Improving Methodology for the Preparation of 2-(Substituted phenyl) -4, 5-bis (4-Methoxyphenyl)-1H-imidazoles from 4, 4'-Dimethoxybenzil under Microwave Irradiation

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Abstract- An efficient synthesis of 2-(2-Substituted Phenyl) -4,5-bis (4-methoxyphenyl)-1H-imidazoles by one step condensation of an substituted aldehyde ,4,4'-dimethyl benzil ,ammonium acetate under microwave irradiation is described .The structure of the product were characterized by 1HNMR ,IR ,elemental analysis , and melting point .The advantage of this method is simple methods ,procedure are a green method ,its milder conditions , necessary shorter reaction time and its higher yields and easy workup.

Index Terms- Imidazoles, Solvent free, MW irradiation, multi-component reaction.

I. INTRODUCTION

Many heterocyclic compounds due to their specific activity are employed in the treatment of many infectious diseases .The toxicity and volatile nature of many organic solvents, particularly chlorinated hydrocarbons that are widely used in huge amounts for organic reactions have posed a serious threat to the environmental [1] .Thus the design of solvent free catalytic reaction has received more attention in recent times in the area of green synthesis [2-3] .The emergence of microwave technology as a tool for increasing reaction rates is well documented [4-5] .Microwave-assisted reactions are extremely attractive to synthetic organic chemists due to their ability to shorten reaction times [6-7]. Reactions that previously required hours to run for completion can now be finished within minutes [8]. Imidazoles are commonly utilizing substructures within the pharmaceutical industry , as these heterocycles impart unique physical and biological properties to compounds of interest [9-10] .Trisubstituted imidazoles derivatives are widely used as organic materials such as to resist composition on textile [11] ,photographic materials[12-13] .Meantime , it was found that these compound play roles in many kinds of biological activities[14-15].This versatile applicability highlights the importance of access to efficient synthetic routes to well-designed and highly substituted imidazole derivatives .There are several methods for the synthesis of 2,4,5-trisubstituted imidazoles by three component cyclocondensation of a 1,2-diketone , with an aldehyde and ammonium acetate which comprise the use of microwave [16-17] ,Ionic liquid [18] , refluxing in acetic acid [19-20] ,Silica sulfuric acid [21] ,$NiCl_2.6H_2O$ / Al_2O_3 ,Iodine [23] ,$Zr(acac)_4$ [24] ,Sodium bisulfite[25] ,L-proline [26] .Most of these synthetic methods suffer from one or more serious drawbacks such as laborious and complex work-up and purification ,significant amounts of waste materials ,high temperature ,low yields , long reaction times and the of expensive reagents

We were promoted a facile , mild and efficient method for one –pot synthesis of 2-(Substituted phenyl)-4,5-bis(4-methoxyphenyl)-1H-imidazole from 4,4'-Dimethoxy benzil and various aromatic aldehydes under solvent free and microwave conditions.

II. EXPERIMENTAL SECTION

Materials - Substituted aromatic aldehyde , Anisaldehyde ,Sodium Cyanide ,ethanol ,Conc. Nitric acid ,Ammonium acetate ,glacial acetic acid is required chemicals perchased from merk and S-d fine chemicals .All the reported melting points were taken in open capillaries and are uncorrected .IR spectra were measured by using Perkin Elmer Model 2000 Spectrophotometer and are given in cm^{-1} using KBr disc ,1HNMR spectra were measured in DMSO by using Bruckner Avance 400MHz spectrophotometer using TMS as an internal standard .The purity of all the synthesized compound was tested by TLC on silica gel plate using ethyl acetate and petroleum ether (80 : 20)and iodine was used as a visualizing agent .Microwave synthesis was carried out on a ETHOS 1600 , Milestone microwave reactor .

- **General procedure for the synthesis of 4,4'-Dimethoxybenzil [1,2-bis(4-methoxyphenyl) –ethan-1,2- dione)] – (B_2)**

Took 7.8 gm 2-hydroxy-1,2-bis-(4-methoxyphenyl)-ethan-1-one dissolved in 22ml glacial acetic acid then added 31 ml Conc. Nitric acid slowly to a reaction mixture with controlled temperature by using ice-bath .Refluxed the reaction mixture for 2 hours until the complete evolution of brown gas , stopped reaction and cooled , poured into crush ice-cold water with stirring obtained a solid product , Filter, dried it and recrystallized from ethanol .

Yield- 67% , M.Pt- 133-135 ^{O}C , M.Wt- 270 , Formula- $C_{16}H_{14}O_4$
IR (KBr cm^{-1}) 3072 (C-H Ar) , 2979 (C-H ali –OCH3), 1690 (C=O) , 1536 (C=C) , 1158 (C-O) .
^{1}HNMR (DMSO) 4.0 (S ,3H ,-OCH3) , 7.3 (d ,2H) , 7.4 (d ,2H) .
Anal .Caculation for $C_{16}H_{14}O_4$

Element	C	H	O
Found	71.16	5.27	23.73
Calcd	71.19	5.31	23.69

***Synthesis of 2-(Substituted phenyl)-4, 5-bis (4-methoxyphenyl)-1H-imidazoles (3a-3l) under Microwave irradiation**

A mixture of 1, 2-bis (4-methoxyphenyl) –ethan-1,2- dione (1 mmol) ,ammonium acetate (7 mmol) , aromatic aldehyde (1 mmol) in a Borosil beaker (50 ml) add 2 to 3 drop of glacial acetic acid .The reaction mixture was mixed properly with the help of glass rod and put in a microwave oven .The mixture was irradiated at 135 W and irradiated for a period 30 sec at a time , After each irradiation the reaction mixture was removed from the microwave oven for shaking .The total period of microwave irradiation was 1- 7 min (Table -1) .After TLC (Petrolium ether : ethyl acetate 9:1) indicating the starting materials of 4,4'-dimethoxybenzil and aldehyde had disappeared .The reaction mixture was cooled to room temperature and poured into ice water (50 ml) obtained solid product , filter washed with water , dried and recrystallized from ethanol to get the corresponding product (3a-3l) were confirmed by IR ,^{1}HNMR and melting point .

***Spectral Data for New derivatives of 2-(Substituted phenyl)-4,5-bis-(4-methoxyphenyl)-1H-imidazoles –**
1. 2-Phenyl-4,5-bis(4-Methoxyphenyl)-1H-imidazole (3a) --

Solid Colourless , M.Pt- 198-200 ^{O}C . Formula – $C_{23}H_{20}O_2N_2$, M.Wt- 356 .
IR (KBr cm^{-1}) 3450 (N-H) ,3048 (C- H arom) , 2977 (C-H aliph) , 1618 (C=N) , 1461.56 (C=C)
^{1}HNMR (400 MHz , DMSO) 3.90 (S, 1H –OCH_3), 3.98 (S, 1H, -OCH_3), 7.46 (d, 2H), 8.36 (d ,2H) 8.05 (s, 1H), 7.51 – 8.69 (m , 8H) , 8.6 (S , N-H) .

Anal. Calculation for $C_{23}H_{20}O_2N_2$ –

Element	C	H	O	N
Found	77.55	5.63	8.98	7.86
Calculated	77.59	5.56	8.96	7.90

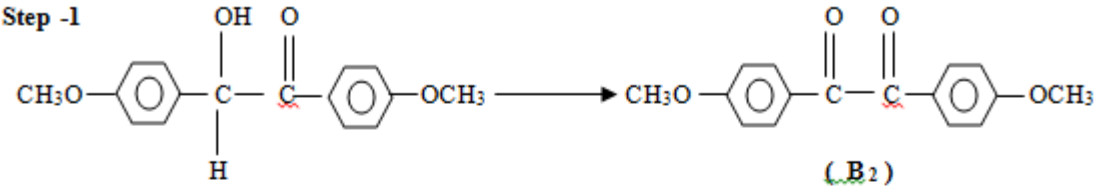
***2-(4-Chlorophenyl)-4,5-bis-(4-Methoxyphenyl)-1H –imidazole (3 b) – Solid , Colour- Yellow , M.Pt- 120 – 122 ^{O}C ,Yield -81% , Formula- $C_{23}H_{19}O_2N_2Cl$, M.Wt- 390.5**
IR (KBr cm^{-1}) 3448 cm^{-1}(N-H) ,3078 cm^{-1}(C-H arom) ,2846 cm^{-1}(C-H ,-OCH_3), 1613 (C=N) , 1536 (C=C) ,1012 (C-O Str) , 829 cm^{-1}(4-Substituted benzene ring) .
^{1}HNMR (DMSO) 3.82 S (6H) ,-OCH_3 x 2 , 6.9-7.5 q (8H) , (C_6H_4 OCH_3) x2 , 6.9 (m, 2H) ,8.4 (m,2H) 9.9 broad Singlet (1H , N-H)

Anal. Calculation for –$C_{23}H_{19}O_2N_2Cl$

Element	C	H	O	N	Cl
Found	**70.72**	**4.83**	**8.17**	**7.14**	**9.07**
Calcd	**7.076**	**4.85**	**8.15**	**7.19**	**9.12**

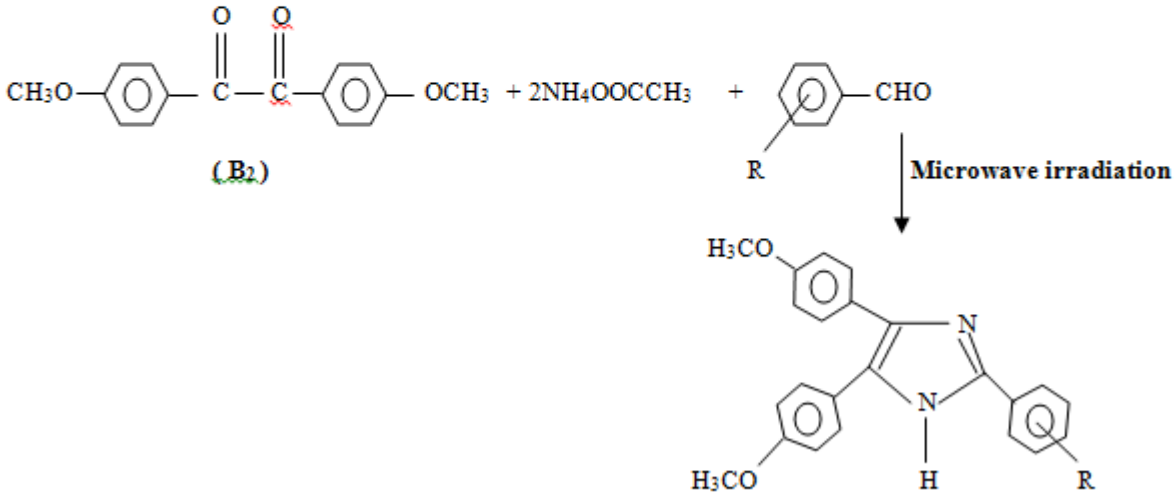
Reaction :-

1) **Step -1**



(B2)

2) **Step-2**



(B2)

R – H , 4Cl , 4-OCH_3 , $4NO_2$, $4N(CH_3)_2$, 2(OH) , 4(OH) -3-(OCH_3) ,3,4,5-(OCH_3) ,2Cl , 4(OH)

The other compounds of this series (3a-3l) were prepared similarly and are recorded in table-1

Table :-1 , Physicochemical data of the synthesized imidazole derivatives (3a-3l)

Entry	R	M.Pt (^{O}C)	Yield (%)	Time (min)	Formula
3a	-H	198-200	85	7	$C_{23}H_{20}O_2N_2$
3b	-4Cl	120-121	81	9	$C_{23}H_{19}O_2N_2Cl$
3c	-4OCH_3	170-171	93	6	$C_{24}H_{22}O_3N_2$
3d	-4NO_2	170-173	80	8	$C_{23}H_{19}O_4N_3$
3e	-2NO_2	209-212	70	5	$C_{23}H_{19}O_4N_3$
3f	-4$N(CH_3)_2$	155-157	71	3	$C_{25}H_{25}O_2N_3$
3g	-2OH	200-203	75	6	$C_{23}H_{20}O_3N_2$
3h	-4(OH)-3-(OCH_3)	228-230	82	3	$C_{24}H_{22}O_4N_2$
3i	3,4,5-(OCH_3)	232-234	93	2	$C_{26}H_{26}O_5N_2$
3j	2-Cl	180-184	79	7	$C_{23}H_{19}O_2N_2Cl$
3k	-4OH	170-173	78	5	$C_{23}H_{20}O_3N_2$
3l	-3NO_2	240-242	79	4	$C_{23}H_{19}O_4N_3$

III. RESULT AND DISCUSSION

2-Substituted-4,5-bis(4-methoxyphenyl)-1H-imidazole (3a-3l) were synthesized by reagent such as P-anisil , Substituted benzaldehyde and ammonium acetate under microwave irradiation in good yield .Ammonium acetate plays an important role in the reaction . If ammonium acetate is deficient , p-anisil can't transform completely .The physical data of compounds were collected and presented under compound name and spectral data.The yield of the compounds was in the range 70 -93 % , most of them are yellow crystalline solids.The IR spectrum of compound 3a shows the characteristic band at 3450 cm^{-1} due to the N-H.The IR spectrum of compound 3a,3b,3c shows the characteristic band at 1500 -1600 cm^{-1} due to –C=N .The

1HNMR spectrum of compound 3a,3b,3c shows signal of N-H at 8.6 ppm , 9.9 ppm , 8.7 ppm single of N-H at which confirmed the presence of N-H bond of imidazole.**We have presented efficient synthesis of 2-Substitutedphenyl-4,5-bis(4-Methoxyphenyl)-1H-imidazoles in the absence of catalyst in microwave irradiation .**

IV. CONCLUSION

In Conclusion a reliable rapid and environmentally benign method for synthesizing 2-Phenyl-4,5-bis(4-Methoxyphenyl)-1H-imidazole(3a-3l) has been developed compared to previous reported methodologies ,**the present protocol features ,simple operations ,short reaction time ,environmental friendliness and good yields ,low pollution and simple experimental procedure and easy workup .**

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