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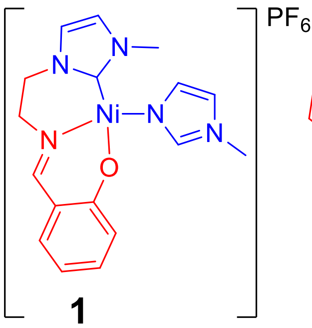
APPLICATION OF NI(II) COMPLEXES OF AIR STABLE SCHIFF BASE FUNCTIONALIZED *N*-HETEROCYCLIC CARBENE LIGANDS AS CATALYSTS FOR CN COUPLING REACTION

*[1]Samaila Abubakar, [2]Dailami S. Adam and [1]Abubakar Abdulkadir
[1]Department of Chemistry, Gombe State University, Gombe, Gombe State, Nigeria
[2]Department of Chemistry, Federal University Lokoja, Kogi State, Nigeria.
*Correspondence to: e-mail- ismailabubakarch@yahoo.com.

ABSTRACT

We reported the applications of square planar nickel(II) complexes in the C-N coupling reaction. The complexes **1–3,** were previously reported for transfer hydrogenation reaction of ketones and are now found to be active in the activation of CN coupling reaction in the presence of KO^{t}Bu, and dioxane as base and solvent respectively. Formation of various aminated products from bromo benzene and aniline with isolated yields up to 85% has been recorded with low catalysts loading of 1 mol% in the presence of base. The scope of the catalysis was further extended to include other substituted halogenated benzenes. The isolated products were analysed using NMR.



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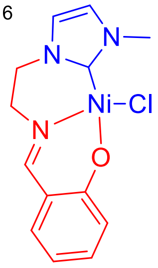

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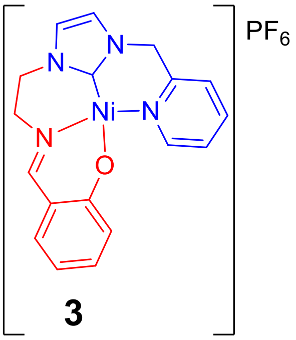

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Keywords: CN coupling, *N*-heterocyclic carbene, nickel complex, Imino-NHC, Schiff base

INTRODUCTION

Development of arylamines is one of the leading areas in organic transformation reactions and this is not by surprise considering the variety of applications of aminated products [1-4]. Aminated products appear in almost all applications of chemistry starting from the pharmaceutical drugs, polymers, materials sciences and various intermediates for pesticides and detergent [5-7]. The challenge is how to develop a mild and convenient ways of making these amazing compounds.

However, the use of transition metal complexes as catalysts in organic transformation reactions has since proven to offer a solution. Reactions that used to be slower and harsh has now become simplified and fast with the aid of transition metal catalysts [8].In this context traditional ways of making CN coupling reactions are now obsolete [9]. For over decade's palladium complexes have taken the lead in the development of the C-N coupling reactions [6, 10, 11]. However, as the attention of the world has moved towards sustainable chemistry, the minimization of the use of heavy metals in our daily chemistry is also necessary [12]. First, raw transition metals also known as earth-abundant metals have been identified as potential candidates in these aspects [13, 14]. They have low cost, and low toxicity and they proved to compete with their heavy metals counterpart. Reports on the use of nickel complexes in the C-N coupling reactions have been well documented [15-17]. However, reports on the use of NHC-Ni complexes are scanty. Recently, imino-NHC-nickel complexes **1**–**3** were developed and applied as precatalysts in the transfer hydrogenation of ketones [18]. Inspired by the thermal stability of the complexes they are now used as catalysts in the C-N coupling reaction. Specifically, since these type of reactions are usually carried out at high temperature, the use of ligands with thermal stability like imino-NHCs are required [19, 20].

MATERIAL AND METHODS

General information

All reactions except where mentioned otherwise, were performed using standard Schleck techniques under an inert atmosphere. All solvents were dried and purified using standard procedures prior to use. Glassware was washed and dried in an oven at 120 ˚C. ^{1}H NMR spectra were measured on a Bruker Avance-III 400 MHz spectrometer at ambient temperature with tetramethylsilane (TMS at 0.00 ppm) as an internal standard. All chemical shifts are quoted in δ (ppm) and coupling constants in Hertz (Hz). Abbreviations used for the multiplicity of the NMR signals are s = singlet, m = multiplet.

Procedure for the CN coupling reaction

Samples for catalytic studies were prepared as follows: A substrate (benzylbromide 1.2 mmol and aniline 1.2 mmol) were placed into a clean Schleck tube fitted with a reflux condenser and a stir bar, followed by the addition of the nickel (II) complexes (**1-3,** 1 mol%) and base (1.2 mmol in 2 mL dioxane). The mixture was then refluxed at 90 ^{o}C for 8 h. Upon cooling, the solvent was evaporated to dryness under reduced pressure and then dissolved in chloroform (10 mL) and washed with two equivalent of distilled water (20 mL). After two further washes the organic layer was collected, dried with Na_2SO_4 and concentrated under reduced pressure. The crude products were purified by column chromatography. Percentage were calculated based on isolated yield and products analyzed using NMR.

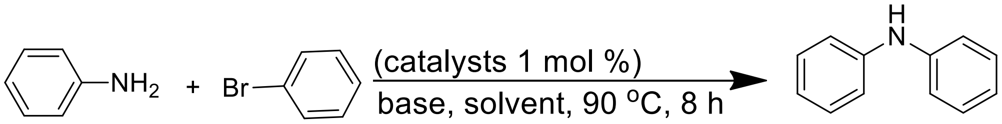
Catalytic study

The complexes were tested as catalysts in the C-N coupling reactions.

An optimization study

Before the exploration of the substrates, the reaction conditions were optimized to determine the best experimental procedure that suits our catalysts system. In efforts to achieve the desired results, initial studies were conducted using aniline and bromobenzene and moderate conversions were recorded based on isolated yields with the catalysts loading of 1 mol%. Using base is crucial in many catalytic systems involving homogeneous catalysts [21]. Therefore, the optimization reaction starts by testing the effect of the catalyst in presence of the different type of base in dioxane at 90 ˚C. And this led to the selection of bases such as KOH, NaOH, $NaCO_3$, $NaHCO_3$ and KO^tBu. No conversions were recorded in the presence of NaOH, and $NaCO_3$. However, complexes **1** yielded 35 and 11 % products with KOH and $NaHCO_3$ respectively (Table 1 entries 1 and 4). Similarly, when strong organic base KO^tBu was used a significant improvement was seen as **1,** yielded 85%, **2,** 80% and **3,** 65% (Table 1 entry 5). Therefore, from the above study, it was noticed that a strong base is required to achieve the desired conversion of the products. Since the solvent is also important in the C-N coupling reactions, the effect of solvent on the catalysts system using KO^tBu as a base of choice was also explored. When the reaction was carried out in toluene as a solvent, the trend reversed showing decrease in the conversion to 57% and 45% for complex **1** and **2** respectively. (Table 1 entry 6). This showed that dioxane has a better potential than toluene in our catalysts system, a similar behaviour was also reported [15]. Other solvents with traces of activity are THF 24%, DMF 23%, and 2-propanol 2% (Table 1 entries 7, 8 and 9). When the reaction was carried out in DMSO, acetonitrile, and DCM no trace of the desired products were recorded (Table 1, entries 10 – 12). But, diethyl ether yielded 80% isolated product using **1** and **2**, presumably the highest activity recorded by our catalysts. However, due to the volatility of the ether, all other substrates were explored using dioxane, and KO^tBu as a solvent and base respectively.

Table 1: base and solvent profile using **1,2** and **3**

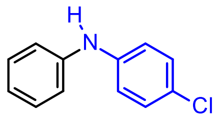
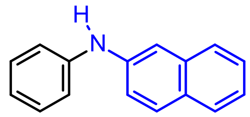
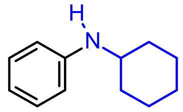
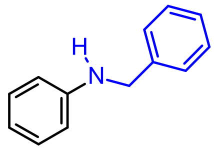
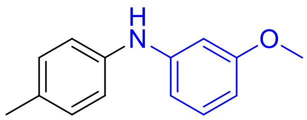
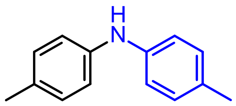
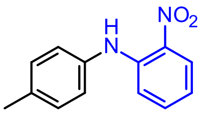
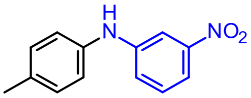


Entry	Solvent	Base	Temperature (˚C)	Yield(%)		
				1	**2**	**3**
1	Dioxane	KOH	90	35	35	n,r
2	,,	NaOH	90	n,r	nr	n,r
3	,,	$NaCO_3$	90	n,r	nr	n,r
4	,,	$NaHCO_3$	90	11	-	n,r
5	**,,**	**KO^{t}Bu**	**90**	**85**	**80**	**65**
6	Toluene	,,	105	57	45	65
7	THF	,,	65	12	8	24
8	DMF	,,	115	23	15	n,r
9	IrPOH	,,	82	1	2	2
10	DMSO	,,	150	n,r	nr	n,r
11	DCM	,,	35	n,r	nr	n,r
12	CAN	,,	85	n,r	nr	n,r
13	**Et_2O**	**,,**	**35**	**80**	**80**	**60**

All reactions were carried out using bromobenzene, (1 mmol), aniline (1.2mmol), base (1.2 mmol), solvent 2mL, reaction time 8 h.

Results for the CN coupling reactions of various substituted aryl bromides and anilines are presented in (Table 2). The results show the relative activity of the imino-NHC nickel complex **1** with isolated yields between 50 to 90% recorded. The turnover frequency of 11 h^{-1} (Table2 entry 6) was an indication that the catalyst can compete favourably with other NHC based transition metal complexes [16], and has better activity over other non-NHC based nickel complexes reported in the literature [22, 23].

Table 2: Scope of the coupling reaction catalysed by **1**

S/no	Product	Yield (%)	TON[a]	TOF[b]
1		87	90	11
2		82	80	10
3		76	80	10
4		85	85	11
5		62	60	8
6		90	90	11
7		45	45	6
8		50	50	6

Reaction conditions arylbromides, (1 mmol), substituted anilines (1.2 mmol), base KO^{t}Bu (1.2 mmol), catalyst **1**, (1 mol %) and solvent 1,2-dioxane (2mL),reaction time 8h. [a]Turnover number = mole product / mole catalyst; [b]Turnover frequency (h^{-1}) = mole product / (mole catalyst x time).

CONCLUSION

In summary, three square planar Ni(II) complexes; **1-3** were utilized as efficient catalysts for the CN coupling reaction. The results for the catalytic studies showed that Ni-NHC complexes stand the chance for use as potential catalysts in the amination reactions. The catalytic results revealed that Ni-NHC complexes **1** and **2** with the methyl group as wingtip displayed relatively higher activity compared with the tetradentate complex **3**.

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Application of Ni(II) complexes of air stable Schiff base functionalized N-heterocyclic carbene ligands as catalysts for CN coupling reaction

Entry 1

^{1}H-NMR ($CDCl_3$) 1.60 (1H, s, NH), 6.61 (5H, m, Ar), 7.10 (4H, m, Ar).

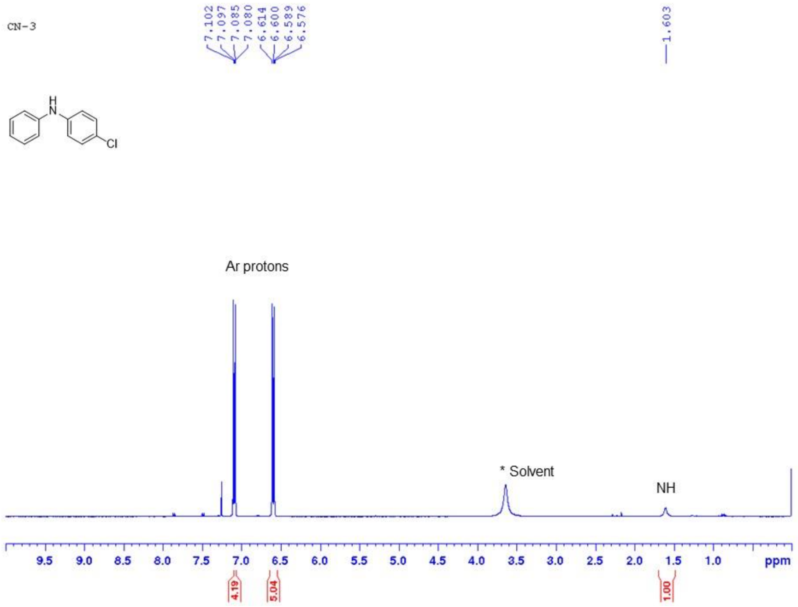


Figure ESI 1.1:^{1}HNMR Spectrum of entry 1 in $CDCl_3$.

Entry 2

^{1}H-NMR ($CDCl_3$) 4.16 (1H, s, NH), 6.78 (2, m, Ar), 7.32 (3H, m, Ar), 7.45 (3H, m, Ar), 7.81 (4H, m, Ar).

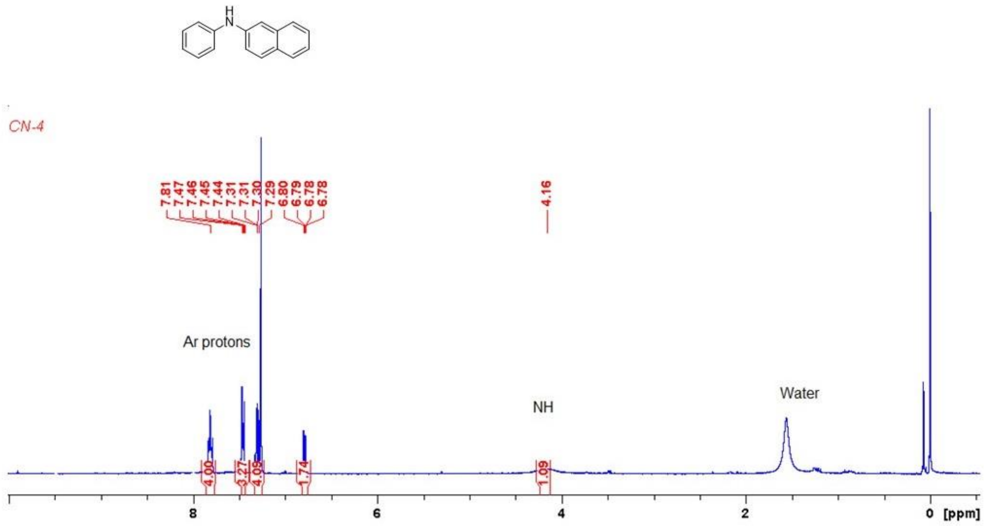


Figure ESI 1.2:^{1}HNMR Spectrum of entry 2 in $CDCl_3$.

Entry 3

^{1}H-NMR (CDCl$_3$) 0.89 (4H, m, CH$_2$), 1.25 (2H, CH$_2$),1.35 (4H, q,CH$_2$), 2.17 (1H, m, 3.49 (1H, s, NH), 6.62 (3H, m, Ar), 7.13 (2H, m, Ar).

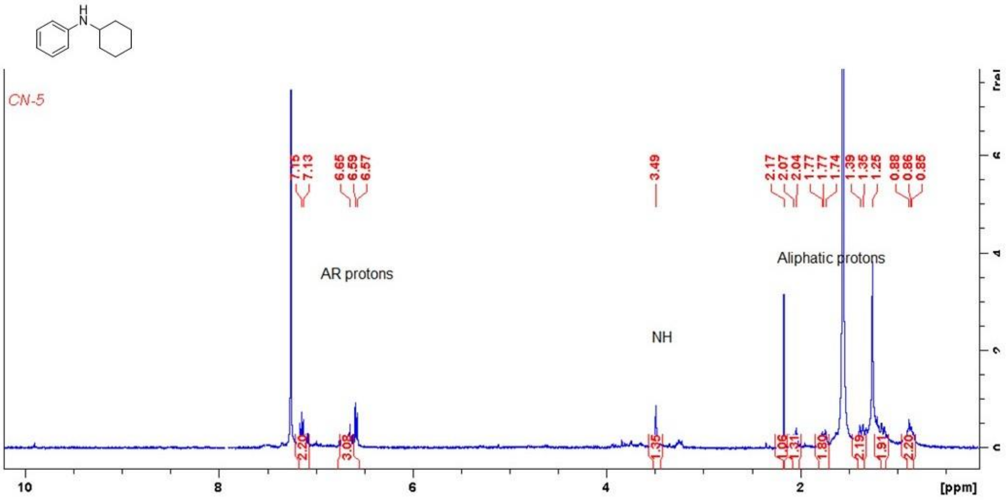


Figure ESI 1.3:^{1}HNMR Spectrum of entry 3 in CDCl$_3$.

Entry 4

^{1}H-NMR (CDCl$_3$) 4.76 (2H, d, CH$_2$), 7.19 (1H, t, Ar), 7.27 (4H, m, Ar), 7.35 (3H, m, Ar), 7.71 (2H, m, Ar), 8.33 (1H, m, Ar).

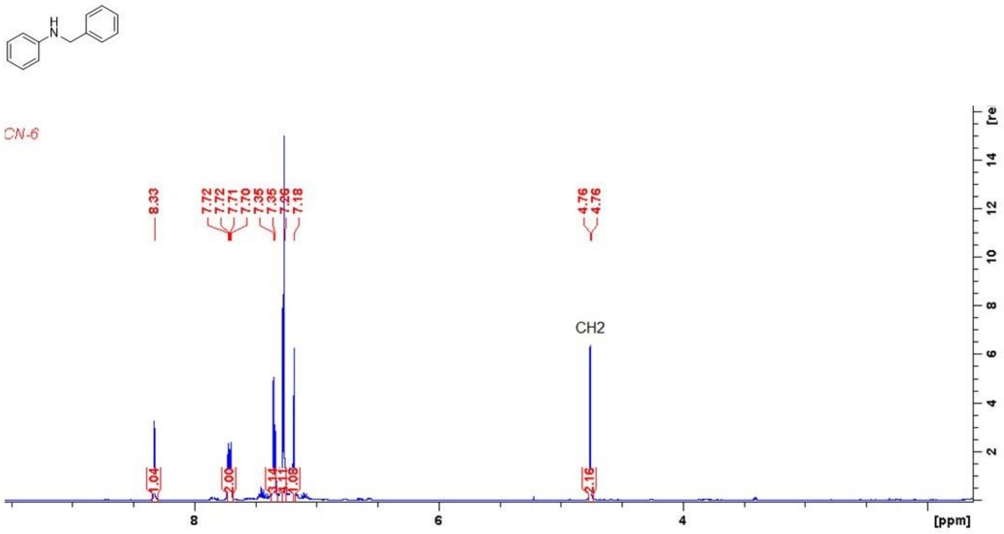
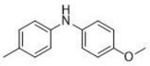


Figure ESI 1.4:^{1}HNMR Spectrum of entry 4 in CDCl$_3$.

Entry 5

^{1}H-NMR ($CDCl_3$) 1.57 (3H, s, CH_3), 3.79 (1H, s, NH), 3.88 (3H, s, OCH_3), 7.00 (4H, m, Ar), 7.88 (4H, m, Ar).



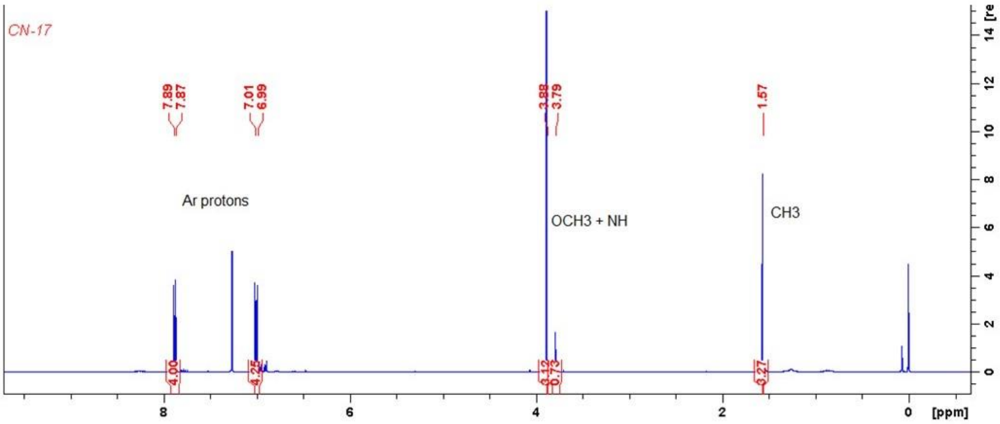
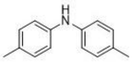


Figure ESI 1.5:^{1}HNMR Spectrum of entry 5 in $CDCl_3$.

Entry 6

^{1}H-NMR ($CDCl_3$) 2.30 (1H, s, NH), 2.43 (6H, s, 2CH_3), 7.30 (4H, m, Ar), 7.81 (4H, m, Ar).



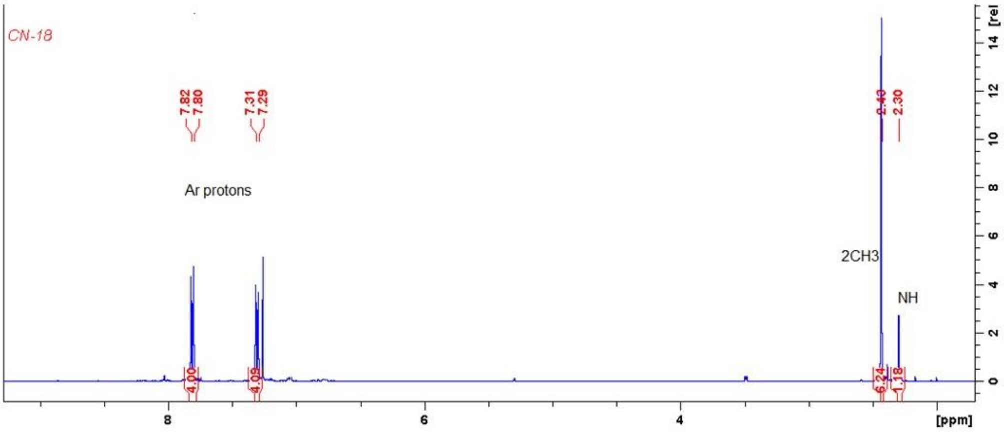
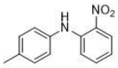


Figure ESI 1.6: ^{1}HNMR Spectrum of entry 6 in $CDCl_3$.

Entry 7

^{1}H-NMR ($CDCl_3$) 1.59 (3H, s, CH_3), 6.06 (1H, m, NH), 6.71 (2H, m, Ar), 6.81 (2H, m, Ar), 7.36 (2H, m, Ar), 8.12 (2H, m, Ar).



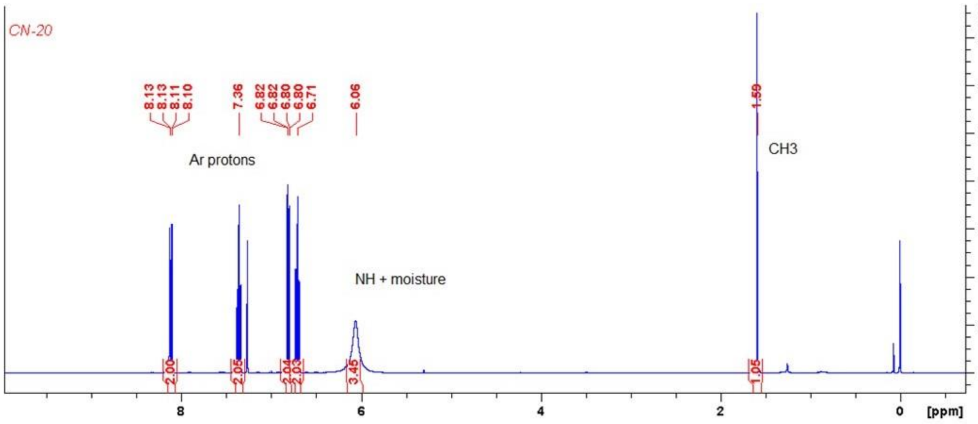
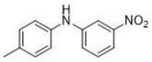


Figure ESI 1.7: ^{1}HNMR Spectrum of entry 7 in $CDCl_3$.

Entry 8

^{1}H-NMR ($CDCl_3$) 1.57 (3H, s, CH_3), 6.06 (1H, m, NH), 6.95 (2H, t, Ar), 7.28 (3H, m, Ar), 7.49 (2H, m, Ar), 7.58 (2H, d, Ar).



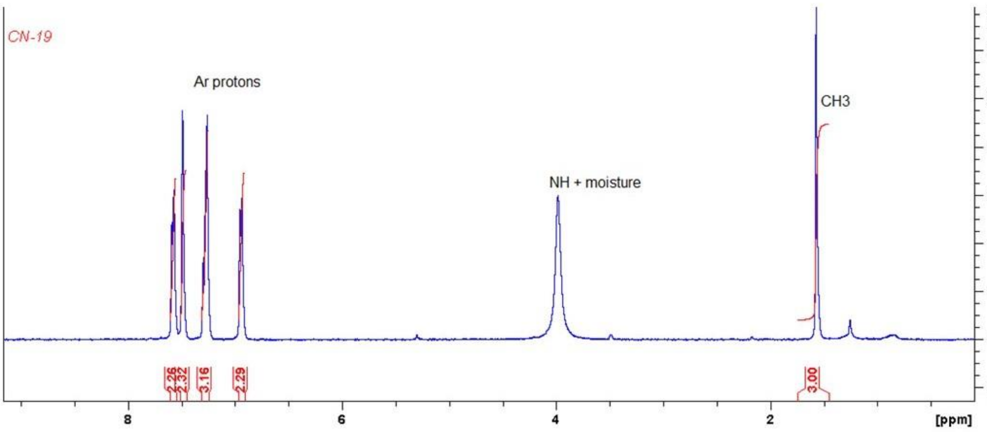


Figure ESI 1.8: ^{1}HNMR Spectrum of entry 8 in $CDCl_3$.