C-H), 1604 (aromatic C-C), 1457 (C-H bend), 1355 (C=N), 1092, 888, 804, 735 (aromatic C-H oop) cm^{-1} . HRMS (ESI): m/z found 426.1383, calcd for $C_{19}H_{28}IN_3$ (M+H)⁺ requires 426.1361.

6.3.9 N-2,4,6-trimethylphenyl-N',N''-dicyclohexylguanidine (**9a**):



¹H NMR(400 MHz, CDCl₃): δ 6.85 (s, 2H, Ar-H), 3.43 (br, 2H, NH), 2.24 (s, 3H, p-CH₃), 2.15 (s, 6H, o-CH₃), 1.91-1.09 (m, 22H, CH and CH₂ of cyclohexyl) ppm. . ¹³C{¹H}NMR (100 MHz, CDCl₃): δ =152.1 (C=N), 145.2, 129.2, 127.8, 126.2 (Ar-C), 55.7 (CH), 34.9 (CH₂), 25.4 (CH₂), 24.7 (CH₂), 21.4 (p-CH₃), 20.4 (o-CH₃). FT-IR (selected frequencies): ν = 3275 (N-H), 3055 (aromatic C-H), 2928 (sp^3 C-H), 2853 (sp^3 C-H), 1604 (aromatic C-C), 1457 (C-H bend), 1355 (C=N), 1092, 888, 804, 735 (aromatic C-H oop) cm^{-1} .

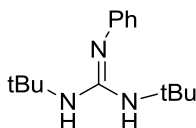
6.3.10 N-2,4-dimethylphenyl-N',N''-dicyclohexylguanidine (**10a**):



Yield: 169 mg, 52%. ¹H NMR (400 MHz, CDCl₃): δ 7.10-7.08 (m, 1H, Ar-H), 6.93-6.92 (m, 2H, Ar-H), 3.35 (br, 2H, NH), 2.2 (s, 6H, CH₃), 1.86-1.18 (m, 22H, CH and CH₂ of cyclohexyl)

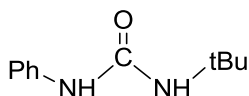
ppm. FT-IR (selected frequencies): $\nu = 3292$ (N-H), 2930 (sp^3 C-H), 2854 (sp^3 C-H), 1587 (aromatic C-C), 1448 (C-H bend), 1344 (C=N), 891 , 839 , 781 , 738 (aromatic C-H oop) cm^{-1} .

6.3.11 N-phenyl-N',N''-di-tert-butylguanidine (**12a**):



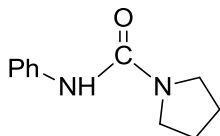
1H NMR (400 MHz, $CDCl_3$): δ 7.27-7.24 (m, 2H, Ar-H), 7.03-6.95 (m, 1H, Ar-H), 6.92-6.90 (d, 2H, Ar-H), 1.56 (br, 2H, NH), 1.25 (s, 9H, CH_3) ppm.

6.3.12 1-(tert-butyl)-3-phenylurea (**13a**):



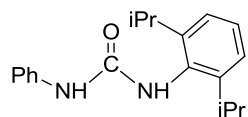
Yield: 183 mg, 75%. 1H NMR (400 MHz, $CDCl_3$): δ 7.38 (s, 1H, PhNH), 7.28-7.22 (m, 2H, Ar), 7.20-7.18 (m, 2H, Ar) 6.97-6.94 (m, 1H, Ar), 5.50 (s, 1H, *t*BuNH), 1.01 (s, 9H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (100, MHz, $CDCl_3$): δ 154.2 (CO), 139 (Ar), 129 (Ar), 122 (Ar), 119.8 (Ar), 50 ($C(CH_3)_3$), 29.3 ($C(CH_3)$) ppm.

6.3.13 N-phenylpyrrolidine-1-carboxamide (**14a**):



Yield: 179 mg, 95%. ^1H NMR (400 MHz, CDCl_3): δ 7.41 (d, 2H, $^3J_{\text{HH}} = 7.20$ Hz, Ar), 7.26 (t, 2H, $^3J_{\text{HH}} = 7.20$ Hz, Ar), 7.94 (t, 1H, $^3J_{\text{HH}} = 7.60$ Hz, ArH), 6.26 (s, 1H, PhNH), 3.44 (q, 4H, $^3J_{\text{HH}} = 6.80$ Hz, CH_2), 1.94 (q, 6H, $^3J_{\text{HH}} = 6.80$ Hz, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100, MHz, CDCl_3) δ 154.0 (CO), 139 (Ar), 128 (Ar), 122 (Ar), 119 (Ar), 45 (CH_2), 25 (CH_2) ppm.

6.3.14 1-(2,6-diisopropylphenyl)-3-phenylurea (**15a**):



Yield: 232 mg, 79%. ^1H NMR (400 MHz, CDCl_3): δ 7.36-7.34 (m, 2H, Ar), 7.24-7.05 (m, 6H, Ar), 6.51 (br, 1H, PhNH), 6.02 (br, 1H, ArNH), 3.34 (br, 2H, CH), 1.18 (br, 12H, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100, MHz, CDCl_3): δ 155 (CO), 128 (Ar), 119 (Ar), 28 (CH), 24 (CH_3) ppm.

Chapter- 2

Lanthanides Mediated Oxidative Cross coupling of Benzyl Alcohols and Various Amines to form corresponding Imines

1. Introduction

Imines, also known as Schiff bases are versatile intermediates having widespread applications in laboratory and industrial synthetic processes.^[40] They are involved in organic synthesis and extensively utilized in the synthesis of pharmaceuticals, fragrances, fungicides, natural products, dyes and agricultural chemicals. They act as electrophiles in many important organic transformations including addition, condensation, reduction, cyclisation, cycloaddition and aziridination reactions. Moreover, imines also serve as common ligands in the field of coordination chemistry. Therefore, the efficient and diverse synthesis of imines is a consistently demanding research topic in the organic synthetic chemistry.

Conventionally, imines were synthesized from the condensation of aldehydes/ketones with amines in the presence of an acid. During the past decade, numerous efforts have been devoted to the direct synthesis of imines, in particular via one pot procedures through an oxidative process to reduce the energy consumption, waste emission, operating and purification steps.^[42] Recently, versatile alternative methods such as oxidation of secondary amines^[43], self-condensation of primary amines upon oxidation^[44], oxidative coupling of alcohols and amines^[45], hydroamination of alkynes with amines^[46] and the partial hydrogenation of nitriles followed by coupling with amines^[47] have been reported. Among the various methodologies for imine formation, mainly three approaches – cross coupling of alcohols with amines, self-coupling of primary amines, and oxidative dehydrogenation of secondary amines have received much more attention and have

been greatly studied because the starting materials are readily available, and green molecular oxygen or air can serve as the terminal oxidant. To create environmentally benign processes, the development of catalytic systems for these reactions has received much attention. From this point of view, an oxidative coupling of alcohols and amines ought to be the most direct, appropriate and efficient way to produce imines due to their wide substrate scope. In the cross-coupling of alcohols with amines, the only by-product is water, and diverse symmetric and unsymmetric imines can be easily synthesized choosing different starting substrates. Moreover, compared to carbonyl compounds alcohols are less toxic, readily available, more stable, inexpensive, and easier to handle. Nevertheless, the selective oxidation of alcohols into aldehyde intermediates under mild conditions is the major challenge for this type of reaction. The development of an effective and general method for the synthesis of imines from alcohols and amines is very prudent due to its potential versatility and broad scope. Recently, quite a number of metal complexes, including complexes of ruthenium^[48], osmium^[49], palladium^[50], manganese^[51], iridium^[52], and copper^[53] have been reported to catalyze this reaction homogeneously.

Although these results are encouraging, there are still some drawbacks associated with these types of reactions such as the use of organic solvents as the reaction medium, the use of expensive metal complexes, and high catalyst loadings. These reactions are also limited to activated (benzylic) alcohols and a maximum turnover number of 50 are reported. The limited availability of these metals and their high cost makes it highly demanding to search for more economical and environmental friendly alternatives. The development of nonprecious metal catalysts would be a significant progress from the perspective of cost, abundance, and sustainable chemistry.

2. Aim of the project

Considerable efforts have been devoted in the recent years for the synthesis of imines including the direct synthesis of imines from amines and alcohols in the presence of catalyst, self-condensation of primary amines with oxidant and oxidation of secondary amines. Several approaches have been developed and explored either by using a homogenous catalyst or heterogeneous catalyst. Among these transformations, oxidative coupling of amines and alcohols represent the most direct and straightforward way to produce imines. Since the ground breaking work of Milstein and co-workers, second-row and third-row transition metals such as ruthenium, palladium, osmium, manganese, iridium, and copper have been reported to catalyze this reaction homogeneously. On the other hand, platinum and gold have also been reported as heterogeneous catalysts.

Considering the limited supply of these rare and precious metals, it is highly urgent and desirable for the chemists to search for more potential, economical and environmental friendly catalysts. However, no attempts were made for the synthesis of imines by the oxidative cross coupling of alcohols and amines using lanthanides as catalysts. So, in this part of my thesis, we wish to explore the efficiency of lanthanides as metal catalysts for this reaction.

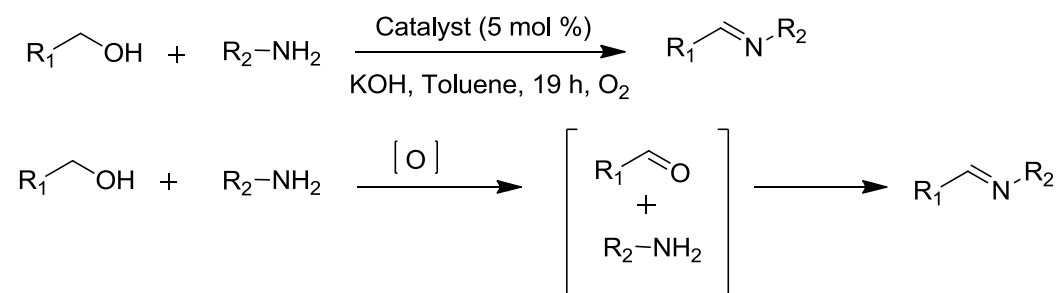
3. Scope of work

As oxidative coupling reaction of alcohols with amines for the synthesis of imines offers the major advantages of mild reaction conditions, high efficiency and wide scope of substrates, a wide variety of catalytic systems has been extensively explored during the past years and significant progress has been made for this particular transformation. In this methodology, aldehydes and ketones are obtained from alcohols by stoichiometric oxidation. Second-row and third-row transition metal complexes such as of ruthenium, osmium, manganese, iridium and palladium have been reported to catalyze this reaction homogeneously. Moreover, platinum and gold have been applied as heterogeneous catalysts. In 2011, Zhang et. al explored the oxidative coupling reaction of alcohols with primary amines to form the corresponding imines using a homogeneous copper catalyst.^[54] They have found that copper (II) salts showed better selectivity than copper(I) salts and benzyl alcohol can be smoothly coupled with various aromatic or aliphatic amines to form corresponding imines in good yields. Recently, Xu et. al showed the oxidative reaction of alcohols and amines using iron catalyst and air as an oxidant.^[55] Despite numerous efforts towards the catalytic synthesis of imines from oxidative coupling reactions of alcohols and amines, all the available reactions have some limitations and only few catalytic systems are available for the transformation of alcohols into aldehydes and ketones using molecular oxygen or air as the ultimate and stoichiometric oxidant. Hence, there is an increasing demand to develop more facile, efficient and environmental friendly catalytic systems for this transformation.

4. Results and discussions

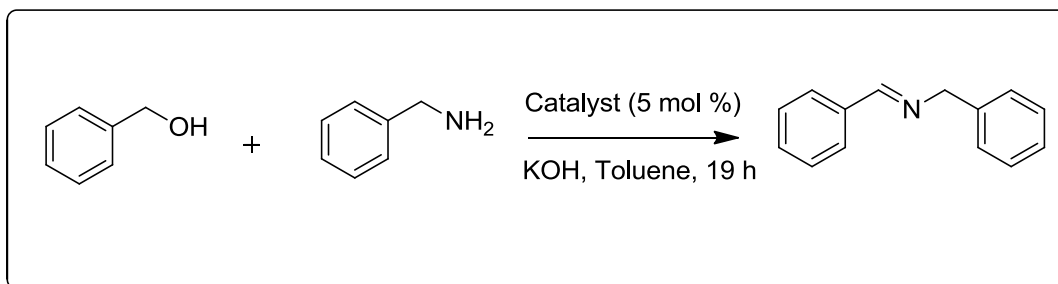
4.1 Preparation of imines by the cross coupling of alcohols and amines

In this study, we examined the synthesis of imines using the lanthanide salts catalyzed oxidative cross coupling of alcohols and amines. Initially, the coupling reaction of benzyl alcohol and benzyl amine was investigated in the presence of commercially available various lanthanide catalysts and 1.5 equivalent of KOH in toluene at 90⁰C for 19 h under O₂ atmosphere (Scheme 2.1).



Scheme 2.1: Lanthanide salts mediated preparation of imines by the oxidative cross coupling of alcohols with amines.

To our delight, the reaction went smoothly to afford the corresponding imines in 90-99% yield with the full conversion of the starting material when the different types of lanthanides were used as catalysts for the transformation (Table 1, entries 1-4).

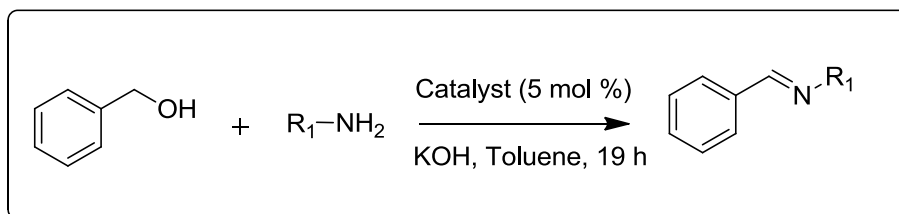
Table 1 : Catalyst Screening for oxidative cross coupling reaction^a

Entry	Alcohol	Amine	Catalyst	Product	Yield(%) ^b
1			LaCl ₃ .6H ₂ O		99
2			ErCl ₃ .6H ₂ O		99
3			La(NO ₃) ₃ .6H ₂ O		97
4			La(OAc) ₃ .1/2H ₂ O		90

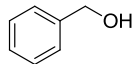
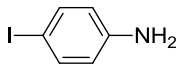
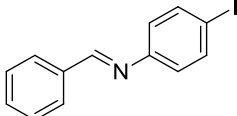
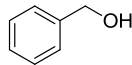
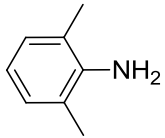
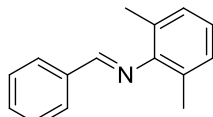
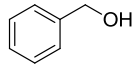
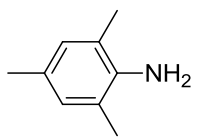
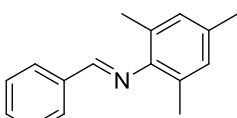
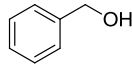
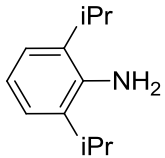
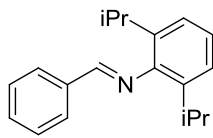
^aReaction Conditions: 5 mol% of catalyst, 1mmol of benzyl alcohol, 1.5 mmol of benzyl amine, 1 ml toluene, 19 hours, 90°C, O₂ atmosphere. All compounds were characterized by ¹H and ¹³C NMR spectroscopy using CDCl₃ as NMR solvent. ^bYields are calculated by ¹H NMR on the basis of amount of alcohol.

Encouraged by these promising results and the efficiency of lanthanides as catalysts, we looked at extending the scope of this reaction for the synthesis of other imines with various amine substrates. We have used 5 mol% of hydrated lanthanum nitrate [La(NO₃)₃.6H₂O] as the catalyst as the optimum condition to evaluate a variety of substituted anilines for imine formation with benzyl alcohols (Table 2). Anilines containing electron withdrawing groups at *ortho* position produced excellent yields (Table 2, entries 2-4). Anilines having halo functional groups such as 2-fluoroaniline, 2-chloroaniline and 2-iodoaniline gave 96%, 95% and 91% yield respectively because of the stronger electron withdrawing effect of halogen groups. To study the effect of groups present at *para* position of the anilines, 4-methylaniline and 4-iodoaniline were employed as substrates for this catalytic reaction. It was noteworthy that no substantial decrease or increase in the yield is observed and the yields of 84% and 80% were obtained with 4-methylaniline and 4-iodoaniline respectively (Table 2, entries 5 and 6). To further validate the scope of this reaction and to study the effect of various groups, anilines bearing electron releasing groups were also examined. It was found out that 2,6-dimethylaniline gave only 15% yield on reaction with benzyl alcohol (Table 2, entry 7). Furthermore, no imine formation takes place when Dip-NH₂ and mesityl aniline were investigated as substrates for the reaction. This is presumably because of the steric hindrance of the bulky electron donating groups.

Table 2 : Catalyzed oxidative cross coupling of alcohols and amines to form imines^a



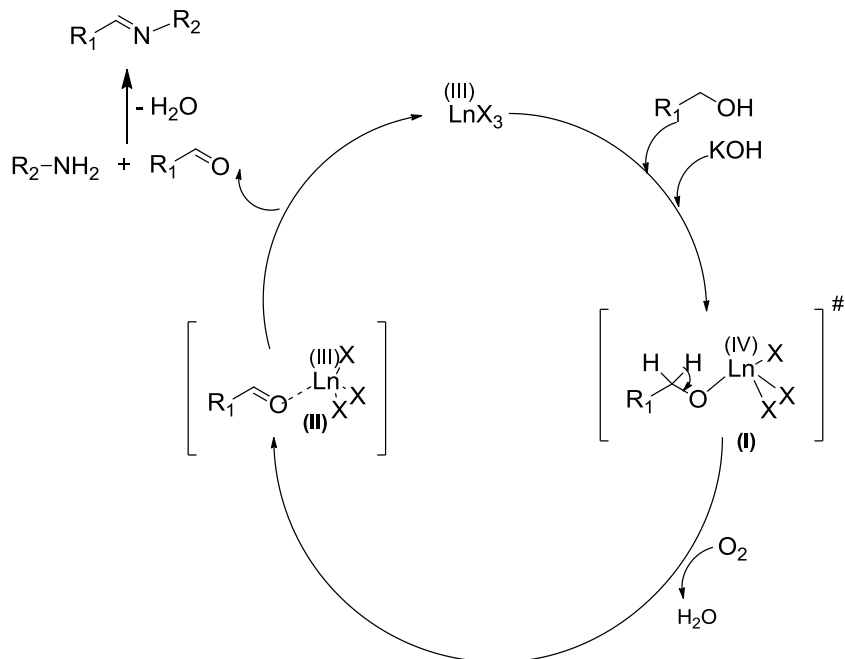
Entry	Alcohol	Amine	Catalyst	Product	Yield (%) ^b
1			La(NO ₃) ₃ ·6H ₂ O	 (1b)	97
2			La(NO ₃) ₃ ·6H ₂ O	 (2b)	96
3			La(NO ₃) ₃ ·6H ₂ O	 (3b)	95
4			La(NO ₃) ₃ ·6H ₂ O	 (4b)	91
5			La(NO ₃) ₃ ·6H ₂ O	 (5b)	84

6			La(NO ₃) ₃ ·6H ₂ O	 (6b)	80
7			La(NO ₃) ₃ ·6H ₂ O	 (7b)	15
8			La(NO ₃) ₃ ·6H ₂ O	 (8b)	0
9			La(NO ₃) ₃ ·6H ₂ O	 (9b)	0

^aReaction Conditions: 5 mol% of catalyst, 1 mmol of benzyl alcohol, 1.5 mmol of benzyl amine, 1 ml toluene, 19 hours, 90°C, O₂ atmosphere. All compounds were characterized by ¹H and ¹³C NMR spectroscopy using CDCl₃ as NMR solvent. ^bYields are calculated by ¹H NMR on the basis of amount of alcohol.

The most plausible mechanism for the lanthanide salts catalyzed oxidative cross coupling of alcohols with amines is given in Scheme 2.2. In the first step, deprotonation of alcohol takes place by base followed by addition of lanthanides to the deprotonated alcohol to form the hypervalent lanthanum (IV) intermediate (I). In the second step, oxidation of alcohol takes place by the atmospheric oxygen and the abstraction of allylic hydrogen takes place releasing water as the by-product and to form another lanthanum (III) intermediate (II). Next, the intermediate (II)

releases the aldehyde and the catalyst. Then the aldehyde couples with the amine leading to imine formation. However we could not able to isolate any of the intermediates.



Scheme 2.2: Most plausible mechanism for the lanthanides mediated oxidative cross coupling of alcohols with amines.

5. Conclusion

In summary, we have developed a new, simple and efficient catalytic system for the oxidative cross coupling of alcohols with amines to form the corresponding imines. Lanthanide salts proved to be the effective and versatile catalysts for synthesis of imines. The major advantages of this method are its general applicability, giving good yields of corresponding imines with various amines, easy transformation and low toxicity. The reaction was performed at atmospheric pressure of molecular oxygen which is considered as an abundant and green oxidant.

6. Experimental Section

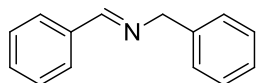
6.1 General information

All reactions were performed in air without any special precautions, unless stated otherwise. Chemicals and solvents were of analytical grade, purchased from Sigma Aldrich and were used without purification. ^1H NMR (400 MHz) and $^{13}\text{C}\{^1\text{H}\}$ (C100 MHz), spectra were recorded on a BRUKER AVANCE III-400 spectrometer.

6.2 General procedure for the cross coupling of alcohols and amines to form imines:

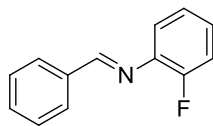
In a typical experiment, alcohol (1.0 mmol), amine (1.50 mmol), catalyst (5 mol%), KOH (84 mg, 1.5 mmol), and toluene (1 mL) were placed in a 10 mL glass tube. Then, the reaction mixture was stirred under oxygen atmosphere at 70 °C for 19 hours before it was quenched by NH_4Cl (2 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried using Na_2SO_4 and concentrated in vacuo. The product was characterized by ^1H and ^{13}C NMR spectroscopy. The yield of product was analysed using ^1H NMR spectroscopy and calculated based on the amount of alcohol.

6.2.1 *N*-benzylidene-1-phenylmethanamine (**2a**):



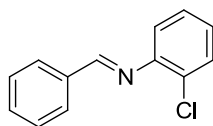
^1H NMR (400MHz, CDCl_3): δ 8.31 (s, 1H, *H*-C=N), 7.72-7.69 (m, 2H, Ar-*H*), 7.34-7.32 (m, 3H, Ar-*H*), 7.20-7.15 (m, 4H, Ar-*H*), 4.74 (s, 2H, CH_2 -N) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.1 (C=N), 139.3, 136.2, 132.0, 130.8, 128.6, 128.5, 128.3, 128.0, 127.3, 127.2, 127.0 (Ar-C), 65.0 (C-N) ppm.

6.2.2 *N*-benzylidene-2-fluoroaniline (**2b**):



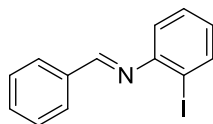
^1H NMR (400MHz, CDCl_3): δ 8.48 (s, 1H, *H*-C=N), 7.92-7.90 (m, 2H, Ar-*H*), 7.50-7.43 (m, 3H, Ar-), 7.14-7.12 (m, 4H, Ar-*H*) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.1 (C=N), 156.5 (C-F), 141.0, 136.0, 131.8, 129.8, 128.8, 127.5, 127.0, 126.7, 124.6, 122.0, 118.7 (Ar-C) ppm.

6.2.3 *N*-benzylidene-2-chloroaniline (**3b**):



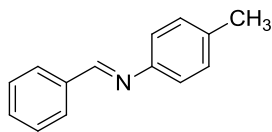
^1H NMR (400MHz, CDCl_3): δ 8.35 (s, 1H, *H*-C=N), 7.93-7.91 (m, 2H, Ar-*H*), 7.47-7.41 (m, 4H, Ar-*H*), 7.24-7.20 (m, 3H, Ar-*H*) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.1 (C=N), 149.6, 143.0, 135.9, 131.9, 130.0, 129.4, 129.2, 128.9, 127.7, 126.4, 120.1, 119.1(Ar-C) ppm.

6.2.4 *N*-benzylidene-2-iodoaniline (**4b**):



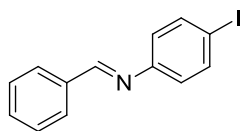
^1H NMR (400MHz, CDCl_3): δ 8.34 (s, 1H, *H*-C=N), 7.78-7.76 (m, 2H, Ar-*H*), 7.32-7.30 (m, 3H, Ar-*H*), 7.00-6.98 (m, 4H, Ar-*H*) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.1 (C=N), 149.6, 143.0, 135.9, 131.9, 130.0, 129.4, 129.2, 128.9, 127.7, 126.4, 120.1, 119.1 (Ar-C) ppm.

6.2.5 *N*-benzylidene-4-methylaniline (**5b**):



^1H NMR (400MHz, CDCl_3): δ 8.45 (s, 1H, *H*-C=N), 7.90-7.88 (m, 2H, Ar-*H*), 7.46-7.45 (m, 3H, Ar-*H*), 7.20-7.18 (m, 2H, Ar-*H*), 7.15-7.13 (m, 2H, Ar-*H*), 2.36 (s, 3H, CH_3) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 159.7 (C=N), 149.5, 143.8, 136.4, 135.9, 131.3, 129.8, 128.8, 127.9, 127.6, 127.0, 120.9, 115.4 (Ar-C), 21.1 (CH_3).

6.2.6 *N*-benzylidene-4-iodoaniline (**6b**):



^1H NMR (400MHz, CDCl_3): δ 8.31 (s, 1H, *H*-C=N), 7.80-7.78 (m, 2H, Ar-*H*), 7.60-7.58 (d, 2H, Ar-*H*), 7.39-7.36 (m, 3H, Ar-*H*), 6.87-6.85 (d, 2H, Ar-*H*) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 161.1 (C=N), 146.1, 140.9, 138.2, 137.9, 131.7, 131.8, 128.9, 128.6, 127.7, 127.1, 123.1, 117.4 (Ar-C) ppm.

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Appendix

Supporting Information:

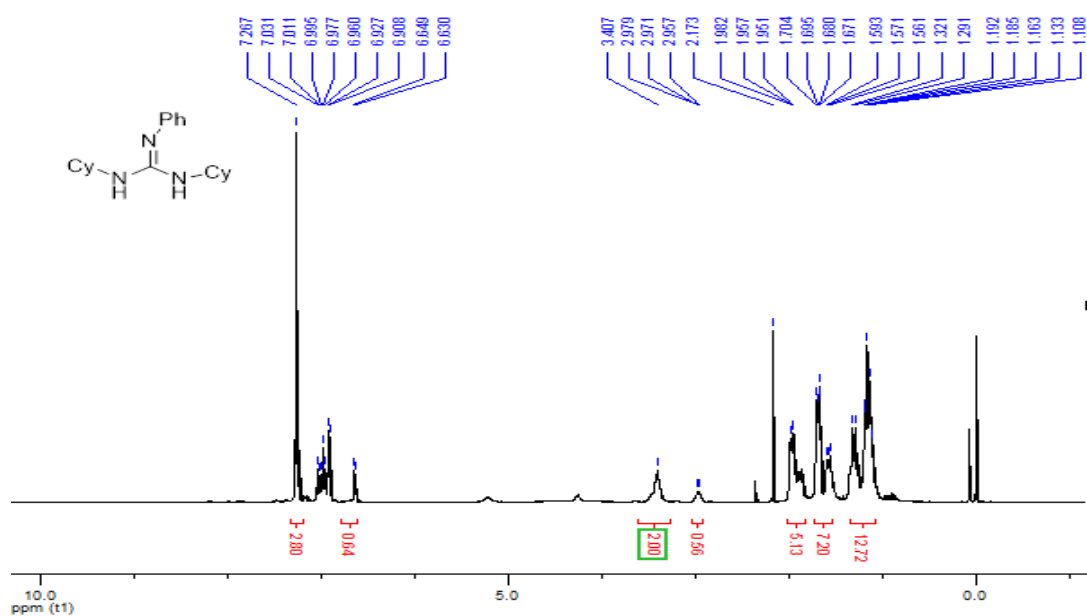


Figure S1: ¹H NMR spectra of compound 1a.

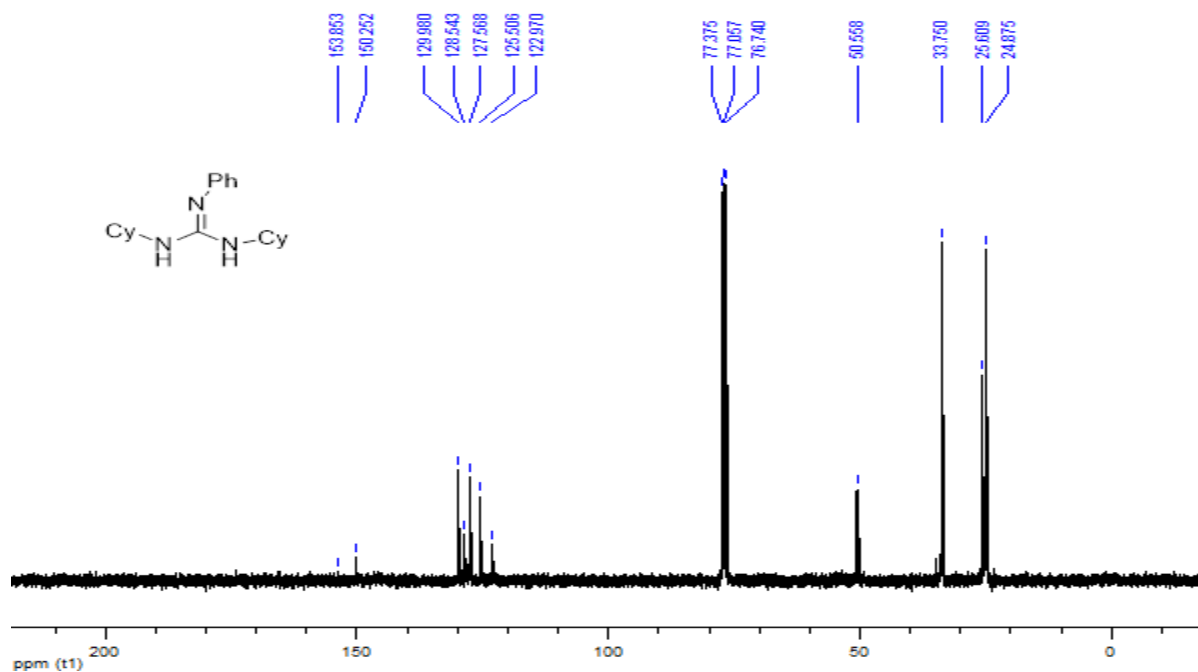


Figure S2: ¹³C NMR spectra of compound 1a.

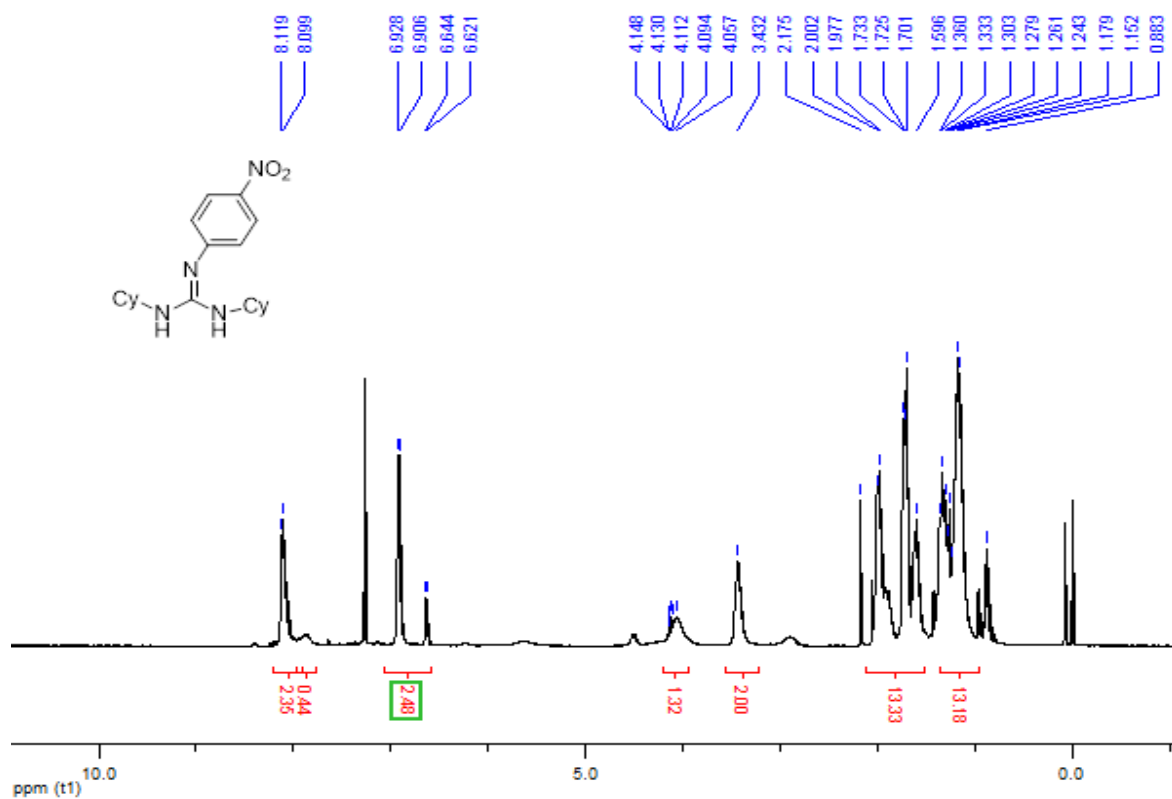


Figure S3: ¹H NMR spectra of compound 2a.

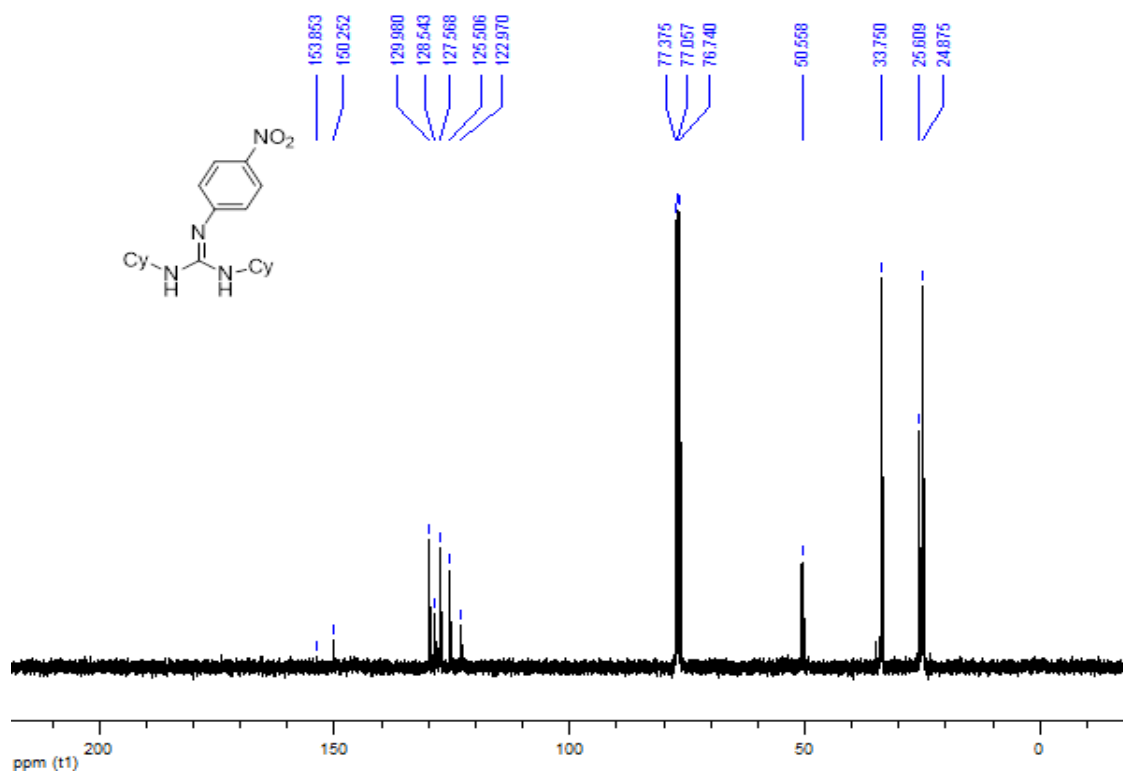
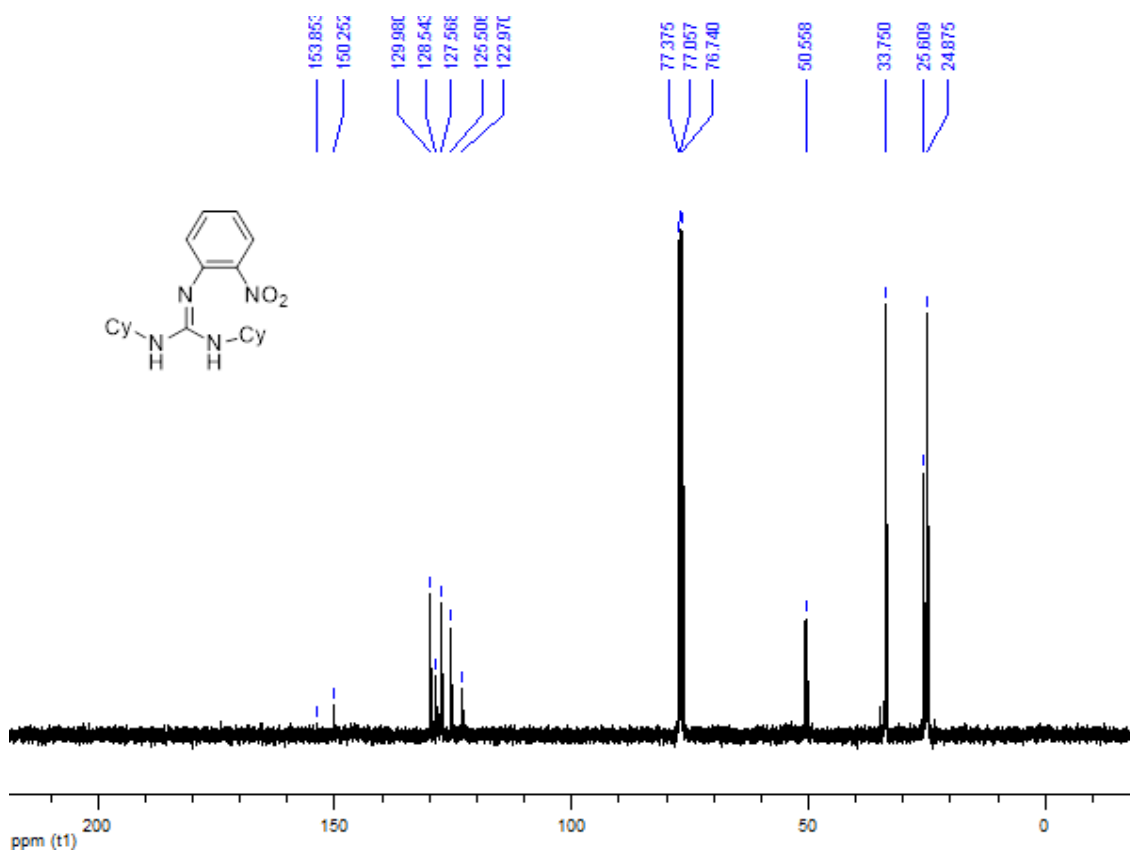
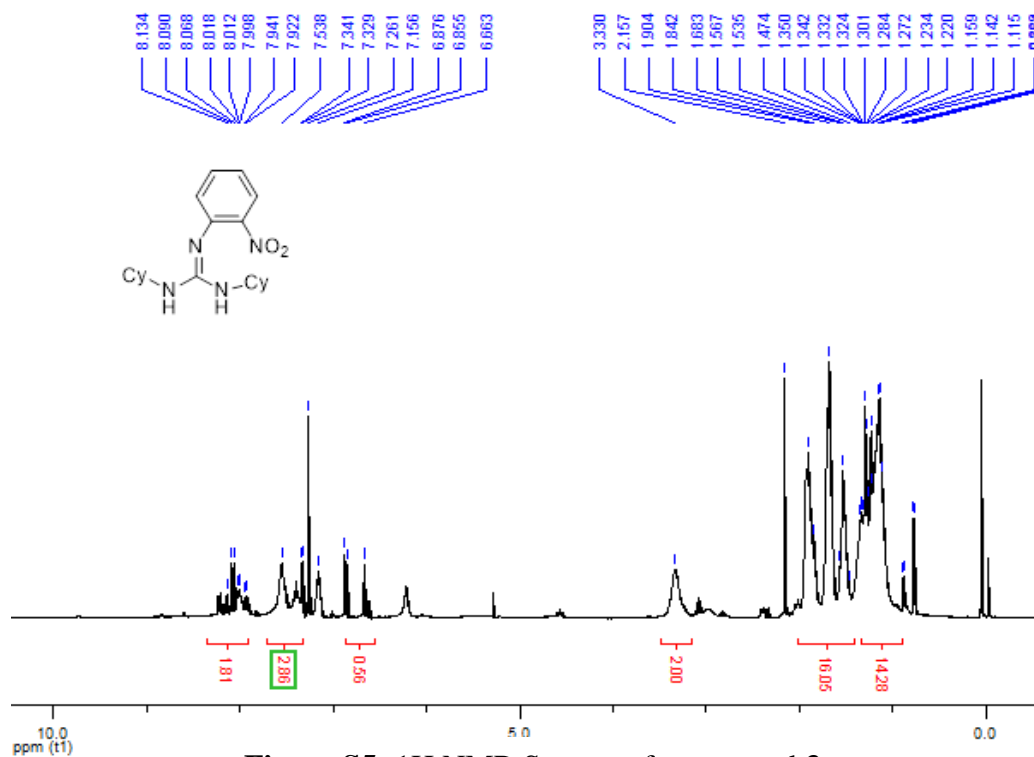


Figure S4: ¹³C NMR spectra of compound 2a.



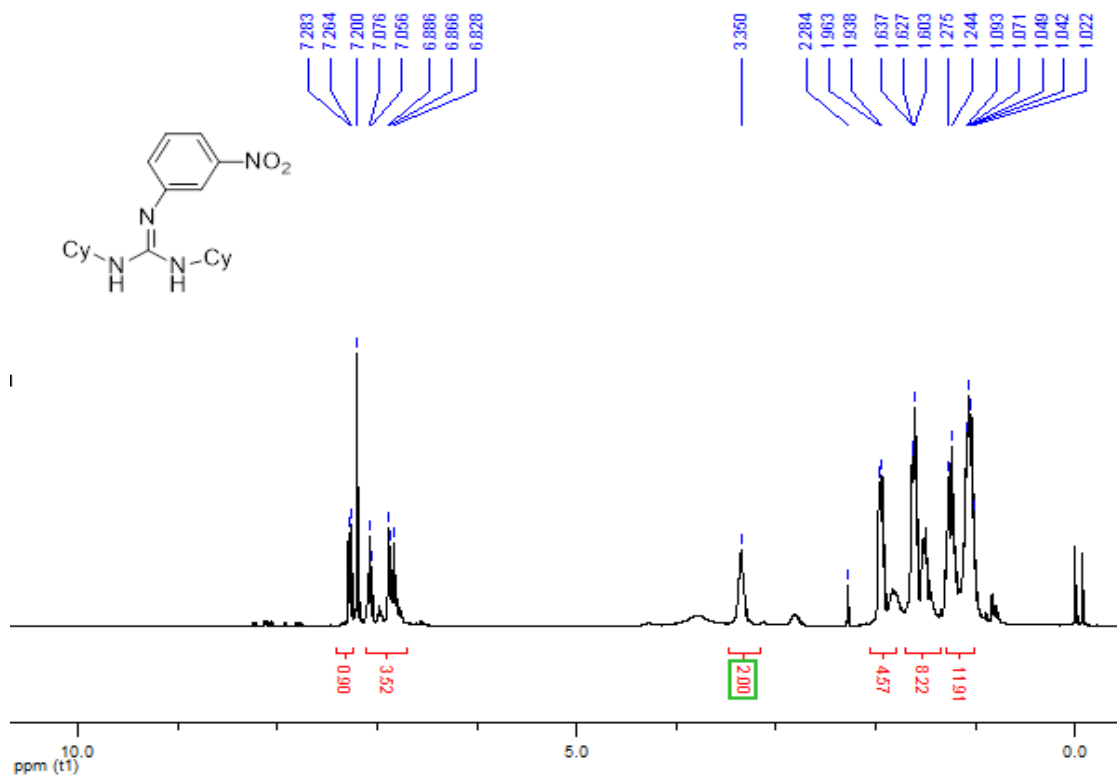


Figure S7: ¹H NMR spectra of compound 4a.

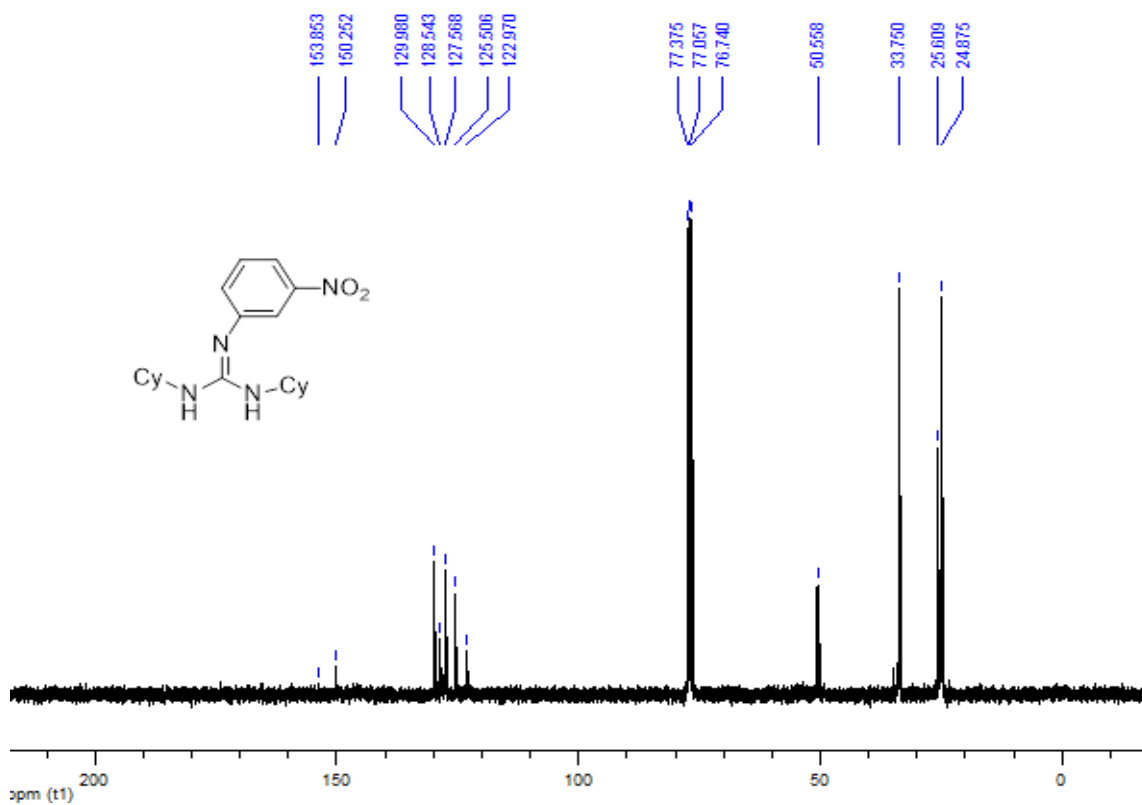


Figure S8: ¹³C NMR spectra of compound 4a.

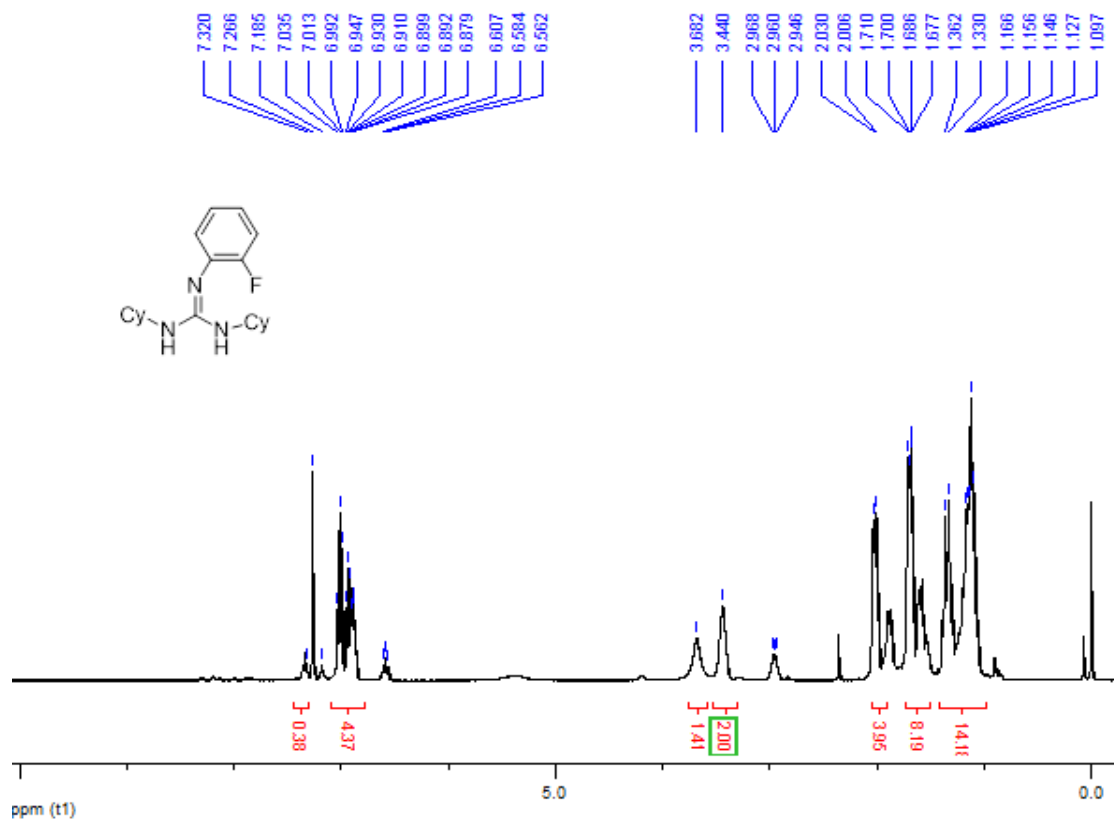


Figure S9: ¹H NMR spectra of compound 5a.

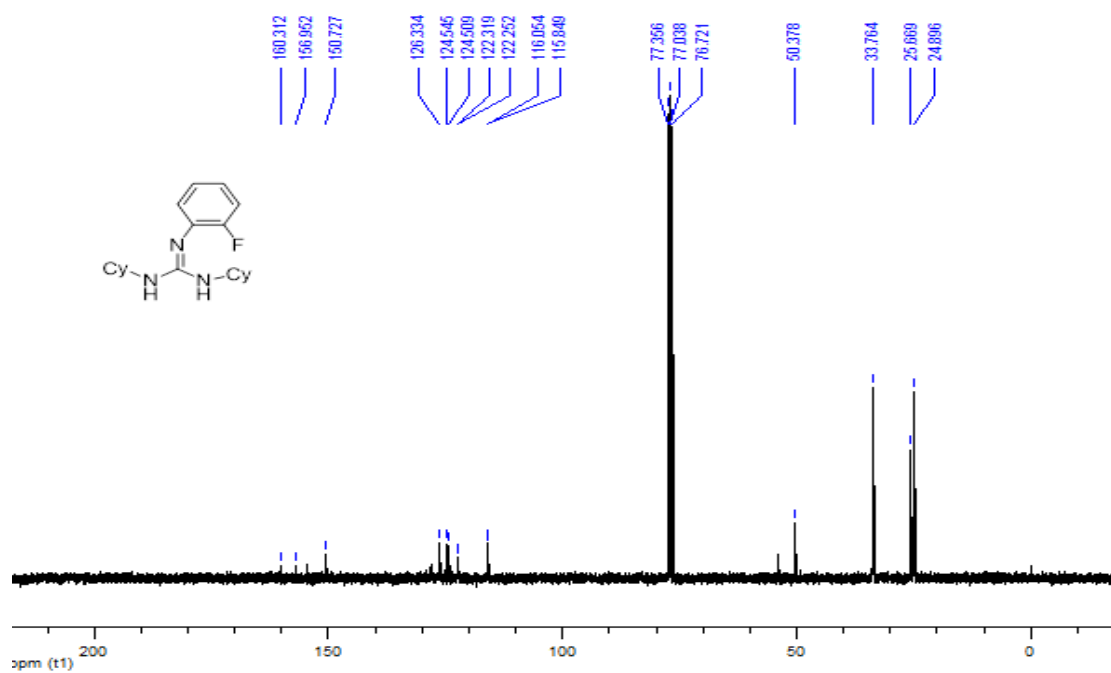


Figure S10: ¹³C NMR spectra of compound 5a.

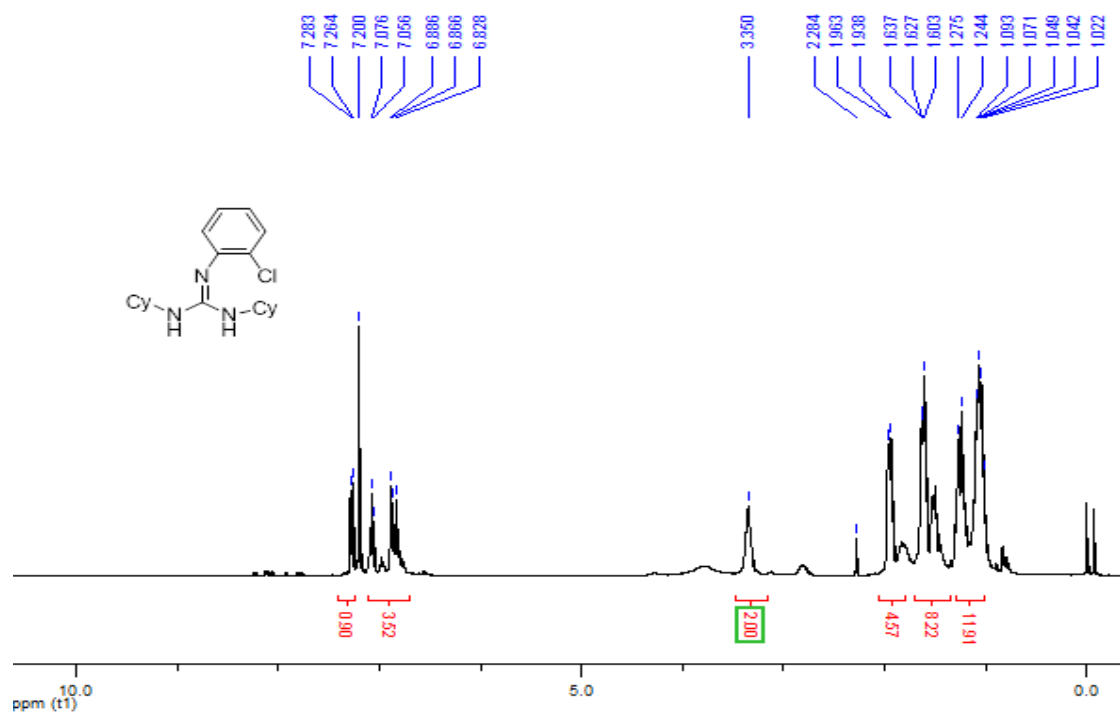


Figure S11: ¹H NMR spectra of compound 6a.

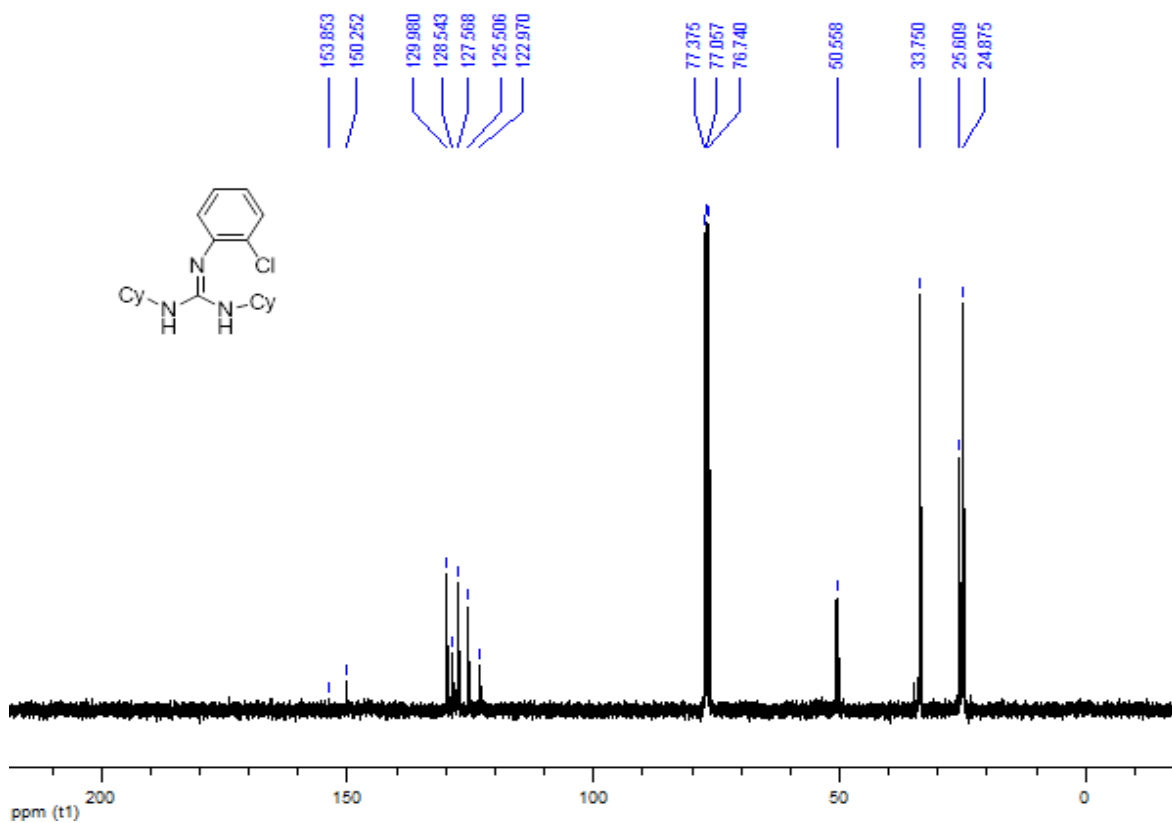


Figure S12: ¹³C NMR spectra of compound 6a.

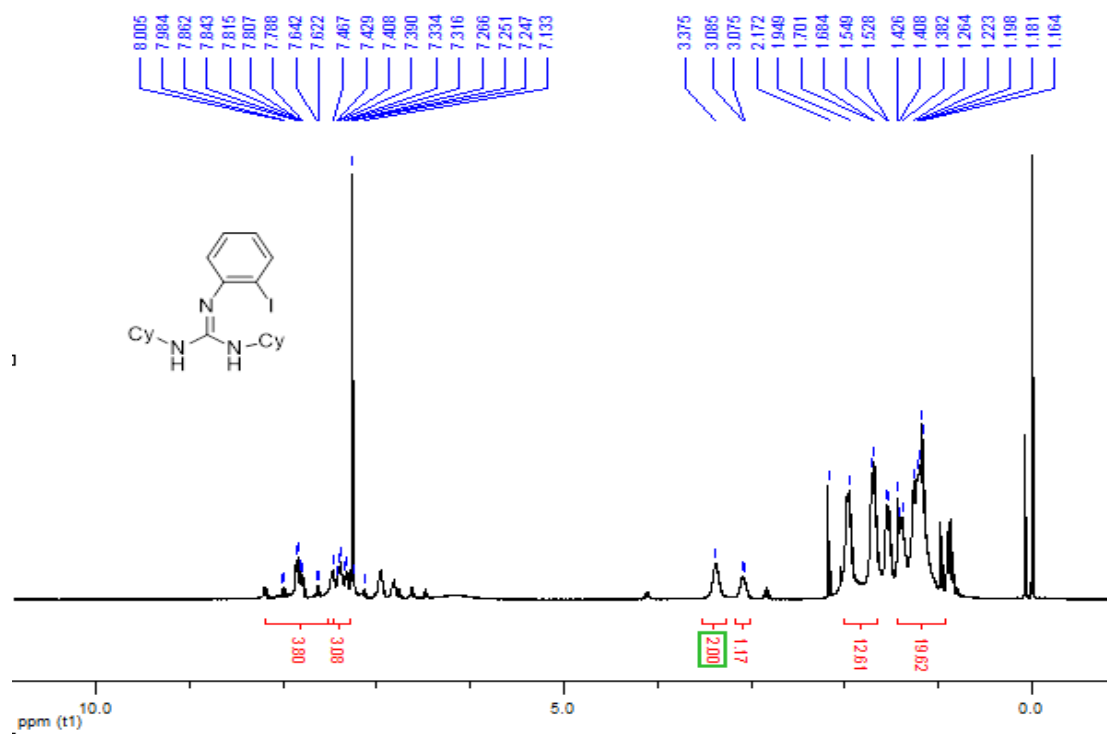


Figure S13: ¹H NMR spectra of compound 7a.

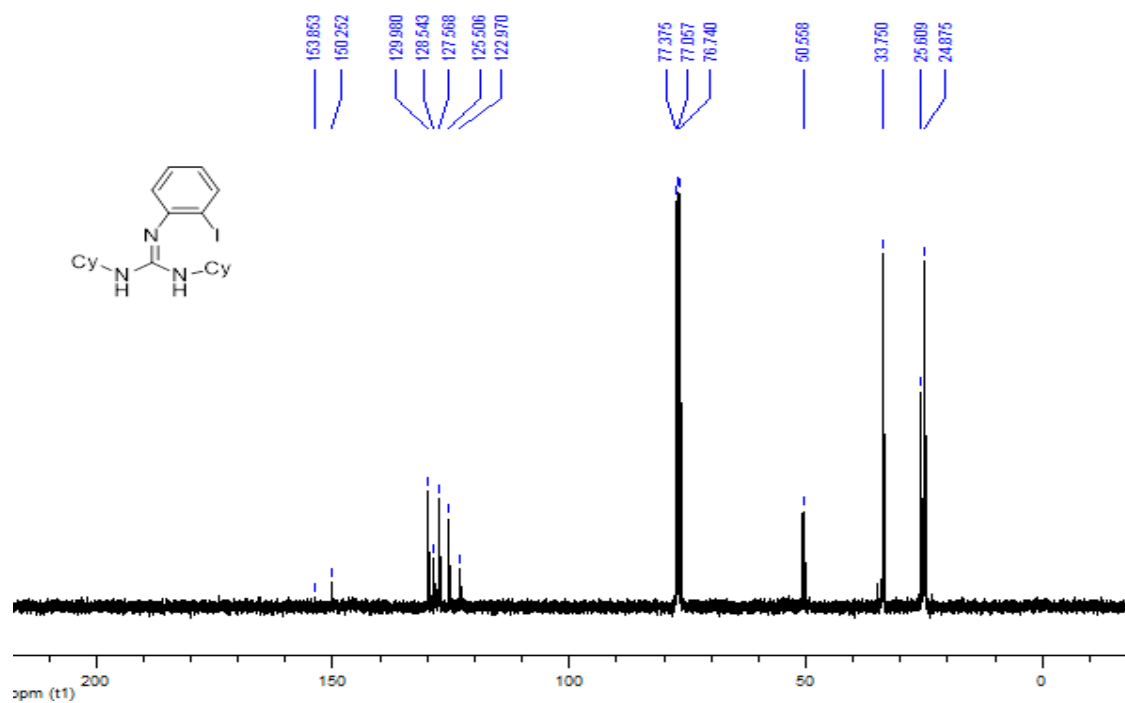


Figure S14: ¹³C NMR spectra of compound 7a.

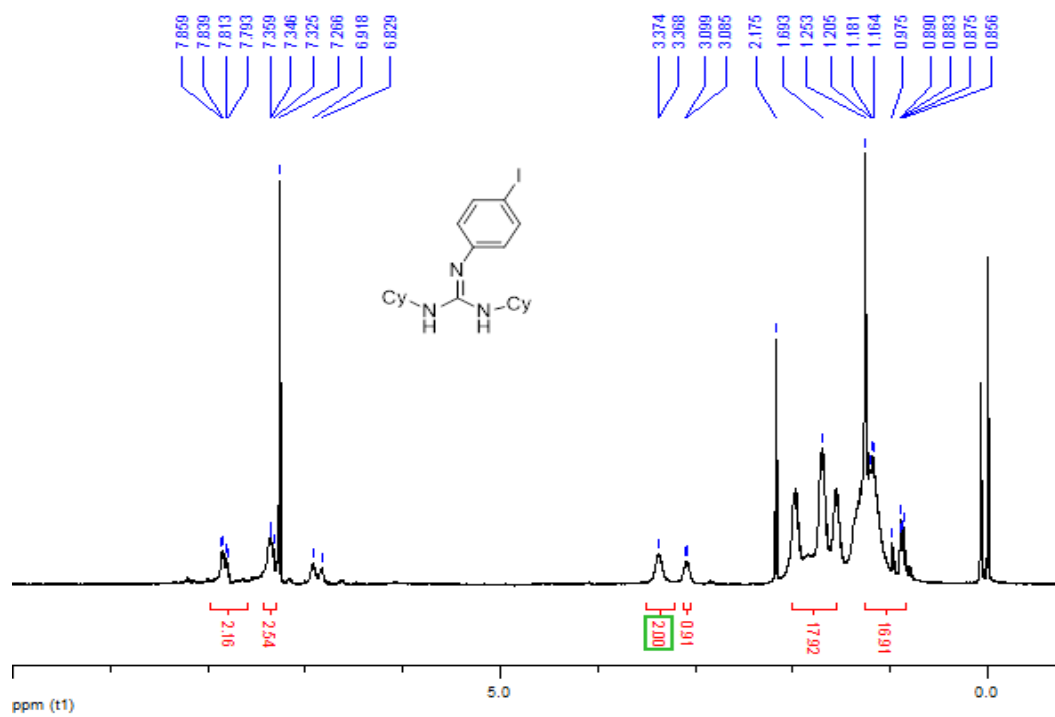


Figure S15: ¹H NMR spectra of compound 8a.

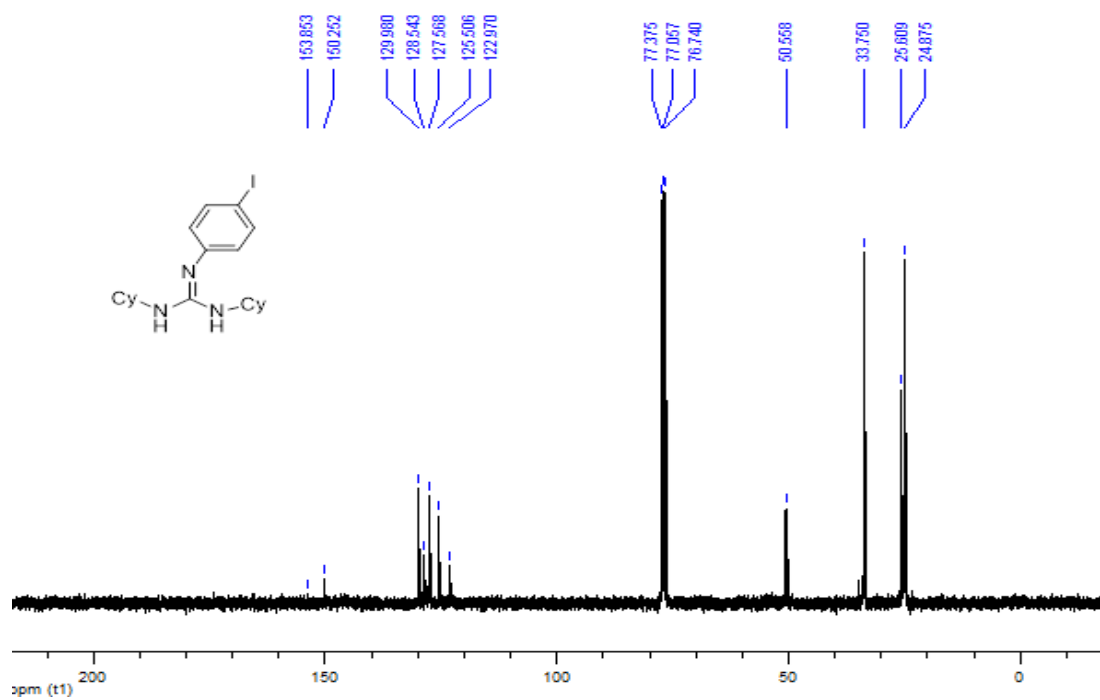


Figure S16: ¹³C NMR spectra of compound 8a.

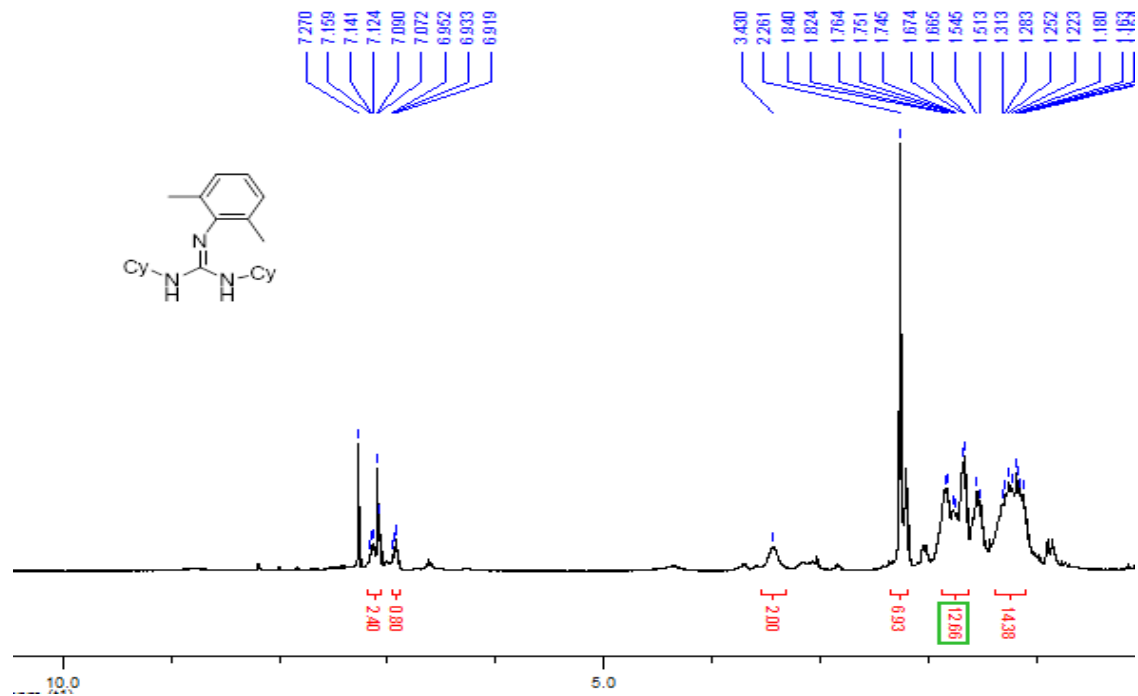


Figure S17: ¹H NMR spectra of compound 10a.

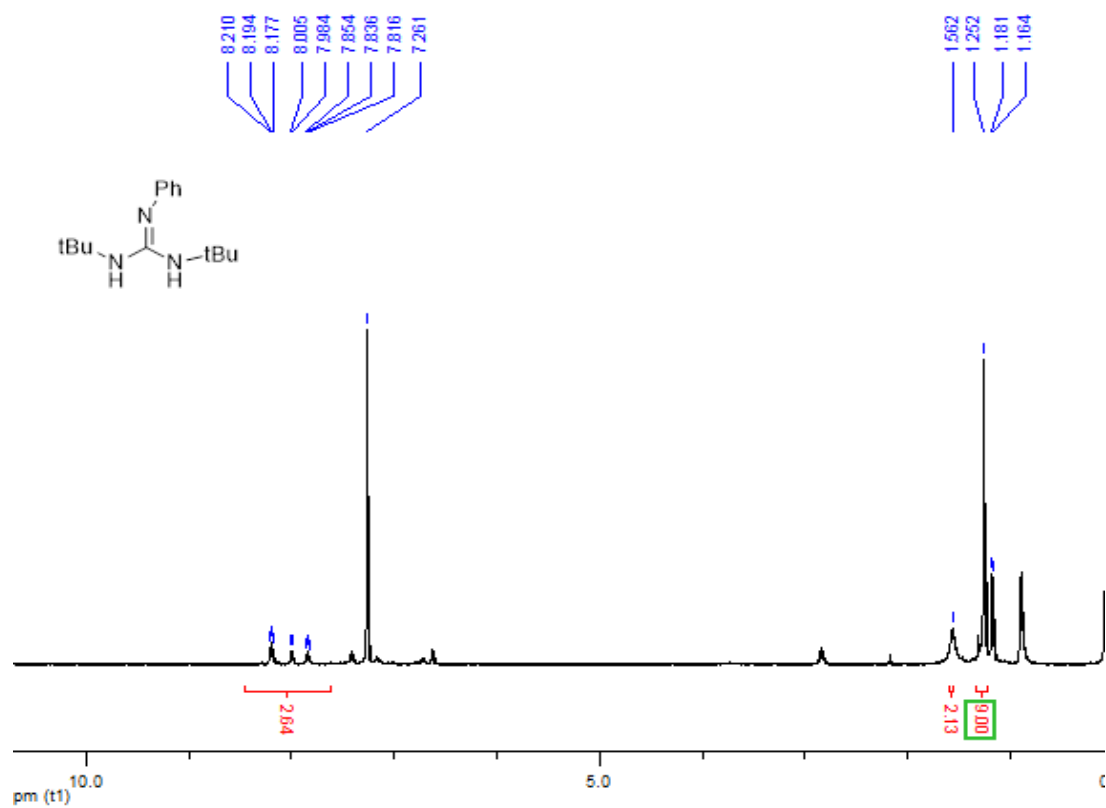


Figure S18: ¹H NMR spectra of compound 12a.

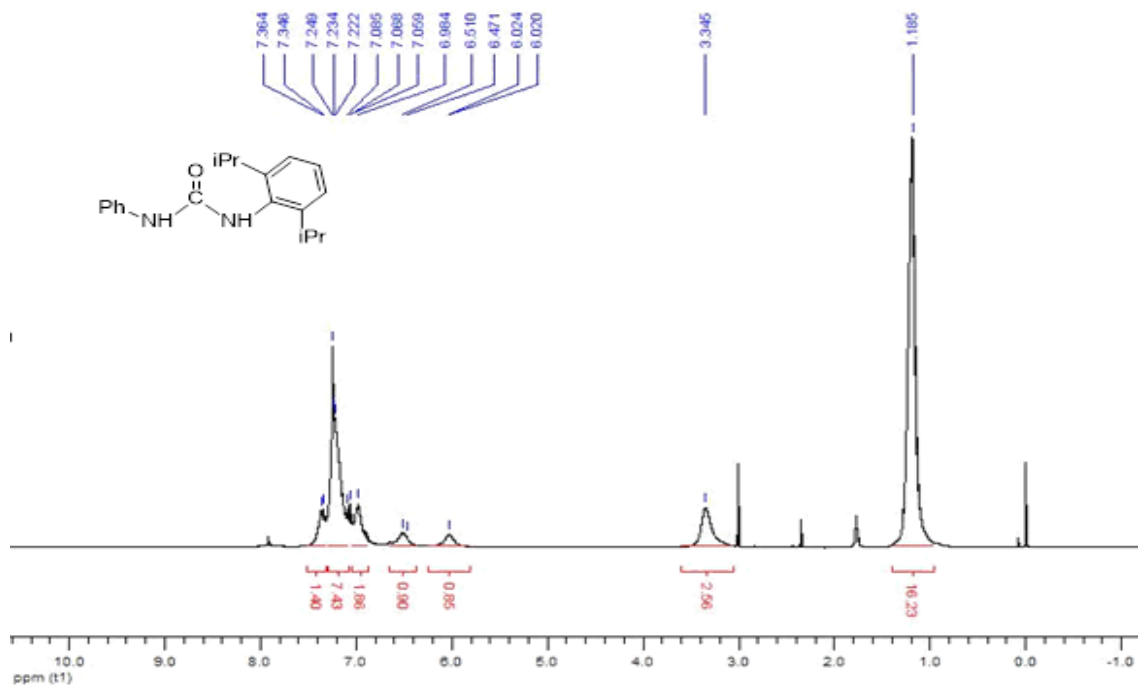


Figure S21: ^1H NMR spectra of compound 15a.

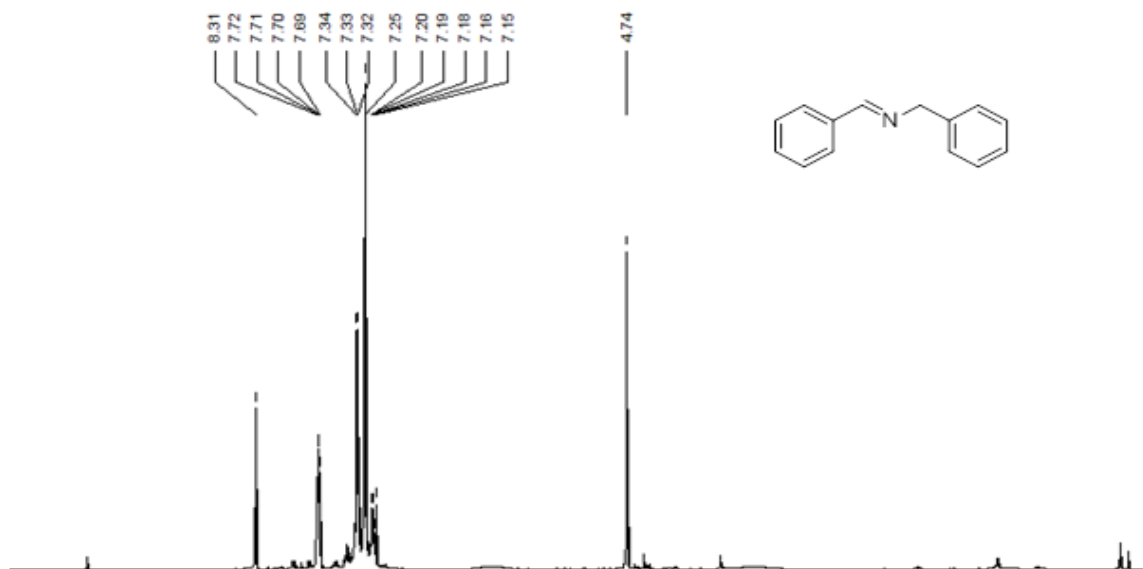


Figure S22: ¹H NMR spectra of compound **1b**.

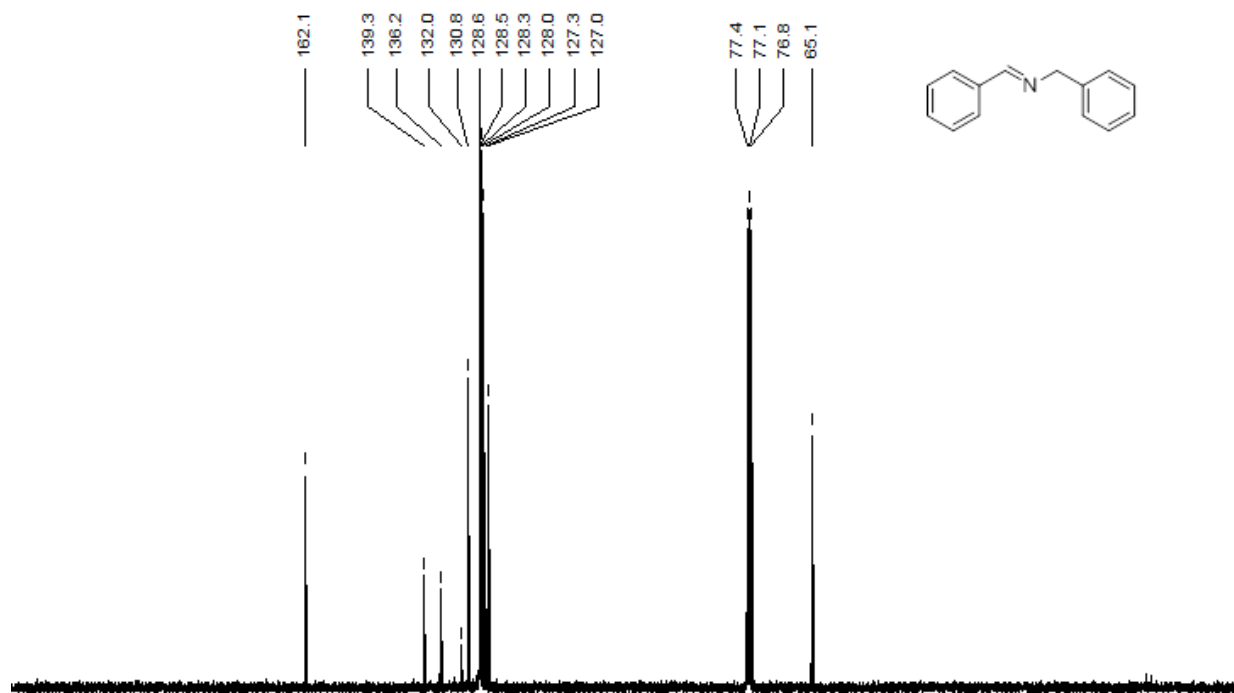


Figure S23: ¹³C NMR spectra of compound **1b**.

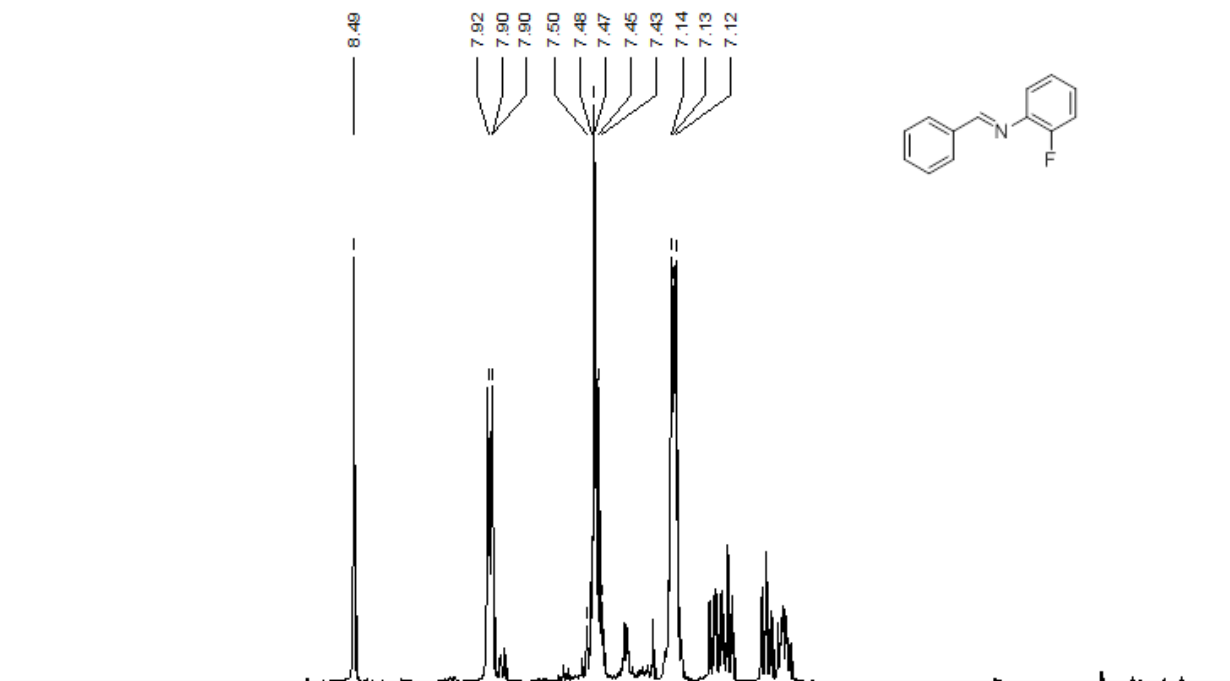


Figure S24: ¹H NMR spectra of compound **2b**.

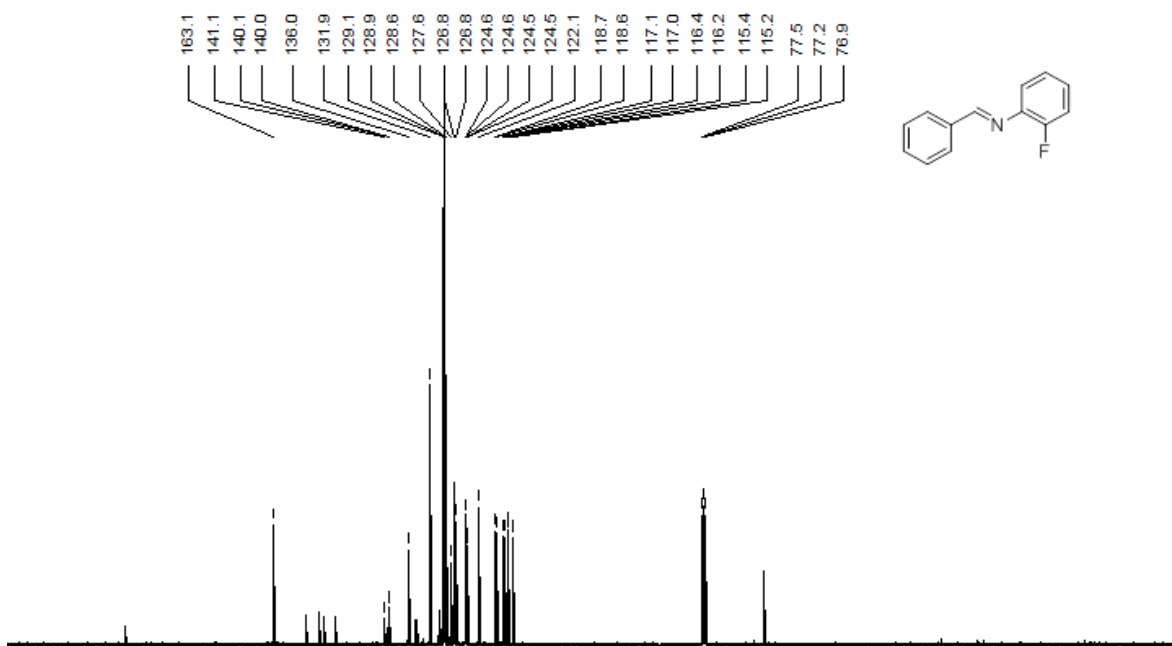


Figure S25: ¹³C NMR spectra of compound **2b**.

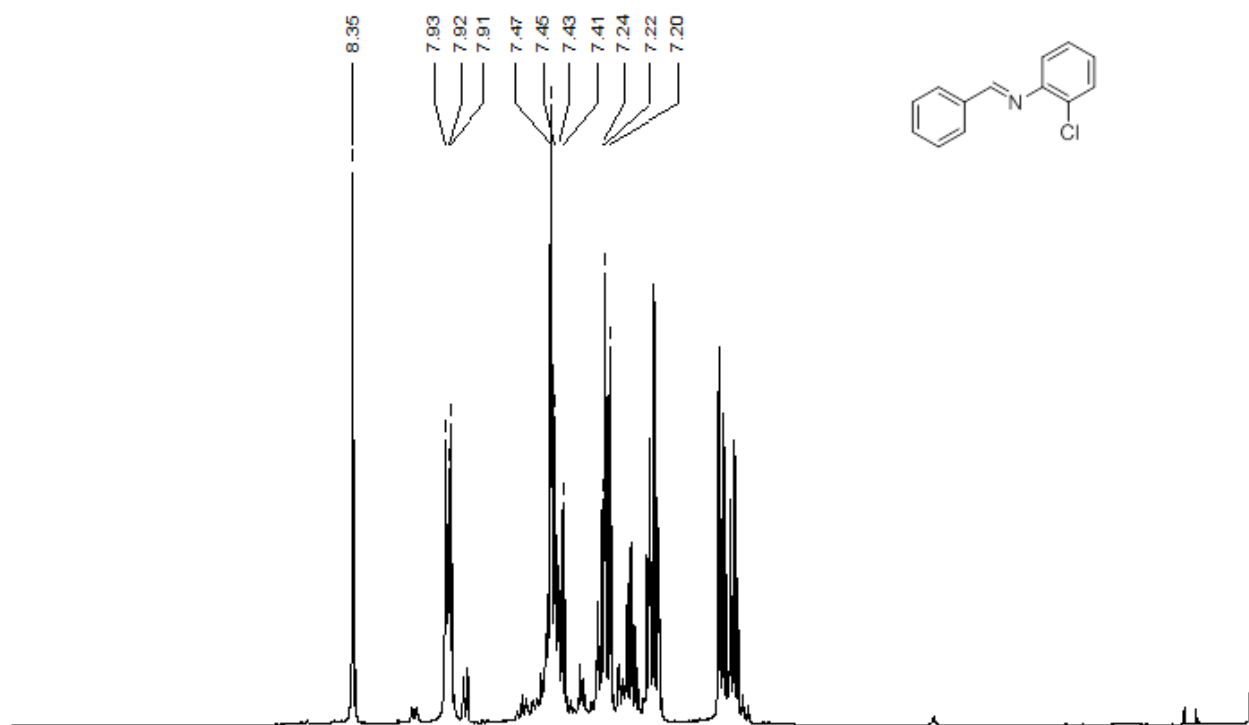


Figure S26: ¹H NMR spectra of compound 3b.

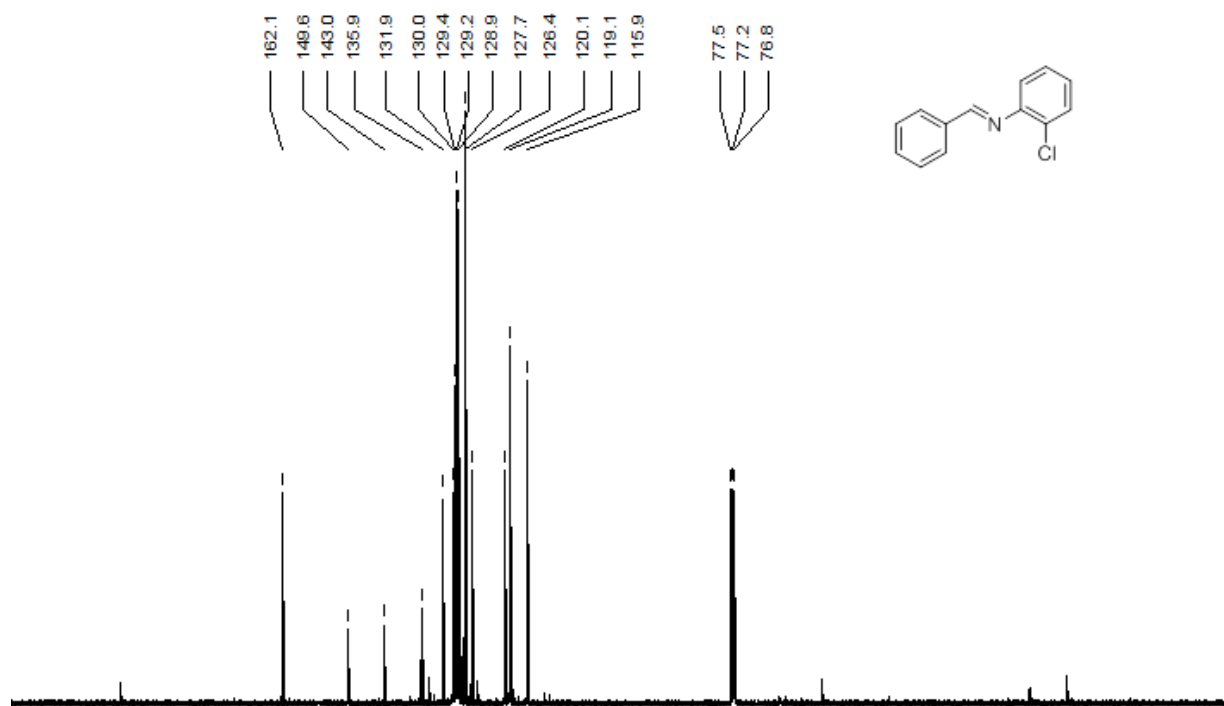


Figure S27: ¹³C NMR spectra of compound 3b.

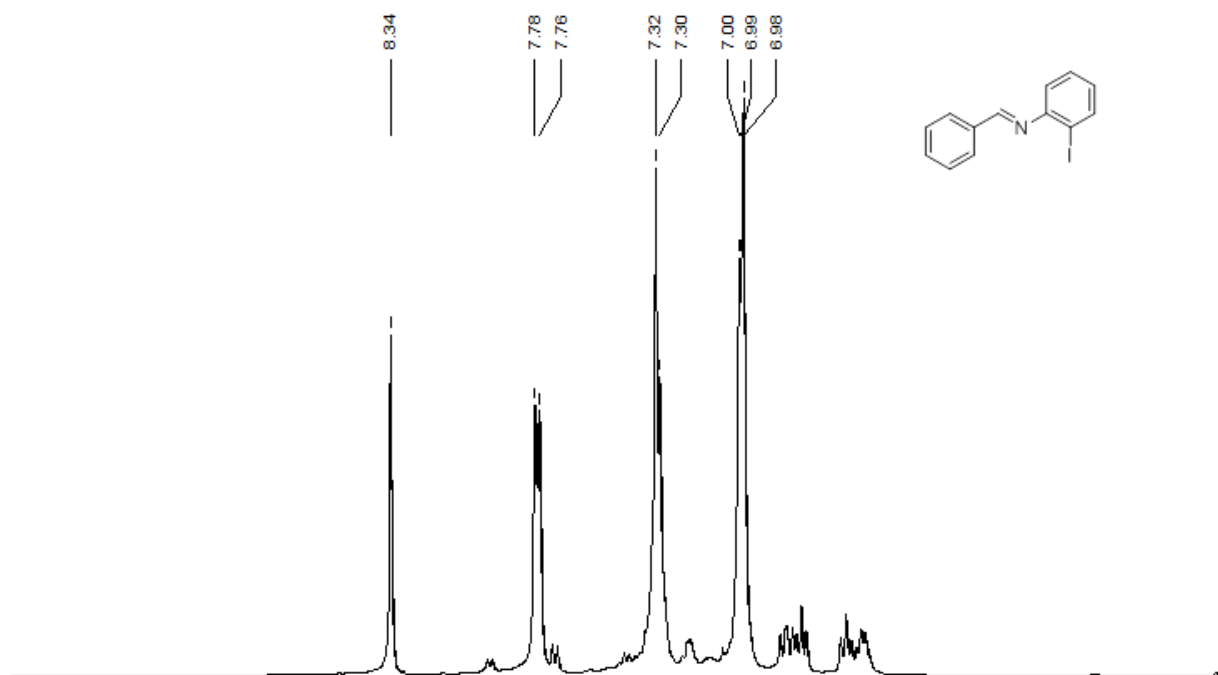


Figure S28: ¹H NMR spectra of compound **4b**.

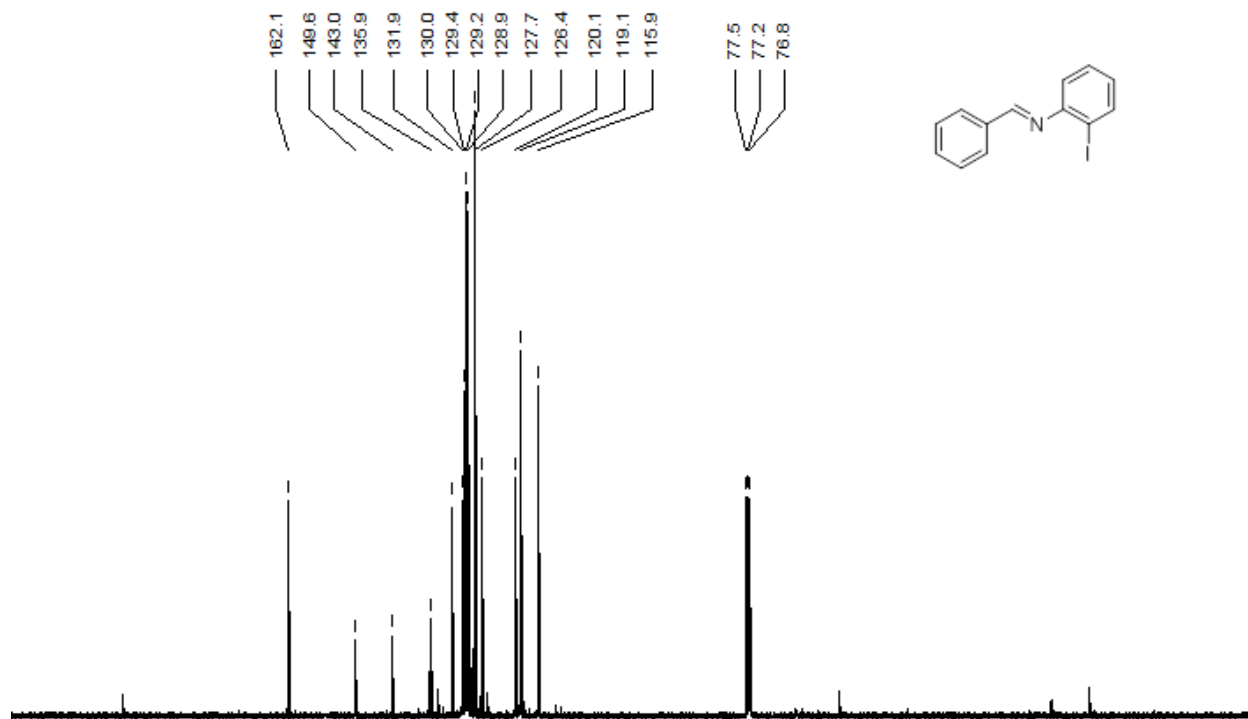


Figure S29: ¹³C NMR spectra of compound **4b**.

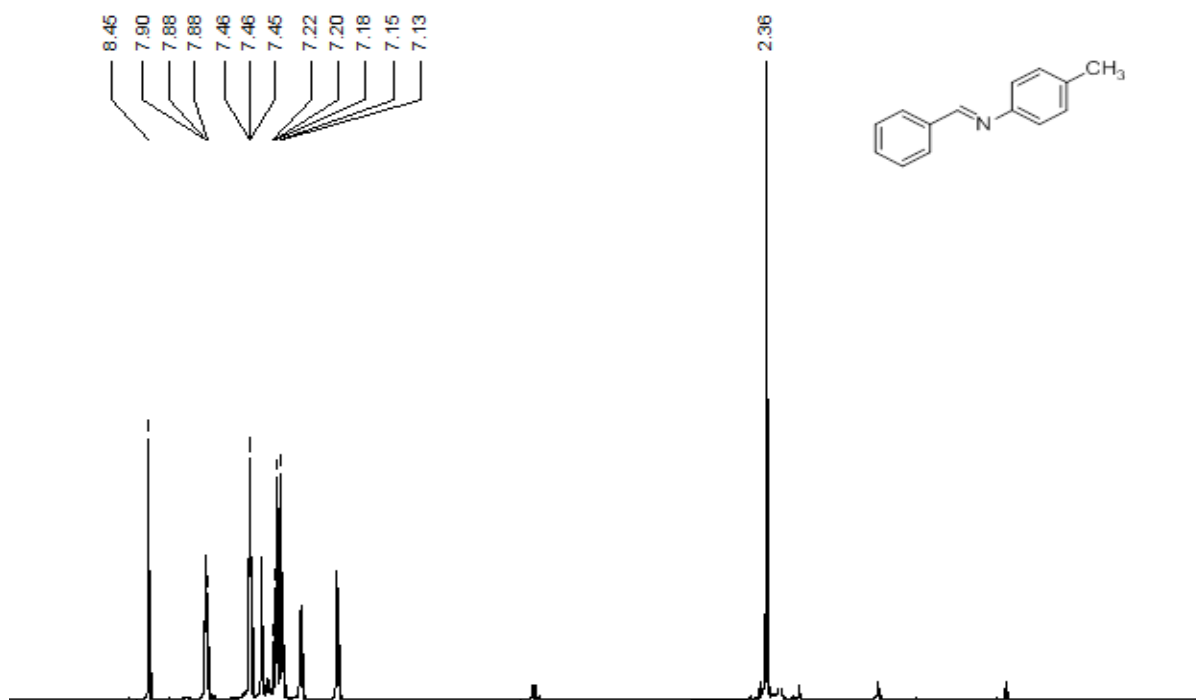


Figure S30: ^1H NMR spectra of compound 5b.

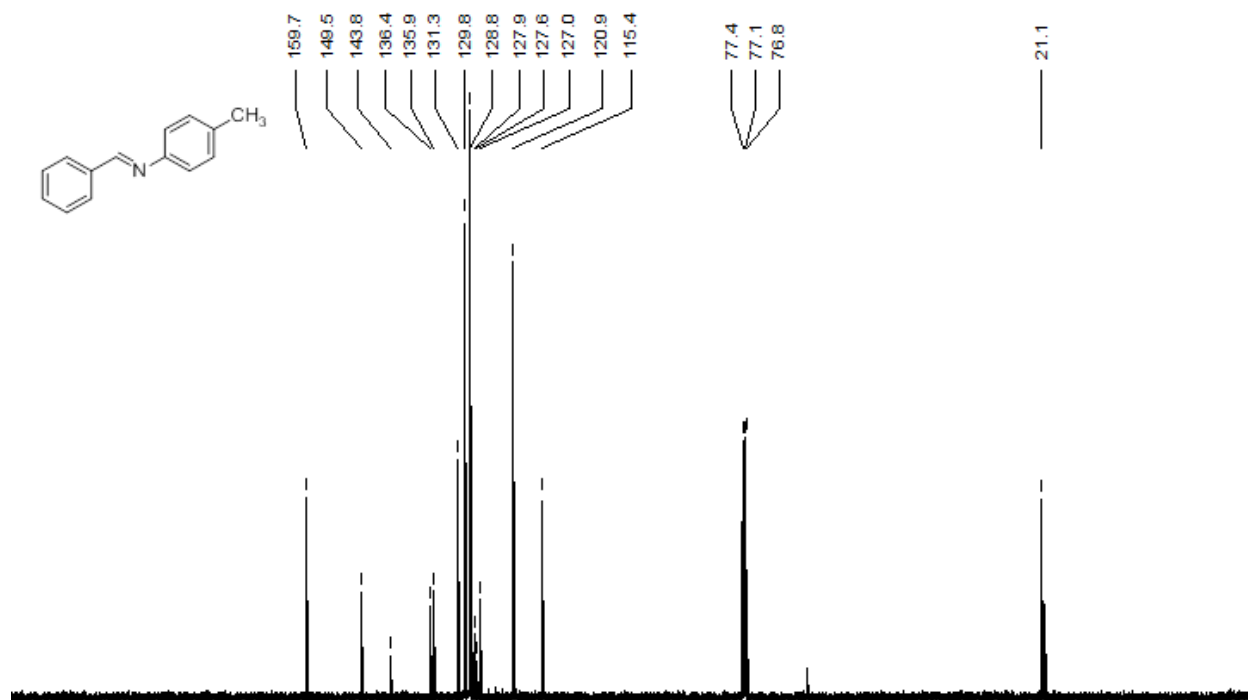


Figure S31: ^{13}C NMR spectra of compound 5b.

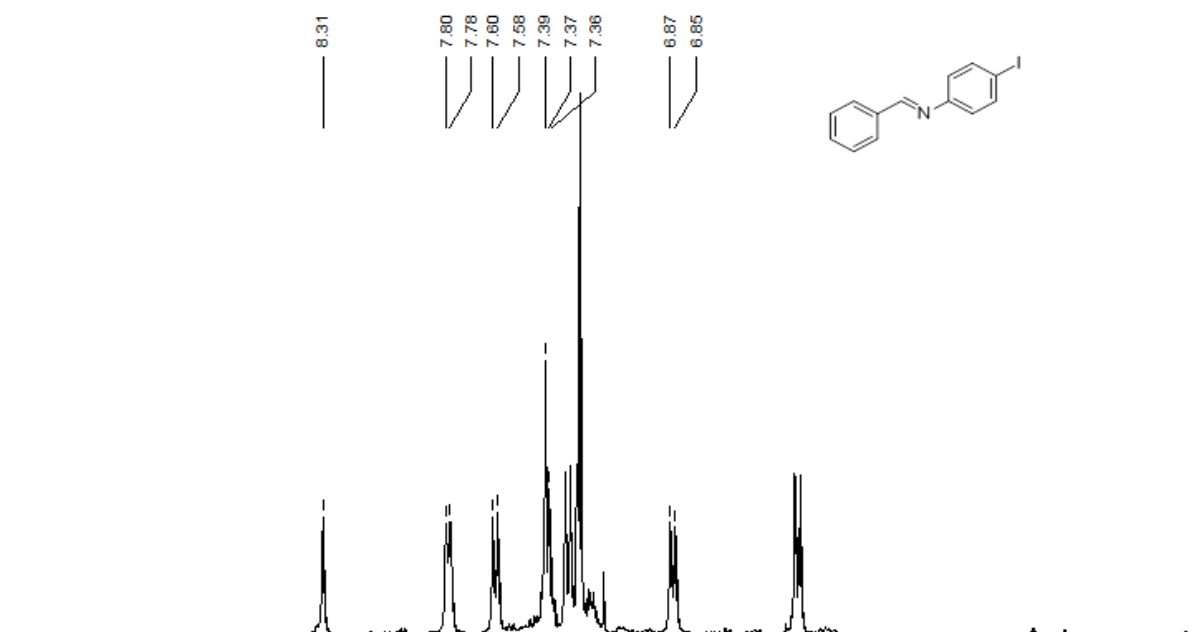


Figure S32: ¹H NMR spectra of compound **6b**.

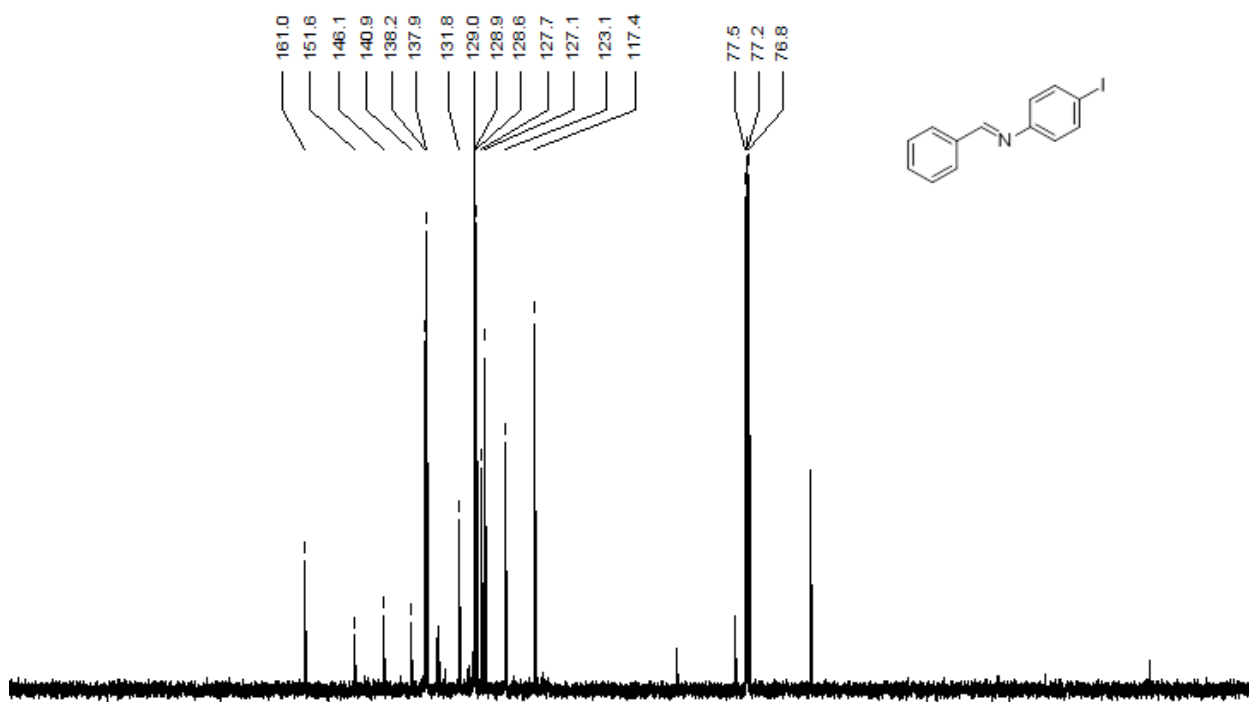


Figure S33: ¹³C NMR spectra of compound **6b**.

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- ❖ Attended '**Polyurethane exhibition and conference**' organized by PU TECH at Indian Expo Centre, Noida during 9-11 March, 2011

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- ❖ Secured All India Rank 217 in JAM (Joint Admission test for M.sc)
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