Synthesis and Characterisation of Novel Pyrazoline Derivatives and Their Biological Activity

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Abstract:
3-phenoxy benzaldehyde reacted with 1-(substituted pheny) ethan-1-one with 10%KOH reflux in alcohol solvent then formed in 2(E)-1-(4-chlorophenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one
2(E)-1-(substituted phenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one reacted pyridine-4-carbohydrazide in DMF solvent and formed 4-[3-(substituted phenyl) -5-(3-phenoxyphenyl) -4,5-dihydro-1H-pyrazole- 1-carbonyl] pyridine(pyrazoline derivatives).synthesized pyrazoline derivatives have been found to possess considerable biological activities, which stimulated the reseach activity in this field. They have several prominent and such as antimicrobial, antifungal.

Keywords: pyrazoline, synthesis, characterization, antimicrobial activity.

I. Introduction

Pyrazolines are well identified and significant nitrogen containing five membered heterocyclic complexes and numerous systems have been operated out for their synthesis. Many pyrazoline derivatives have been create to possess considerable biological activities, which inspired the investigation activity in this field. They have created to possess anti-fungal, anti-bacterial, anti-inflammatory, anti-oxidant, anti-convulsant, anti-depressant, antiviral, anti-cancer, anti-microbial, anti-tumor, antidiabetic, anti-malarial, anesthetic, blue photo luminescence and electro luminescence, food and chemical toxicology, herbicidal, hypoglycemic, hypertensive. Moreover, many selectively chloro-substituted organic complexes display peculiar pharmacological and agrochemical properties.

Experimental

The chemical used in the present work were AR grade and LR grade, purchased from, Merck, S.D. fine chemicals and research lab and used as received. The list of chemicals used were 4-hydroxyacetophenone, 4-methylacetophenone,2—acetyl furan, 4-methoxy benzaldehyde,4-fluoro benzaldehyde, sodium hydroxide, 2,4-dintrophenyl hydrazine, ethyl-acetate,HCl, light paraffin oil, pet ether, glacial acetic acid, chloroform. The water used was double distilled deionized water. All the compounds showed satisfactory elemental analysis for C, H&N

1.melting point determination:
The melting point of the synthesized compounds were determined using veego Vmp-I melting point apparatus and recored in degree Celsius.

2. Thin layer chromatography:
Thin layer chromatography was performed on percolated silica gel plates with suitable solvent system. The R_f values were recorded accordingly .

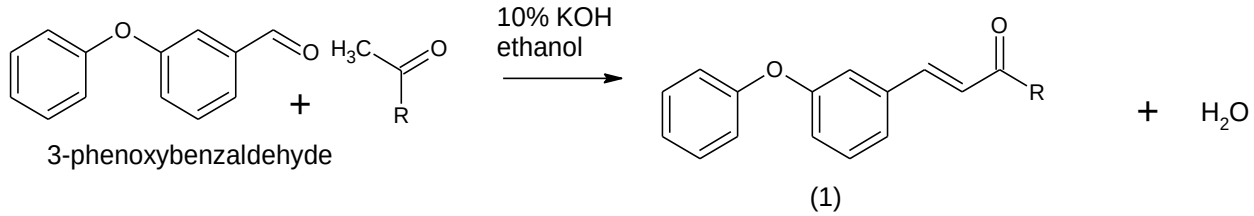
3. Infrared spectroscopy:
The infrared spectra for the synthesized compounds were recorded using JASCO-FTIR 8400 spectrophotometer using potassium bromide pellet technique.

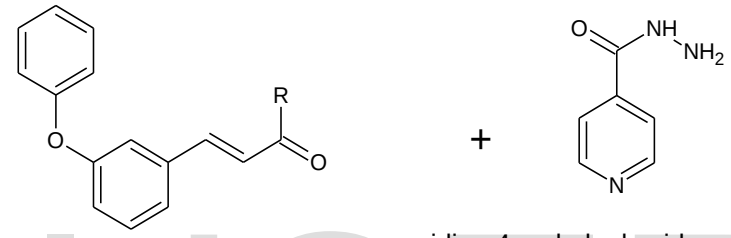
4. Nuclear magnetic resonance spectroscopy:
HNMR spectra of the synthesized compounds were taken using tetramethyl silane as an internal standard. HNMR spectra were recorded with DMSO and CDCl3 as a solvent and the chemical shift data were expressed as δ values relative to TMS, CNMR spectra were recorded with DMSO and CDCL3 as a solvent and the chemical shift data were expressed as δ values relatives to TMS.

General procedure for the synthesis of new phenyl pyrazoline derivatives from 2(E)-1-(4-chlorophenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one : 3-phenoxy benzaldehyde reacted with 1-(4-chlorophenyl) ethan-1-one with 10%KOH reflux in ethanol solvent then formed in 2(E)-1-(4-chlorophenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one

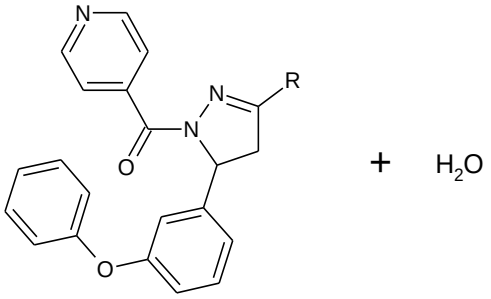
2(E)-1-(4-chlorophenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one reacted pyridine-4-carbohydrazide in DMF solvent and formed 4-[3-(4-chlorophenyl)-5-(3-phenoxyphenyl) -4,5-dihydro-1H -pyrazole-1-carbonyl] pyridine

Scheme:





DMF



where R =

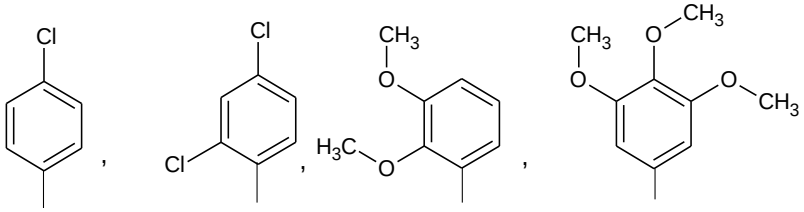


TABLE 1

PHYSICAL CHARACTERIZATION DATA OF SYNTHESIZED COMPOUND

Pyrazolines derivatives (1a-d)

Compound	Yield (%)	M.P. (°C)	Molecular Formula
1a	75	242	$C_{27}H_{20}O_2N_3Cl$
1b	75	257	$C_{27}H_{19}O_2N_3Cl_2$
1c	78	264	$C_{29}H_{25}O_4N_3$
1d	75	272	$C_{30}H_{27}O_5N_3$

Identification and characterization of synthesized products:

(1).4-[3-(4-chlorophenyl)-5-(3-phenoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbonyl] pyridine (1a)

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.58 – 7.52 (m, 2H), 7.49 (s, 5H), 7.45 – 7.39 (m, 2H), 7.39 – 7.32 (m, 2H), 7.23 – 7.17 (m, 1H), 7.10 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.88 – 6.82 (m, 1H), 6.79 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.51 (dt, *J* = 2.6, 0.8 Hz, 1H), 5.46 (t, *J* = 6.6 Hz, 1H), 3.84 (dd, *J* = 14.7, 6.6 Hz, 1H), 3.22 (dd, *J* = 14.7, 6.6 Hz, 1H).

IR (Kbr)cm^{-1}) - 688-(C-H-def), 751-(C-Cl), 801-(=C-H o.o.p.def), 1054-(C-O-C(asym)), 1085-(C-H i.p.def), 1220-(C-O-C str.(sym)), 1382-(= C-N-), 1514 –(= N-ph),1594 –(C=Nstr), 1612-(C=C str aromatic), 1679-(C=O conjugated), 3032-(C-H str aromatic ring)

Anal.calcd. for $C_{27}H_{20}ClN_3O_2$: C,71.44, H, 4.44, N,9.26, O,7.05, Cl, 7.80. Found: : C,71.50, H, 4.40, N,9.30, O,7.00, Cl, 7.80.

(2).4-[3-(2,4-dichlorophenyl)-5-(3-phenoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbonyl] pyridine (1b)

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.72 – 8.68 (m, 2H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.77 – 7.70 (m, 3H), 7.65 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.23 – 7.17 (m, 1H), 7.10 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.88 – 6.82 (m, 1H), 6.79 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.51 (dt, *J* = 2.6, 0.8 Hz, 1H), 5.46 (t, *J* = 6.6 Hz, 1H), 3.98 (dd, *J* = 14.5, 6.6 Hz, 1H), 3.36 (dd, *J* = 14.5, 6.6 Hz, 1H).

IR (Kbr)cm^{-1} -691-(C-H-def), 753-(C-Cl),802-(=C-H o.o.p.def), 1055-(C-O-C(asym)), 1087 –(= C-H i.p.def), 1221-(C-O-C str.(sym)), 1384-(= C-N-), 1514-(= N-ph), 1596–(=C=Nstr), 1615-(C=C str aromatic), 1676 –(C=O conjugated), 3037-(C-H str aromatic ring).

Anal.calcd. for $C_{27}H_{19}Cl_2N_3O_2$: C,66.40, H, 3.92, N,8.60, O,6.55, Cl, 14.52. Found: : C,66.40, H, 3.90, N,8.60, O,6.60, Cl, 14.50.

(3).4-[3-(2,3-dimethoxyphenyl)-5-(3-phenoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbonyl] pyridine (1c)

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.72 – 8.68 (m, 2H), 7.77 – 7.73 (m, 2H), 7.55 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.23 – 7.14 (m, 2H), 7.14 – 7.06 (m, 1H), 7.06 – 7.02 (m, 2H), 7.01 (d, *J* = 1.5 Hz, 1H), 6.88 – 6.82 (m, 1H), 6.79 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.51 (dt, *J* = 2.6, 0.8 Hz, 1H), 5.46 (t, *J* = 6.6 Hz, 1H), 3.98 (dd, *J* = 14.5, 6.6 Hz, 1H), 3.87 (d, *J* = 9.9 Hz, 6H), 3.36 (dd, *J* = 14.5, 6.6 Hz, 1H).

IR (Kbr)cm^{-1} -687 –(C-H-def),-804-(=C-H o.o.p.def), 1054-(C-O-C(asym)), 1087-(C-H i.p.def), 1168-(O-CH3), 1222- (C-O-C str.(sym)), 1384-(C-N-), 1515-(= N-ph), 1595-(=C=Nstr), 1615-(C=C str aromatic), 1680-(C=O conjugated), (3034 -(C-H str aromatic ring

Anal.calcd. for $C_{29}H_{25}N_3O_4$: C,72.64, H, 5.26, N,8.76, O,13.35. Found: : C,72.70, H, 5.30, N,8.70, O,13.30.

(4). 4-[5-(3-phenoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1h-pyrazole-1-carbonyl]pyridine (1d)

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.72 – 8.68 (m, 2H), 7.77 – 7.73 (m, 2H), 7.39 – 7.31 (m, 2H), 7.23 – 7.17 (m, 1H), 7.10 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.88 – 6.82 (m, 1H), 6.79 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.51 (dt, *J* = 2.6, 0.8 Hz, 1H), 5.46 (t, *J* = 6.6 Hz, 1H), 3.88 (s, 6H), 3.86 – 3.76 (m, 4H), 3.18 (dd, *J* = 14.7, 6.7 Hz, 1H).

IR (Kbr)cm^{-1}- 687-(C-H-def), 801-(=C-H o.o.p.def)**,**1054-(C-O-C(asym))**,** 1084-(C-H i.p.def)**,** 1165-(O-CH3)**,** 1220-(C-O-C str.(sym)**,** 1382-(= C-N-), 1514-(= N-ph)**,** 1593-(=C=Nstr)**,** 1611-(C=C str aromatic)**,** 1675-(C=O conjugated), 3036-(C-H str aromatic ring).

Anal.calcd. for $C_{29}H_{27}N_3O_5$: C,70.71, H, 5.34, N,8.25, O,15.70. Found: : C,70.70, H, 5.30, N,8.30, O,15.70.

Table 1; antimicrobial activity of the compounds (1a-d)

Compound name	Diameter of Zone of Inhibition (In mm)				
	B.Subtilis	**S.aureus**	**E.Coli**	**Ps. aeruginosa**	**C.albicans**
1a	17	16	16	18	14
1b	18	17	15	17	15
1c	16	15	11	12	10
1d	15	16	15	14	13
Ampicillin	18	16	17	16	08
Griseofulvin	17	14	16	13	15

B=Bacillus Subtillis, S= Staphylococcus aureus, E= Escherichia coli, Ps=Pseudomonas aeruginosa, C=candida albicans

Results and discussion:

The compounds tested for antimicrobial activity are listed in Table-1 show size of zone of inhibition of bacterial growth procedure by test compounds for broad range of antimicrobial activity inhibiting growth of Gram-positive bacterial strains B.Subtillis and S.Aureus and Gram-negative bacterial strains E.coli and P.Aeruginosa.

Among pyrazoline derivatives (1a-d) compounds 1a and 1b shows good antimicrobial activity.

Conclusion:

The synthetic scheme reported in this study design is novel example in hetero cyclic synthesis of pyrazoline derivatives was carried out in two steps these are as

1.formation of chalcone

2.cyclisation to form pyrazolines

Infirtly, when substistuted aldehyde treated with substituted ketone to form chalcone. Further treated with suitable pyridine-4-carbohydrazide to form corresponding pyrazolines . the yield of all derivatives were lies in the ranging from 75% to 78% All synthesized compounds were meeting the expected spectral data. General structure confirm from the collected spectral data is as follows

All synthesized compounds characterized by spectral analysis.

All synthesized compounds are screened for antimicrobial activity and compared with standard drug. From the results

it can be concluded that the modified pyrazoline shows remarkable antimicrobial activity.

CONFLICT OF INTEREST:

The authors confirm that this article content has no conflict of interest.

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