

An Efficient Synthesis of 2-Substitutedphenyl-4-(4-Methoxyphenyl)-5-phenyl-1H-imidazole from 4-Methoxybenzil under Microwave irradiation

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Abstract- An eco-friendly method has been employed for the synthesis of 2-Substitutedphenyl-4-(4-methoxyphenyl)-5-phenyl -1H-imidazole under microwave irradiation .The synthesis of 2-Substituted phenyl -4- (4-methoxyphenyl)-5-phenyl-1H-imidazoles by one step condensation of an substituted aldehyde ,4-methoxyl benzil ,ammonium acetate.The structure of the product were characterized by ¹HNMR ,IR ,elemental analysis , and melting point .In conclusion of this method gives some advantages such as a green method , good yield , simple procedure , easy work up , needed short reaction time , less expenditure of energy , and less pollution .

Index Terms –Trisubstituted imidazoles, Solvent free, MW irradiation, multi-component reaction.

I. INTRODUCTION

Imidazole is an organic aromatic heterocyclic compound with the formula $C_3H_4N_2$. Imidazole ring system has many pharmacological properties and play important roles in biochemical processes. Derivatives of imidazole were reported for anti-inflammatory ¹⁻⁴, analgesic ⁵, anti-convulsant ⁶⁻⁷. Triarylimidazoles are used in photography ⁸ as photosensitive compounds. Many of the substituted imidazoles are known as inhibitors of fungicides, and herbicides, plant growth regulators and therapeutic agents ⁹. Several substituted imidazole are known as inhibitors of p-38 Kinase ¹⁰. Highly substituted imidazole , like Lipidilines A and B¹¹ used to exhibit micro molar cytotoxicity against several human cancer cell lines .Literature survey reveals that there are several methods for synthesizing them , mainly using nitriles and esters ¹²⁻¹⁴.In recent years , substituted imidazoles are substantially used in ionic liquids ¹⁵ that has been given a new approach to “Green Chemistry ”.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 ,NiCl₂.6H₂O / Al₂O₃ ,Iodine ²³ ,Zr(acac)₄²⁴ ,Sodium bisulfite²⁵ ,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 reported a reliable , rapid , and environmentally benign method for the synthesis of 2-Substitutedphenyl-4-(4-methoxyphenyl)-5-phenyl-1H-imidazoles has been developed under microwave irradiation .Compared to previous reported methodologies , the present protocol features , simple operations , short reaction time , environmental friendliness , less pollution , saving of energy and good yield .

II. EXPERIMENTAL SECTION

Materials - Substituted aromatic aldehyde , Anisaldehyde , Benzaldehyde , Sodium Cyanide ,ethanol ,Conc. Nitric acid ,Ammonium acetate ,glacial acetic acid is required chemicals purchased 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 , ^1H NMR 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 , 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-Methoxybenzil [1-(4-Methoxyphenyl)-2-phenylethan-1,2-dione] (C₂)**

Took 5.5 gm 2-hydroxy-1-(4-methoxyphenyl)-ethan-1-one (C1)dissolved it in 12ml glacial acetic acid then added 18 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, the crude product was recrystallized from ethanol .

Yield- 65% , M.Pt- 63^oC , M.Wt- 240 , Formula- C₁₅H₁₂O₃.

IR (KBr cm^{-1}) 3071.27 (C-H Ar) , 2991.10 (C-H ali -OCH₃) , 1676.27 (C=O) , 1535.59 (C=C) , 1208.17 (C-O) .

^1H NMR (400MHz, DMSO) 3.9 (s ,3H , -OCH₃) , 7.2 (d ,2H, phenyl) , 7.5 (d ,2H , phenyl) , 7.96 (1H phenyl) , 8.0 to 8.6 (m , 4H) .

Anal .Caculation for C₁₅H₁₂O₃

Element	C (%)	H(%)	O(%)
Found	75.06	4.91	19.85
Calcd	75.00	4.95	19.83

***Synthesis of 2-(Substituted phenyl)-4-(4-Methoxyphenyl)-5-phenyl-1H-imidazoles (4a-4l) under Microwave irradiation :-**

A mixture containing 1-(4-methoxyphenyl)-2-phenylethan-1,2-dione (0.1 mol) ,ammonium acetate (0.2 mmol) , aromatic aldehyde (0.1 mmol) was taken in a 100ml beaker added 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 145 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- 6 min (Table -1) .After TLC (Petroleum ether: ethyl acetate 9:1) indicating the starting materials of 4-methoxybenzil 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 (4a-4l) were confirmed by IR ,¹HNMR melting point , and elemental analysis .

***Spectral Data of 2-(Substitutedphenyl)-4-(4-methoxyphenyl)-5-phenyl-1H-imidazoles: –**

1. 2-Phenyl-4-(4-Methoxyphenyl)-5-phenyl-1H-imidazole (4a) --

Solid Colourless , M.Pt- 210⁰C . Formula – C₂₂H₁₈ON₂, M.Wt- 326.

IR (KBr cm⁻¹) 3440 (N-H) ,3021 (C- H arom) , 2920 (C-H aliph) , 1675 (C=N) , 1426 (C=C aro)
1092 (C- O)

¹HNMR (400 MHz , DMSO)4.04(s, 3H –OCH₃), 6.8 (d, 2H) , 7.0 (d, 2H),7.2 (d ,2H) ,7.3 to8.1(m ,8H) , 9.2 (s , 1H , N-H)

Anal. Calculation for C₂₂H₁₈ON₂–

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-(4-Methoxyphenyl)-5-phenyl-1H-imidazole (4 b) –**

Colourless solid , M.Pt- 242 ⁰C , Formula- C₂₂H₁₇N₂OCl , M.Wt- 360.5

IR (KBr cm⁻¹) 3454 cm⁻¹(N-H) ,3054 cm⁻¹(C-H arom) ,2938 cm⁻¹(C-H ,aliph) , 1682 (C=N) , 1426 (C=C) ,1092 (C-O Str) , 761 cm⁻¹(C- Cl) .

¹HNMR (DMSO)4.09 (s , 3H , -OCH₃) , 6.9(d ,2H) , 7.2(d, 2H) ,7.3 (d ,2H) ,7.4 to 8.1 (m, 7H) , 9.31 broad Singlet (1H , N-H)

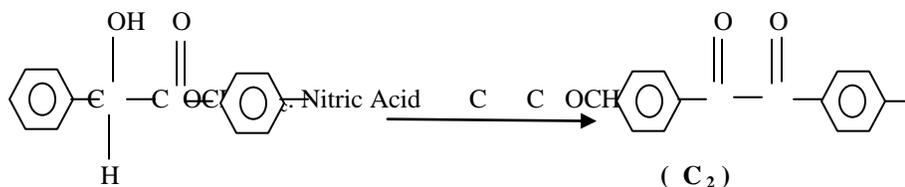
Anal. Calculation for –C₂₂H₁₇N₂OCl .

Element	C (%)	H(%)	O(%)	N(%)	Cl(%)
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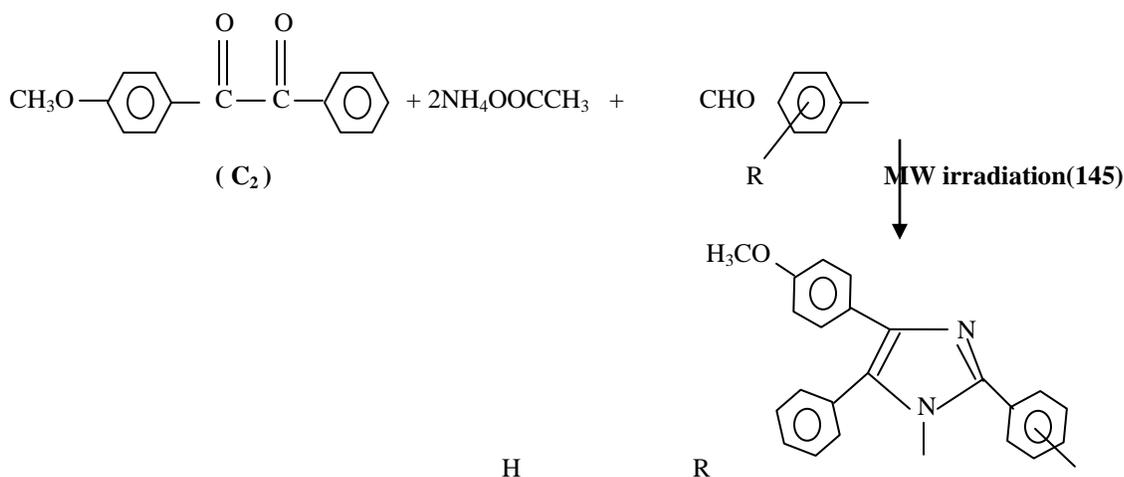
Found	73.20	4.76	4.45	7.80	9.81
Calcd	73.23	4.71	4.43	7.76	9.84

Reaction :-

1) **Step -1**



2) **Step-2**



R – H , 4Cl , 4-OCH₃ , 4NO₂ , 4N(CH₃)₂ , 2(OH) , 4(OH) -3-(OCH₃) , 3,4,5-(OCH₃) , 2Cl , 4(OH)

The other compounds of this series (4a-4l) were prepared similarly and are recorded in table-1

Table :-1 , Physicochemical data of the synthesized imidazole derivatives (4a-4l)

Entry	R	M.Pt (°C)	Yield (%)	Time (min)	Formula
4a	-H	210	85	4	C ₂₂ H ₁₈ ON ₂
4b	-4Cl	242	81	5	C ₂₂ H ₁₇ ON ₂ Cl
4c	-4OCH ₃	208	93	4	C ₂₃ H ₂₀ O ₂ N ₂
4d	-4NO ₂	212	80	5	C ₂₂ H ₁₈ O ₃ N ₃
4e	-2NO ₂	178	85	3	C ₂₂ H ₁₈ O ₃ N ₃
4f	-4N(CH ₃) ₂	200	71	4	C ₂₄ H ₂₃ ON ₃
4g	-2OH	223	79	4	C ₂₂ H ₁₈ ON ₂
4h	-4(OH)-3-(OCH ₃)	239	80	4	C ₂₃ H ₂₀ O ₃ N ₂

4i	3,4,5-(OCH ₃)	232	87	5	C ₂₅ H ₂₄ O ₄ N ₂
4j	2-Cl	180	79	3	C ₂₂ H ₁₇ ON ₂ Cl
4k	-4OH	195	83	6	C ₂₂ H ₁₈ O ₂ N ₂
4l	-3NO ₂	187	91	5	C ₂₂ H ₁₈ O ₃ N ₃

III. RESULT AND DISCUSSION

We have modified the solid supported technique to an environmentally friendly neat synthesis in which the reaction is carried out in the absence of catalyst. 2-Substitutedphenyl-4-(4-methoxyphenyl)-5-phenyl-1H-imidazole (4a-4l) were synthesized by reagent such as 4-Methoxybenzil, 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, 4-methoxybenzil 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 71 -93 %, most of them are colorless crystalline solids. The IR spectrum of compound 4a shows the characteristic band at 3440 cm⁻¹ due to the N-H. The IR spectrum of compound 4a,4b,4c shows the characteristic band at 1500 -1600 cm⁻¹ due to -C=N. The ¹H NMR spectrum of compound 4a,4b shows signal of N-H at 9.2, 9.3 single of N-H at which confirmed the presence of N-H bond of imidazole. **We have presented efficient synthesis of 2-Substitutedphenyl-4-(4-Methoxyphenyl)-5-phenyl- 1H-imidazoles in the absence of catalyst under microwave irradiation .**

IV. CONCLUSION

In Conclusion a reliable rapid and environmentally benign method for synthesizing 2-Substitutedphenyl-4-(4-methoxyphenyl)-5-phenyl-1H-imidazole(4a-4l) 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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