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A Convenient Method of Synthesis of 2-(Substituted Phenyl)-4-(4-Dimethylaminophenyl)-5-Phenyl-1H-imidazoles from4-Dimethylaminobenzil in the Absence of Catalyst

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Abstract **-** In this study new imidazoles derivatives were synthesized.The first stage involved preparation of 2-hydroxy-1-(4-dimethylaminophenyl)-ethan-1-one (F_1) by reacting 4-dimethylaminobenzaldehyde with benzaldehyde in presence of sodium cyanide catalyst .The second stage involved the synthesis of 1-(4-dimethylaminophenyl)-2-phenylethan-1,2-dione(f_2) using nitric acid in glacial acetic acid. Finally the compound (5a-5l) were synthesized using the three component system (Compound F_2 , Substituted benzaldehyde and ammonium acetate) .The structure of all compounds were confirmed by elemental analysis ,NMR and IR data and by melting point .In conclusion this method give some advantages such as good yield ,simple procedure , low cost of chemicals and easy work up .

Index Terms **–** 4-dimethylaminobenzil, ammonium acetate, substituted benzaldehyde, imidazole derivatives.

I. INTRODUCTION

Substituted imidazoles, many of which play important roles in the biologically significant processes have been prepared by a variety of synthetic methods [1.] Imidazoles and their derivatives play important role as versatile building blocks for the synthesis of natural products and as therapeutic agents [2].Compounds with imidazole moiety have also been found to process many pharmacological properties and are widely implicated in biochemical processes [3] .The study of triphenyl imidazole derivatives has been a developing field within the realm of heterocyclic chemistry for the post several decades because of their ready accessibility through synthesis , wide range of chemical reactivity and manifold biological activities .The compounds with imidazole ring system have many pharmacological properties and play an important role in biochemical process .The structures of trisubstitued imidazoles are prevalent in natural products and pharmacologically active compounds ,such as p38 kinase inhibitors I (SB 203580) [4] and cyclooxygenase-2(Cox-2) inhibitor II [5] ,fungicides and herbicides [6].Recent advances in green chemistry and organ metallic chemistry have extended the boundary of imidazoles to the synthesis and application of a large class of imidazoles as ionic liquid and imidazole related N-heterocyclic Carbenes (NHC) [7,8] .Several routes have been developed for the synthesis of substituted imidazoles, such as hetero-cope rearrangement [9].The synthesis of imidazoles from1,2-diketone and aldehyde in presence of variety of catalysts by using microwave (MW) irradiation have been reported including MW / Silica-gel

[10] , MW / Silica –gel H-Y [11], MW / Al_2O_3 [12] ,$NiCl_2.6H_2O$ [13] ,Iodine [14], acetic acid [15] , sodium disulphide [16], ammonium acetate [17] **.** However these methods require exotic reaction condition and high cost of catalyst.

Keeping in view of their biological activity , synthesis of some new 2-(Substituted phenyl) -4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole derivatives has been carried out without using a catalyst .The 4-dimethylaminobenzoin was synthesized by benzoin condensation using benzaldehyde and and 4-dimethylaminobenzaldehyde in presence of sodium cyanide as a catalyst .The 4-dimethylaminobenzoin was oxidized using Conc. Nitric acid in presence of glacial acetic acid to obtained 4-dimethylaminobenzil.The 4-dimethylaminobenzil was reacted with substituted aromatic aldehyde ,ammonium acetate in glacial acetic acid to obtained the 2-(Substitutedphenyl)-4-(4-dimethyaminopenyl)-5-phenyl-1H-imidazoles.

II. EXPERIMENTAL SECTION

Materials - Substituted benzaldehyde, 4-dimethylaminobenzadehyde, 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 Bruckner 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-dimethylaminophenyl)-2-hydroxy-2-phenylethan-1-one (F_1) -**To the mixture of 4-dimethylaminobenzaldehyde (0.15mol) in 65 ml ethylalcohol, added benzaldehyde (0.15mol) and aq. solution of sodium cyanide (0.1 mol) .It was reflux for 3 hour. The reaction mixture was cooled under the tap water with continuous shaking for 10 min and poured into ice-cold water, kept it long time on table obtained the crude product, Filter it, wash by water, dried and recrystallized from mixture of ethanol and water. Colour - Yellow , Yield – 78 % , M.Pt- 158 ^{O}C Formula – $C_{16}H_{17}O_2N$, M.Wt – 255.31.

IR (KBr cm-1) 3368.40 (O - H) , 3010 (Ar C-H) , 2870 (Ali C-H) , 1610.40 (C=O)
1552.05 (C= C), 1234 .80 (C – O), 751.32 (p- substituted –CH_3) .

1HNMR (400 MHz , DMSO) – 2.98 (S , 3H ,- CH_3) , 3.05 (S , 3H , -CH_3) , 5.89 (S , 1H , C-H)
6.00 (S , 1H , O-H) , 6.55 to 7.96 (m , 9H ,aromatic) .

Anal.Calcd for $C_{16}H_{17}O_2N$ 1) Found - C: 75.35, H: 6.72, O: 12.65, N: 5.55
2) Calcd - C :75.29 , H : 6.66 , O : 12.54 , N :5.49 .

***General procedure for the synthesis of 1-(4-dimethylaminophenyl) -2- phenylethan-1,2-dione (F_2) –**

Took 12.3 gm of 2-hydroxy-1-(4-dimethylaminophenyl)-ethan-1-one (F_1) dissolved it in 25 ml glacial acetic acid ,then added 36 ml Conc. Nitric acid slowly to the reaction mixture (Kept in an ice-bath),Refluxed the reaction mixture for 2 hour , until the complete evolution of brown gas. Stopped reaction, cooled and poured it to ice-cold water, obtained a solid product, to neutralized the excess acid add small amount of dil. sodium hydroxide. Filter the solid product and recrystallized from ethanol.

Colour – Greenish Yield- 60% Formula – $C_{16}H_{15}O_2N$, M.Wt – 253.29 , M.Pt - 112 ^{O}C .

IR(KBr cm^{-1}) - 3092 (aro C-H) , 2929(ali C-H) , 1620 (C=O), 1586 (C=C) .

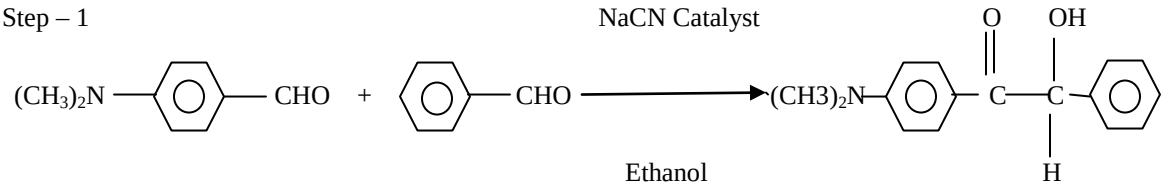
1HNMR (400 MHz ,DMSO) - 3.08 (S ,6H ,CH_3) ,6.90(S ,2H ,C-H) , 7.5(d , 2H C-H) ,7.72(d ,2H,C-H)

7.90 (d ,H , CH) , 8.9 (d , 2H , C-H) .

***Procedure for the synthesis of 2-(Substituted phenyl)-4-(4-dimethylaminophenyl) -5-phenyl-1H- imidazole (5a – 5 l):-** A mixture containing 1-(4-dimethylaminophenyl) -2-phenylethan-1,2-dione (0.01 mol) , benzaldehyde (0.01 mol) ,ammonium acetate (0.07 mol) was taken in a 100 ml round bottom flask .It was dissolved in 25 ml glacial acetic acid and refluxed for 6 hour .Check the progress of reaction by TLC plate .Cooled the reaction mixture and poured to ice cold water, kept for 10 minutes ,obtained a solid product . Filtered it and wash with cold water .Recrystallized it from ethanol.

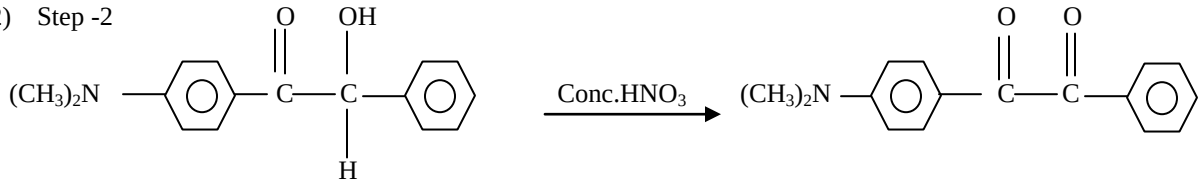
Reaction:-

1) Step – 1



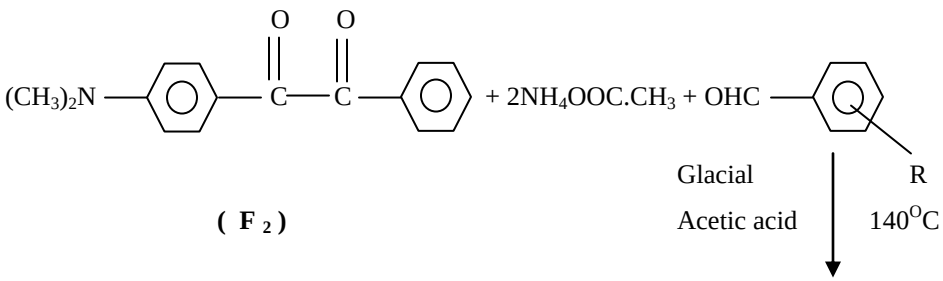
(F_1)

2) Step -2

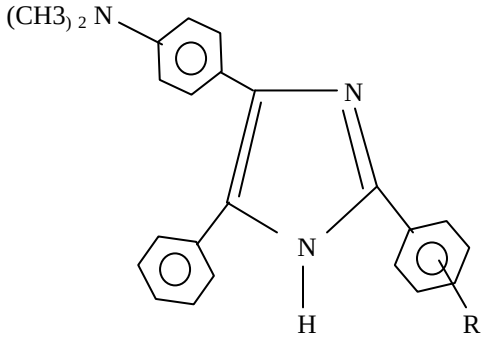


(F_1) **(F_2)**

3) Step-3



(F_2)



(5a – 5l)

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 – 1) 2-Phenyl-4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole (5a) –

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Colourless solid, M.Pt – 243 ^{O}C, Formula –$C_{24}H_{21}N_3$, M.Wt – 351.

IR (KBr cm^{-1}) – 3468 (N-H) , 3092 (Aro ,C-H) , 2927 (C-H alip) , 1621 (C=N) , 1408 (C= C aro).

^{1}HNMR - 3.10 (d ,6H –CH_3) ,7.0(d , 2H) ,8.0(S 1H) , 8.2(d,2H) ,8.2 to 8.8 (m ,9H) ,8.9 (S , N-H)

Anal.Calcd for $C_{24}H_{21}N_3$: Calcd – C:82.05 H:5.98 N: 11.96 .

Found – C: 82.17 H: 5.92 N: 11.98.

Spectral Data - 2) 2-(4-Chlorophenyl)-4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole (5b) –

Colourless solid, M.Pt -275^{O}C, Formula – $C_{24}H_{20}N_3Cl$ M.Wt- 385.5

IR (KBr cm^{-1}) 3353 (N-H) , 3093 (C-H aro) , 2927 (C-H aliph) , 1683 (C= N) , 1408 (C=C aro) ,

745 (C-Cl).

^{1}HNMR - 3.0 (S , 3H , -CH_3) , 7.0 (d , 2H) , 7.2 (d , 2H) ,7.4 (d, 2H) , 7.5 to 8.9 (m ,7H)

9.7 (S, 1H, N-H) .

Anal . Calcd for - $C_{24}H_{20}N_3Cl$,Found C:74.65, H:5.20, N:10.81 , Cl:9.28,

Calcd C: 74.70 H: 5.18, N: 10.89, Cl:9.20

The other compounds of this series (5a – 5l) were prepared similarly and are recorded in table- 1

Table -1 Chemical Data of the synthesized compounds

S.No	Code	R	Formula	M.Wt	%of Yield	M.Pt (^{O} C)
1	5a	-H	$C_{24}H_{21}N_3$	351	79	243
2	5b	-4Cl	$C_{24}H_{20}N_3Cl$	385.5	82	275
3	5c	-4OCH_3	$C_{25}H_{23}N_3O$	369	65	236
4	5d	-4NO_2	$C_{24}H_{20}N_4O_2$	368	85	242
5	5e	-2NO_2	$C_{24}H_{20}N_4O_2$	368	83	265
6	5f	-4$N(CH_3)_2$	$C_{26}H_{26}N_4$	394	68	209
7	5g	-2(OH)	$C_{24}H_{21}N_3O$	354	86	227
8	5h	-4(OH)-3-(OCH_3)	$C_{25}H_{23}N_3O_2$	404	59	190
9	5i	-3,4,5-$(OCH_3)_3$	$C_{27}H_{27}N_3O_3$	425	78	211
10	5j	-2Cl	$C_{24}H_{20}N_3$.Cl	373.5	80	249
11	5k	-4 OH	$C_{24}H_{21}$.N_3.O	354	63	237
12	5l	-3NO_2	$C_{24}H_{20}N_4$.O_2	368	81	240

III. RESULT AND DISCUSSION.

2-Substituted -4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole (5a- 5l) were synthesized by condensation reaction involving reactant such as 4-dimethylaminobenzil ,substituted benzaldehyde ,ammonium acetate in glacial acetic acid .The sodium cyanide is a best catalyst which gives the cross benzoin condensation between benzaldehyde and 4-dimethylaminobenzaldehyde to form 4-dimethylaminobenzoin . Nitric acid with glacial acetic acid is an oxidizing agent which oxidized 4-dimethylaminobenzoin into 4-dimethylaminobenzil. The physical data of compound were collected and presented under compound name and spectral data. The yield of the compound was in the range of 59-86 %. Most of them are colorless crystalline solid .The IR spectrum of compound shows N-H band at 3468 to 3350 cm-1.The characteristic band at 1500-1650cm-1 due to C=N group .The 1HNMR spectrum of compound (5a- 5l) shows signal of N-H at 9.8 ,8.9 ppm which confirm the presence of N-H band of imidazole .

The synthesis of 2-Substitutedphenyl-4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole from mixed benzil is very difficult .**We have reported the efficient method of synthesis of 2-Substitutedphenyl-4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole in the absence of catalyst for synthesis required less compound which gives high yield of product by avoiding the excess used of catalyst .In using of ethanol as a solvent give less product, but in glacial acetic acid occurred increased the yield of product .This synthesis is easy to follow and required low cost reactant .The reaction has advantages such as excellent yield, simple procedure .**

IV. CONCLUSION.

In Conclusion ,we have developed an efficient and convenient method for the synthesis of 2-(Substituted phenyl)-4-(4-dimethylaminophenyl)-5-phenyl-1H-imidazole derivatives using mixed benzil in absence of catalyst .**The notable**

merits offered by this methodology are mild reaction condition , simple procedure, required less reactant and gives excellent yield of products .

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