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Synthesis of New 2-(Substituted Phenyl) -4-(4-Methoxyphenyl) -5- Phenyl -1H- Imidazoles from 4-Methoxybenzil in the Absence of Catalyst

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Abstract- In this study new imidazole derivatives were synthesized .The first stage involved preparation of 2-hydroxy-1-(4-methoxyphenyl)-ethan-1-one(C_1) by reacting 4-methoxybenzaldehyde with benzaldehyde in presence of sodium cyanide catalyst .The second stage involved the synthesis of 1-(4-methoxyphenyl) -2-phenylethan-1,2-dione(C_2) using nitric acid in glacial acetic acid .Finally the compound (4a to 4l) were synthesized using the three-component system (Compound C_2 , Substituted benzaldehyde ,and ammonium acetate) .The structures of all compounds were confirmed by elemental analysis , NMR , IR data and melting point .In conclusion ,this method offer some advantages such as good yield , simple procedure , low cost of chemicals and easy work up .

Index Terms- 4-methoxybenzil, ammonium acetate, substituted benzaldehyde , imidazole derivatives.

I. INTRODUCTION

The importance of imidazoles in biological system has attracted much interested due to their involvement in chemical and biochemical processes [1] . Compounds with imidazole ring system have many pharmacological properties and play important role as versatile building blocks for the synthesis of natural products and as therapeutic agents [2] .The structure of trisubstituted imidazoles are prevalent in natural products and pharmacologically active compounds such as p38 kinase inhibitor I [3] and cyclooxygenase-[2] inhibitor II [4], fungicides , herbicides[5] plant growth regulators [6] and therapeutic agents[7] . Several routes have been developed for the synthesis of substituted imidazoles ,Such as hetero-cope rearrangement [8],four component condensation of aryl ,glyoxals ,primary amines ,carboxylic acids and isocyanides on Wang resin [9] .The synthesis of imidazoles from 1,2-diketone and aldehyde in presence of variety of catalysts by using microwave (MW) irradiation have been reported including MW/Silica-gel [10].2,4,5-Trisubstitutd -1H-imidazoles can be synthesized in presence of catalyst such as Zeolite HY / Silica gel [11] , $ZrCl_4$ [12] , $NiCl_2.6H_2O$ [13] , Iodine [14] , acetic acid [15]. However these methods required prolong reaction time and high cost of catalyst.

Keeping in view their biological activity ,synthesis of some new 2-(Substituted phenyl)-4-(4-methoxyphenyl)-5-phenyl-1H-imidazole derivatives has been carried out **without using a catalyst** .The 4-methoxybenzoin was synthesized by benzoin condensation using benzaldehyde and anisaldehyde in presence of sodium cyanide as a catalyst. The 4-methoxybenzoin was oxidized using conc. Nitric acid in presence of glacial acetic acid to obtain 4-methoxybenzil. The 4-methoxybenzil was reacted with substituted aromatic aldehydes , ammonium acetate in glacial acetic acid to obtain the 2-(Substitutedphenyl)-4-(4-methoxyphenyl)-5-phenyl-1H-imidazoles.

II. EXPERIMENTAL SECTION

Materials - Substituted benzaldehyde , 4-Methoxybenzaldehyde ,Sodium cyanide ,Ethanol ,Conc,nitric acid , ammonium acetate , glacial acetic acid is required chemicals . All the reported melting points were taken in open capillaries and are uncorrected .Infrared spectra were measured by using Perkin Elmer model 2000 spectrophotometer and are given in cm^{-1} using KBr disc .^{1}HNMR spectra were measured by Brucker Avance 400 MHz spectrophotometer using TMS as an internal standard .The purity of all the synthesized compounds was tested by TLC on silica gel plate using ethyl acetate and petroleum ether (80:20) and iodine was used as a visualizing agent.

***General procedure for the synthesis of 1-(4-methoxyphenyl)-2-hydroxy-2-phenylethan-1-one (C_1):-**

To the mixture of 4-methoxybenzaldehyde (0.15 mol) in 60 ml ethyl alcohol, added benzaldehyde (0.15 mol) and aq. Solution of sodium cyanide (0.1 mol) .It was refluxed for 3 hours .The reaction mixture was cooled under the tap water with continuous shaking for 10 min ,and poured to ice-cold water . Kept it overnight ,Obtained the crude product , remove the oily material from product ,wash it with water , dried and recrystallized from ethanol .

Colour - Yellow , Yield- 52 % , M.Pt- 104^{O}C , M.Wt- 242 , Formula – $C_{15}H_{14}O_3$

IR (KBr cm^{-1}) 3478.50 (O-H) ,3062.86 (Ar –CH) ,2966.75 (Ali C-H)1662.73 (C=O) ,1600(C=C)1263.59 (C-O).

^{1}HNMR (400MHz ,DMSO)– 3.79(S ,3H ,-OCH_3) , 5.89(S,1H,C-H) , 6.83 (S,1H,OH) ,6.9 to 7.6 (m, 9H ,aromatic) .

Anal,Calcd for-$C_{15}H_{14}O_3$ 1. Found – C: 74.33,H:5.83,O:19.89 2.Calcd- C:74.38,H:5.78 ,O:19.83

***General procedure for the synthesis of 1-(4-methoxyphenyl)-2-phenylethan-1,2-dione (C_2) :-**

Took 6 gms of 2-hydroxy-1-(4-methoxyphenyl)-ethan-1-one (C_1) dissolved it in 12 ml glacial acetic acid, then added 18ml conc. nitric acid slowly to the reaction mixture(kept in an ice bath) .Refluxed the reaction mixture for 2 hours until the evolution of brown gas .Stopped reaction , cooled and poured it to ice-cold water .Obtained green solid product , filtered it , The crude product was recrystallised from ethanol .

Colour – Green , Yield-65%, M.Pt- 63^{O}C , M.Wt-240 . formula –$C_{15}H_{12}O_3$

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

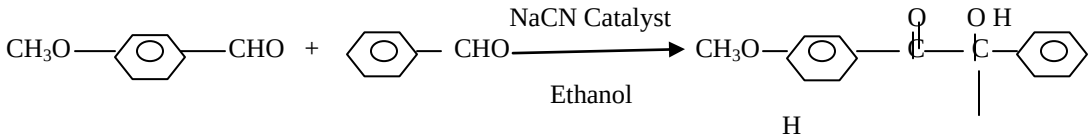
^{1}HNMR (400MHz ,DMSO) 3.9 (S,3H –OCH_3),7.2(d ,2H ,phenyl),7.5(d ,2H ,phenyl),7.96(1H phenyl), 8.0 to 8.6 (m, 4H). Anal,Calcd for-$C_{15}H_{12}O_3$ 1. Found – C: 75.06,H:4.91,O:19.85 2.Calcd- C:75.00,H:4.95,O:19.83.

***Procedure for the synthesis of 2-(Substitutedphenyl)-4-(4-methoxyphenyl)-5-phenyl-1H-imidazoles–(4a- 4 l)**

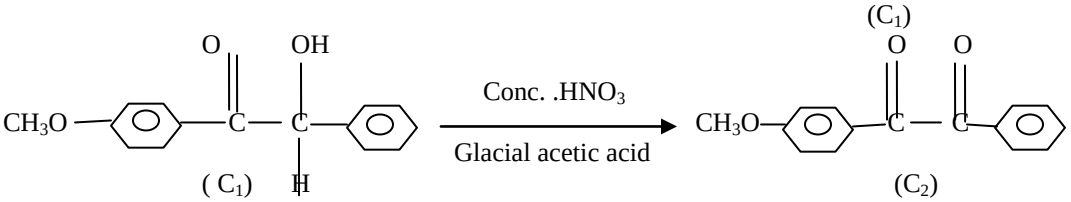
A mixture containing 1-(4-methoxyphenyl)-2-phenylethan-1,2-dione(0.01mol) , benzaldehyde (0.01mol) ammonium acetate (0.02 mol) was taken in a 100ml round bottom flask.It was dissolved 15 ml glacial acetic acid and refluxed for 4 hours . Cooled the reaction mixture and poured to ice cold water , kept it for 10 minutes ,obtained a solid product .filtered it and washed with cold water .Recrystallized it from ethanol .
Color- Colorless, Yield- 62% M.Pt- 209 ^{O}C.

Reaction: -

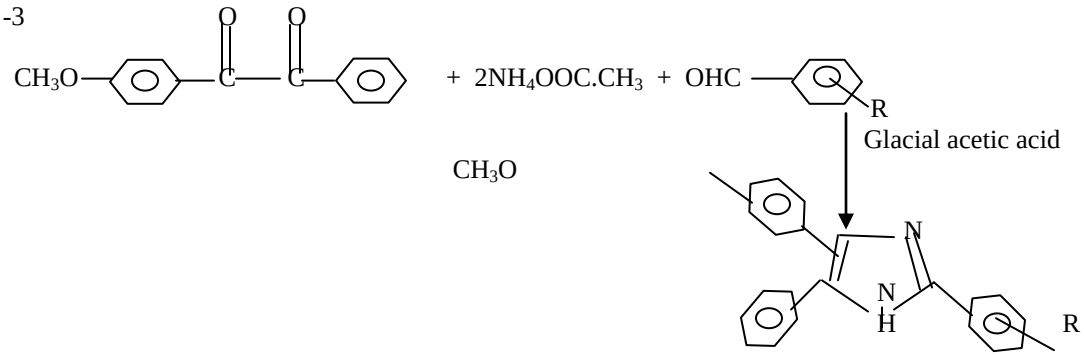
1) Step -1



2) Step-2



3) Step -3



2-(Substituted phenyl)-4-(4-methoxyphenyl) -5-phenyl-1H-imidazole
(4a to 4l)

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

Spectral Data –

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

Colourless solid , M.Pt – 210^{O}C , Formula- $C_{22}H_{18}N_2O$, M.Wt – 326 .

IR (KBr cm^{-1}) 3440 (N-H) ,3021 (C-H ,Aro) ,2920 (C-H Alip),1675 (C=N),1426 (C=C Aro) , 1092 (C-O)

^{1}HNMR – 4.04 (S ,3H ,-OCH_3) , 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 .Calcd for $C_{22}H_{18}ON_2$ Found -C:80.98, H:5.52, O: 4.95,N: 4.29. Calcd - C : 80.95 H:5.57, O :4.97N: 4.32

2-(4-Chlorophenyl)-4-(4-methoxyphenyl) -5-phenyl-1H-imidazole (4b) –

Colourless solid , M.Pt-242 ^{O}C , Formula – $C_{22}H_{17}N_2OCl$, M.Wt – 360.5

IR (KBr cm^{-1}) - 3454 (N-H) , 3054 (C-H Aro) , 2938 (C-H ,aliph), ,1682 (C=N),1426(C=C Aro),1092(C-O) , 761 (C-Cl) .

1HNMR - 4.09 (S, 3H, $-OCH_3$),6.9(d,2H),7.2(d,2H),7.3(d,2H),7.4 to 8.1 (m,7H) , 9.31(S ,1H ,N-H).

Anal .Calcd for – $C_{22}H_{17}N_2OCl$. Found – C: 73.20, H:4.76, O:4.45, N:7.80, Cl:9.81

Calcd : C: 73.23, H: 4.71, O: 4.43, N: 7.76 , Cl: 9.84

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

Table- 1 . Physicochemical data of the synthesized compound

S.No	Code	R	Formula	M.Wt	% yield	M.Pt (^{O}C)
1	4a	-H	$C_{22}H_{18}ON_2$	326	81	210
2	4b	-4Cl	$C_{22}H_{17}ON_2Cl$	361.5	72	242
3	4c	$-4OCH_3$	$C_{23}H_{20}O_2N_2$	356	70	209
4	4d	$-4NO_2$	$C_{22}H_{18}O_3N_3$	372	65	213
5	4e	$-2NO_2$	$C_{22}H_{18}O_3N_3$	372	64	178
6	4f	$-4N(CH_3)_2$	$C_{24}H_{23}ON_3$	369	69	199
7	4g	-2OH	$C_{22}H_{18}O_2N_2$	342	70	223
8	4h	$-4OH-3-(OCH_3)$	$C_{23}H_{20}O_3N_2$	372	68	239
9	4i	$-3,4,5-(OCH_3)_3$	$C_{25}H_{24}O_4N_2$	416	55	232
10	4j	-2Cl	$C_{22}H_{17}ON_2Cl$	361.5	70	180
11	4k	-4OH	$C_{22}H_{18}O_2N_2$	342	66	195
12	4l	$3NO_2$	$C_{22}H_{18}O_3N3$	372	56	188

III. RESULTS AND DISCUSSION

2-Substitutedphenyl -4-(4-methoxyphenyl)-5-phenyl-1H-imidazoles (4a- 4l) were synthesized by condensation reaction involving reactant such as 4-methoxybenzil , Substituted benzaldehyde ,ammonium acetate in glacial acetic acid .The sodium cyanide is a best catalyst which gives the cross benzoin condensation between benzaldehyde and anisaldehyde to form 4-methoxybenzoin .Nitric acid is an oxidizing agent which oxidized 4-methoxybenzoin into 4-methoxybenzil .The physical data of compounds were collected and presented under compound name and spectral data .The yield of the compound was in the range of 55 -81% .Most of them are colorless ,crystalline solid .The IR spectrum of compounds shows N-H band at 3450 to 3410 cm^{-1}. The characteristic band at 1500 -1600 cm^{-1} due to C=N group .The 1HNMR spectrum of compounds (4a-4l) shows signal of N-H at 8.9 ,9.8 ,9.9 ppm which confirm the presence of N-H band of imidazole .

The synthesis of 2-Substitutd-4, 5-diphenyl-1H-imidazole from mixed benzil is very difficult **We have reported the efficient method of synthesis of 2-Substitutedphenyl-4(4-methoxyphenyl)-5-phenyl -1H-imidazole in the absence of catalyst for synthesis required less compound which gives high yield of product by avoiding the excess use of catalyst** .This synthesis is easy to follow and required low cost reactants.

IV. CONCLUSION

In conclusion ,we have developed an efficient and convenient method for the synthesis of 2-(Substituted phenyl)-4-(4-methoxyphenyl)-5-phenyl-1H-imidazole derivatives using mixed benzil **in absence of catalyst** .**The notable merits offered by this methodology are mild reaction conditions ,simple procedure and excellent yield of products.**

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