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Synthesis And Characterisation Of Substituted Diaryl Pyrazoline

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ABSTRACT

Pyrazoline moieties attracted considerable attention of medicinal chemists as they are endowed with a wide range of diverse biological activities such as anti-inflammatory, analgesic, antimicrobial, anti-oxidant activity etc. The proposed work involves synthesis of some new pyrazoline from substituted flavanone. The substituted flavanone in turn were obtained from substituted chalcone and the chalcone is prepared from acetophenone and variedly substituted aromatic aldehydes in presence of acetic anhydride and anhydrous sodium acetate. Here in the synthesis of pyrazolines reflux time was reduced significantly. The characterization of these compounds was made by chemical properties, elemental analysis as well as spectral analysis (like IR, ^{1}H-NMR). The purity of the compounds was tested by TLC on a chromatographic paper of 0.3 mm thickness.

Keyword:- Phenyl Acetate, acetophenone, flavanone,diaryl pyrazoline

MATERIALS & METHODS :-

1) Acetic anhydride
2) 2,4 dichloro phenol
3) Sodium acetate
4) Anhydrous $AlCl_3$
5) 2 hydroxy benzaldehyde
6) Hydrazine hydrate & Phenyl hydrazine
7) Pipyridine
8) DMSO
9) NaOH,KOH, $NaHCO_3$ Ethanol , methenol ETC.
S d fine, merk and loba companies chemicals are used in the synthesis of diaryl pyrozolines.

INTRODUCTION

Pyrazole refers both to the class of simple aromatic ring organic compounds of the heterocyclic diazole series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions, and to the unsubstituted parent compound. Chincholkar and jamode[1], have reported the synthesis of some new 4-aroylsubsituted pyrazolines by the condensation of hydrazine hydrate and phenyl hydrazine. Behrooz Maleki[2], A simple, green and cost-effective protocol was used for the aromatization of 1,3,5-trisubstituted-2-pyrazolines to the corresponding pyrazoles by in situ generation of iodine (I+) from H_2O_2/A_COH or SSA or oxalic acid /KI or NaI system under thermal condition with moderate to good yields. Baker et al[3] reported the formation of 1-phenyle-(2-hydroxy-4-methox phenyl)-3-methoxyfrom 2-hydroxy-4-methoxy strylmethyle ketone. On treatment with phenyl hydrazine. Govindraju[4] the tetra-substituted pyrazoles were synthesized by 1,3-dipolar cyclo addition of nitrile imines generated in situ by the oxidative dehydrogenation aldehyde hydrazones using chloramine-T as

mild oxidant with 1, 3-diphenylprop-2-yn-1-one in good yields. The synthesized compounds were tested for their antimicrobial susceptibility activity against different fungi and bacteria species by paper disc diffusion method the structures of the new pyrazoles were confirmed by spectral studies and elemental studies. Wadokar[5] further reported the synthesis of 3,5-diaryle-1-phenyle pyrazoline from flavononeand phenyl hydrazinehydrochloride in DMF. Arora[6] Pyrazole belongs to the "diazole" class of heterocycles and is the most important moiety found in large number pharmaceutical agents. One of the earliest methods of pyrazole synthesis is refluxing the contents high yields in a lesser time duration. In the present review, an attempt has been made to describe the various development stages in the synthesis of pyrazole analogues. Jamode[7] reported the formation of 2-hydroxychalcone phenylehydradation of hydrazine hydrochloride of flavonone and itsconvers ion into phenyl pyrazoline. Ayman El sayed Rashad [8]synthesized some biologically active pyrazoles and were tested for antimicrobial activity. The new derivative of pyrazoles some of the synthesized compound shows anti-microbial activity. G. Huang [9,] An easy and efficient copper-catalyzed reaction for the synthesis of polysubstituted pyrazoles from phenyl hydrazones and dialkyl ethylene dicarboxylates tolerates a range of functionalities, and the corresponding adducts can be obtained in moderate to good yields. D. E. Frantz[10]A tandem catalytic cross-coupling/electro cyclization allows the conversion of differentially substituted acyclic and cyclic enoltriflates and an elaborated set of diazoacetates to provide the corresponding 3,4,5-trisubstituted pyrazoles with a high degree of structural complexity. Chincholkar and Jamode[11] reported the synthesis of some new 4-aroylsubstituted pyrazolines by the condensation of hydrazine hydrate and phenyl hydrazine with 3-aroylflavonones in pyridine. Rault[12], general two-step synthesis of substituted 3- aminoindazoles from 2-bromobenzonitriles involves a palladium-catalyzed arylation of benzophenonehydrazone followed by an acidic deprotection cyclization sequence. This procedure offers a general and efficient alternative to the typical Ar-SN reaction of hydrazine with o-fluorobenzonitriles.

MATERIAL AND METHODS

Step-1:- Preparation of 2,4 - dichloro Phenyl Acetate.

2,4-dichloro phenol (25gm) was mixed with acetic anhydride (30ml) and anhydrous sodium acetate (2.5gm).The mixture was refluxed about 2hrs. It was cooled and poured in cold water. The acetate layer was separated and washed with water several times and finally it was purified by distillation and hence distilled compound (A) was collected at about 240^0C.

Step-2:- Preparation 2-hydroxy 3,5 dichloro acetophenone.

Take 2,4dichloro Phenyl Acetate layer was mixed with anhydrous $AlCl_3$ (1:3) and heated at 120^0 C for 45 min on sand bath. The reaction in mixture was decomposed with ice cold water containing a little HCl to get crude product with constant stirring, A pinkish solid obtained which is compound (B) it can be recrystallized by ethanol.

Melting point- 91^0 C Yield –70%

Step-3:- Preparation of Synthesis of 1(3, 5–dichlaro–2–hydroxylphenyl)–3–(4-methoxy phenyl) prop-2-en –1–one.

Take 2-hydroxy 3,5 dichloro phenyl acetate (0.01 mole.) was dissolve in ethanol (10ml) with 2-hydroxy benzaldehyde (0.01mole) & added to the solution 1or 2 drops of pipyridine solution & mixture was heated to boiling to this solution add aq. KOH solution (40%) (10ml) was added drop wise with constant stirring. The mixture was stirred mechanically at room temperature for 30 minutes and kept for overnight and then it was acidified by HCl (50%) solution. The solid product thus separated out was filtered and washed with sodium bicarbonate (10%) followed by water the crude product (c) was recrystallized by ethanol. Melting point=180^{0}C Yield: 68%

Step-4:- Preparation Synthesis of 6,8 dichloro-2-6(2-hydroxyphenyle-4H-chromen-4-one from 1-(3,5-dichloro-2-hydroxyphenyle)-3-(-2-hydroxyphenyle)prope-2-en-1-one.

Substituted chalcone (0.001) dissolved in methanol (50 ml) in 200 ml beaker. The resulting solution was made alkaline (pH10) with potassium hydroxide pellets and was allowed to react for 2-3 hours. At room temperature (the reaction time for different chalcones very from 1-3 hours). The reaction mixture was then acidified (using 10%aqueous hydrochloric acid: ice cold) to precipitate the flavonone. The product was filtered with suction on a Buchner funnel, washed with cold water the washing were neutral to litmus and then with 5 ml of ice cold rectified sprite. The dried product was recrystallized from ethanol.

Melting point=106 0c Yield:66%

IR : 3164cm-1 (Ar,C-H str);3067cm-1(aliph,C-H str);1638cm-1(C=O str);1537(C=N);1432(Ar,C=C str);1297(C-N str);1250(C-O str);692(C-Br str)

^{1}H-NMR (DMSO):-9.8 (Ar-OH); 7 -7.6(Ar –CH) 6.43(CH_2) 2.2 (CH_2-CH)

Step-5:- Preparation of 3-(2,-hydroxy-4-,benzyloxyphenyle)-5-phenyle pyrazoline.

2,-hydroxy-4-,benzyloxy chalcone (0.5gm.1.5151 mmoles) was dissolve in 1o ml of DMSO and then hydrazine hydrate (5 ml, [80%solution]) was added drop wise with constant stirring at room temp. The yellow coloured solution turned colourless with the formation of precipitate when crushed ice (20 gm) was added to it. The colourless pr oduct obtained was filtered, washed with water and dried. The crude product was recrystallized from methanol.

Melting point = 138^{0}C Yield = 60%

IR : 3164cm-1 (Ar,C-H str);3067cm-1(aliph,C-H str);1638cm-1(C=O str);1537(C=N);1432(Ar,C=C str);1297(C-N str);1250(C-O str);692(C-Br str)

^{1}H-NMR (DMSO):-9.8 (Ar-OH); 7 -7.6(Ar –CH) 6.43(CH_2) 2.2 (CH_2-CH)

Step-6:-preparation of 3-(2,-hydroxy-4-benzyloxyphenyle)-5-phenyle pyrazoline.

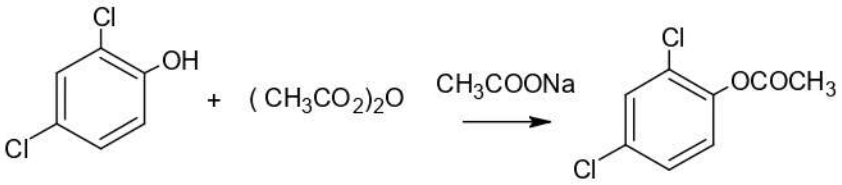
2,-hydroxy-4-,benzyloxy chalcone (0.5gm.1.5151 mmoles) was dissolve in 10 ml of DMSO and then phenyl hydrazine (5 ml, [80%solution]) was added drop wise with constant stirring at room temp. The yellow coloured solution turned colourless with the formation of precipitate when crushed ice (20 gm) was added to it. The colourless product obtained was filtered, washed with water and dried. The crude product was recrystalised from methanol.

Melting point= 132^{0}C Yield:= 55%

IR : 3164cm-1 (Ar,C-H str);3067cm-1(aliph,C-H str);1638cm-1(C=O str);1537(C=N);1432(Ar,C=C str);1297(C-N str);1250(C-O str);692(C-Br str)

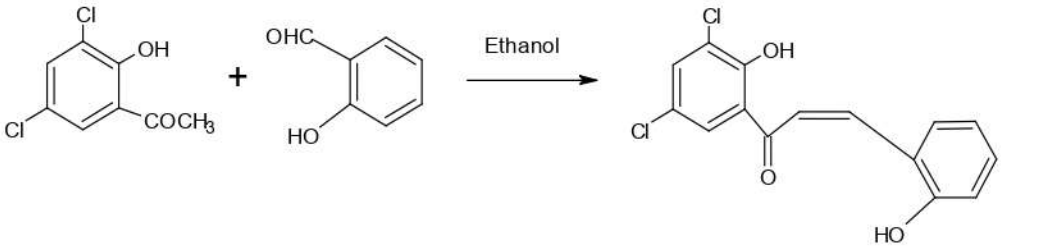
^{1}H-NMR (DMSO):-9.8 (Ar-OH); 7 -7.6(Ar –CH) 6.43(CH_2) 2.2 (CH_2-CH

Scheme:-

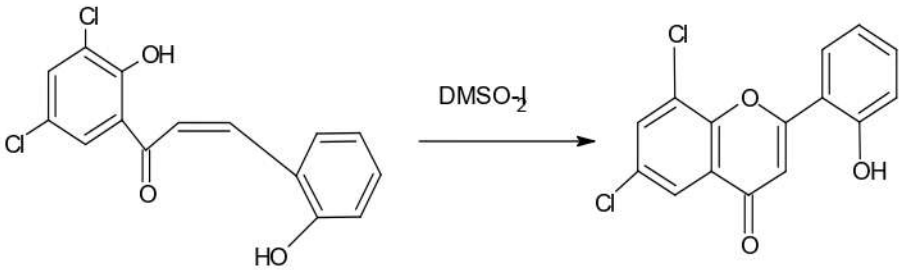


2,4-dichlorophenyl acetate

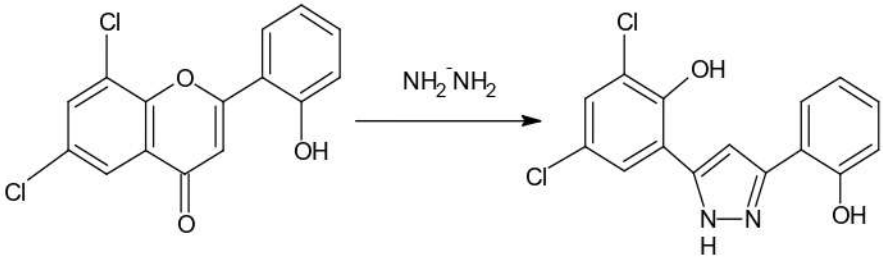
1-(3,5-dichloro-2-hydroxyphenyl)ethanone



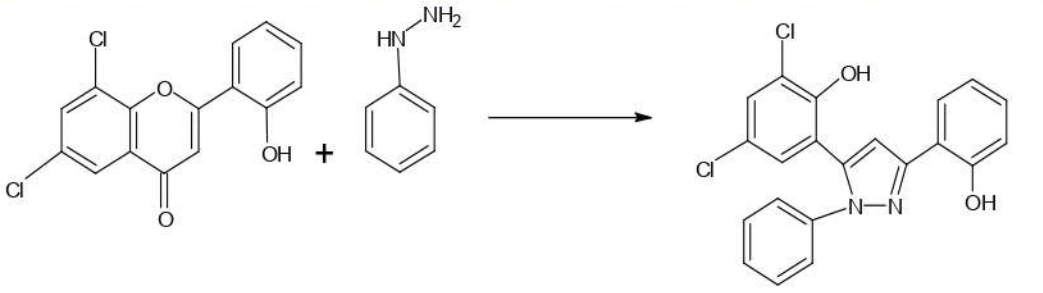
(2Z)-1-(3,5-dichloro-2-hydroxyphenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one



6,8-dichloro-2-(2-hydroxyphenyl)-4*H*-chromen-4-one



2,4-dichloro-6-[3-(2-hydroxyphenyl)-1*H*-pyrazol-5-yl]phenol



2,4-dichloro-6-[3-(2-hydroxyphenyl)-1-phenyl-1*H*-pyrazol-5-yl]phenol

RESULT & DISCUSSION:-

Physical characterization data of all the compounds are given in Table-1.

TABLE-1

CHARACTERIZATION DATA OF NEWLY SYNTHESIZED COMPOUNDS

Compound	Mol. Formula	M.P. (^{0}C)	Yield (%)	R_f
A	$C_8H_6O_2Cl_2$	240^{0C}	70	0.75
B	$C_8H_6Cl_2O_2$	91^{0C}	68	0.80
C	$C_{13}H_8Cl_2O_3$	180^{0C}	66	0.82
D	$C_{12}H_7Cl_2O_3$	106^{0C}	60	0.80
E	$C_{12}H_8Cl_2N_2O_2$	138^{0C}	55	0.89
F	$C_{18}H_{13}Cl_2N_2O_2$	132^{0C}	55	0.80

CONCLUSION

Thus it was possible for us to reduce reflux time and increase percent yield of newly synthesized products. The use of DMSO as a solvent afforded rapid synthetic route to pyrazoline and also easy work up of the products. These newly synthesized compounds contain many bioactive substituents and therefore should be screened for their antibacterial activity.

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