Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(7):35-45
(http://derpharmachemica.com/archive.html)

Design, synthesis of pyrazol-1-carbaldehyde derivatives under microwave irradiation in solvent-free conditions and their biological investigation

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ABSTRACT

*A new series of pyrazol-1-carbaldehydes **5(a-f)** were synthesized by reacting chalcones **3(a-d)** with hydrazine **4** using ion exchange resins viz. amberlite formate and amberlyst 15 DRY as reusable heterogeneous catalysts in solvent free conditions. The present methodology offers several advantages such as simple procedure with an easy work-up, shorter reaction times, and high yields. The structures of newly synthesized compounds have been established by spectral, elemental analysis and evaluated for their antioxidant, antibacterial, and antifungal activity. Some of them were found to possess significant activity, when compared to standard drugs.*

Keywords: Pyrazol-1-carbaldehyde, Amberlyst 15 DRY, Amberlite formate, Antioxidant, Antibacterial, Antifungal activity.

INTRODUCTION

Pyrazole derivatives are well established in the literatures as important biologically effective heterocyclic compounds. These derivatives are the subject of many research studies due to their widespread potential pharmacological activities such as anti-inflammatory [1], antipyretic [2], antimicrobial [3], antiviral [4], antitumour [5], anticonvulsant [6], antihistaminic [7] and antidepressant [8] activities. The widely prescribed anti-inflammatory pyrazole derivatives, celecoxib [9] and deracoxib [10] are selective COX-2 inhibitors with reduced ulcerogenic side effects.

In the present communication, we have focused on microwave-assisted synthesis because this technique has gained popularity over non-conventional techniques for the rapid synthesis [11,12, 13,14]. With the help of this technique many researchers have accelerated organic synthesis and since last couple of years a large number of research papers have appeared in the scientific journals. This has proved the utility of microwave assisted synthesis in various branches of chemistry. Microwave assisted organic synthesis may be helpful to increase the yield, decrease the reaction time and minimize the formation of hazardous by-products. With the help of this technique solvent free reactions can be easily carried out for eliminating toxicity and flammability issues which are a major concern with classical solvents.

The physical and chemical properties of ion exchange resins (IER) are highly customizable, as such; they may find a practical application as catalysts for biodiesel production [15]. IER are widely used in industrial water softening,

food preparation, pharmaceuticals, and in medical applications [16]. As catalysts IER are commonly applied to organic chemical reactions such as esterification, alcoholysis, hydrolysis and inversion of sugars [17]. Ion-exchange resins can be used in any type of reactor and in any solution. Ion-exchange resins offer a wide variety of support structures and functional groups. Several published works have examined IER in transesterification for biodiesel production [18-20]. Cation exchange resins are more commonly found in literature on biodiesel production [21, 22]. One study found base-functionalized anion exchange resins to be highly active [23].

In conjunction with the ongoing work in our laboratory on the synthesis of biologically active ingredients [24-26], using ion exchange resins [27, 28] and microwave irradiation technique [29, 30], herein we wish to report a microwave accelerated synthesis of pyrazol-1-carbaldehydes **5(a-f)** in solvent-free conditions by the reaction of chalcones **3(a-d)** with hydrazine **4** using ion exchange resins *viz.* amberlite formate and amberlyst 15 DRY as reusable heterogeneous catalysts respectively (Scheme **1**).

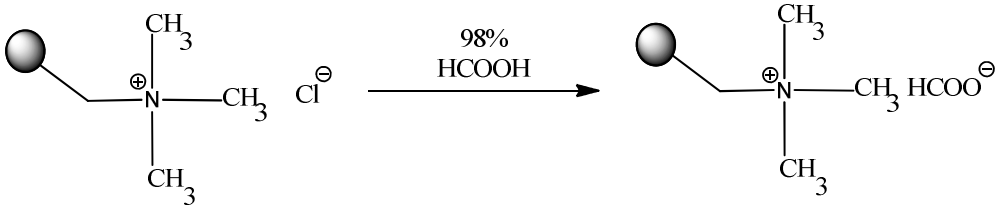
MATERIALS AND METHODS

General

All chemicals used are commercially available. All the reactions were carried out in commercial microwave oven YW 1600 multimode reactor equipped with condenser. The melting points were determined in open capillary tube using precision melting point apparatus and are uncorrected. Thin-layer chromatography was performed with fluorescent silica gel plates HF 254 (Merck), and they were viewed under UV 254 and 265 light. Infrared spectra's were recorded on a Shmadzu FT-IR 4000 using KBr disks. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-400 spectrophotometer in $CDCl_3$ using TMS as internal standard reference. Peaks are reported in ppm downfield of TMS. Mass spectra were recorded on JEOL spectrophotometer. All yields refer to the isolated yields.

Preparation of amberlite formate:

Amberlite formate is not commercially available, it was prepared by using Ambrelite IRA 900C (Cl^- form) anion exchange resin. The formyl group donor was prepared by washing Amberlite IRA 900C (Cl^- form) resin with formic acid (98%) and subsequently with water until no further chloride was eluted. The resulting solid was dried under vacuum over P_2O_5. The resin thus obtained was ready for further application in cyclization and formylation reactions.



Amberlite Chloride Amberlite formate

General procedure for the synthesis of chalcone derivatives 3(a-d)

A solution of acetophenone **(1)** (0.01 mol), benzeldehyde **(2)** (0.01 mol) and Amberlyst 15 DRY (0.50 mg) was taken in a 100 mL borosil flask fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation at 25% microwave power (300 W) for a period specified as in Table **1** with short interval of 30 seconds to 1 min, the reaction mixture was cooled, filtered, washed with water (250 ml) and recrystallized from ethanol to afford analytical samples of compounds **3(a-d)**. All these chalcones have already been reported and therefore have been identified by comparing their melting points with the literature values [31, 32]. The catalyst Amberlyst 15 DRY, used for their preparation has not been used earlier.

General procedure for the synthesis of pyrazol-1-carbaldehydes 5(a-f)

An intimate mixture of compound **3(a-d)** (0.01 mol), hydrazine hydrate **(4)** (0.01 mol) and amberlite formate (0.50 mg) was subjected to MWI at 450 watt power for 3-5 minutes. After the completion of the reaction as indicated by TLC, the residue was cooled to room temperature. It was dissolved in ethanol. The insolubles were filtered off and the filtrate was concentrated in vacuum. On keeping at room temperature, a solid was separated which was filtered, dried and recrystallized by ethanol to afford pure products **5(a-f)** with good to excellent yield. The synthesized

products **5(a-f)** are new and characterized by spectroscopic techniques like ^{1}H, ^{13}C, Mass (LCMS) and IR. The physical data of all the synthesized compounds are provided in Table **1.** Spectroscopic data for newly synthesized compounds are shown below.

3,5-diphenyl-2,3-dihydro-1*H*-pyrazol-1-carbaldehyde (5a)
M.p. 108-110; ^{1}H-NMR ($CDCl_3$) δ: 8.2 (CHO proton), 7.3-7.9 (aromatic protons), 6.1 (-NH proton), 5.1 (pyrazoline ring proton); ^{13}C-NMR ($CDCl_3$) δ: 160.66 (C=O carbon atom), 138.28, 99.51, (C-N pyrazoline ring carbon atoms) 134.96-122.15 (aromatic carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3380, 3200, 2810, 1090; LCMS: m/z (%): 250 (M^+), 221.

2,3,5-triphenyl-2, 3-dihydro-1*H*-pyrazol-1-carbaldehyde (5b)
M.p. 123-125; ^{1}H-NMR ($CDCl_3$) δ: 8.3 (CHO), 6.97.6 (aromatic protons), 5.8 (pyrozoline ring proton); ^{13}C-NMR ($CDCl_3$) δ: 167.79 (-C=O carbon atom), 97.50, 139.51 (pyrazoline carbon atoms), 47.63-113.53 (aromatic carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3070, 2820, 1740, 1210; LCMS: m/z (%): 327 (M^+), 298, 221.

5-(3-methoxyphenyl)-2, 3-dihydro-1*H*-pyrazol-1-carbaldehyde (5c)
M.p. 112-114; ^{1}H-NMR ($CDCl_3$) δ: 8.2 (C=O), 6.7-7.4 (aromatic protons), 5.3 (pyrazoline ring proton), 3.8 (-OCH_3 protons); ^{13}C-NMR ($CDCl_3$) δ: 146.70 (C=O, carbon atom), 134.65, 98.20, 70.9 (pyrazoline ring carbon atoms), 55.26 (-OCH_3 carbon atom), 158.94, 111.62 (aromatic ring carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3070, 2820, 2740, 1705; LCMS: m/z (%): 357 (M^+), 328, 326.

5-(2-hydroxyphenyl)-3-phenyl-2,3-dihydro-1H-pyrazole-1-carbaldehyde (5d)
M.p. 150-152; ^{1}H-NMR ($CDCl_3$) δ: 6.9-7.5 (aromatic protons), 8.7(-CHO proton), 5.2 (-NH proton), 4.5 (-OH proton), 7.3 & 6.4 pyrazoline ring protons); ^{13}C-NMR ($CDCl_3$) δ: 156.21 (-C=O carbon atom), 134.45, 100.20, 69.84 (pyrazoline ring carbon atoms) 118.54-108.60 (aromatic carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3280, 3100, 2750, 1110, 650; LCMS: m/z (%): 266 (M^+), 238, 250.

3-phenyl-5-(pyridine-3-yl)-2,3-dihydro-1*H*-pyrazole-1-carbadehyde (5e)
M.p. 110-112; ^{1}H-NMR ($CDCl_3$) δ: 8.3 (-CHO proton), 6.8-7.6 (phenyl ring & pyridine ring protons) 5.2 6.2 (pyrazoline ring protons); ^{13}C-NMR ($CDCl_3$) δ: 159.12 (-C=O, Carbon atom), 135.41, 102.20, 65.10 (pyrazoline ring carbon atoms), 150.366, 154.35, 123.85, 132.31, 129.01 (pyridine ring carbon atoms), 145.71-120.11 (aromatic carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3260, 3060, 1735, 1520, 1440; LCMS: m/z (%): 251 (M^+), 222, 174, 145, 116.

2,3-diphenyl-5-(pyridine-3-yl)-2,3-dihydro-1*H*-pyrazole-1-carbadehyde (5f)
M.p.133-135; ^{1}H-NMR ($CDCl_3$) δ: 6.8-7.4 (aromatic protons), 8.3 (-CHO proton), 5.8 (pyrazoline ring proton); ^{13}C-NMR ($CDCl_3$) δ: 160.65 (-C=O carbon atom), 136.86, 104.50, 71.23 (pyrazoline ring carbon atoms), 151.55, 149.25, 136.64, 122.01, 130.64 (pyridine ring carbon atoms), 151.55-113.21 (aromatic carbon atoms); IR (ν_{max}.; KBr, cm^{-1}): 3100, 2760, 1760, 1610; LCMS: m/z (%): 327 (M^+), 298, 221, 193.

Free radical scavenging activity
The free radical scavenging activity of the synthesized compounds was tested by DPPH assay. DPPH is a free radical and accepts one electron or hydrogen radical to become a stable diamagnetic molecule. DPPH in ethanol shows a strong absorption band at 517 nm (independent of pH from 5.0 to 6.5) and the solution appears to be deep violet in color. As the DPPH radical is scavenged by the donated hydrogen from the antioxidant, the absorbance is diminished according to the stoichiometry. The degree of discoloration indicates the scavenging potential of the antioxidant compounds. At first 5 test tubes were taken to make aliquots of 4 different concentrations level (4, 8, 15 and 30 μg/mL). Tested samples and ascorbic acid were weighed 3 times and dissolved in ethanol to make the required concentrations by dilution technique. DPPH was weighed and dissolved in ethanol to make 0.004% (w/v) solution. To make homogeneous solutions of the tested samples, magnetic stirrer was used. After making the desired concentrations, 2 mL of 0.004% DPPH solution was applied on each test tube by using pipette. The room temperature was recorded and kept the test tubes for 30 minutes in light exposure to complete the reactions. DPPH was also applied on the blank test tubes at the same time where only ethanol was taken as blank. After 30 minutes, absorbance of each test tube was determined by UV spectrophotometer. Ascorbic acid was used as a positive control. The percentage of scavenging activity was calculated by using the formula:

% Inhibition = (Ac – At / Ac) x 100

Where, Ac = absorbance of control, At = absorbance of test compound/ascorbic acid.

The percentage (%) inhibition curves for ascorbic acid and samples were plotted against concentration, from which IC_{50} values of percentage inhibition of DPPH by ascorbic acid and samples were calculated using regression equation. Calculated antioxidant data of all the test samples **5(a-f)** were summarized in (Table **6**).

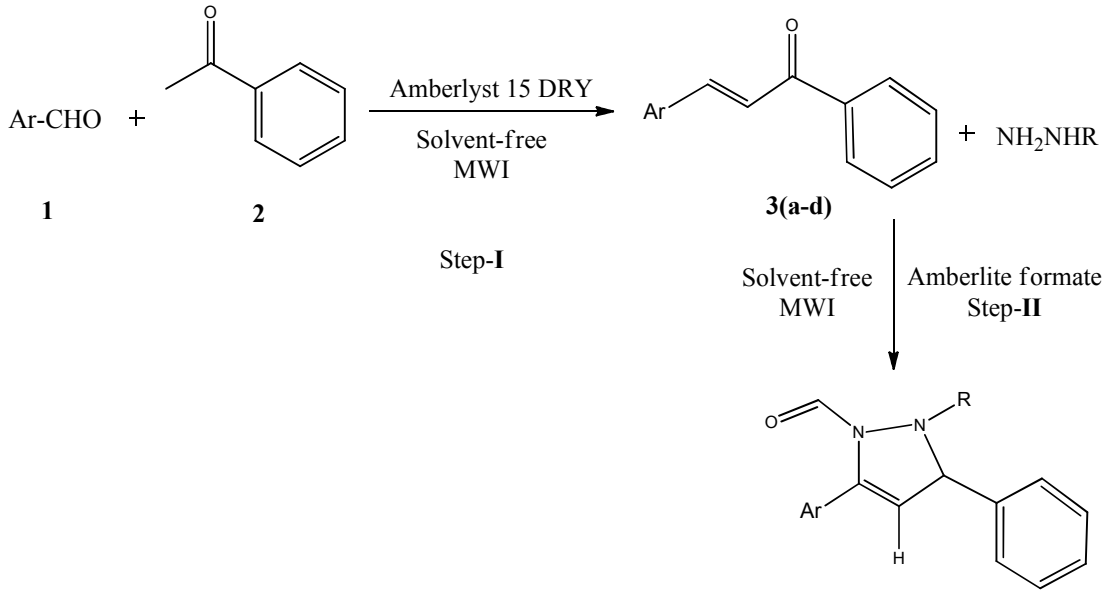
Antibacterial activity

Antibacterial activity of the prepared compounds **5(a-f)** was tested by the disk diffusion method against two gm +ve and two gm -ve bacteria *Bacillus subtilis, Micrococcus, Salmonella typhi, Escherichia coli* respectively. Whatman No. 1 filter paper disks were sterilized by autoclaving for 1 h at 140^0C. All the synthesized compounds were dissolved in DMSO for dilution to prepare stock solutions of 100 μg/mL for antibacterial assay. Agar plates were uniformly surface inoculated with fresh broth culture of *B. subtilis, Micrococcus, S. typhi, E. coli.* The impregnated disks were placed on the medium suitably spaced apart and the plates were incubated at 30^0C for 1 h to permit good diffusion and were then transferred to an incubator at 37 ± 2^0C for 24 h. The zones of inhibition were measured on mm scale and recorded (Table **7**). Ciprofloxacin was used as standard antibacterial drug. Dimethylsulphoxide was used as solvent control.

Antifungal activity

Antifungal susceptibility test was done by disk diffusion method [34] using Sabouraud's dextrose agar medium. After sterilization, the medium was inoculated with *Aspergillus niger, Aspergillus flavus, Alternaria.* The standard antifungal agent Griseofulvin (100 μg/mL), solvent control (0.5% v/v Tween 80), and the newly synthesized compounds **5(a-f)** in a concentration of 100 μg/ml were then added by sterile micropipette. The plates were then incubated at 37^0C for 24 h and the diameter of zone of inhibition was measured and recorded (Table **8**).

RESULTS AND DISCUSSION



Scheme-1 **5(a-f)**

The method used in the present work is general and can be used for wide range of reactants with different groups. We have synthesized some new compounds containing 1-*H*-pyrazol-1-carbaldehyde moiety (Table **1**). All the reactions delivered good to excellent yield with range of diversities. All the final products **5(a-f)** obtained are new and were synthesized from chalcones **3(a-d)**. In the present work, different aldehydes were condensed with acetophenone to give respective chalcones as intermediates with an excellent yield (95%) (step **1**). These products **3(a-d)** were further used to synthesize series of new 1-*H*-pyrazol-1-carbaldehydes (step **2**), in which they condensed with hydrazines to form substituted N-formylated pyrazolines. All the reactions were carried out in solvent free

condition. We found that the use of non conventional heating method reduced the rection time with several folds. The pure products were isolated by simple filtration without use of any separation technique.

Table 1 - Physical data of synthesized compounds 3(a-d) & 5(a-f)

Product	Ar	R	Time (min)	M.P. (°C)	Yield[a] (%)	Elemental analysis Calculated Observed
3a	C_6H_5	---	4	55-56	85	C, 80.36; H, 5.30; C, 80.37; H, 5.29;
3b	m-$C_6H_4(OCH_3)$	---	3	72-73	88	C, 80.65; H 6.35; C, 79.65; H,6.92;
3c	$C_6H_4(OH)$	---	3	153-155	95	C, 80.34; H, 5.39 C, 81.34; H, 5.39
3d	C_5H_4N	----	2	157-159	85	C, 80.34; H, 5.39 C, 81.34; H, 5.39
5a	C_6H_5	H	2	108-110	90	C, 76.78; H, 5.64; N,11.90 C, 76.68; H,5.35; N, 11.36
5b	C_6H_5	C_6H_5	4	123-125	88	C, 80.96; H, 5.56; N, 8.58 C, 80.96; H, 5.56; N, 8.01
5c	m-$C_6H_4(OCH_3)$	C_6H_5	3	112-114	74	C,71.70; H, 5.25; N, 16.72 C, 70.90; H, 5.45; N, 16.21
5d	O-$C_6H_4(OH)$	H	4	150-152	80	C, 72.58; H,6.09; N, 9.96 C, 72.55; H, 6.00; N, 9.56
5e	C_5H_4N	H	2	110-112	79	C, 71.70; H, 5.25; N,16.72 C, 70.70; H, 5.25; N, 16.04
5f	C_5H_4N	C_6H_5	3	133-135	85	C, 77.04; H,5.23; N,12.84 C, 76.99; H, 5.01; N,11.92

[a]*Isolated Yields*

The important feature of the present scheme is the use of ion exchange resins as catalysts in both the steps of scheme *viz.* Amberlyst 15 DRY and Amberlite formate in macro reticular bead form. Being heterogeneous, they can be easily separated from reaction mixture making the work up procedure simple and can be recycled and reused for several times.

Amberlyst 15 DRY a strong acidic cation exchange resin was used in step **1** and it was realized that there is complete transformation of starting material into desired product. Amberlyst 15 DRY is heterogeneous in nature and is easy to remove by simple filtration. It was observed that reaction works very fast and efficient in solvent free condition and with simple work-up procedure. Microwave irradiation reduces reaction time from hrs to minutes and reaction was completed in 2-4 min with excellent yields. The results were compared by carrying out synthesis of **3a** as a model reaction using other acidic resins catalysts and are summarized in Table **2**.

Table 2: Synthesis of 3a using different acidic resin catalysts

Entry	Ion exchange resin	Time (min)[a]	Yield (%)[b]
1	Amberlite IRA 120	5-7	58
2	Indion 130	9-10	64
3	Amberlyst15 DRY	2-4	88

[a]*Reaction condition: Ketone (0.01 mol), aldehyde (0.01 mol) Amberlyst 15 DRY (0.50mg), MWI-4min, solvent-free condition.* [b] *isolated yields.*

In order to optimize the reaction conditions the synthesis of compound **3a** was used as the model reaction. Therefore, a mixture of acetophenone (1.0 mol), aldehyde (1.0 mol) and different amounts of Amberlyst 15 DRY was taken (Table **3**). The efficiency of the reaction is affected by amount of catalyst. Maximum yield was obtained at 0.50 mg. This was the optimum amount of catalyst for the reaction.

Table 3: Synthesis of 3a using different amounts of Amberlyst 15 DRY

Entry	Amount of catalyst (mg)	Time (min)	Yield (%)
1	Nil	8	Nil
2	0.25	6.5	60
3	0.50	3	90
4	0.75	3	85
5	1.0	3	80

Condensation of chalcones which were prepared in step **1** was carried out with different hydrazines to give pyrazolines by using amberlite formate anion exchange resin which was prepared from commercially available Amberlite 900C (Cl^- form). Amberlite formate is a macro reticular heterogeneous catalyst which exchanged formate ion with hydroxyl ion produced in the reaction. Due to heterogeneous nature it was separated by simple filtration, and could be recycled and reused. Microwave irradidiation (MWI) made the reaction more efficient as it reduced reaction time to significantly short period, and reaction was completed in 2-4 min with excellent yields of products **5(a-f)**. The results were compared by carrying out synthesis of **5a** as a model reaction in MWI using other N-formylating reagents and are summarized in Table **4**.

Table 4: Synthesis of 5a using different formylating agents

Catalyst	Condition	Time (min)	Yield (%)
Ammonium formate	Solvent free/300watt	5	60
SiO_2/HCOOH	solvent free/450watt	7.5	74
Amberlite formate	solvent free/300watt	4	92

In order to optimize the reaction conditions the synthesis of compound **5a** was used as the model reaction. Therefore, a mixture of chalcone and hydrazine (1:1) using different amounts of amberlite formate was taken. The efficiency of the reaction was affected by amount of catalyst. Maximum yield was obtained at 150 mg (Table **5**). So it was the optimum amount of catalyst for the reaction.

Table 5: Synthesis of 5a using different amounts of Amberlite formate

Entry	Amount of Catalyst (mg)	Time (min)	Yield (%)
1	Nil	5	Nil
2	100	4	55
3	125	3	87
4	150	3	91
5	200	3	86

Synthesis of these compounds revealed that it is safe, rapid, economic and convenient, eco friendly method. Pollution free synthesis, lesser reaction time, and easy work-up, are the major advantages of this technique. An important advantage of this method is selection of solvent free condition which prevents the formation of by-products and also makes it economical. It can be termed as e-chemistry because it is easy, effective, economical and eco-friendly and is believed to be a step towards green chemistry. In general the reactions are cleaner, fast and high yielding. The applications of microwave irradiation as a non conventional energy sources for the activation of reaction has now become popular and useful technology in organic reactions.

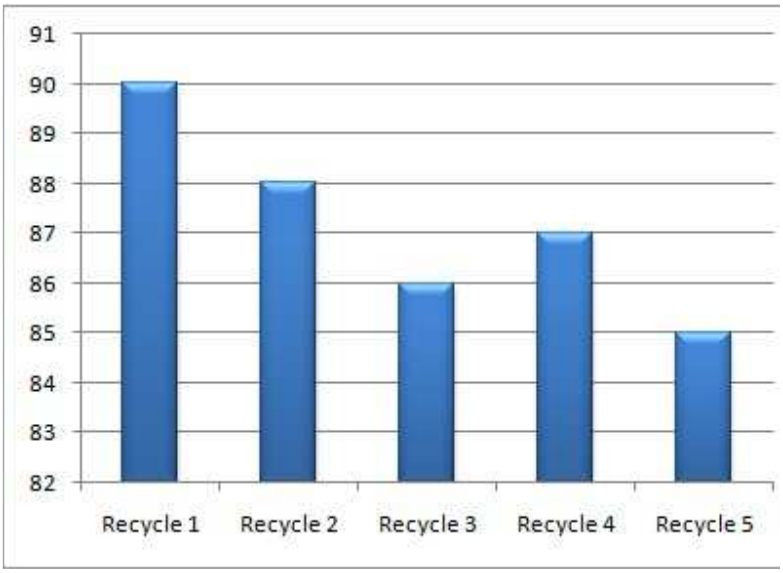
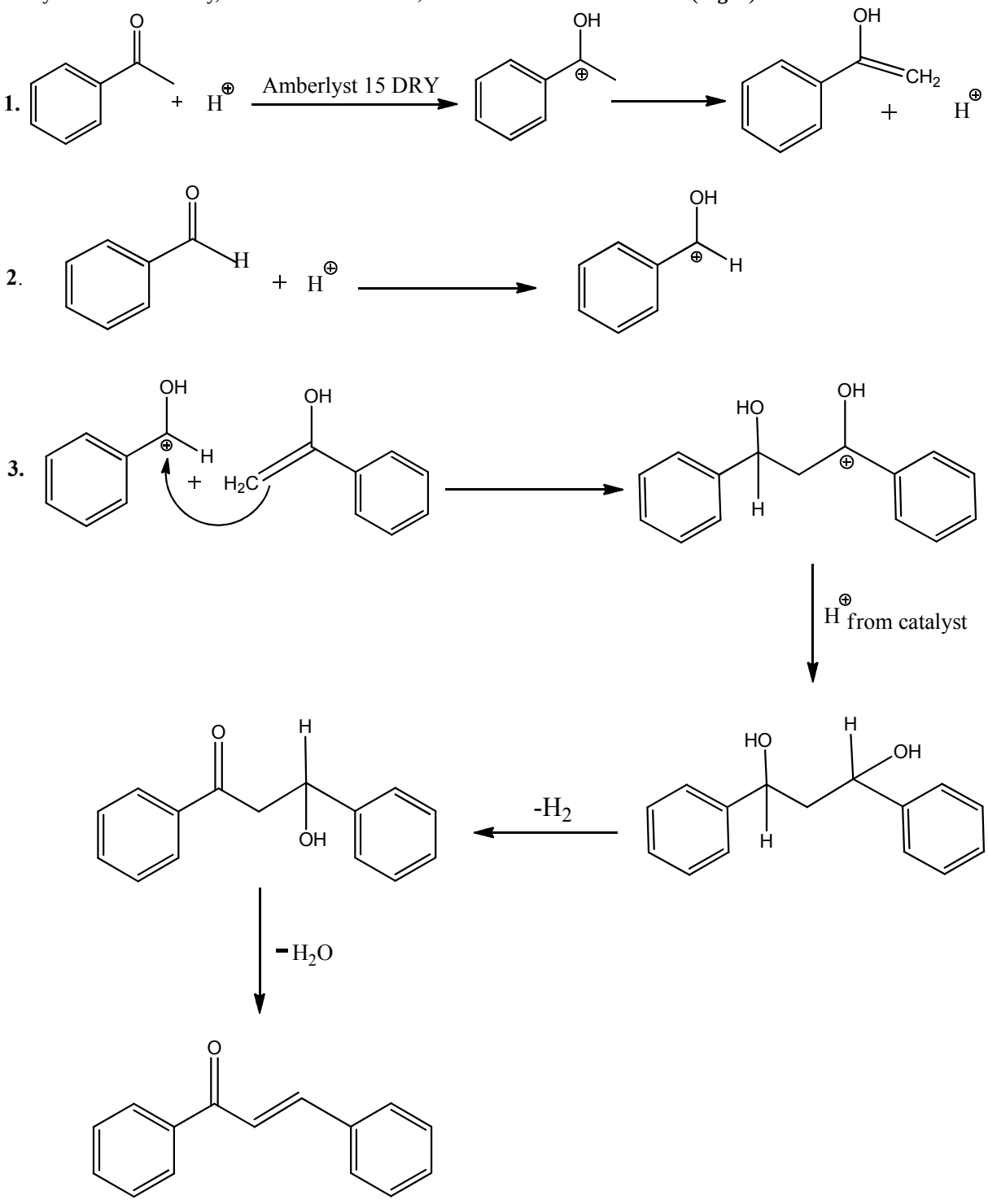


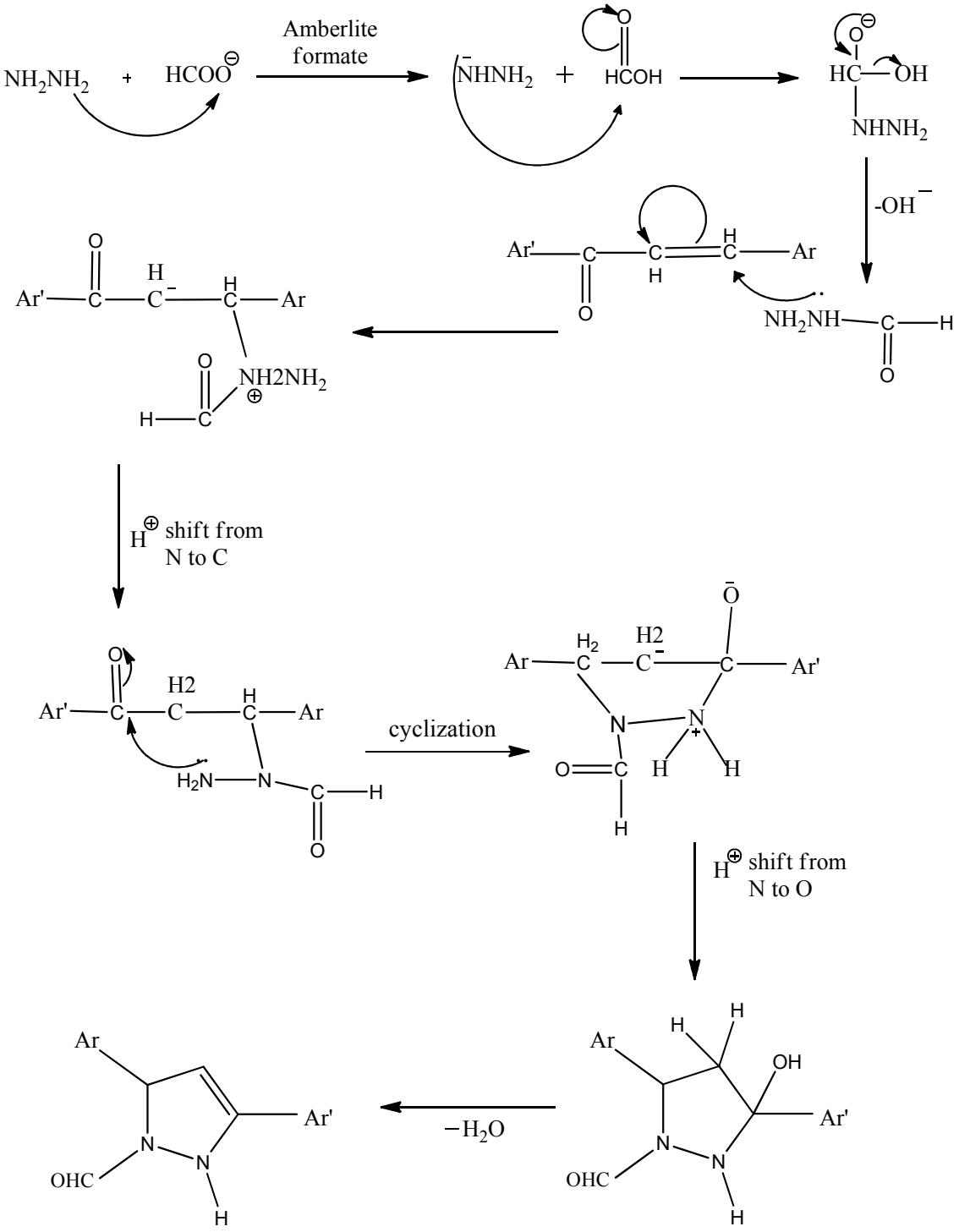
Fig.1: Recyclization chart of amberlite formate showing %yield

We found that amberlite formate shows good catalytic activity and could be recovered and recycled for 4-5 times without significant loss of activity. At the end of each reaction, the catalyst was filtered, washed with hot ethanol and diethyl ether successively, dried at 160°C for 1 hr, and reused in another reaction (**Fig. 1**).



3(a-d)

Proposed mechanism for the formation of Chalcones 3(a-d) using Amberlyst15 DRY (Step1)



Proposed mechanism for the formation of 1-*H*-pyrazol-1-carbaldehydes 5(a-f) using Amberlite formate (Step 2)

In step1, the Amberlyst 15 DRY catalyses the reaction by protonating carbonyl oxygen of acetophenone and aldehyde thereby producing carbonium ion intermediates which then undergo condensation to form chalcones **3(a-d)**. However in step **2**, amberlite formate which is an anion exchange resin provides formate ion and takes up OH^- ion produced in the reaction. The formate ion reacts with hydrazine to produce formyl hydrazine, which further

reacts with chalcone to form N-formyl pyrazoline ring. And thus, new products, 1-*H*-pyrazol-1-carbaldehyde derivatives **5(a-f)** were obtained.

As per chemical structural features there were six different types of compounds **5(a-f)** synthesized under the study area. All the compounds have N-H bonding in the pyrazoline ring system so that hydrogen radical could be generated and the ring-nitrogen radical can scavenge the damaging radicals to prevent further oxidation. But compound **5f** was found to be the most efficacious antioxidant among all compounds. Actually pyrazoline ring is responsible to initiate the free radical scavenging activity by means of reactive nitrogen species (RNS). In the compounds **5a** and **5b** pyrazoline ring is associated with unsubstituted phenyl rings so these compounds showed milder activity whereas in the compound **5c, 5d** pyrazoline ring system is associated with methoxy and hydroxy substituted phenyl ring which enhanced the activity. **5e** and **5f** showed most significant activity due to greater number of nitrogen atoms in different ring systems of the compounds.

Table 6: In vitro free radical scavenging effect of drugs by DPPH Method for compounds 5(a-f)

Entry	Drug	% Scavenging activity (Mean ± SEM)				IC_{50}
		Dose Concentration µg/ml				
		4 µg/ml	8 µg/ml	15 µg/ml	30 µg/ml	
1	**Ascorbic acid**	21.35 ± 0.002	22.54 ± 0.002	31.4 ± 0.001	23.77 ± 0.001	15.5
2	**5a**	24.00 ± 0.002	32.11 ± 0.002	14.35 ± 0.001	34.06 ± 0.002	21.6
3	**5b**	33.80± 0.001	45.22 ± 0.002	56.17 ± 0.001	43.13 ± 0.002	20.5
4	**5c**	42.44 ± 0.002	44.03 ± 0.002	54.11 ± 0.002	49.55 ± 0.002	17.6
5	**5d**	42.78± 0.001	46.28 ± 0.001	45.45 ± 0.002	65.22 ± 0.002	8.4
6	**5e**	35.17 ± 0.002	40.33 ± 0.002	67.27 ± 0.002	34.26 ± 0.001	7.45
7	**5f**	31.28 ± 0.001	40.33 ± 0.001	61.47 ± 0.004	75.23 ± 0.002	12.13

Values are expressed as mean ±SEM;

The compounds **5(a-f)** were screened against two Gm -ve and two Gm +ve bacteria and the results indicated that (Table **7**) all the compounds showed antibacterial activity using Ciprofloxacin as a control. Among all the compounds **5f** was found to be most active against all the tested microorganisms. **5e** gave good activity against *Bacillus subtilis* and *Micrococcus* (Gm +ve) bacteria but the compound **5c** was found to be merely active against most of the selected microorganisms. The compounds **5a** and **5b** exhibited significant activity against all screened bacteria. **5d** was found to be most sensitive against *Salmonella typhi* and *E.coli* (Gm -ve).

Table 7: Screening of compounds 5(a-f) for their antimicrobial activity *in vitro* (zone of inhibition in mm diameter)

Culture	Compound						
	Standard (Ciprofloxacin)	5a	5b	5c	5d	5e	5f
Gm +ve bacteria							
Bacillus Subtilis	34	20	20	06	12	16	20
Micrococcus	12	-	18	09	10	10	25
Gm-ve bacteria							
Salmonella typhi	25	25	20	-	24	06	20
Escherichia Coli	28	16	18	-	28	08	12
DMSO	-	-	-	-	-	-	-

The synthesized compounds **5(a-f)** were screened against three fungi *viz. Aspergillus nigar*, *Aspergillus flavus* and *Alternaria*. The results (Table **8**) indicated that almost all the compounds show antifungal activity. Among these compounds, **5f** and **5d** showed excellent antifungal activity against all the fungi. **5c, 5d** and **5e** were found to be most active against *Aspergillus nigar* but show good activity against *Aspergillus flavus* and *Alternaria*. **5a** was found to be inactive against *Aspergillus nigar* and *Aspergillus flavus*. **5b** showed good to better activity against all the microorganisms.

Table 8: Screening of compounds 5(a-f) for their antifungal activity in vitro (zone of inhibition in mm diameter)

Culture	Compound						
	Standard (Griseofulvin)	5a	5b	5c	5d	5e	5f
Aspergillus niger	11	-	11	24	23	25	16
A. Flavus	09	-	06	18	16	10	12
Alternaria	14	12	08	10	14	10	14

CONCLUSION

In summary, we have reported an efficient, simple, convenient, and practical procedure for the synthesis of pyrazol-1-carbaldehyde derivatives **5(a-f)** under microwave irradiation in aqueous media. Reaction of hydrazine on the synthesized chalcones **3(a-d)** gave corresponding products **5(a-f)** in good yields. All starting materials are readily available from commercial sources. Moreover, there is no need for dry solvents or protecting gas atmospheres. Using of ion exchange resin catalysts *viz.* Amberlyst 15 DRY, Amberlite formate and microwave irradiation offers advantages including simplicity of operation, easy workup, time minimizing, and high yields of products. The procedure is very simple and can be used as an alternative to the existing procedures.

Acknowledgements
The authors are thankful to SAIF - IIT Bombay for providing spectral analysis and Department of Chemistry, Vikram University, Ujjain for extending laboratory facilities and IR data. The authors are also grateful to Anis Shaik, Institute of Pharmacy, Vikram University, Ujjain for providing microbiological facilities.

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