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Microwave Assisted Synthesis and Antimicrobial Activity of Some Novel Isonicotinoyl-Pyrazol Derivatives

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Abstract: Syntheses of some pyrazole derivatives have been carried out under microwave irradiation and compared with conventional procedure. To start with, the compound 1a, that is, 3-amino-1-isonicotinoyl-1H-pyrazol-5 (4H)-one is prepared from condensation reaction of isonicotinohydrazide and ethyl 2-cyanoacetate. Target compounds substituted 3-(benzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one has been synthesized by the condensation reaction of 1a with various substituted benzaldehydes. The final products have been characterized by spectral analysis. All these compounds have also been screened for their antimicrobial activity against bacteria E.coli, S. aureus, P. eruginosa and S. progenies and fungi such as C.albicans and A.niger. Introduction of Cl, F, NO_2, and OH groups in the heterocyclic framework enhanced antibacterial and antifungal activities.

Key Words: Microwave, Isonicotinohydrazide, Ethyl 2-cyanoacetate and Furan-2-carbaldehyde.

Introduction

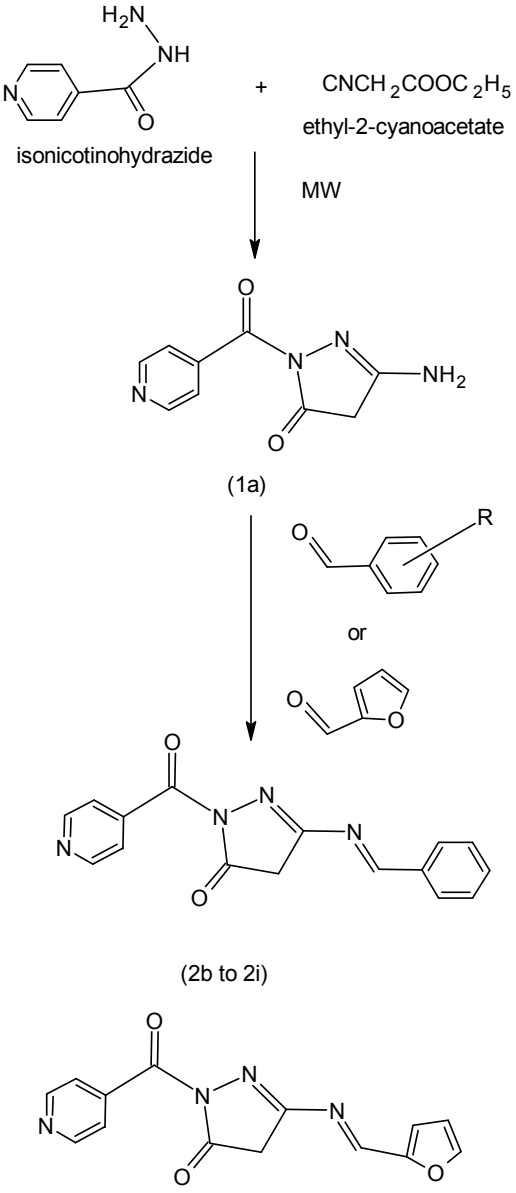
Organic synthesis, especially diversity-oriented synthesis, may likely to play a vital role in drug discovery in the future. However, the manufacture of fine chemicals and pharmaceuticals through traditional processing generates a lot of waste, the bulk of which consists of byproducts and inorganic salts. Hence, for cleaner production, waste minimization is essential which can be achieved using newer techniques. Microwave assisted organic synthesis offers a cleaner and greener route, since higher yields are obtained in few minutes, leading to minimization of wastes.

Isoniazid is reported as a well known drug.[1-3] Isoniazid is one of the primary drugs used in combination with ethanbutol, rifampin, streptomycin and pyrazinamide to treat tuberculosis.[4] Despite the large number of compounds containing the isoniazid moiety which have already been synthesized and tested, there is still a need for new compounds of this kind,[5] due to the increasing resistance of bacterial strains of certain type of antibiotics.[6] The efficiency of pyrazole as chemotherapeutic agent is well established and their chemistry has been extensively studied. Pyrazole and its synthetic analogues have been found to exhibit industrial, agricultural and biological applications.[7-11] Pyrazoles are an interesting group of compounds many of which possess broad spectrum pharmacological properties, such as analgesic, agents and play a vital role in the biological system. Looking to the great-diversified role of pyrazole moieties as drugs, synthesis of some pyrazole derivatives have been carried out under microwave irradiation and compared with conventional procedure. In conventional method, it took 6-12 hours for completion of reaction whereas under microwave irradiation, only 2-4 min. are required. Consequently, the microwave irradiation method provided higher

product yields in a very short period of time. Thus, the ever-increasing demands of economic and safety considerations offer many opportunities for microwave chemistry in the development of eco-friendly methods for the preparation of pharmaceuticals. The microwave-assisted reactions are rapid, safe, high yielding and superior to conventional methods.

Experimental

All the reactions were carried out in a domestic microwave oven (Kenstar, Model No: OM26.EGO). Melting points of synthesized compounds were determined in open capillaries in liquid paraffin and are uncorrected. Purity of the compounds was ascertained by TLC using silica gel-G as an adsorbent and ethyl acetate: n-hexane (7:3) as an eluent and spots were detected using iodine vapors. The IR (KBr pellets) spectra were recorded on a Perkin Elimer-1800- Spectrophotometer and ^{1}HNMR spectra were recorded on Brucker DRX-300 MHz; FT- NMR Spectrophotometer (TMS as internal reference) and chemical shifts were expressed in δ. Mass spectra were recorded on Jeol D30 Spectrophotometer. Percentage of C, H and N were determined by using a Perkin - Elmer C, H, and N analyzer. The starting compound isonicotinohydrazide was a product from BDH.



R= (a) H, (b) 4-F, (c) 4-Cl, (d) 4-OCH_3, (e) 4-OH, (f) 2-OH, (g) 3-OH, (h) 3-NO_2, (i) 4-NO_2 (j) Furan-2-carbaldehyde

Reaction Scheme

Synthesis of 3-amino-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (1a).

Isonicotinohydrazide (0.01 mole) and ethyl 2-cyanoacetate (0.01 mole) was taken in an Erlenmeyer flask and mixed thoroughly. The mixture was irradiated under microwave for 2 min at 500 W power with intermittent radiation of 30 sec interval. The progress of the reaction was examined by TLC; the mixture was poured onto the ice-cold water. The crude product was filtered, dried, and recrystallized from methanol to give product (1a). The physical data and R_f value are given in Table1.

Elemental analysis (Found): C, 53.25; H, 4.24; N, 27.77; (calculated): C, 52.92; H, 3.95;N, 27.44; Mol.Formula: $C_9H_8N_4O_2$; **IR** (KBr,): 3334, 3218, 1698, 1672, 1554**;** cm^{-1} **^{1}H NMR** (400 MHz, DMSO**)** δ**:** 7.20-7.77 (m, 4H, pyridine); 5.12 (s, 2H, NH_2), 3.33 (s, 2H, CH_2); **MS** (EI, 70 eV)**:** m/z $[M]^+$ 204

Synthesis of 3-(benzylideneamino)-1-isonicotinoyl-1H-pyrazole-5 (4H)-one. (2a).

A mixture of 3-amino-1-isonicotinoyl-1H-pyrazol-5 (4H)-one, substituted benzaldehydes or furan-2-carbaldehyde (0.01 mole), and a catalytic amount of acetic acid and DMF (10.0mL) was taken in Erlenmeyer flask and mixed thoroughly. The mixture was subjected to microwave irradiation at 400 W at 30 sec intervals for 3-5 min. On completion of reaction, as monitored by TLC, the reaction mixture was cooled and poured onto the crushed ice. The precipitate thus obtained was filtered, washed with water and purified by recrystallization from methanol. Similarly, other derivatives **(2b-2j)** were prepared by the minor change in this method. The physical data and R_f value are given in Table -1

3-(Benzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2a).

Elemental analysis (Found) C, 66.05; H, 4.44; N, 19.37; (calculated) C, 65.75; H, 4.14; N, 19.17; Mol.Formula: $C_{16}H_{12}N_4O_2$; IR (KBr,): 1703, 1680, 1609, 1574, 1527 cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.84-8.11 (m, 4H, pyridine), 7.32-7.55 (m, 4H,Ar-H), 8.68 (s, 1H, N=CH-Ar), 3.60 (s, 2H, CH_2, pyrazolidine); **MS:** m/z 292.

3-(4-Fluorobenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2b).

Elemental analysis (Found) C, 62.25; H, 3.37; N, 18.36; (calculated) C, 61.93; H, 3.57; N, 18.06; **Mol.Formula:** $C_{16}H_{11}FN_4O_2$; **IR** (KBr): 1695,1673, 1619,1574,1525,752, cm^{-1}**;** **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.52-7.85 (m, 4H, pyridine), 6.93-7.32 (m, 4H,Ar-H), 8.66 (s, 1H, N=CH-Ar), 3.72 (s, 2H, CH_2, pyrazolidine); **MS:** m/z $[M]^+$ 310.

3-(4-Chlorobenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2c).

Elemental analysis (Found) C, 58.52; H, 3.67; N, 17.46; (calculated) C, 58.22; H, 3.39; N, 17.15; **Mol.Formula:** $C_{16}H_{11}ClN_4O_2$ **IR** (KBr): 1703, 1686, 1596, 1510, 1500, 762, cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.74-8.11 (m, 4H, pyridine), 6.95-7.46 (m, 4H, Ar-H) 8.68 (s, 1H, N=CH-Ar), 3.33 (s, 2H, CH_2, pyrazolidine); **MS** (EI, 70 eV)**:** m/z $[M]^+$ 326, $[M^{+2}]$ 328.

3-(4-Methoxybenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2d).

Elemental analysis (Found) C, 63.52; H, 4.67; N, 17.66; (calculated) C, 63.35; H, 4.38; N, 17.38; **Mol.Formula:** $C_{17}H_{14}N_4O_3$ **IR** (KBr): 1688, 1664, 1587, 1561, 1511, cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.85-8.24 (m, 4H, pyridine), 6.95-7.55 (m, 4H, Ar-H) 8.79 (s, 1H, N=CH-Ar), 2.93 (s 2H, CH_2, pyrazolidine), 4.31 (s, 3H, CH_3); **MS** (EI, 70 eV)**:** m/z $[M]^+$ 323.

3-(4-Hydroxybenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2e).

Elemental analysis (Found) C, 62.52; H, 4.17; N, 18.46; (calculated) C, 62.33; H, 3.92; N, 18.17; **Mol. Formula:** $C_{16}H_{12}N_4O_3$; **IR** (KBr): 3625, 1680, 1660, 1610, 1568, 1532 cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.55-8.01 (m, 4H, pyridine), 6.79-7.21 (m, 4H, Ar-H), 8.89 (s, 1H, N=CH-Ar), 10.35 (s, H, OH), 2.72 (s, 2H, CH_2, pyrazolidine); **MS:** m/z $[M]^+$ 308.

3-(2-Hydroxybenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one. (2f).

Elemental analysis (Found) C, 62.58; H, 4.10; N, 17.86; (Calculated) C, 62.33; H, 3.92; N, 18.17; **Mol. Formula:** $C_{16}H_{12}N_4O_3$ **IR** (KBr): 3615, 1690, 1663, 1609, 1574, 1530, cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ7.74-8.11 (m, 4H, pyridine), 6.52-7.21 (m, 4H, Ar-H), 8.32 (s, 1H, N=CH-Ar), 9.07 (s, H, OH) 2.87 (s, 2H, CH_2, pyrazolidine); **MS** (EI, 70 eV)**:** m/z $[M]^+$ 308.

3-(3-Hydroxybenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2g).

Elemental analysis (Found) C, 62.08; H, 4.19; N, 18.36; (Calculated) C, 62.33; H, 3.92; N, 18.17; **Mol. Formula:** $C_{16}H_{12}N_4O_3$; IR (KBr,): 3620, 1688, 1666, 1615, 1570, 1525 , cm^{-1}**;** **^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.85-8.42 (m, 4H, pyridine), 6.93-7.74 (m, 4H,Ar-H), 8.79 (s, 1H, N=CH-Ar), 10.43 (s, H, OH) 3.64 (s, 2H, CH_2, pyrazolidine); **MS** (EI, 70 eV): m/z $[M]^+$ 308.

3-(3-Nitrobenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2h).
Elemental analysis (Found) C, 57.28; H, 3.49; N, 20.46; (Calculated) C, 56.98; H, 3.29; N, 20.76; **Mol. Formula**: $C_{16}H_{11}N_5O_4$, **IR** (KBr): 1706, 1685, 1615, 1570, 1529, 1375, cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 8.22-8.42 (m, 4H, pyridine), 7.55-8.01 (m, 4H, Ar-H), 9.04 (s, 1H, N=CH-Ar), 4.31 (s, 2H, CH_2, pyrazolidine); **MS** (EI, 70 eV)**:** m/z $[M]^+$ 337.

3-(4-Nitrobenzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2i).
Elemental analysis (Found) C, 56.68; H, 3.09; N, 21.16; (Calculated) C, 56.98; H, 3.29; N, 20.76; **Mol. Formula:** $C_{16}H_{11}N_5O_4$; **IR** (KBr): 1680, 1667, 1605, 1565, 1525, 1370, cm^{-1}; **^{1}H NMR**: (400 MHz, DMSO**)** δ: 8.57-8.91 (m, 4H, pyridine), 8.08-8.32 (m, 4H,Ar-H), 10.35 (s, 1H, N=CH-Ar), 3.72 (s, 2H, CH_2, pyrazolidine), **MS** (EI, 70 eV)**:** m/z $[M]^+$ 337.

3-(Furan-2-ylmethyleneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (2j). Elemental analysis (Found) C, 59.28; H, 3.89; N, 19.56; (Calculated) C, 59.57; H, 3.57; N, 19.85; **Mol. Formula:** $C_{14}H_{10}N_4O_3$; **IR** (KBr): 1693, 1670, 1607, 1565, 1533 cm^{-1}**; ^{1}H NMR**: (400 MHz, DMSO**)** δ: 7.85-8.22 (m, 4H, pyridine), 6.79-7.21 (m, 3H, Furan), 8.98 (s, 1H, N=CH-Ar), 3.64 (s, 2H, CH_2 pyrazolidine),); **MS** (EI, 70 eV): m/z $[M]^+$ 282.

Antimicrobial Activity

Antibacterial activity: The antibacterial activity of the synthesized compounds was studied systematically against four different strains of bacteria (two gram-positive and two gram-negative) by the agar diffusion method[13-14] **.**
Bacterial strains used are Staphylococcus *aureus, Bacillus subtillis* (gram-positive) and *Eschrichia coli* and *Pseudomonas eruginosa* (gram-negative). The organisms were subcultured using nutrient agar medium. The tubes containing sterilized medium were inoculated with respective bacterial strain. After incubation at 37 ± 1°C for 24 hr. they were stored in a refrigerator. Thus stock cultures were maintained. Bacterial inoculum was prepared by transferring a loopful of stock culture to nutrient broth (100.0 mL) in a clean and sterilized conical flask (250.0 mL). The flasks were incubated at 37 ± 1°C for 18 hr. before the experimentation.
Solutions of the test compounds were prepared by dissolving 5.0, 10.0 and 20.0 mg of each in dimethylsulfoxide (10.0 mL AR). A reference standard was prepared by dissolving accurately weighed quantity of streptomycin in dimethylsulfoxide. The nutrient agar medium was sterilized by autoclaving at 121°C (15 lb/sq. inch). The petri-plates, tubes and flasks plugged with cotton were sterilized in hot air-oven at 160°C for an hour. Into each sterilized petri-plate (10 cm diameter), about 30.0 mL each of molten nutrient bacteria (6.0 mL of inoculum to 300 mL of nutrient agar medium) was transferred, aseptically. The plates were left at room temperature to allow the solidification. In each plate, four cups of 6 mm diameter were made with a sterile borer. Then, 0.1 mL of the test solution was added to the cups, aseptically and labeled, accordingly. The plates were kept undisturbed for at least 2 hrs at room temperature to allow diffusion of the solution properly, into nutrient agar medium. After incubation of the plates at 37 ± 1°C for 24 hr. the diameter of the zone of inhibition surrounding each of the cups was measured with the help of an 'antibiotic zone reader'. All the experiments were carried out in triplicate. Simultaneously, controls were maintained employing 0.1 mL of dimethylsulfoxide to observe the solvent effects.

Antifungal activity

All these compounds were screened for their antifungal activity were also tested for their antifungal activity. The fungi used for screening were: *Asperigillus niger* and *Candida albicans*.
The test organisms were sub-cultured using potato-dextrose agar medium. The tubes containing sterilized medium were inoculated with test fungi and after incubation at 25°C for 48 hr., they were stored 4°C in a refrigerator. The inoculum was prepared by taking a loopful of stock culture to about 100.0 mL of nutrient broth; in 250.0 mL clean and sterilized conical flasks. The flasks were incubated at 25°C for 24 hr. before use.
The solutions of test compounds were prepared by a similar procedure described under the antibacterial activity. A reference standard was prepared by dissolving 5.0, 10.0 and 20.0 mg of Amphotericin-B in 10.0 mL of dimethylsulfoxide (DMSO) to obtain solutions of 50 µg/mL, 100 µg/mL and 200 µg/mL concentrations.
The potato-dextrose agar medium was sterilized by autoclaving at 121°C (15 ib/sq. inch), for 15 minutes. The petri-plates, tubes and flasks plugged with cotton plugs were sterilized in hot air-oven at 150°C, for an hour. Into each sterilized petri-plate (10.0 cm diameter), about 30.0 mL each of molten potato-dextrose agar medium inoculated with respective fungus (6.0 mL of inoculum to 300.0 mL of potato-dextrose-agar medium) was transferred, respectively. After solidification of the medium at room temperature four cups of 6.0 mm diameter were made in each plate with a sterile borer. Accurately 0.1 mL (50 µg/mL conc., 100µg/mL conc. and 200 µg/mL conc.) of test solution was transferred to the cups, aseptically and

labeled, accordingly. The reference standard 0.1 mL (50 µg/mL conc., 100 µg/mL conc., 200 µg/mL conc.) was also added to the cups in each plate. The plates were kept undisturbed for at least two hours at room temperature to allow diffusion of the solution properly, into potato-dextrose-agar medium. Then the plates were incubated at 25°C for 48 hr. The diameter of the zone of inhibition was read with help of an 'antibiotic zone reader'. The experiments were performed in triplicate in order to minimize the errors.

Table.1: The physical data and R_f value of the synthesized compounds1a & 2a –2j.

Compounds	R (For 2a-2j)	Molecular Formula	Mol. Wt.	Conventional Method		Microwave Method		m.p (°C)	R_f
				Yield (%)	Reaction time (Hours)	Yield (%)	Reaction time (min).		
1a	-	$C_9H_8N_4O_2$	204	51	10	88	2.0	116	0.72
2a	H	$C_{16}H_{12}N_4O_2$	292	47	8	87	3.0	122	0.77
2b	4-FC_6H_4	$C_{16}H_{11}FN_4O_2$	310	52	6	88	2.5	124	0.72
2c	4-ClC_6H_4	$C_{16}H_{11}ClN_4O_2$	326	53	11	86	3.5	136	0.74
2d	4-$OCH_3C_6H_4$	$C_{17}H_{14}N_4O_3$	322	50	9	87	3.0	145	0.75
2e	4-OHC_6H_4	$C_{16}H_{12}N_4O_3$	308	49	12	88	3.0	134	0.79
2f	2-OHC_6H_4	$C_{16}H_{12}N_4O_3$	308	50	13	83	3.5	189	0.71
2g	3-OHC_6H_4	$C_{16}H_{12}N_4O_3$	308	48	12	84	4.0	169	0.78
2h	3-$NO_2C_6H_4$	$C_{16}H_{11}N_5O_4$	337	45	10	80	3.5	187	0.73
2i	4-$NO_2C_6H_4$	$C_{16}H_{11}N_5O_4$	337	45	12	84	4.0	156	0.76
2j	2-Furaldehyde	$C_{14}H_{10}N_4O_3$	282	45	13	87	4.5	169	0.71

Table.2: Antibacterial activity of the synthesized compounds 2a –2j

Compounds.	Zone of inhibition (mm)											
	E.coli			*P. aeruginosa*			*B.subtitis*,			*S.aureus*		
	50 µg /mL	100 µg /mL	200 µg /mL	50 µg /mL	100 µg /mL	200 µg /mL	50 µg /mL	100 µg /mL	200 µg /mL	50 µg /mL	100 µg /mL	200 µg /mL
2a	05	10	15	04	08	13	05	09	11	04	08	14
2b	06	13	16	04	08	14	05	05	14	**06**	**10**	**20**
2c	**06**	**12**	**18**	04	08	12	**05**	**13**	**23**	04	10	14
2d	05	10	14	06	10	12	05	10	18	04	10	14
2e	05	12	19	05	09	18	05	11	13	04	09	14
2f	05	12	20	05	08	12	05	10	14	04	06	14
2g	**05**	**12**	**20**	04	08	12	05	09	13	04	10	15
2h	**06**	**15**	**21**	**07**	**12**	**20**	**07**	**10**	**18**	04	10	16
2i	**05**	**13**	**20**	06	10	14	05	10	18	04	09	14
2j	03	13	18	05	09	14	03	09	13	**05**	**10**	**19**
Streptomycin	12	19	27	11	18	26	10	17	28	12	19	25

Table3: Antifungal activity of the synthesized compounds 2a –2J

Compounds	Zone of inhibition (mm)					
	C. albicans			*A. niger*		
	50 µg/mL	100 µg/mL	200 µg/mL	50 µg/mL	100 µg/mL	200 µg/mL
2a	06	10	15	05	11	12
2b	07	12	20	06	12	21
2c	06	13	22	05	08	12
2d	06	09	15	06	12	14
2e	05	09	13	06	09	14
2f	06	09	12	05	10	13
2g	05	08	13	05	10	12
2h	07	10	20	06	13	20
2i	06	10	18	05	11	19
2j	05	08	16	04	10	16
Amphotericin-B	13	19	26	11	15	25

Results and Discussion

As many as 10 new compounds were synthesized by conventional and Microwave Induced Organic Reaction Enhancement technique and characterized by their physical, analytical and spectral data. The solvent free condensation of isonicotinohydrazide with ethyl 2-cyanoacetate under microwave irradiation afforded 3-amino-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (**1a**) in quantitative yield. It is noteworthy that the reaction was completed within 2 min. However, by conventional heating in DMF, the same reaction resulted in the formation of (**1a**) in low yields and required 10-11 hours. The IR spectrum of **(1a)** showed absorptions at 3334 and 3218 cm^{-1} (NH_2 group) and 1698, 1672 (C=O), 1574, 1556 (C=N), ^1H NMR of **(1a)** showed broad singlet at 4.68 δ due to NH_2 protons whereas signals of pyridine protons are in the region 7.20-7.77 δ (4 protons), a singlet at 3.33 δ due to two protons of -CH_2- group supported the formation of the desired product. Mass spectrum showed molecular ion peak at m/z 204.

When 3-amino-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (**1a**) was condensed with substituted benzaldehydes (2a-2i) or furan-2-carbaldehyde for (**2j**) and a catalytic amount of acetic acid in DMF under microwave irradiation, product 3-(substituted benzylideneamino)-1-isonicotinoyl-1H-pyrazol-5 (4H)-one (**2a-2j)** were obtained in good yields (Table 1). IR, ^1H NMR and mass spectral data have characterized these compounds. ^1H NMR showed broad singlet at 8.64 to10.35 due to proton N=CH-Ar and at 3.42 to 3.77 for CH_2 protons. Multiplets for aromatic protons in the range 6.52-8.32 for benzene and 7.52-8.91 for pyridine were observed. When the same reaction was carried out under conventional heating conditions, products **(2a-2j)** were obtained in very low yield and reaction took 6-13 hours for completion. Under microwave yields were (>83%) whereas by conventional method less yields of products (45-52%) were obtained. Thus comparing the two methods, it has been concluded that microwave assistance synthesis offers an eco-friendly, therefore greener path for the synthesis of target compounds.

All the synthesized compounds were tested for *in vitro* antimicrobial activity by the broth dilution method. The results are summarized in Table-2 and Table-3. Reference drugs used were Streptomycin and Amphotricin-B, respectively for antibacterial and antifungal activity. The tested compounds exhibited mild to moderate antibacterial activity against all four strains of bacteria. The compounds, 2c, 2g, 2h and 2i are active on *E. coli* and 2h is active on *P. aeruginosa*. Whereas compounds 2c and 2h are active on *B. subtitis*. It has also been observed that compounds 2b and 2j showed activity against *S. aureuss*. The antifungal activity of the compounds were studied for the two pathogenic fungi. Amphotricin-B was used as reference for inhibitory activity against fungi. It was observed that compounds 2b, 2h and 2i had showed good activity against *C. albicans* and *A. niger*. It has also been observed that compound 2c showed good activity against *C. albicans*. On the basis of biological activity results, it may be concluded that the introduction of Cl, F, NO_2, and OH groups to the heterocyclic framework enhanced antibacterial and antifungal activities.

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