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SYNTHESIS AND CHARACTERISATION OF NOVEL INDAZOLE DERIVATIVES AND THEIR BIOLOGICAL ACTIVITY

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Abstract: 2-nitro-5-phenoxybenzaldehyde reacted with 4-substituted aniline with reflux in ethanol solvent then formed in (E)-1-(2-nitro-5-phrnoxyphenyl)-N-(4-substitutedphenyl)methanimine. Then (E)-1-(2-nitro-5-phrnoxyphenyl)-N-(4-substitutedphenyl)methanimine reacted triethyl phosphite at 150˚C and formed 5-phenoxy-2-(4-substitutedphenyl)-2H-indazole(Indazole derivative). synthesized Indazole 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: Indazole, synthesis, characterization, antimicrobial activity.

I. INTRODUCTION

The indazole nucleus is a very significant heterocyclic agenda in medicinal chemistry. This scafford is current in a large number of complexes with a wide range of biological activities. Some indazole derivatives have lately been testified as antiprotozoals, with activity compared to E. histolytica and T. uaginalis. Transferable diseases began by protozoa, bacteria, and yeasts have a major effect on human health. Enteric pathogenic protozoa and bacteria are a common cause of duodenal sickness which, in turn, is a significant cause of illness and mortality everywhere the world. Two significant etiological agents of duodenal parasitic sicknesses are the protozoa Giardia intestinalis and Entamoeba histolytica, which have been projected to affect 280 million and 50 million people universal each year, correspondingly. Moreover, some bacterial strains have been recognized as responsible for severe duodenal sickness. Example of these are pathogenic strains of Escherichia coli,e,g, enterohemorrhagic E.coli (EHEC) and enteroaggregative E.Coli (EAEC), and Salmonella enterica serovar Typhi. Duodenal sicknesses caused by protozoa and bacteria mark persons of all ages, but have a high occurrence in children. Even though contaminations linked with each pathogen show particular clinical symptoms, all of them are fundamental agents of transferrable diarrhea with severe health significances and that could principal to death.

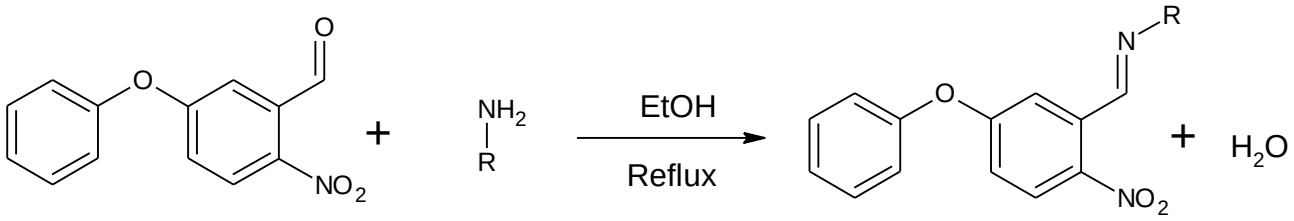
Experimental

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 2-nitro-5-phenoxy benzaldehyde, aniline, 4-aminophenol, triethyl phosphite, ethanol, 4-methoxyaniline, 4-(methylsulfanyl)aniline. The water used was double distilled deionized water. All the compounds showed satisfactory elemental analysis for C, H&N

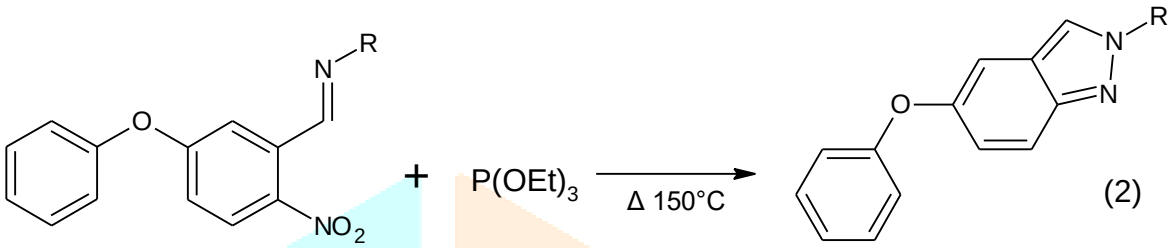
1. Thin layer chromatography: Thin layer chromatography was performed on percolated silica gel plates with suitable solvent system. The R_f values were recorded accordingly .
2. Infrared spectroscopy: The infrared spectra for the synthesized compounds were recorded using JASCO-FTIR 8400 spectrophotometer using potassium bromide pellet technique.
3. 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.

General procedure for the synthesis of new indazole derivatives from 2-nitro-5-phenoxybenzaldehyde : 2-nitro-5-phenoxybenzaldehyde reacted with 4-substituted aniline with reflux in ethanol solvent then formed in (E)-1-(2-nitro-5-phrnoxyphenyl)-N-(4-substitutedphenyl)methanimine(1). Then(E)-1-(2-nitro-5-phrnoxyphenyl)-N-(4-substitutedphenyl) methanimine reacted triethyl phosphite at 150˚C and formed 5-phenoxy-2-(4-substitutedphenyl)-2H-indazole(2).

Scheme:



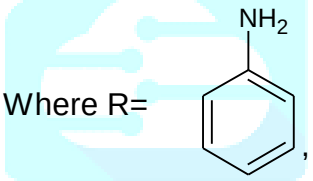
2-nitro-5-phenoxybenzaldehyde (1)



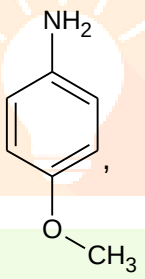
(2)

Indazole derivative

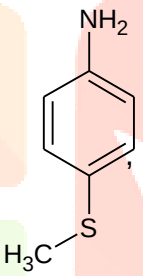
Where R=



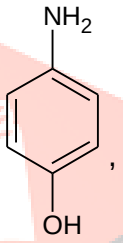
(1a)



(1b)



(1c)



(1d)

TABLE 1

PHYSICAL CHARACTERIZATION DATA OF SYNTHESIZED COMPOUND

Indazole derivatives (1a-d)

Compound	Yield (%)	Molecular Formula
1a	78	$C_{19}H_{14}ON_2$
1b	77	$C_{20}H_{16}O_2N_2$
1c	81	$C_{20}H_{16}ON_2S$
1d	83	$C_{19}H_{14}O_2N_2$

Identification and characterization of synthesized products:

1.Synthesis of 5-phenoxy-2-phenyl-2H-indazole

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 1.8 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.53 – 7.39 (m, 4H), 7.39 – 7.31 (m, 2H), 7.10 (tt, *J* = 7.7, 1.7 Hz, 2H), 7.05 – 6.99 (m, 2H).

IR (Kbr)cm^{-1}) – 834-(C-H o.o.p.def), 1023-(C-H i.p.def), 1237-(C-O-C vinyl ether), 1510-(= N-ph), 1525-(C=C aromatic ring), 1579-(C=N indazoline ring), 3038-(C-H aromatic ring).

Anal.calcd. for $C_{19}H_{14}N_2O$: C,79.70, H, 4.93, N,9.78, O,5.59. Found: : C,79.70, H, 4.90, N,9.80, O,5.60.

2.Synthesis of 2-(4-methoxyphenyl)-5-phenoxy-2H-indazole

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 1.8 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.51 (t, *J* = 1.9 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.14 – 7.06 (m, 2H), 7.05 – 6.99 (m, 2H), 6.97 – 6.91 (m, 2H), 3.82 (s, 3H).

IR (Kbr)cm^{-1}) -834-(C-H o.o.p.def), 1024-(C-H i.p.def), 1175-(OCH3 str.), 1242-(C-O-C vinyl ether), 1505-(= N-ph), 1527-(C=C aromatic ring), 1589-(C=N indazoline ring), 3040-(C-H aromatic ring).

Anal.calcd. for $C_{20}H_{16}N_2O_2$: C,75.93, H, 5.10, N,8.86, O,10.11. Found: : C,75.90, H, 5.10, N,8.90, O,10.10.

3.Synthesis of 2-[4-(methylsulfanyl)phenyl]-5-phenoxy-2H-indazole

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 1.8 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.61 – 7.57 (m, 2H), 7.51 (t, *J* = 1.9 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.28 (s, 1H), 7.14 – 7.06 (m, 2H), 7.05 – 6.99 (m, 2H).

IR (Kbr)cm^{-1}) -692-(C-S), 833-(C-H o.o.p.def), 1025-(C-H i.p.def), 1247-(C-O-C vinyl ether), 1438-(C-H alkane ch3), 1510-(=N-ph), 1527-(C=C aromatic ring), 1582-(C=N indazoline ring), 3038-(C-H aromatic ring).

Anal.calcd. for $C_{20}H_{16}SN_2O$: C,72.26, H, 4.85, N,8.43, O,4.81, S, 9.64. Found: : C,72.30, H, 4.90, N,8.40, O,4.80, S, 9.60.

4.Synthesis of **4-(5-phenoxy-2H-indazol-2-yl)phenol**

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 1.8 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.51 (t, *J* = 1.9 Hz, 1H), 7.39 – 7.27 (m, 5H), 7.14 – 7.06 (m, 2H), 7.05 – 6.99 (m, 2H), 6.12 (s, 1H).

IR (Kbr)cm^{-1}) -834-(C-H o.o.p.def), 1025-(C-H i.p.def), 1237-(C-O-C vinyl ether), 1438-(C-H alkane ch3), 1509-(=N-ph), 1525-(C=C aromatic ring), 1580-(C=N indazoline ring), 3040-(C-H aromatic ring), 3163-(C-OH group).

Anal.calcd. for $C_{19}H_{14}N_2O_2$: C,75.48, H, 4.67, N,9.27, O,10.58. Found: : C,75.50, H, 4.65, N,9.25, O,10.60.

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	15	16	17	14
1b	16	14	10	11	9
1c	19	17	14	16	15
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 Indazole derivatives (1a-d) compounds 1a and 1c shows good antimicrobial activity.

Conclusion:

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

1.formation of (1)

2.cyclisation to form Indazole(2)

Infirtly, when 2-nitro-5-phenoxybenzaldehyde treated with substituted aniline to form (1). Further treated with suitable triethyl phosphite to form corresponding Indazoles. the yield of all derivatives were lies in the ranging from 78% to 83% 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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