MINOR RESEARCH PROJECT

Project Title

"Copper Catalyzed Direct and Site Selective Arylation Reaction under Mild Conditions"

1398-MRP/14-15/KABA108/UGC-SWRO

Final report

Submitted To

The Joint secretary and Head

South Western Regional Office (SWRO)

University grants commission

P.K. Block, Gandhinagar

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Accredited by NAAC with 'A' Grade & International Accreditation Organization (IAO)

Recognised by UGC under section 2(f) & 12(B)

DECLARATION AND CERTIFICATE

I hereby declare and certify that, the Minor Research Project entitled "**COPPER CATALYZED DIRECT AND SITE SELECTIVE ARYLATION REACTION UNDER MILD CONDITIONS " 1398-MRP/14-15/KABA108/UGC-SWRO** is a bonafide record of research work carried out by me during the year 2014- 2015. Further certify that the work presented in the report is original and carried out according to the plan in the proposal and guidelines of the University Grants Commission.

Principal Investigator

CONTENTS

1. ANNUAL REPORT (ANNUAL BASIS) OF THE MINOR RESEARCH PROJECT

First year

Exclusive literature survey was conducted regarding copper catalyzed reactions for the formation of C-H bond i.e, arylation at hydrogen. This was achieved by collecting journals and from valid references. Then chemicals, glasswares and rotary evaporator were planned and purchased to implement the study.

Various copper catalysts were first screened during the optimization studies for this purpose. During screening copper sulfate was found to be efficient than other copper catalyst for this C-H bond formation reaction.

The reactivity of this catalyst was compared with similar transition metal catalysts which were readily accessible. For this purpose familiar and readily available metal salts such as ferrous sulfate and zinc sulfate have been chosen.

The formation of Ar-H bond was achieved with various aromatic amines through treatment of diazonium salts with copper sulfate and other metal catalysts. During the study, diazonium salts were prepared from aromatic amines and without isolation converted to corresponding arenes in the presence of copper catalysts. This study revealed that metal catalyst with incomplete *d*-orbitals such as copper sulfate and ferrous sulfate were found to be efficient than catalyst such as zinc sulfate which has complete *d*-orbitals.

Overall, this study indicated that copper catalysts can be employed in the formation of C-H bond and similar arylation reactions in the place of expensive catalysts like palladium and gold.

Second year

Second installment was requested to stop because of completion of work in the first installment itself.

2. INTRODUCTION

Metal catalyzed reactions probably represent one of the single most useful synthetic tools for the preparation of organic compounds. The formation of C-H, C-C, C-N bonds could be achieved very easily by this protocol when compared to other available methods. It is always challenging to make such bonds when synthesizing a drug or natural product in the laboratory. The discovery of arylation reactions via coupling reaction is one of the most striking breakthrough in organic chemistry and it has brought us a lot of benefit:

(i) it has expanded the scope for what we can synthesize and
(ii) it has changed the methodology for the retrosynthesis, enabling us to shorten the synthetic procedures.

Review of Research and Development in the Subject

Copper-catalyzed coupling reactions have longer history than Pd-catalyzed ones: for example, Glaser coupling was reported in 1869, almost 100 years before Mizoroki-Heck reaction was reported in 1971, 1972. In these days, however, copper is again attracting the attention of researchers around the world as an alternative of Palladium in arylation through coupling reactions like Heck coupling, Kumada coupling, Sonogashira coupling, Negishi coupling, Stille coupling, Suzuki coupling, Hiyama coupling and Buchwald-Hartwig coupling because palladium is a precious metal. The reserve is much less than copper, so it will cost more to use palladium in arylation methods.

The fact is verified that the oxidative addition and reductive elimination of Cu(I) Cupric ion [Cu(I)] can occur in the presence of aryl halide [ArX], so it is possible that Cu(I) undergoes the steps similar to Pd(0) in coupling reactions through which usually arylation for the formation of C-H, C-C and C-N bonds were achieved.

Diazo group is a very good leaving group and diazonium salts can be synthesized easily in the lab through simple chemical procedure. Even though unstable in nature they can be used as potential substrates for the formation of C-H, C-C bonds efficiently. The research in this area is still under development using transition metal catalysis. In this project work, by using diazonium salts formation of C-H bond by arylation at hydrogen is discussed.

Significance of the study

The C-H (arylation at hydrogen) bond formation is a very interesting protocol and very less methods using copper catalyzed reactions are available as compared to other transition metals. In the present project arylation at hydrogen for the formation of C-H bond via hydrodediazoniation reaction (here it is considered as knocking of amino group as diazo group and placing hydrogen for the formation of Ar-H bond) using copper salts and comparison with other metal salts for reactivity is discussed.

There is always a demand for synthesizing drugs in which formation of C-H takes place. To achieve this protocol, methods discussed in this work could be used as a supplement for existing procedures would be significance. Employing copper as a catalyst in this project in the place of palladium and other expensive metal compounds is another significance because copper salts are inexpensive. The scopes of these reactions are very high and versatile and have lot of applications in organic synthesis.

3. METHODOLOGY

Selective Arylation at hydrogen

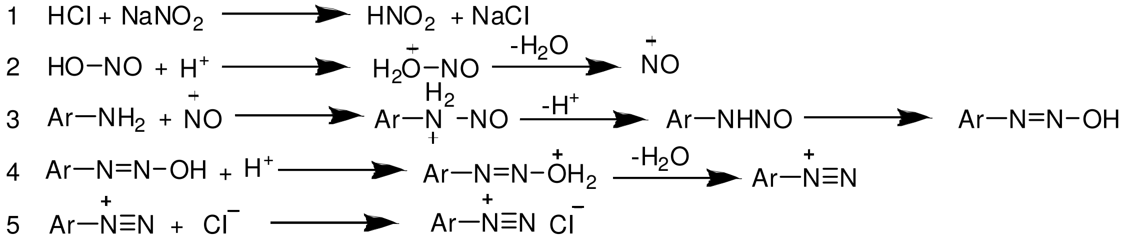
Formation of C-H bond through arylation at hydrogen (hydrodediazoniation reaction) using copper catalyst and comparison of reactivity with other metal salts

When aromatic primary amines such as aniline, toluidine etc., reacted with nitrous acid form aromatic *diazonium* compounds. They are denoted by the general formula ArN_2X where Ar and X are aromatic and nucleophilic groups (Cl^-, Br^-, NO_3^-, HSO_4^-) respectively. They derived their name from *di* meaning two and *azo* meaning nitrogen; indicating thereby the presence of two nitrogens per aryl group. The *'onium'* of the word diazonium is derived from ammonium for these compounds. The process of the formation of diazonium salt by the interaction of aromatic primary amine, sodium nitrite and an inorganic acid like HCl preferably at 0 ^oC is known as *diazotization*. These compounds are unstable and highly reactive and serve as potential intermediates in the synthesis of a numerous number of aromatic compounds and azo-dye stuffs.[1]

Reaction

$$ArNH_2 + 2HCl + NaNO_2 \longrightarrow ArN_2Cl + NaCl + 2H_2O$$

Mechanism



$$\begin{array}{ll}
1 & HCl + NaNO_2 \longrightarrow HNO_2 + NaCl \\
2 & HO{-}NO + H^+ \longrightarrow H_2\overset{+}{O}{-}NO \xrightarrow{-H_2O} \overset{+}{N}O \\
3 & Ar{-}NH_2 + \overset{+}{N}O \longrightarrow Ar{-}\underset{+}{\overset{H_2}{N}}{-}NO \xrightarrow{-H^+} Ar{-}NHNO \longrightarrow Ar{-}N{=}N{-}OH \\
4 & Ar{-}N{=}N{-}OH + H^+ \longrightarrow Ar{-}N{=}N{-}\overset{+}{O}H_2 \xrightarrow{-H_2O} Ar{-}\overset{+}{N}{\equiv}N \\
5 & Ar{-}\overset{+}{N}{\equiv}N + Cl^- \longrightarrow Ar{-}\overset{+}{N}{\equiv}N\ Cl^-
\end{array}$$

Scheme 1: Probable mechanism of diazotization

Since the diazonium salts are unstable and explosive in nature, they are not isolated in solid state but reactions are carried out directly in solution. The general reaction for its formation and mechanism is given in **Scheme 1**.

The mechanism involves the formation of nitrosonium ion generated by protonation of nitrous acid. This ion reacts further with aromatic amine to form *N*-nitrosoamine which is a slow and rate determining step of the reaction. The formed *N*-nitrosoamine under go protonation to generate diazohydroxide. This diazohydroxide after protonation eliminates a molecule of water producing diazonium ion which combines with the halide ion present in the medium to form diazonium salt. The diazonium group of the formed salt can be replaced by various functional groups which are hydrogen, hydroxyl, alkoxyl, acyloxy, halides, cyano, nitro, aryl etc., using appropriate reagents producing various range of products.

The replacement of diazo- group by hydrogen is called as *hydrodediazoniation* reaction.[1b] The history of this reaction is more than a century older and always has been an interest for organic chemist. This method is useful to remove aromatic amino groups *via* diazotization reaction. This protocol can be considered as arylation at hydrogen for the formation of C-H bond by knocking amino group and placing hydrogen in its place. Various reagents have been employed as hydrogen donors but hypophosphorus acid is the most useful reagent.[2-17]

Reaction

$$ArN_2^+X^- \xrightarrow{\text{Reducing Agent}} Ar\text{-}H$$

Reducing agent

H_3PO_2
H_3PO_3
$NaBH_4$, DMF
$SnCl_2$, NaOH
cat.Cu_2O, Dioxane
CH_3ONa, CH_3OH
t-BuOK, *t*-BuOH, Et_2O
HMPA

Scheme 2: Hydrodediazoniation- Historical methods

Recent studies revealed that dimethylformamide and related compounds were also used as a source of hydrogen for this reduction reaction. Few reactions reported in the literature are given in **Scheme 2**.

This reaction is carried out usually in the presence of cuprous ion as a catalyst. Wassmundt et al. have reported the hydrodediazoniation reaction using ferrous sulphate-dimethylformamide as the catalytic system.[1b] Based on this work, a comparative study of ferrous, cupric and zinc sulfates which are actually d^6, d^9 and d^{10} systems were investigated.

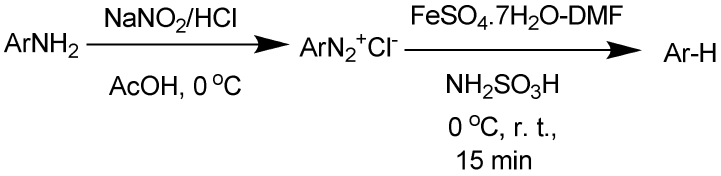
4. RESULTS

To compare the reactivity of cupric and zinc sulfate, initially reactions were carried out with ferrous sulfate-dimethylformamide system reported in the literature. The metal ion exist in d^6 configuration in this system. The results are summarized in **Table 1** with this catalytic system. Firstly, reaction was carried out with aniline (**1**) as the substrate which produced benzene (**1a**) in 90% yield. Substrates such as *p*-toluidine (**2**), *p*-aminophenol (**3**) and *p*-aminobenzene sulphonic acid (**4**) were chosen to check the reactivity studies in this reaction. In the case of *p*-toluidine and *p*-aminophenol substituents present are electron donating and hydrodediazoniation proceeded smoothly delivering the products toluene (**2a**) and phenol (**3a**) in high yields (81% and 67%). On the otherhand, due to presence of electron withdrawing sulphonic acid group in *p*-aminobenzene sulfonic acid, the expected product benzene sulfonic acid (**4a**) was formed in low yield (24%) with this catalytic system. This observation revealed that substrate with electron withdrawing groups is not suitable for this reaction.

Then copper sulfate-dimethylformamide system has been chosen to study the reactivity pattern in this reaction. It is well known that metal in this catalytic system have d^9 configuration. It is also well known that this d^9 configuration has exceptional reactivity. The results were summarized in **Table 1.** From **Table 1** it is clear that aniline, *p*-toluidine and *p*-aminophenol reacted moderately delivering the expected products in reasonable yields (47%, 71% and 38%). However, *p*-aminobenzene sulfonic acid gave only 5% of the product and the reason is attributed to presence of electron withdrawing group on the aromatic nucleus in this substrate.

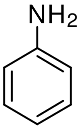
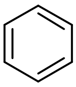
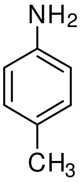
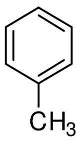
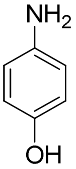
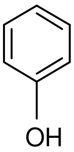
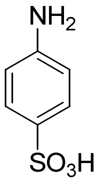
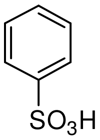
Further studies have been carried out to check the reactivity of zinc sulfate-dimethylformamide catalytic system under the same conditions which were carried out for cuprous and ferrous sulfate Metal ion in zinc sulfate have d^{10} configuration which is more stable. The results observed are summarized in **Table 2**. From **Table 2** it is clear that aniline, *p*-toluidine and *p*-aminophenol reacted producing moderate yield (40%, 54% and 38%) of the product. On the otherhand, *p*-aminobenzene sulfonic acid under the same reaction medium didn't reacted indicating the effect of electron withdrawing sulfonic acid group of the substrate which retards the reaction.

Reaction



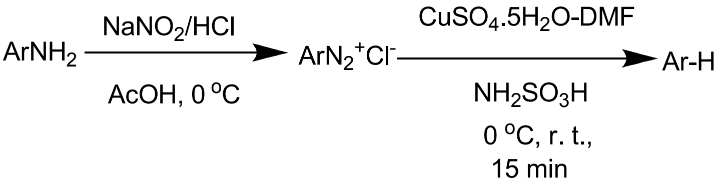
$$\mathrm{ArNH_2} \xrightarrow[\mathrm{AcOH,\ 0\ ^{\circ}C}]{\mathrm{NaNO_2/HCl}} \mathrm{ArN_2^{+}Cl^{-}} \xrightarrow[\mathrm{NH_2SO_3H},\ 0\ ^{\circ}\mathrm{C,\ r.\ t.,\ 15\ min}]{\mathrm{FeSO_4.7H_2O\text{-}DMF}} \mathrm{Ar\text{-}H}$$

Table 1: Hydrodediazoniation using $FeSO_4.7H_2O$–DMF system[a-c]

S.No.	Substrate	Product	Yield (%)
1	 **(1)**	 **(1a)**	90%
2	 **(2)**	 **(2a)**	81%
3	 **(3)**	 **(3a)**	67%
4	 **(4)**	 **(4a)**	24%

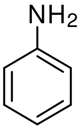
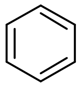
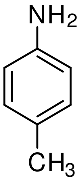
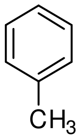
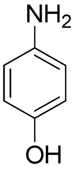
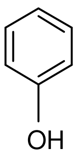
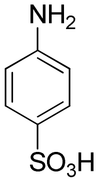
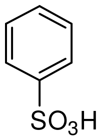
[a] $ArNH_2$ (1 equiv), $NaNO_2$ (1.08 equiv) and $FeSO_4.7H_2O$ (1 equiv) were used. [b] Sulfamic acid (0.5 g), AcOH (4 mL), HCl (2.2 mL) and DMF (20 mL) were used. [c] Isolated yields.

Reaction



$$ArNH_2 \xrightarrow[AcOH,\ 0\ ^{o}C]{NaNO_2/HCl} ArN_2^{+}Cl^{-} \xrightarrow[NH_2SO_3H,\ 0\ ^{o}C,\ r.\ t.,\ 15\ min]{CuSO_4.5H_2O\text{-}DMF} Ar\text{-}H$$

Table 2: Hydrodediazoniation using $CuSO_4.5H_2O$– DMF system[a-c]

S.No.	Substrate	Product	Yield (%)
1	 **(1)**	 **(1a)**	47%
2	 **(2)**	 **(2a)**	71%
3	 **(3)**	 **(3a)**	38%
4	 **(4)**	 **(4a)**	6%

[a] $ArNH_2$ (1 equiv), $NaNO_2$ (1.08 equiv) and $CuSO_4.5H_2O$ (1 equiv) were used. [b] Sulfamic acid (0.5 g), AcOH (4 mL), HCl (2.2 mL) and DMF (20 mL) were used. [c] Isolated yields.

Reaction

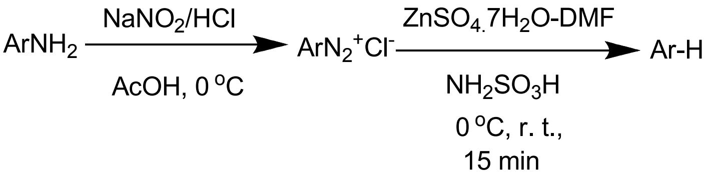
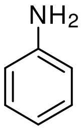
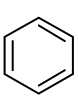
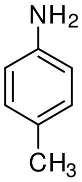
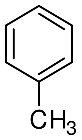
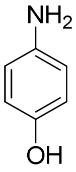
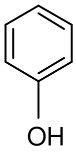
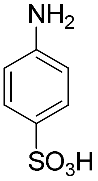
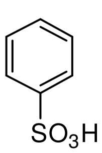


Table 3: Hydrodediazoniation using $ZnSO_4.7H_2O$-DMF system[a-c]

S.No.	Substrate	Product	Yield (%)
1	 **(1)**	 **(1a)**	40%
2	 **(2)**	 **(2a)**	54%
3	 **(3)**	 **(3a)**	38%
4	 **(4)**	 **(4a)**	-

[a] $ArNH_2$ (1 equiv), $NaNO_2$ (1.08 equiv) and $ZnSO_4.7H_2O$ (1 equiv) were used. [b] Sulfamic acid (0.5 g), AcOH (4 mL), HCl (2.2 mL) and DMF (20 mL) were used. [c] Isolated yields.

Overall comparison of all the three systems with d^6, d^9 and d^{10} configuration indicating that ferrous and copper sulfate were preferred than zinc sulfate. This study also revealed that compounds with *d*-orbitals such as $d^6$and d^9 which have vacant orbitals are highly reactive and can be utilized in this kind of reaction. However, completely filled *d*-orbital containing substances cannot be utilized as a catalyst because in those reactions yields are found to be lesser as in the case of zinc sulfate.

5. DISCUSSION

In this section mechanism of this Ar-H bond formation i.e., arylation at hydrogen and experimental part were discussed.

5.1 *Mechanism*

Experimental studies from literature strongly implicates that this reaction involves free-radical chain mechanism if ferrous sulfate is used a catalyst which is given in **Fig.8**. It involves the electron transfer from ferrous ion (Fe^{2+}) to diazonium cation which leads to reduction reaction

$$1)\ M^{2+} + ArN_2^{+} \longrightarrow M^{3+} + Ar\dot{N}_2$$

$$2)\ Ar\dot{N}_2 \longrightarrow Ar^{\bullet} + N_2$$

$$3)\ Ar^{\bullet} + HCON(CH_3)_2 \longrightarrow Ar\text{-}H + HCO(CH_3)C\dot{H}_2\ \&\ CO\dot{N}\,(CH_3)_2$$

M = Fe, Cu & Zn

Fig.8: Probable mechanism of hydrodediazoniation reaction

and forms diazenyl radical and ferric ion (Fe^{3+}). This diazenyl radical undergoes cleavage forming molecular nitrogen and aryl radical. The aryl radical thus formed abstracts a proton from dimethylformamide producing the reduced product.[1b]

The involvement of Cu^{2+}-Cu^{3+} and Zn^{2+}-Zn^{3+} in the case of cupric and zinc sulphate salts are less probable and energetically unfavorable. However it is possible to invoke in situ generation of Cu^{+} which gets converted to Cu^{2+} after the reduction. There are few reports from the literature which has proven the existence of Zn^{3+} ion even though which is difficult to generate from a stable d^{10} system. In the present study the consideration has been made in which an electron is transferred from metal to arene diazonium ion irrespective of nature of the metal. Exact mechanism for individual catalyst is under investigation and will be carried out in further studies.

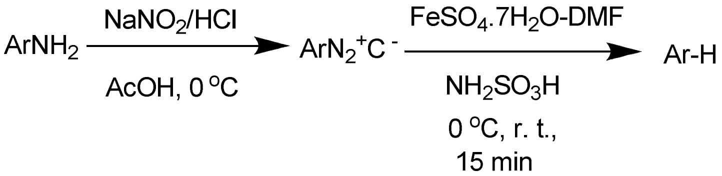
5.2 *Experimental Section*

i) General

All the reactions were carried out in oven dried conical flasks. The thin layer chromatography (TLC) was performed using silica gel 60 F_{254} (Merck) and was visualized by exposure to iodine crystals. The column chromatography was performed employing 60-120 silica gel (sd fine chem) using ethyl acetate/petroleum ether as an eluent system. Materials were purchased from aniline (Merck), *p*-toluidine, *p*-amino phenol, *p*-amino sulphanilic acid, sulfamic acid, ferrous sulfate, copper sulfate, zinc sulfate, sodium nitrite, hydrochloric acid and dimethylformamide (sd fine chem) and used further without purification. The obtained products were characterized by boiling point measurement and correlated with literature data.

ii) Representative procedure for hydrodediazoniation using $FeSO_4.7H_2O$

Reaction



$$ArNH_2 \xrightarrow[\text{AcOH, 0 °C}]{NaNO_2/HCl} ArN_2^+C^- \xrightarrow[\substack{NH_2SO_3H \\ \text{0 °C, r. t.,} \\ \text{15 min}}]{FeSO_4.7H_2O\text{-DMF}} Ar\text{-}H$$

A hot-oven dried conical flask was charged with an aromatic amine (1 equiv) and acetic acid and stirred. To this mixture was added conc. HCl (2.2 mL) and ice (12 g) and stirred further. Now a concentrated solution of $NaNO_2$ (1.08 equiv) was added dropwise to this mixture and stirring was continued for 15 min. To this mixture was added sulfamic acid to destroy the excess nitrous acid. This solution contains diazotized amine which was added dropwise to a mixture of $FeSO_4.7H_2O$ (1 equiv) and DMF (20 mL) with stirring. Water (300 mL) was added to the contents and the solid portion was filtered using a suction pump. The filtrate was extracted with ether (2 x 15 mL) and the combined organic layers were washed with water (1 x 15 mL), brine solution (1 x 15 mL) and dried over Na_2SO_4. Evaporation of the solvent gave the crude product. The crude product thus obtained was further purified by distillation to give the pure product.[1b] The obtained products were given in **Table 6.**

iii) Representative procedure for hydrodediazoniation using $CuSO_4.5H_2O$

Reaction

$$\mathrm{ArNH_2} \xrightarrow[\mathrm{AcOH,\ 0\ ^{o}C}]{\mathrm{NaNO_2/HCl}} \mathrm{ArN_2^{+}Cl^{-}} \xrightarrow[\substack{\mathrm{NH_2SO_3H} \\ \mathrm{0\ ^{o}C,\ r.\ t.,} \\ \mathrm{15\ min}}]{\mathrm{CuSO_4.5H_2O\text{-}DMF}} \mathrm{Ar\text{-}H}$$

A hot-oven dried conical flask was charged with an aromatic amine (1 equiv) and acetic acid and stirred. To this mixture was added conc. HCl (2.2 mL) and ice (12 g) and stirred further. Now a concentrated solution of $NaNO_2$ (1.08 equiv) was added dropwise to this mixture and stirring was continued for 15 min. To this mixture was added sulfamic acid to destroy the excess nitrous acid. This solution contains diazotized amine which was added dropwise to a mixture of $CuSO_4.5H_2O$ (1 equiv) and DMF (20 mL) with stirring. Water (300 mL) was added to the contents and the solid portion was filtered using a suction pump. The filtrate was extracted with ether (2 x 15 mL) and the combined organic layers were washed with water (1 x 15 mL), brine solution (1 x 15 mL) and dried over Na_2SO_4. Evaporation of the solvent gave the crude product. The crude product thus obtained was further purified by distillation to give the pure product. The obtained products were given in **Table 7.**

iv) Representative procedure for hydrodediazoniation using $ZnSO_4.7H_2O$

Reaction

$$\mathrm{ArNH_2} \xrightarrow[\mathrm{AcOH,\ 0\ ^{o}C}]{\mathrm{NaNO_2/HCl}} \mathrm{ArN_2^{+}Cl^{-}} \xrightarrow[\substack{\mathrm{NH_2SO_3H} \\ \mathrm{0\ ^{o}C,\ r.\ t.,} \\ \mathrm{15\ min}}]{\mathrm{ZnSO_4.7H_2O\text{-}DMF}} \mathrm{Ar\text{-}H}$$

A hot-oven dried conical flask was charged with an aromatic amine (1 equiv) and acetic acid and stirred. To this mixture was added conc. HCl (2.2 mL) and ice (12 g) and stirred further. Now a concentrated solution of $NaNO_2$ (1.08 equiv) was added dropwise to this mixture and stirring was continued for 15 min. To this mixture was added sulfamic acid to destroy the excess nitrous acid. This solution contains diazotized amine which was added dropwise to a mixture of $ZnSO_4.7H_2O$ (1 equiv) and DMF (20 mL) with stirring. Water (300 mL) was added to the contents and the solid portion was filtered using a suction pump. The filtrate was extracted with ether (2 x 15 mL) and the combined organic layers were washed with water (1 x 15 mL), brine solution (1 x 15 mL) and dried over Na_2SO_4. Evaporation of the solvent gave the crude product. The crude product thus obtained was further purified by distillation to give the pure product. The obtained products were given in **Table 8.**

Table 6 : Hydrodediazoniation using $FeSO_4.7H_2O$–DMF system[a,b]

Chemicals	**Mol. Weight**	**mMole**	**Molar ratio**	**Quantity**	**Yield (%)**
$ArNH_2$	93.13 for **(1)** 107.15 for **(2)** 109.13 for **(3)** 173.19 for **(4).**	10.73 for **(1)** 9.33 for **(2)** 9.16 for **(3)** 5.80 for **(4)**	1	1.0 g	Ar-H **(1a)** - 90% **(2a)** - 81% **(3a)** - 67% **(4a)** - 24%
$NaNO_2$	69.00	11.6 for **(1)** 10 for **(2)** 9.9 for **(3)**	1.08	0.8 g for **(1)** 0.69 g for **(2)** 0.68 g for **(3)**	

		5.5 for **(4)**		0.37 **g** for **(4)**	
$FeSO_4.7H_2O$	278.01	10.73 for **(1)** 9.33 for **(2)** 9.16 for **(3)** 5.80 for **(4)**	1	2.98 g for **(1)** 2.59 g for **(2)** 2.54 g for **(3)** 1.60 g for **(4)**	

[a] **(1)**, **(2)**, **(3)** & **(4)** – represents aniline, *p*-toludine, *p*-amino phenol, *p*-amino sulfanilic acid.

[b] **(1a)**, **(2a)** , **(3a)** & **(4a)** – represents benzene, toluene, phenol, benzene sulfonic acid.

Table 7: Hydrodediazoniation using $CuSO_4 .5H_2O$–DMF system[a,b]

Chemicals	**Mol. Weight**	**mMole**	**Molar ratio**	**Quantity**	**Yield (%)**
$ArNH_2$	93.13 for **(1)** 107.15 for **(2)** 109.13 for **(3)** 173.19 for **(4)**	10.73 for **(1)** 9.33 for **(2)** 9.16 for **(3)** 5.80 for **(4)**	1	1.0 g	Ar-H **(1a)** – 47.2% **(2a)** - 71% **(3a)** – 38% **(4a)**- 6%
$NaNO_2$	69.00	11.6 for **(1)** 10 for **(2)** 9.9 for **(3)**	1.08	0.8 g for **(1)** 0.69 g for **(2)** 0.68 g for **(3)**	

		5.5 for **(4)**		0.37 g for **(4)**	
$CuSO_4.5H_2O$	249.68	10.73 for **(1)** 9.33 for **(2)** 9.16 for **(3)** 5.80 for **(4)**	1	2.67 g for **(1)** 2.32 g for **(2)** 2.28 g for **(3)** 1.44 g for **(4)**	

[a] **(1)**, **(2)**, **(3)** & **(4)** – represents aniline, *p*-toludine, *p*-amino phenol, *p*-amino sulfanilic acid.

[b] **(1a)**, **(2a)** , **(3a)** & **(4a)** – represents benzene, toluene, phenol, benzene sulfonic acid.

Table 8: Hydrodediazoniation using $ZnSO_4.7H_2O$–DMF system[a,b]

Chemicals	**Mol. Weight**	**mMole**	**Molar ratio**	**quantity**	**Yield (%)**
$ArNH_2$	93.13 for **(1)** 107.15 for **(2)** 109.13 for **(3)** 173.19 for **(4)**	10.73 for **(1)** 9.33 for **(2)** 9.16 for **(3)** 5.80 for **(4)**	1	1.0 g	Ar-H **(1a)** – 40% **(2a)** – 54.11% **(3a)** – 38%
$NaNO_2$	69.00	11.6 for **(1)** 10 for **(2)** 9.9 for **(3)**	1.08	0.8 g for **(1)** 0.69 g for **(2)** 0.68 g for **(3)**	

		5.5 for (**4**)		0.37 g for (**4**)	
$ZnSO_4.7H_2O$	287.54	10.73 for **(1)** 9.33 for (**2**) 9.16 for **(3)** 5.80 for **(4)**	1	3.08 g **(1)** 2.68 g **(2)** 2.63 g **(3)** 1.66 g **(4)**	

[a]**(1)**, **(2)**, **(3)** & **(4)** – represents aniline, *p*-toludine, *p*-amino phenol, *p*-amino sulfanilic acid.

[b]**(1a)**, **(2a)** , **(3a)** & **(4a)** – represents benzene, toluene, phenol, benzene sulfonic acid.

5.3 CONCLUSION

In conclusion, d^6, d^9 and d^{10} configuration have been found to catalyze hydrodediazoniation reaction which can be considered as arylation at hydrogen for the formation of C-H bond using copper and other metal salts. This comparative study revealed that catalyst such as ferrous and copper sulfate with d^6 and d^9 configuration are effective in catalyzing this reaction together with dimethylformamide may be due to presence of incomplete *d*-orbitals. The studies carried out with zinc sulfate-dimethylformamide as a catalytic system indicated that *d*-orbitals with completely filled electrons as in the case this d^{10} system is less efficient in hydrodediazoniation reaction. Overall results imply that various transition-metal salts can serve as catalysts but the preferred one was those with incomplete *d*-orbitals such as copper sulfate would be efficient for arylation reactions to construct C-H bond.

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Annexure -VI

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
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Final Report of the work done on the Minor Research Project

1	Project report No. 1st /Final	Final
2	UGC Reference No.F	1398-MRP/14-15/KABA108/UGC-SWRO
3	Period of report	31.03.2015 to 31.03.2016
4	Title of research project	COPPER CATALYZED DIRECT AND SITE SELECTIVE ARYLATION REACTION UNDER MILD CONDITIONS
5	(a) Name of the Principal Investigator	Dr. V. Venkatesh
	(b) Deptt.	PG Department of Chemistry
	(c) College where work has progressed	The Oxford College of Science, No.32, 19th Main, 17th 'B' Cross, Sector-4, HSR Layout, Bangalore-560 102
6	Effective date of starting of the project	22.01.2015
7	Grant approved and expenditure incurred during the period of the report:	
	a. Total amount approved Rs.	**Rs. 1,50,000.00** Amount Released as 1st instalment (90% Recurring and 10% Non-Recurring)
	b. Total expenditure Rs.	**Rs. 1,51,073.00**
	c. Report of the work done	**Report Enclosed**
8	i. Brief objective of the project	i) Copper catalyzed arylation reaction to form C-H bond

		ii) Arylation occurs with hydrogen through hydrodediazoniation reaction iii) The reactivity of other catalysts of iron and zinc also were compared
	ii. Work done so far and results achieved and publications, if any, resulting from the work (Give details of the papers and names of the journals in which it has been published or accepted for publication	(Work done given in report) Arylation at hydrogen for the formation Ar-H bond was achieved using copper catalyst. The final output is the construction of C-H bond. During the process hydrodediazoniation methodology is employed in which diazo group was knocked from the parent aromatic amine substrate and hydrogen was placed in its place.
	iii. Has the progress been according to original plan of work and towards achieving the objective. if not, state reasons	The progress of the project work is according to the original plan
	(iv). Please indicate the difficulties, if any, experienced in implementing the project	The main objectives of the project has been successfully completed accordingly
	iv. Please enclose a summary of the findings of the study. One bound copy of the final report of work done may also be sent to the concerned Regional Office of the UGC.	Final Report attached
	v. Any other information	2nd installment was requested to stop from the funding agency.

Principal Investigator

Dr. V. Venkatesh

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