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Coupling reactions involving aryldiazonium salt: Part-II. Chemoselective condensation with acetyl acetone and antibacterial activity

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ABSTRACT

The aryldiazonium salt Ar-$N_2^{\oplus}Cl^{\ominus}$ are highly reactive compounds. It is used as intermediate in different reactions. These reactions, either, losses nitrogen containing function or without loss of nitrogen function. First category includes replacement by -H, -OH, -Br, -F, -I, -CN, -NO_2, aryl- etc. and the latter involves reduction and diazo coupling type reaction. In the present piece of work we have reacted the aryldiazonium salt with Active Methylene Group(AMG) containing compound, Pentane-2,4-dione or Acetyl acetone(AA). The final product formed has potential to use as precursor for synthesis of 4-methyl-3-acetylcinnoline or derivatives thereof. These compounds were tested for the antibacterial activity against gram negative bacteria, E. coli.

Keywords: Schiff base, aryldiazonium salt, active methylene group, antibacterial activity.

INTRODUCTION

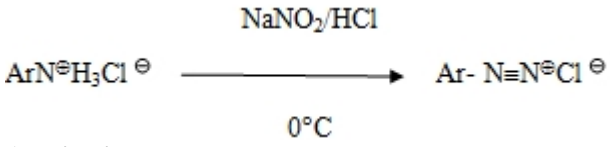
There are many classes of compounds in organic chemistry like aldehyde, ketone, nitrile, ester, lactone, anhydride, imine and azo compounds etc likewise aryldiazonium compounds also plays an important role in synthetic organic chemistry. The aryldiazonium salt were synthesized and reacted upon with AMG containing compound like Pentane-2,4-dione or Acetyl acetone(AA). Heterocyclic rings[1-2], which were the reason for the activity of Most of the drugs of natural origin leads to the discovery of the many synthetic drugs possessing the heterocyclic rings. Heterocyclic nitrogenous[3-4] compounds and their fused analogues represent an important class of heterocyclic compounds exist in numerous natural products displaying a wide range of biological and pharmaceutical activities.

Diazonium Salts

Aromatic diazonium salts, represented by the general formula, Ar-$N_2^{\oplus}X^{\ominus}$, are highly reactive compounds and serves as intermediate in the synthesis of a wide variety of organic aromatic compounds. In fact, they are comparable to Grignard reagents in their versatility i.e ease of processing. They are regarded as salt of the aryldiazonium hydroxide Ar-N≡$N^{\oplus}OH^{\ominus}$.

Method of Formation:

As described earlier, the aryldiazonium salts are commonly prepared by the diazotization of primary aromatic amines at low temperature in acidic solutions.



Applications:
The aryldiazonium compound shows a lot of reactions, few to mention here are as discussed below. The reactions, either, losses nitrogen containing function or without loss of nitrogen function.

a) With loss of N-function:
On Replacement by Bromine group
Replacement by Cyano group

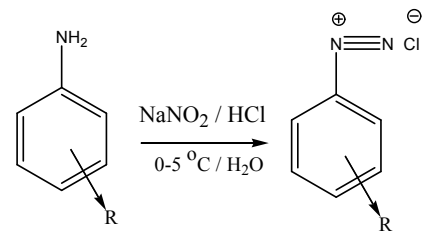
b) Without loss of N-function:
Diazo coupling
Reaction with ester function
Reduction

First category includes replacement by H, -OH, -Br, -F, -I, -CN, -NO_2, aryl- etc. and the latter involves reduction and diazo coupling type reaction. In the present piece of work the aryldiazonium salt was reacted with AMG containing compound, Pentane-2,4-dione viz. Acetyl acetone(AA).

Similar to Sitosterol[5] and Cholesterol etc. Cinnolines are from the class of bioactive compounds due to their remarkable biological and pharmacological property[6]. Cinnoline and its derivatives also shows biological activities such as antihypertensive[7], bacteriocides[8] and analgesic[9] activity. This type of compound requires the intermediates of the type (Phenylhydrazono)-acetyl acetone or similar compounds. In view of synthesis of newer 4-Methyl-3-acetylcinnoline or derivatives thereof are of importance, their intermediates are considered worthwhile to study their synthesis. Similar type of reactions were also reported by Mittal and Singhal[10] and recently from our laboratory[11].

In the present work the type of ketone compounds i.e the intermediates of the type (Phenylhydrazono)-acetyl acetone, **IIIa-d** and its varied derivatives are synthesized (**Scheme-I**). Review of literature indicated that such ketone derivatives are valuable synthones for the synthesis of 4-Methyl-3-acetylcinnoline or derivatives thereof.

Scheme-1:

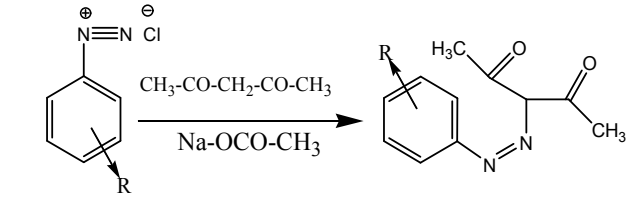


Substituted-aniline derivative **Ia-d**

Substituted-phenyldiazonium chloride **IIa-d**

where, R = a) o-Cl, b) o-NO_2-, c) m-NO_2- and d) p-NO_2-.

Scheme-2:



4-Substituted-phenyl diazonium chloride **IIa-d**

2-(4-Substituted-phenylhydrazono) acetylacetone, **IIIa-d**

where, R = a) o-Cl, b) o-NO_2-, c) m-NO_2- and d) p-NO_2-.

MATERIALS AND METHODS

General: All the chemicals and solvents were obtained from E-Merck, India and are of synthesis and the Spectroscopic grade respectively. They were used without further purification. Silica gel-G was used to monitor the progress of reactions, by TLC and visualized by iodine vapour-chamber. The colour observed was recorded by visual method and melting point range was taken in an one end open capillary tube. The purity of the compounds was ascertained by melting point range determination (in one end open capillary method), and by Silica gel-G TLC. The UV-Vis spectra were recorded on a Shimadzu-1800 instrument (wavelength, λ in nm). Quartz cuvette of path length 1 cm was used for measurements in solution. The FTIR spectra were recorded on a Shimadzu FTIR 8400 spectrophotometer (Model- IRAffinity-1) using sample mixed in powder form with KBr powder, the frequency values, 'ν', are in cm^{-1}. The overall purity and structural assignment of the products was based respectively on the elemental (CHN) analyses, TLC and UV-Vis, FTIR spectral data.

Stage-I. General Procedure for Preparation of Diazonium Salt, IIa-d: Charge 0.02 M aniline (or its derivative) in a beaker Add to it mixture of 10 ml con. HC1 and 5 ml water and stir with the glass rod to get clear solution, cool the solution to 0°C by keeping in an ice bath. Meanwhile dissolve (0.025 M) sodium nitrite in 8 ml water. Cool the solution in ice bath to 0°C, after attaining 0°C add $NaNO_2$ solution in to aniline hydrochloride solution dropwise with constant stirring (Do not allow to rise temperature above 5°C during addition) test the diazotized solution impart dark blue colour to starch iodide paper(blue colour is obtained on the potassium-iodide starch paper). Decompose the excess of nitrous acid by adding pinch of urea filter the solution and collect the filtrate which is diazonium salt solution.

Stage-II. General Procedure for Synthesis of (Phenylhydrazono)-acetyl acetone, IIIa-d: Add aryldiazonium salt solution (from **Stage-I**) slowly, to the well cooled mixture of, Pentane-2,4-dione viz. Acetyl acetone(AA) (0.018 M) dissolved in 5 ml ethanol and NaOAc, 8-10 gm in 4-5 ml of water(to keep the mixture alkaline to litmus), a coloured precipitate is separated, then add 20 ml of con. HCl then filter and check the absence of ester and thus the product obtained is recrystallized by using solvent ethanol, dry it. Record the dried weight (in gms) and the physical constant i.e m. p. range of the compound.

The synthesized compounds were tested for the antibacterial activity against *E. coli* as per the method described in literature [12] and compared with ampicillin as standard drug.

RESULTS AND DISCUSSION

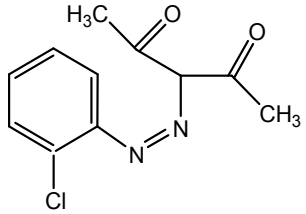
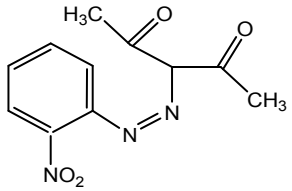
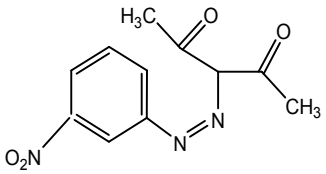
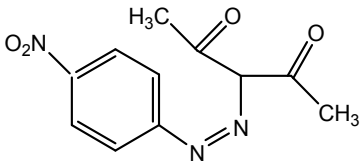
In the present study, diazonium intermediates of aniline and substituted anilines are synthesized, reacted with active methylene compound(acetyl acetone) and screened for antibacterial activity. All the compounds were obtained in high purity. The progress of reactions was monitored by Silica gel-G TLC, visualized by iodine vapour. The purity of the compounds was ascertained by melting point determinations (open capillary method), and by Silica gel-G TLC. The structural assignment of the products was based on UV-Vis and FTIR spectral data and elemental (CHN) analyses. The spectral data are in close agreement with the structures of the synthesized compounds. All compounds gave satisfactory elemental analysis. Values are in the close agreement with the values calculated for expected molecular formulae assigned to these compounds and are in 5 % in statistics.

The data showing result of synthesis study and their analytical details such as colour and physical constants etc. are depicted in the **Table-1**.

Thin layer chromatography indicate for the preparation of the final intermediates, **IIIa-d**, compared with the starting raw material. Thus the synthesized compounds viz. (Phenylhydrazono)-acetyl acetone, **IIIa** or derivatives thereof, **IIIb-d** are synthesized and are now available for the further use.

The FITR spectra of the synthesized final products, **IIIa-d** are depicted below in Fig. **1A** to **1D**. The related data of FTIR characteristic frequency (in cm^{-1}) of the groups indicated in the **Table-2**.

Table-1: Structures of Products, IIIa-d and their Colour, Physical constant and % Practical yield

Sr. No.	Starting Material	Product	Colour	Physical constant, m. p. range, °C	% Practical yield
1	2-Chloro aniline, **Ia**	 2-Chloro-phenylhydrazono acetylacetone, **IIIa**	Yellow	110-111	87.39
2	2-Nitro aniline, **Ib**	 2-Nitro-phenylhydrazono acetylacetone, **IIIb**	Yellow	132-133	83.73
3	3-Nitro aniline, **Ic**	 3-Nitro-phenylhydrazono acetylacetone, **IIIc**	pale yellow	98-100	43.97
4	4-Nitro aniline, **Id**	 4-Nitro-phenylhydrazono acetylacetone, **IIId**	Yellow	119-121	22.48

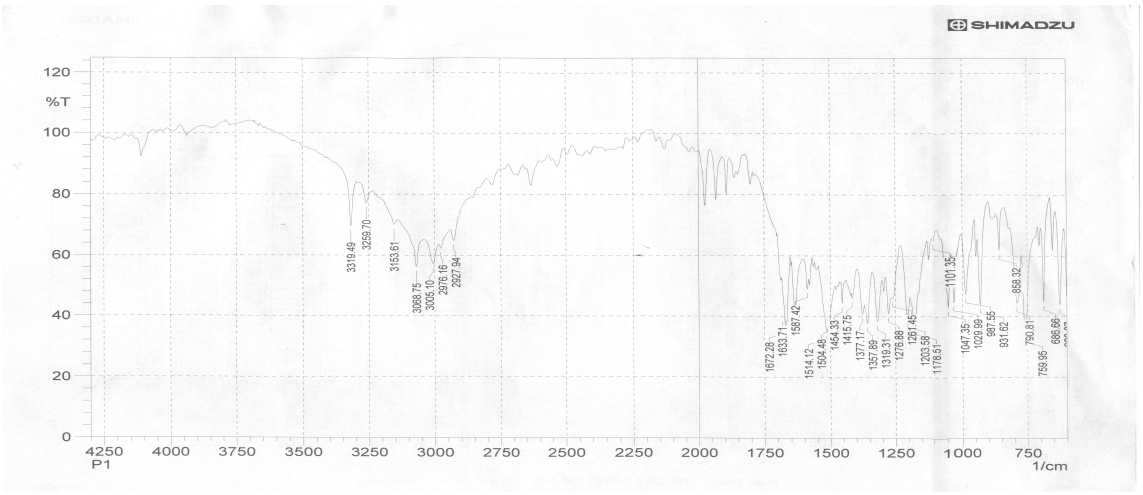


Fig.1A: FTIR spectra for the (2-Chloro-phenylhydrazono)-acetyl acetone, III_a (P1)

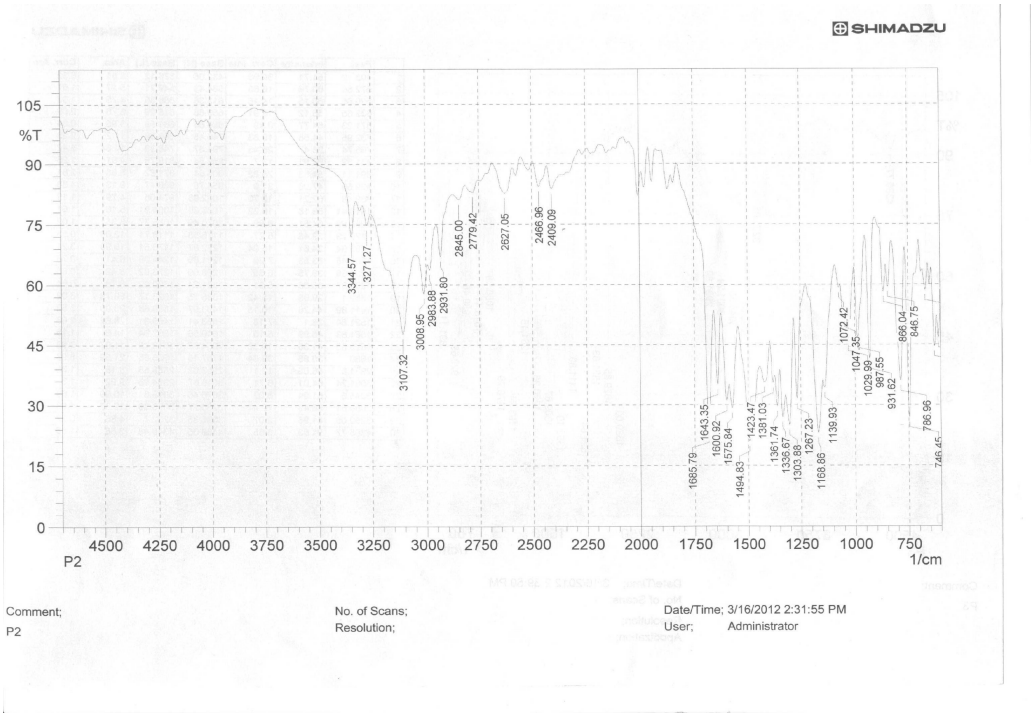


Fig.1B: FTIR spectra for the (2-Nitro-phenylhydrazono)-acetyl acetone, III_b (P2)

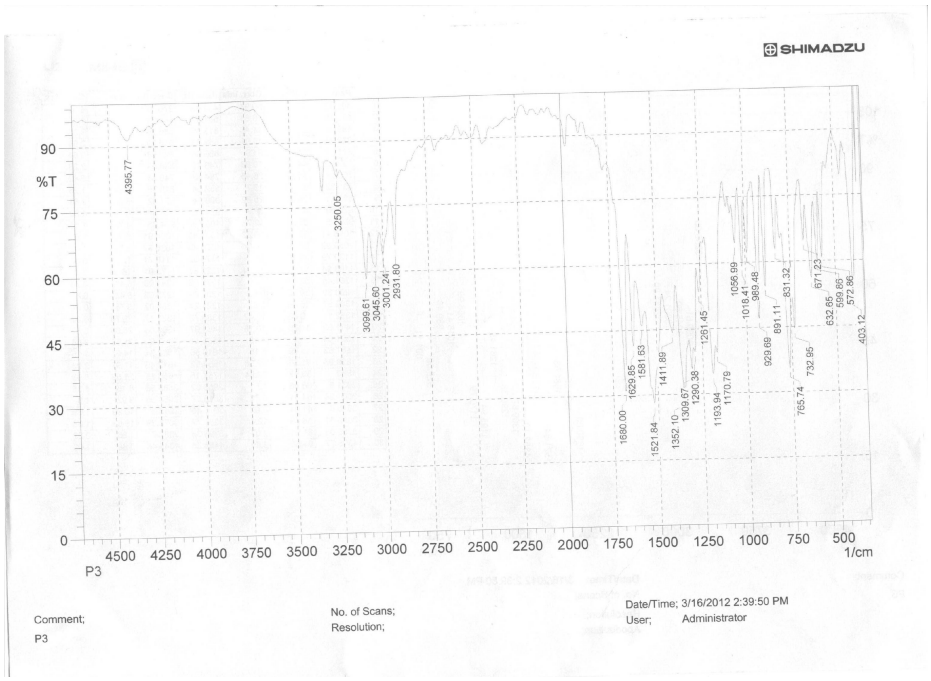


Fig.1C: FTIR spectra for the (3-m-Nitro-phenylhydrazono)-acetyl acetone, III_c (P3)

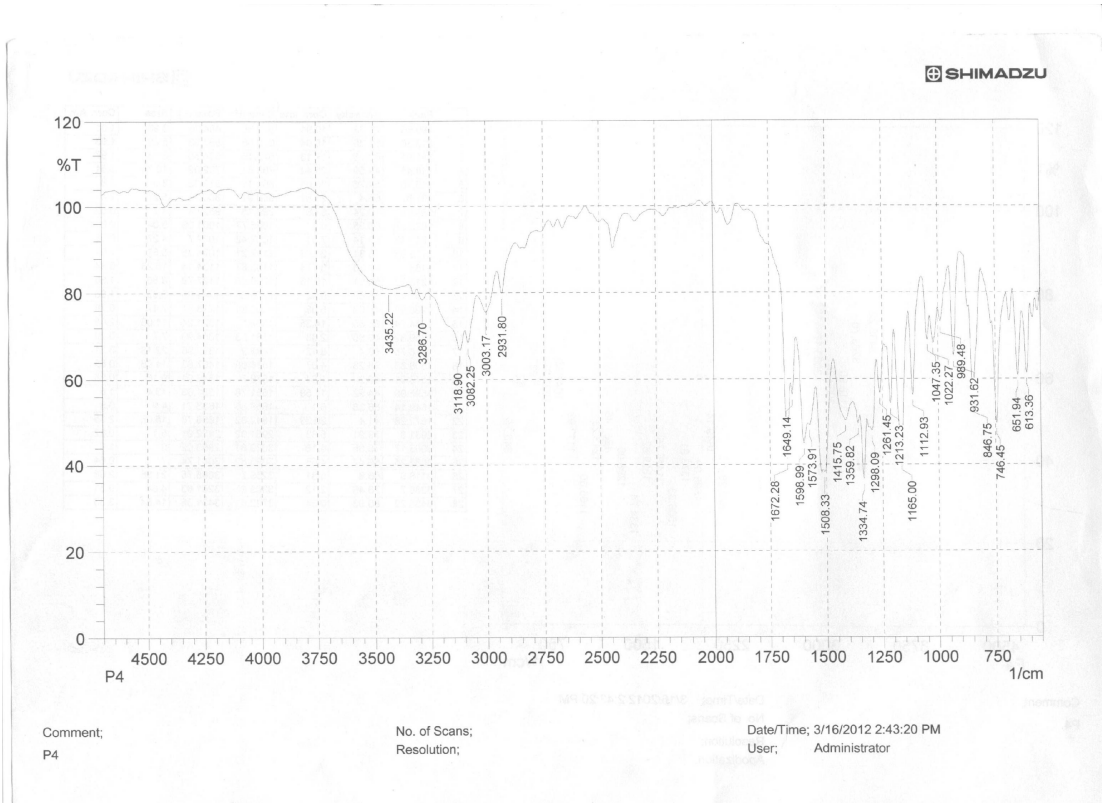
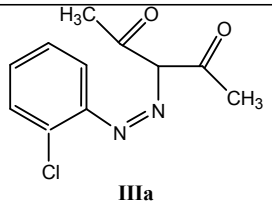
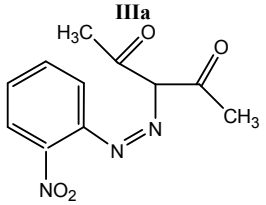
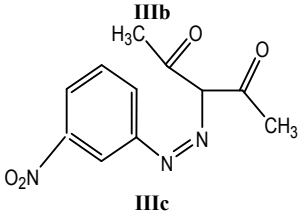
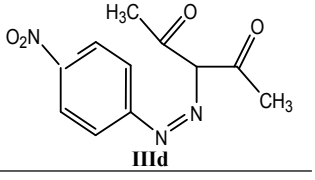


Fig.1D: FTIR spectra for the (4-Nitro-phenylhydrazono)-acetyl acetone, III$_d$ (P4)

Table-2. The Characteristic FTIR Spectral data of the synthesized compounds, IIIa-d

Sr. No.	Name of the Compound	Spectral absorptions (cm^1)	Structure assigned
IIIa	(2-Chloro-phenylhydrazono)-acetyl acetone	ν-N=N- = 1261 νAr-H- = 1504 ν-C-H = 3068 ν>C=O = 1672 ν-(CH3)CO- = 1377 ν-C-Cl = 790	 **IIIa**
IIIb	(2-Nitro-phenylhydrazono)-acetyl acetone	ν-N=N- = 1267 νAr-H- = 1600 ν>C=O = 1643 ν-(CH3)CO- = 1361 νo-NO2- = 1303	 **IIIb**
IIIc	(3-Nitro-phenylhydrazono)-acetyl acetone	ν-N=N- = 1261 νAr-H- = 1521 ν>C=O = 1653 ν-(CH3)CO- = 1352 νm-NO2- = 1309	 **IIIc**
IIId	(4-Nitro-phenylhydrazono)-acetyl acetone	ν-N=N- = 1261 ν Ar-H- = 1508 ν >C=O = 1672 ν-(CH3)CO- = 1359 νp-NO2- = 1305	 **IIId**

Antibacterial activity of all the synthesized compounds were screened against gram-negative bacteria, *E. coli* for two different concentration of 100 µg/ml and 200 µg/ml, as per the method described in[12]. The results of antimicrobial testing are depicted in **Table-3**.

Table-3: The results of antimicrobial testing against *E. coli*

Compound I.D.	*E. coli*	
	100 µg/ml	200 µg/ml
IIIa	7	9
IIIb	5	6
IIIc	7	10
IIId	6	8
Positive Control	+ ve	+ ve
Negative Control	- ve	- ve
Ampicillin	16	24

CONCLUSION

Aniline and substituted anilines are used for the preparation of diazoninium salt then they are reacted upon with Acetyl acetone to give (Phenylhydrazono)-acetyl acetone, **IIIa-d** or derivatives thereof. These compounds will be useful as building block for organic researchers in the near future.

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REFERENCES

[1] a) A. R. Katritzky, W. R. Charles, *Comprehensive Heterocyclic Chemistry,* **1990**, 3, 22, *Trend in Heterocyclic Chemistry,* 248; b) A. R. Katritzky, Chairman of the Editorial Board, W. R. Charles, FRS Co Chairman of the Editorial Board, FRS, Comprehensive Hetrocyclic Chemistry the Structure Reaction Synthesis & Use of Hetrocyclic Compounds Vol-3 (Pergamon Press) UK p. 2.
[2] P. Matyus, K. Czako, *Trend in Heterocyclic Chemistry*, **1993**, 2(3) 249.
[3] M. Tisler and B. Stanovic, In: A. R. Katritzky and A. J. Boulton (Ed.), Advance in Heterocyclic Chemistry, (Academic Press, **1979)** 408.
[4] A. Stanczak and W. Pakulska, *Pharmazie*., **2001**, 56(6) 501.
[5] M. C. Patil and R. T. Mahajan, *Int. J. Pharm. Sci. Rev. Res.,* **2013**, 21(2) n^0 53, 297.
[6] P. Parasuraman, R. S. Shanmugarajan, T. Aravazhi, K. Nehru, T. Mathiazhagan and R. Rajakumari, *Int. J. Pharm. Life Sci.,* **2012,** 3(2) 1430.
[7] J. W. Adwards, *A Survey of Antimalerial Drugs*, **1976**, 11, 946.
[8] H. Eisako, JP 7010349, C.A. **1970**, 73, 45529.
[9] A. M. Amer, M. M. El-Mobayed and S. Asker, *Monatsh. Chem.,* **2004**, 135, 595
[10] A. K. Mittal and O. P. Singhal, *J. Ind. Chem., Soc,* **1982**, 59, 711-712.
[11] C. J. Patil, P. A. Patil, P. B. Patil and M. C. Patil, *Der. Chemica. Sinica.,* 6(5) (2015) 109-114.
[12] C. J. Patil, C. A. Nehete and H. A. Mahajan, *Int J Green and Herbal Chem,* **2013**, 2(2), 241.