SYNTHESIS AND CHARACTERIZATION OF SCHIFF BASES AND THEIR USE FOR THE SYNTHESIS OF DIPHENYL AMINE

A

thesis submitted

in partial fulfillment of requirement for the

Degree of Master of Science in Chemistry

Submitted by

Shalni

(Regd No. 300802004)

Supervisor

Dr. Manmohan Chhibber

Assistant Professor

School of Chemistry and Biochemistry

Thapar University

Patiala 147001

July 2010


DEDICATED TO MY PARENTS

Acknowledgement

It's said that life is a carnival of experiences and a journey with various goals. So in my journey where I experienced this project I want to thank the supreme almighty for his presence in my soul and in my mind.

I take this opportunity to thank my guide Dr. Manmohan Chhibber, Lecturer, School of Chemistry and Biochemistry without whose presence the whole project just would have been a dream . I am extremely indebted to him for the scientific attitude and utmost patience he has installed in me which will definitely stand in all future endeavour and it was because of him that I was able to learn so much in this short period.

My sincere thanks to Dr. Susheel Mittal, Head, School of Chemistry and Biochemistry for his guidance and suggestions. I express my regards to all faculty members of School of Chemistry and Biochemistry for their help and moral support during my stay.

I express my gratitude to my golden friends Shilpa Narang , Charanjeet , jasneet, Ankush and Rohit whose support and friendship was like a cold shower in the heat of work and pressure .

I am highly obliged to Chander sir and other laboratory staff who were very helpful in every possible way.

I thank my labmates Shilpa Narang, Charanjeet and Navjot to cooperate me in the laboratory. It was like a family with them. A vote of thanks goes to PhD. Schlors.Miss Ramandeep,Vishal sir, Ankush sir Rohit sir and Hemant sir For their suggestions and help. A special thanks to my brother Harry who not just encouraged me with his words but also kept me going with his unpredictable fights.

Last but not least I owe my thesis to my parents who are the building pillar of my life.

Shalni

Dated: July 15, 2010.

Candidate's Declaration

I hereby declare that the work being presented in the dissertion entitled "Synthesis and characterization of Schiff bases and their use for the synthesis of diphenyl amine" , in partial fulfillment of the requirement for the award of degree of Masters of Science (Chemistry), School of Chemistry ans Biochemistry (SCBC), Thapar University , Patiala, is my own work during the period of January 2010 to May 2010, under the supervision of Dr. Manmohan Chhibber, Lecturer , School of Chemistry and Biochemistry , Thapar University, Patiala. I have not submitted the matter embodied in this dissertation for the award of any other degree.

Patiala

Date : 15 July 2010

Shalni

This to certify that the above statement made by the candidate is correct and true to the best of our knowledge.

Dr. Manmohan Chhibber

Project Supervisor,

Assistant Professor (SCBC),

Thapar University

Dr. Susheel Mittal 15/7/X

Head, SCBC

Thapar University

Certificate

This is to Certify that the project entitled "Synthesis and characterization of Schiff bases and their use for the synthesis of diphenyl amine", being submitted by Miss SHALNI in partial fulfillment of the requirement for the award of degree of Master of Science (Chemistry), Thapar University , Patiala, is a bonafide work carried out under the supervision of Dr. Manmohan Chhibber and that no part of this project has been submitted for the award of any other degree.

Dr. Manmohan Chhibber

Project Supervisor,

Thapar University

Head,

Dr. Susheel Mittal

School of Chemistry and Biochemistry,

Thapar University

Dean , Academic Affairs,

(Dr. R.K. Sharma)

Thapar University

List of Contents

Introduction

In 1864 Schiff Hugo Josef, a German chemist, discovered the condensation products of aldehydes and amines, now known as Schiff bases. Formally, Schiff base may be defined as any of a class of bases of the general formula RR′C=NR that are obtained typically by condensation of an aldehyde or ketone with a primary amine with elimination of water. These compounds are usually used as intermediates in organic synthesis and in some cases as dyes. This reaction is routinely used as test for the presence of an aldehyde group or a primary amine in organic molecule [1]. These compounds are also referred to as imines.

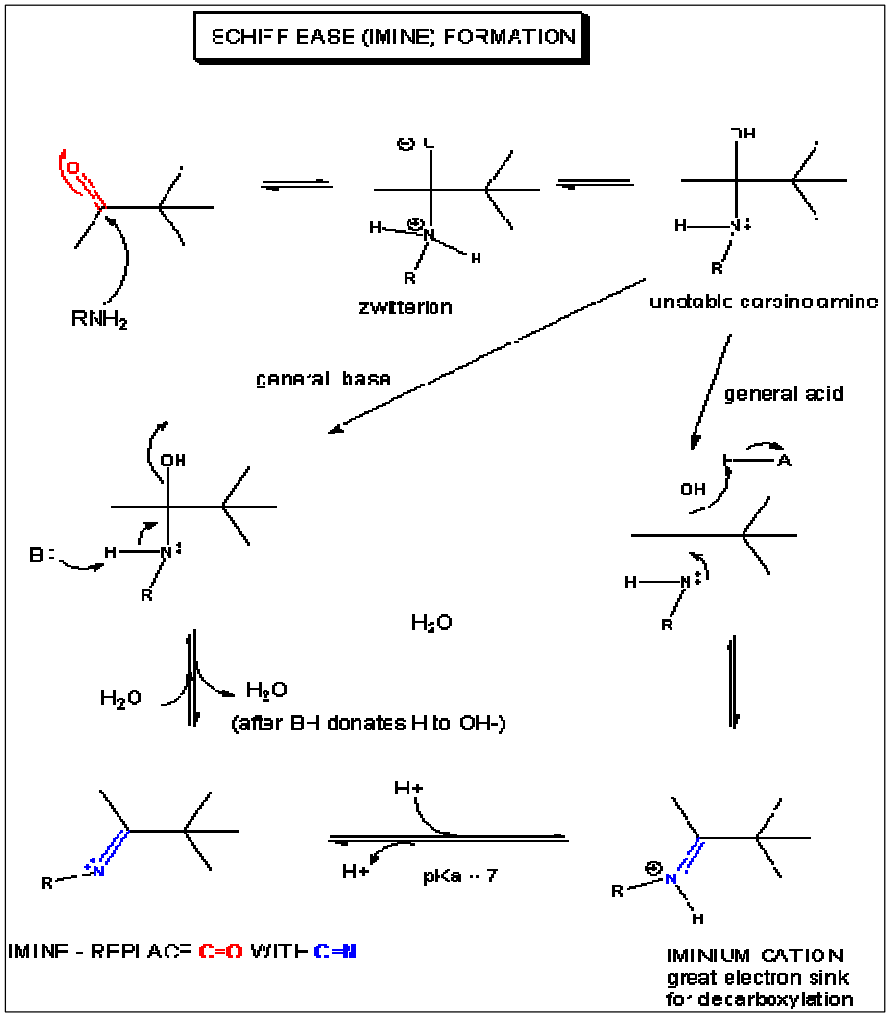
The formation of Schiff's base **(Scheme-A)** occurs by the transformation of electrons from N atom of the amine to carbonyl group of aldehyde followed by the Zwitterion formation. The Zwitterion rearranges to form carbinolamine which being unstable reacts with general acid or base to remove the water. In case of reaction with acid, an iminium cation is formed that finally loses a proton to give Schiff base [2].

Ever since their discover, Schiff bases find applications almost in all the areas of chemistry. Besides being useful as synthetic intermediates, there are studies that demonstrate their use in medicine, pH [3], optical and electrochemical sensors, their biological applications include antibacterial, antifungal, and antitumor activities [4].

One of the important properties of aromatic Schiff bases is to form complexes with metal ions. A hydroxyl or methoxy group, present ortho to C=N bond forms a very convenient site for transition metal ions. This is because nitrogen of Schiff base and oxygen of the hydroxyl or methoxy induce two opposite electronic effects. The phenolate oxygen is regarded a hard donor, which stablizes the higher oxidation states while the imine nitrogen is a softer donor and will hence stabilize the lower oxidation states of metal ions. Because of their metal complexing properties these compounds are used as catalysts in combination with appropriate

metal ions. For example, they have been used as for oxygenation [5], [6] hydrolysis [7], electro-reduction [8] and decomposition [9].

Scheme-A



Present work relates to the synthesis and characterization of Schiff bases and their utilization for synthesis of diphenyl amines.

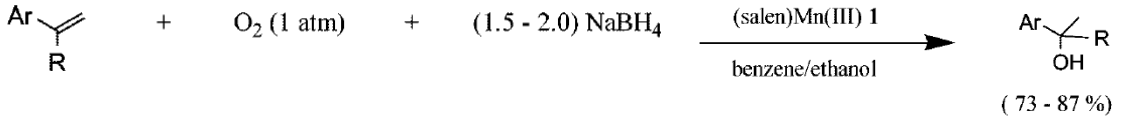
Literature Review

Schiff's bases are considered "privileged ligands" [10] that have been been extensively studied in coordination chemistry. These receptor compounds are able to stabilize many different metals in various oxidation states, controlling the performance of metals in a large variety of useful catalytic transformations such as enantioselective – epoxidation and aziridination and mediating organic redox reactions. Due to their ability to complex with different metal ions Schiff's bases have been used in areas as diverse as electrochemistry, bioinorganic, catalysis, metallic deactivators, separation processes and environmental chemistry.

A brief literature survey of Schiff base catalyzed organic reactions is presented in following lines. Wang et.al.[11] have reported oxidation of olefins with molecular oxygen in presence of amino acid Schiff base manganese complex that was prepared with L-phenylalanine, salicylaldehyde and $Mn(OAc)_2 \cdot 4H_2O$. Cyclohexaene on oxidation gave 2-cyclohexen-1-ol (–OH), 2-cyclohexen-1-one (C=O) and 2-cyclohexen-1-hydroperoxide (–OOH) as major products. The influence of reaction temperature and additive for oxidation was studied and it was observed that selectivity of 2-cyclohexen-1-hydroperoxide varied with reaction time and different additives.

Molecular oxygen in organic synthesis is the most effective oxidant considering costs and environmental considerations. Lee et al [12] have reported the oxidative conversion of olefins to the alcohols, where molecular oxygen was used as the oxidant in the presence of Mn (III) complexes of Schiff bases. They synthesized (salen) Mn(III)Cl complex as the catalyst and sodium borohydride as the one-oxygen reducing agent

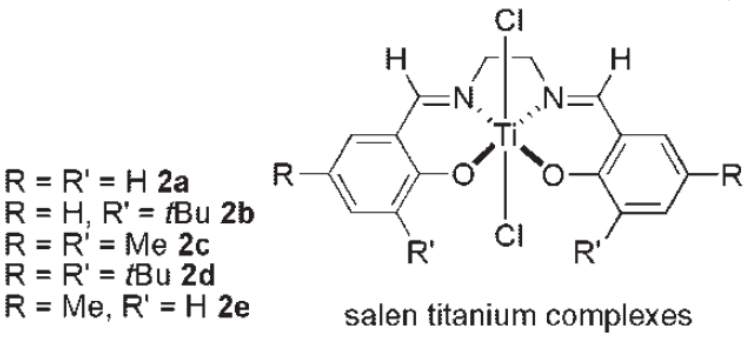
Scheme-B



Using these mild conditions, only conjugated vinyl arene substrates were oxidized with high efficiency **(Scheme-B).** Other olefin substrates, for example non-conjugated or non-vinylic olefins, showed very low reactivity.

Schiff base complexes of titanium have been synthesized and used as replacement of Ziegler-Natta polymerization. A series of salen titanium complexes **(Figure-1)** were used as catalyst precursors for the syndiospecific polymerization of styrene[13] .

Figure-1

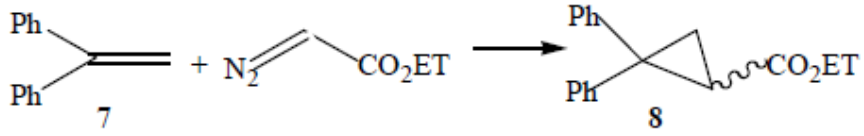


salen titanium complexes

These complexes in the presence of methylalumoxane (MAO) yielded syndiotactic rich polystyrenes. The activity and syndiospecificity of the complexes were dependent on the bulkiness of the ortho substituents in the aryl ring of the ligand and temperature of the reaction. Bulkier groups such as tert-butyl at these positions at 70^0C gave very good yields.

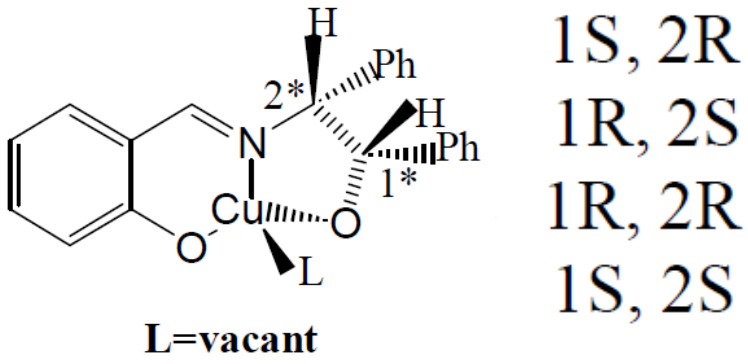
Jiang et. al.[14] have very elegantly used four stereoisomers of a copper-(Schiff-base) complex having two chiral centers to catalyze the asymmetric cyclopropanation reaction **(Scheme-C)**.

Scheme- C



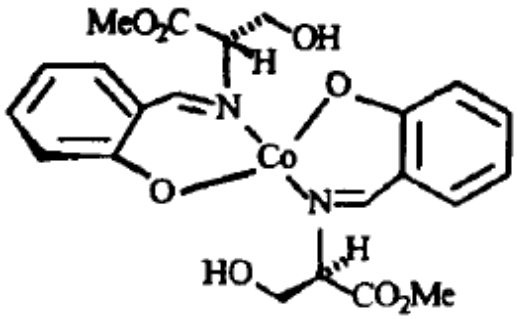
Two of the complexes among foue were efficient catalyst for cyclopropanation of 1,1-diphenylethene with ethyl diazoacetate, affording high enantiomeric excesses of up to 91.8%. The reaction is an important discovery because catalytic asymmetric cyclopropanation of diazoacetates with olefins has attracted much attention due to their use in synthesizing important drug molecules. Following **Figure – 2** describes the structure of four chiral Schiff base complexes.

Figure – 2



Punniyamurthy et. al. [15] has demonstrated oxidation of a wide range of organic substrates in the presence of carbonyl compounds and dioxygen. Studies on complex shown in **Figure-3** indicate that these reactions proceed via cobalt (III)-superoxo complex formed under the aegis of carbonyl compounds and dioxygen. The complex is also is also efficient in oxidizing a wide range of organic substrates in the presence of carbonyl compounds and dioxygen.

Figure- 3



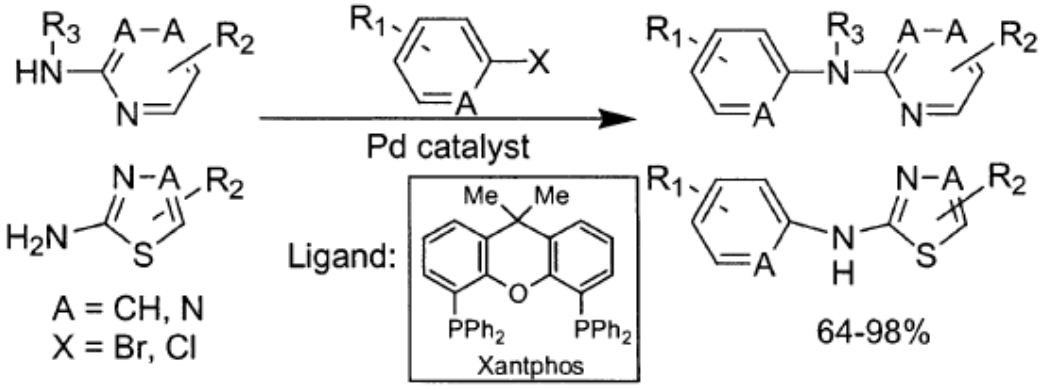
Some studies have demonstrated that even cobalt (II) complexes of the Schiff bases have been used as oxidation catalysts and for selective enrichment of oxygen by making use of their ability to absorb and desorb oxygen. If however, they are brought in contact with water or protic solvents such as water or ethanol they are irreversibly oxidized to hydroxocobalt (III) Schiff base complexes there by losing its tendency to utilize oxygen. Interestingly, in another study Akoi et. al [16] have described a method for reducing a hydrocobalt (III) Schiff

base complexes to cobalt (III) Schiff base complex simply by heating the hydroxo compound below the decomposition temperature of the Cobalt (III) Schiff base complex.

N-Arylamines, N-arylpyrroles, N-arylindoles, N-arylimidazoles, and N-arylpyrazoles are prevalent in compounds that are of biological, pharmaceutical, and materials interest[17] Copper-catalyzed Ullmann-type reactions are traditional methods to assemble these compounds. For a long time, these reactions had been carried out at high temperatures and many functional groups could not be tolerated, and therefore their usage was greatly limited [18] To overcome these drawbacks, several Pd-catalyzed C-N formation methods have been discovered **(Scheme- D)** , which, upon using some sterically hindered phosphine ligands, allowed many coupling reactions of aryl halides with N-containing compounds to proceed under relatively mild conditions and low temperature[19] However, industrial use of these methods is problematic in many cases due to the air and moisture sensitivity, as well as the higher costs of Pd catalysts and the relative ligands.

During the past years, we have witnessed great progress on the modification of Ullmann-type coupling reactions [20]. which highly relied on the utilization of some special bidentate additives such as aliphatic diamines[21] , ethylene glycol[22] , diethylsalicylamide[23], 1,10-phenanthroline and its derivatives[24], oxime-type and Schiff base ligands[25], thiophene-2-carboxylate[26], and amino acids[27].

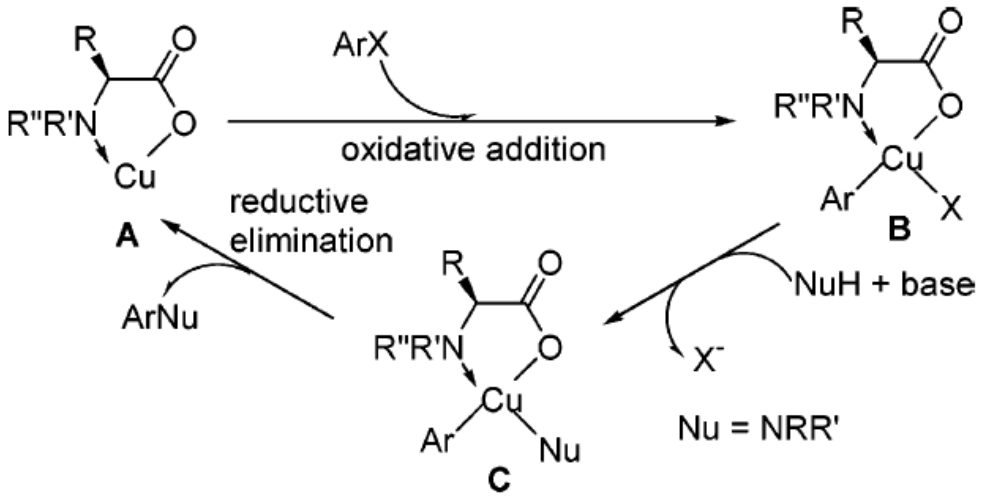
Scheme- D



Ziang et. al .[28] have demonstrated L-proline as a reliable promoter for the following four types of reactions at relatively low temperature, (a) coupling reaction of aryl iodides, and aryl bromides with aliphatic primary amines, aliphatic cyclic secondary amines, and electron-rich

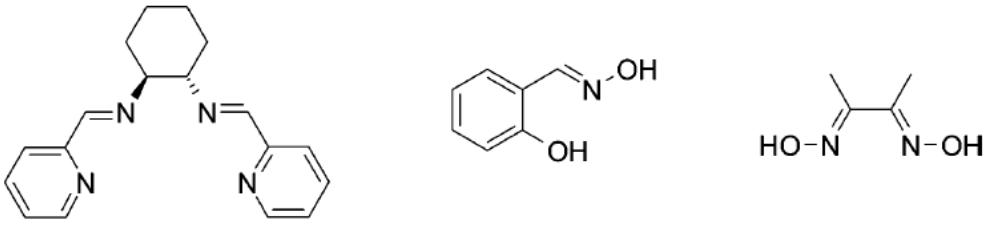
arylamines, (2) intramolecular coupling reaction between aryl chloride and primary amine moieties, (3) coupling reaction of aryl iodides with indole, pyrrole, carbazole, imidazole, or pyrazole and (4) coupling reaction of electron-deficient aryl bromides with imidazole or pyrazole. The mechanism proposed for the study has been shown in **scheme-E** where the chelation of Cu(I) with an amino acid makes Cu(I) species more reactive toward the oxidative addition, or/and stabilize the oxidative addition intermediates **B**, thereby promoting the coupling reaction.

Scheme- E



An efficient method for the synthesis of diaryl ethers under particularly mild conditions is described[29] Inexpensive Schiff base based ligands **(Figure - 4)** were found to greatly accelerate the Ullmann-type coupling of aryl bromides or iodides with phenols in acetonitrile Cs_2CO_3 and catalytic copper(I) oxide.

Figure- 4



The reaction tolerates substrates with unfavorable substitution patterns, such as sterically hindered coupling partners or electron-rich aryl halides.

The references cited above demonstrate the application of Schiff bases for the synthesis of various aromatic systems. These systems have great importance in biological, pharmaceutical and materials interest. Present work has been initiated with an objective of synthesizing and characterizing Schiff bases of salicyaldehyde. The prepared Schiff base ligands will be used for their application in the synthesis of diaryl amines.

MATERIALS AND METHODS

A. Source of reagents and analytical facilities

All the amines used were procured from Aldrich. LR grade solvents were used for the synthesis and procured from S.D. Fine -Chem Limited, Mumbai, India. ^{1}H NMR Spectral analysis were performed on BRUCKER ADVANCE II 400MHz spectrometer.

B. Experimental

2-((Methylimino)methyl)phenol (Table-1, Compound-1): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. Methyl amine (0.1 ml, 2.25mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H NMR:** δ 8.33 (s, 1H), 3.46-3.47 (s, 3H), 13.42 (s, 1H), 6.84-7.54 (m, 4H).

2-((Ethylimino)methyl)phenol (Table-1, Compound-2): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. Ethyl amine (0.13 ml, 2.44mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H NMR:** δ 8.34 (s, 1H), 13.65 (s, 1H), 6.83-7.31 (m, 4H), 3.59-3.65 (m, 2H), 1.30-1.33 (m, 3H).

2-((3-methoxypropylimino)methyl)phenol (Table-1, Compound-3): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. 3-Methoxy propylamine (0.2 ml, 2.04mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H**

NMR: δ 8.35 (s, 1H), 13.57 (s, 1H), 3.34 (s, 1H), 6.84-7.32 (m, 4H), 2.21 (m, 2H), 3.45-3.48 (t, 2H), 3.66-3.70 (t, 2H)

2-((5-Hethoxypentylimino)methyl)phenol (Table-1, Compound-4): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. 5-hydroxy pentylamine (0.2 ml, 2.08mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H NMR :** δ 8.33 (s,1H), 13.65 (s, 1H), 6.84-7.32 (m,4H), 3.66 (s,1H), 3.38-3.62 (t,2H), 3.62-3.65 (t,2H), 1.69-1.77 (m, 2H), 1.54-1.65 (m, 2H), 1.73-1.75 (m, 2H) .

Salen (Table-1, Compound-5): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. Ethylenediamine (0.7 ml, 1.0mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H NMR:** δ 8.35 (s, 2H), 13.22 (s, 1H), 6.83-7.31 (m, 8H), 3.9 (m, 4H).

2-((2-Mehoxyphenylimino)methyl)phenol (Table-1, Compound-6): Salicylaldehyde (250 mg, 2.04mmol) was taken in 50ml beaker containing methanol (10ml) and refluxed the content on a sand bath for 10 minutes at 60-70°C. Anisidine (0.27 ml, 2.45mmol) was added after 10 minutes and reaction mixture again refluxed on sand bath for 5-minutes at 60-70°C. On cooling, a yellow viscous solution was formed that was subjected to rotary evaporator and then high vacuum to evaporate methanol. The viscous mixture of Schiff base was monitored by thin layer chromatography in chloroform methanol (90:10). **^{1}H NMR:** δ 8.67 (s, 1H), 3.82 (s, 3H), 6.74-7.37 (m, 8H)

General procedure for diaryl amine (Scheme-2, L4): 2-Nitrofluoro benzene (0.75 mmol), 2-nitoaniline (0.5 mmol) were taken in a round bottom flask and acetonitrile (10 ml) added. 20 mol % ligand and 5 mol % copper catalyst were added and reaction mixture heated to a

temperature of 90^0C for 12 hrs. TLC monitoring was done to confirm the presence of product and compared with that obtained from proline.

Results and discussion

a) *Preparation and characterization of Schiff bases*

Schiff base ligands using salicylaldehyde and aliphatic amines were synthesized with an objective to use them for the synthesis of diphenyl amines, which are an important class of compounds from biological, pharmaceutical, and materials point of view.[17].

A mixture of salicyaldehyde and amine, dissolved in methanol were heated on sand bath to a temperature of 60-70^{0}C. The progress of the reaction was monitored using thin layer chromatography. In a solvent system consisting of chloroform and methanol a clear spot of ormed Schiff base was observed. **Figure- 5** clearly shows a spot of product in lane 3 **(L3)** which is different from amine or aldehyde. Although the spot for aldehyde and product have almost same R_f value, the more intense spot of product clearly differentiates itself from the starting material.

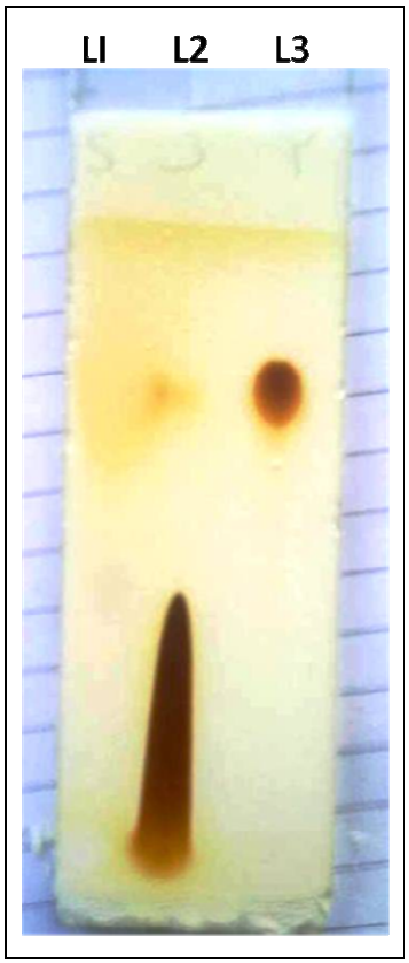


Figure-5: LI, L2 and L3 represent Lane1, Lane 2 and Lane 3 for *Salicyaldehyde, 3-methoxy propyl amine and product respectively.*

All the synthesized ligands were characterized using ^{1}H NMR spectroscopy. Replacement of proton for salicyaldehyde's aldehyde group at 9.8 ppm by the the one appearing at 8.0 ppm for (-C**H**=N-) confirmed the presence of Schiff base. The product obtained in most of the cases was pure except in case of ethyl and methyl amines where signal for residual aldehyde was observed.

Various amines used for the synthesis of ligands were methyl amine, ethyl amine, 3-methoxypropyl amine, 5-amino alcohol and anisidine. The procedure followed for most of the amines was same as described above except in case of anisidine where the reaction mixture had to be refluxed for long hours before desired product was obtained. **Scheme-1** and **Table-1** summarize the amines that were used for the synthesis of products.

Scheme-1

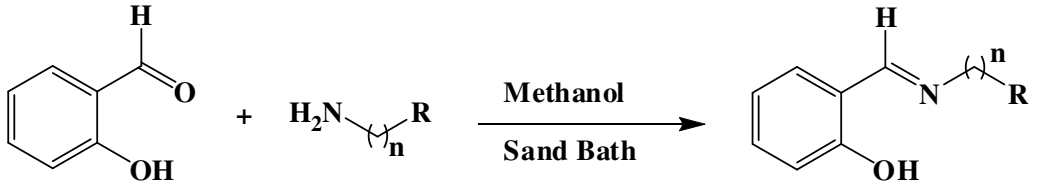
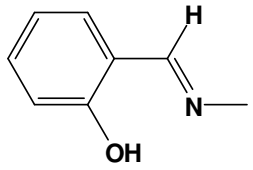
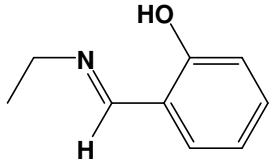
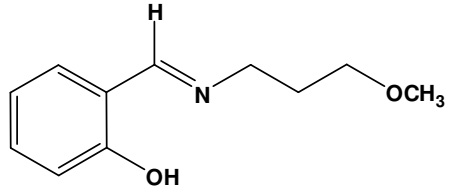
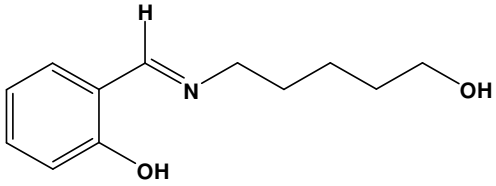
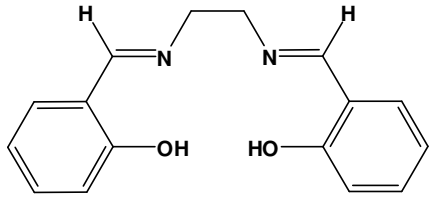
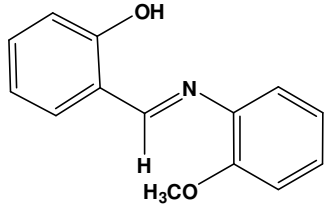


Table-1

S.No	n	R	Product	% Yield
1.	0	CH_3		65
2.	1	CH_3		62
3.	3	OCH_3		72
4.	5	OH		67
5.	2	-		86
6.	-	-		45

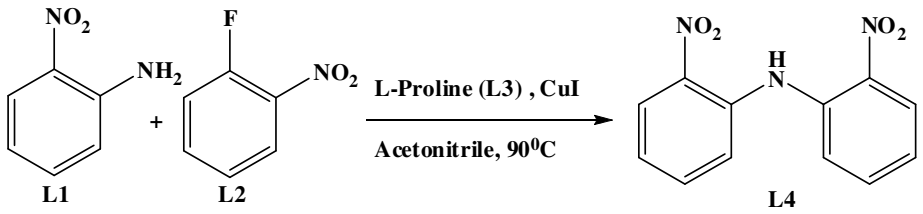
b) *Synthesis of Diarylamines using prepared Schiff bases.*

Several mild conditions for CuI-catalyzed coupling of aryl halides with aliphatic and aromatic amines have been reported in the literature. Venkataraman and coworkers have described a technique where soluble copper (I) catalysts, $Cu(neocup)(PPh_3)Br$ [24] was employed for elaborating diaryl or triarylamines. Buchwald and co workers have found that the combination of CuI and L-proline could catalyze the coupling reaction of iodobenzene with aniline at 90 °C to provide diphenylamine in 66% yield

We have demonstrated that above synthesized ligands act as promoter for the synthesis of diaryl amines. All the reactions carried out for diaryl amines were analysed by TLC only. The reaction conditions reported for the synthesis of diaryl ethers by Ziang et. al[28] were followed for the standard reaction using L-proline as the promoter. Coupling of o-nitro fluorobenzene with o-nitro aniline in the presence of CuI and ligand was carried out in acetonitrile at 90^0C **(Scheme-2)**. **Figure- 6** below shows a spot in lane 4 **(L4)** for the anticipated diaryl amine. Other spots in Lane 1, 2 and 3 **(L1**, **L2** and **L3)** correspond to o-nitroaniline, o-nitrofluorobenze, and proline respectively.

Figure-6

Scheme-2



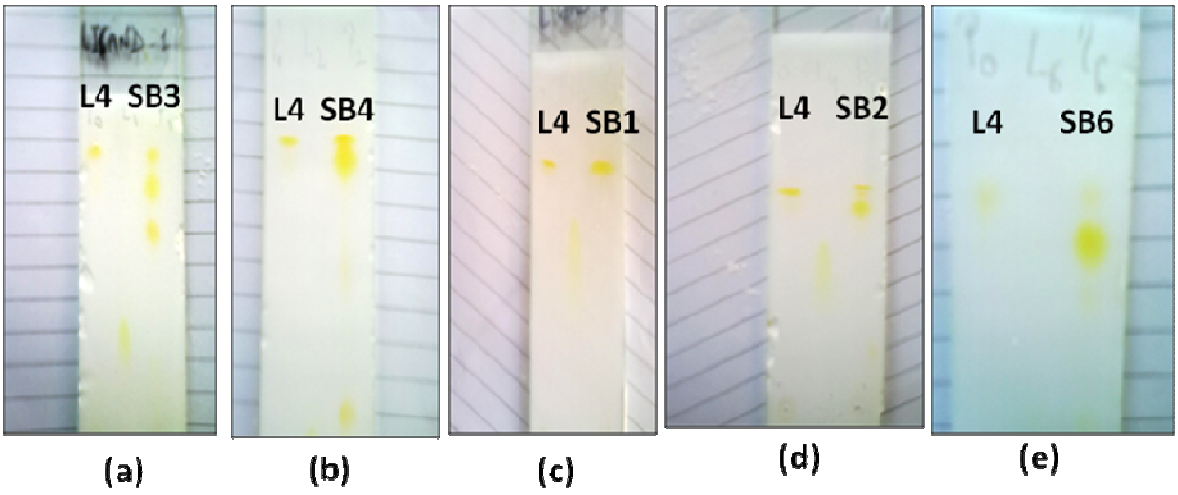
The diaryl amine product **(L4)** obtained from above reaction was used as standard for monitoring the promoting ability of Schiff base ligands to carry out this reaction. Using substrates same as taken in **Scheme-2** above reaction was carried out in the presence of 20 mol % of ligands and 5 mol % of CuI at 90^0C in acetonitrile.

Encouraging results were obtained in case of Schiff bases **1**, **2**, **3** and **4** **(Table-1)** as is evident from TLC pictures shown in **Figure-7**. The best yields as shown by TLC is for Schiff base-1 **(SB1)** made from methyl amine **(Figure-7, C)**. In case of Schiff base synthesized using 3-methoxy propyl amine **(3, Table-1)** a clear residual starting material spots can be seen **(SB3)**. In all the cases a spot of blank Schiff base was also compared (not

labeled on TLC) plate. Almost negligible product was observed in case of salen Cu complex **(5)** and Schiff base made from anisidine.

A comparison of structure of Schiff base **(1)** with salen **(5)** clearly shows that available number of binding sites for later is more. The insignificant yields in case of compound **(5)**

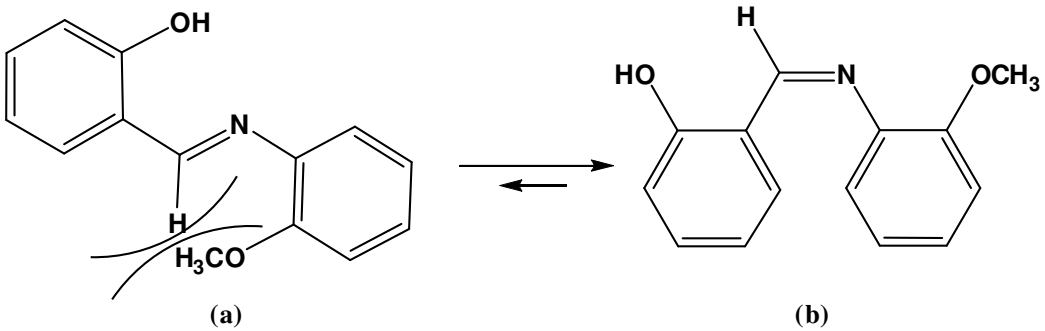
Figure-7



may be because of strong binding of the metal ion by ligand. As a result **(Scheme-D above)** the oxidative addition of the aryl halide and subsequent nucleophilic addition cannot take place on metal resulting in extremely low yields.

Schiff base synthesized from anisidene may not be able to coordinate with metal ions due to its orientation in the more stable form as shown in **(Figure-8b)** where the hydroxyl and C=N orient in opposite directions.

Figure-8



Conclusion

A number of Schiff base ligands were prepoared and used for the synthesis of Ullmann-type coupling reaction of diaryl amines. The Schiff bases synthesized from methyl amine and ethyl amine gave a clear reaction product in TLC, however characterization of the product using 1H , 13 C NMR and mass spectroscopy techniques needs to be done. The initial results of this novel way of synthesizing diaryl amines can be helpful in the prepration of these important synthetic intermediates.

References

1. IUPAC *Compendium of Chemical Terminology*, **1995**, 65, 1364.
2. E. H. Cordes, W. P. Jencks **,** *J. Am. Chem. Soc***., 1962,** 84, 832–837**.**
3. Cemal Hezneci, kadriye Ertekin, Berrin yenigul *and Engin Cetinkaya, Dyes and pigment,* **2004,** *1, 35-41.*
4. Shalin Kumar, Durga Nath Dhar and PN Saxena. *Journal of Scientific and Industrial Research*, **2009**, 68, 181-187.
5. Nishinaga A, Yamada T, Fujisawa H, and Ishizaki K, *J Mol Catal*, (**1988)**, 48, 249-64.
6. Z Xi , w Liu , G Cao , W DU , J Huang, K Cai and , Cuihau Xuebao *, Catalytic oxidation of naphthol by metalloporphyrins ,* **(1986)** , 7 , 357-363 .
7. Chakraborty H, Paul N and Rahman M L, esters, *Trans Met Chem (lond)*, (**1994)**, 19, 524-526.
8. Y D Zhao, D W Pang, Z Zong, J K Cheng, Z F Luo, C J Feng, H Y Shen, and X C Zhung, H Xuebao, **(1988)**, 56, 178-183.
9. R Sreekala, K K Yusuff and Mohammed, *Catal Pap Natl Symp* , **(1994)** 507-510 .
10. P Tehshik. Y, Eric Jacobsen. *Science***, (2003),** 299, 1691-1693.
11. Wang R-M, Hao C-J, Wang Y-P, Li-S-B, *Journal of Molecular Catalysis A*, **1999,** 173-178.
12. Nam Ho Lee, Jong Chul Byun, Jong Seok Baik, Chung-Hun Han, and Sung-bin Han , *Korean Chem. Soc, .* **2002**, 1365.
13. Anthony M, Granville, *Macromol. Rapid Commun*. 2004, 25, 1319–1323.
14. X Wang, *Chinese Chemical Letters*, **2002.**
15. T. Punniyamurthy, M. Madhava Reddy, Swinder Jeet Singh Kalra and Javed Iqbal, *Pure & Appl. Chem.,***1996***,* 68, 619-622 .
16. Akoi, *US Patent, 1988*, 748.
17. O'Hagan, D. *Nat, Prod. Rep*. **2000**, *17*, 435.
18. F Ullmann ,. *Ber. Dtsch. Chem. Ges***. 1903**, *36*, 238.
19. J. P Wolfe, S Wagaw, J F Marcoux, S. L Buchwald, Acc. *Chem. Res.* **1998**, 31, 805.
20. I. P Beletskaya, A. V Cheprakov, *Coord. Chem. Rev*. **2004**, *248*, 2337).
21. Klapars, A., Antilla, J. C., Huang, X., Buchwald, S. L. J. Am.*Chem. Soc*. **2001**, 123, 7727

22. Kwong, F, Y, Klapars, Buchwald, S.L. *Org. lett*. **2002**, 4, 581.

23. Kwong, F, Y, Buchwald, S.L. *Org. lett*. **2003**, 5, 793.

24. Gujadhur, R. K., Bates, C. G., Venkataraman, D. *Org. Lett.* **2001**, 3, 4315.

25. Cristau, H.-J., Cellier, P. P, Spindler, J.-F., Taillefer, M. *Eur. J. Org. Chem.* **2004**, 695.

26. Zhang, S., Zhang, D. , Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.

27. Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem Soc*. **1998**, *120*, 12459

28. Zhang, Q Cai, and D Ma, *J. Org. Chem.* **2005**, *70*, 5164-517.

29. Bouchard, N Blouin, A Michaud, M Leclerc, *Org. Lett*., **2004**, 6, 913