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Synthesis of 2-[{2-(1-Acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy}methyl]-5-aryl-1,3,4-oxadiazoles and related compounds as potential pesticides

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Cyclization of substituted chalkones **3a,b** with hydrazine hydrate followed by acylation of the resulting 3-aryl-4,5-dihydro-5-(2-hydroxyphenyl)-1*H*-pyrazoles (**4a,b**) with alkanoic acids furnished 1-acyl-3-aryl-4,5-dihydro-5-(2-hydroxyphenyl)-1*H*-pyrazoles (**5a-d**). The compounds **5a-d** are also directly prepared by refluxing **3a,b** with hydrazine hydrate in alkanoic acids. Alkylation of **5a-d** with ethyl chloroacetate yields the corresponding aryloxyacetates **6a-d**. Aminolysis of the ester **6a-d** results in the formation of corresponding substituted aryloxyacetamides **7a-ℓ**. Hydrazinolysis of esters **6a-d** with hydrazine hydrate followed by cyclization of the resulting aryloxyacetic acid hydrazides **8a-d** with aromatic acids in refluxing $POCl_3$ affords the title compounds **9a-t**. The compounds **3-9** have been evaluated for their *in vitro* growth-inhibitory activity against four fungal pests, *Alternaria helianthus, Colletotrichum falcatum, fusarium oxysporum* and *Rhizoctonia solani*. Many of the compounds have displayed promising activity at different concentrations ranging from 3.13 – 100 mg L^{-1}.

Keywords: Dihydropyrazoles, Oxadiazoles, Pyrazolyloxadiazoles, Antifungal activity, Pesticidal activity

The derivatives of 3,5-diaryl-4,5-dihydro-1*H*-pyrazoles (**A**) have gained the reputation as useful agrochemicals for their various pesticidal and related activities like antifungal, antibacterial, insecticidal etc.[1-7] 2-Aryl-5-aryloxymethyl-1,3,4-oxadiazoles (**B**) are also reported to posses useful biological activities.[8-16] With a hope to improve upon the activity of such compounds, we report, herein, the synthesis of the hitherto unknown title compounds 2-[{2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)-phenoxy}methyl]-5-aryl-1,3,4-oxadiazoles (**9**) and related derivatives which incorporate structural features of both **A** and **B** and their *in vitro* growth-inhibitory activity against some fungal pests (Fig. 1).

Experimental Details

The melting points were determined in open glass capillaries on an electrically heated melting point apparatus and are uncorrected. Homogeneity of the compounds was routinely checked on silica gel G TLC plates using hexane - ethyl acetate or methanol ethyl acetate mixtures as irrigants. The IR spectra in KBr pallets were recorded on a Perkin-Elmer infrared spectrophotometer model 621 and frequencies are expressed in cm^{-1}. The ^1H NMR spectra were recorded on a Bruker AC 300 F instrument (300 MHz) in deuterochloroform or otherwise indicated using tetramethylsilane as an internal reference and chemical shifts are expressed in δ values. The compounds were analyzed for C, H and N and the values were found within ±0.4% of the theoretical values.

The representative examples of synthetic methods adopted for preparation of various compounds (Scheme 1) are described below. Other analogs are prepared using similar methods from appropriate starting compounds. The compounds showed expected spectral characteristics. However, only those spectral data, which have a direct relevance towards structural elucidation, are included here. The characterization data of the compounds is given in Table 1.

2-Hydroxy-4'-methylchalkone (3b): A mixture of 4-methylacetophenone (**1b**, 13·4 g, 0.1 mol) and salicylaldehyde (**2**, 12.2 g, 0.1 mol) was added to a cold (10°C) methanolic solution of potassium hydroxide (5.6%, 200 mL) with constant stirring. The stirring was continued for 48 h. The reaction mixture was diluted with water, and acidified with dilute sulfuric acid. The solid, thus separated, was filtered, washed with water, dried and recrystallized from methanol to give 11.9 g of **3b**, yield 50%, m.p. 160°C. ^1H NMR : 2.42 (s, 3H, CH_3), 6.86 [dd (t), 1H, H-5,

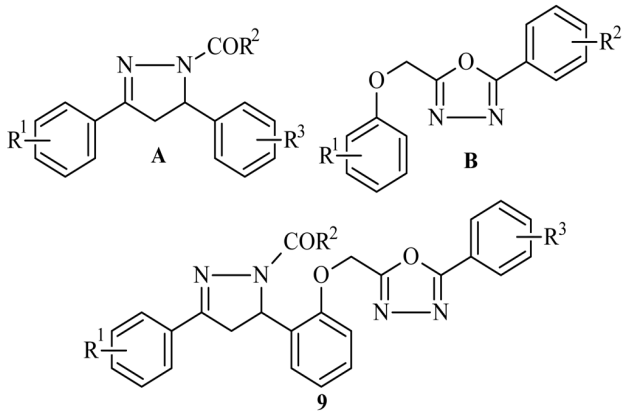
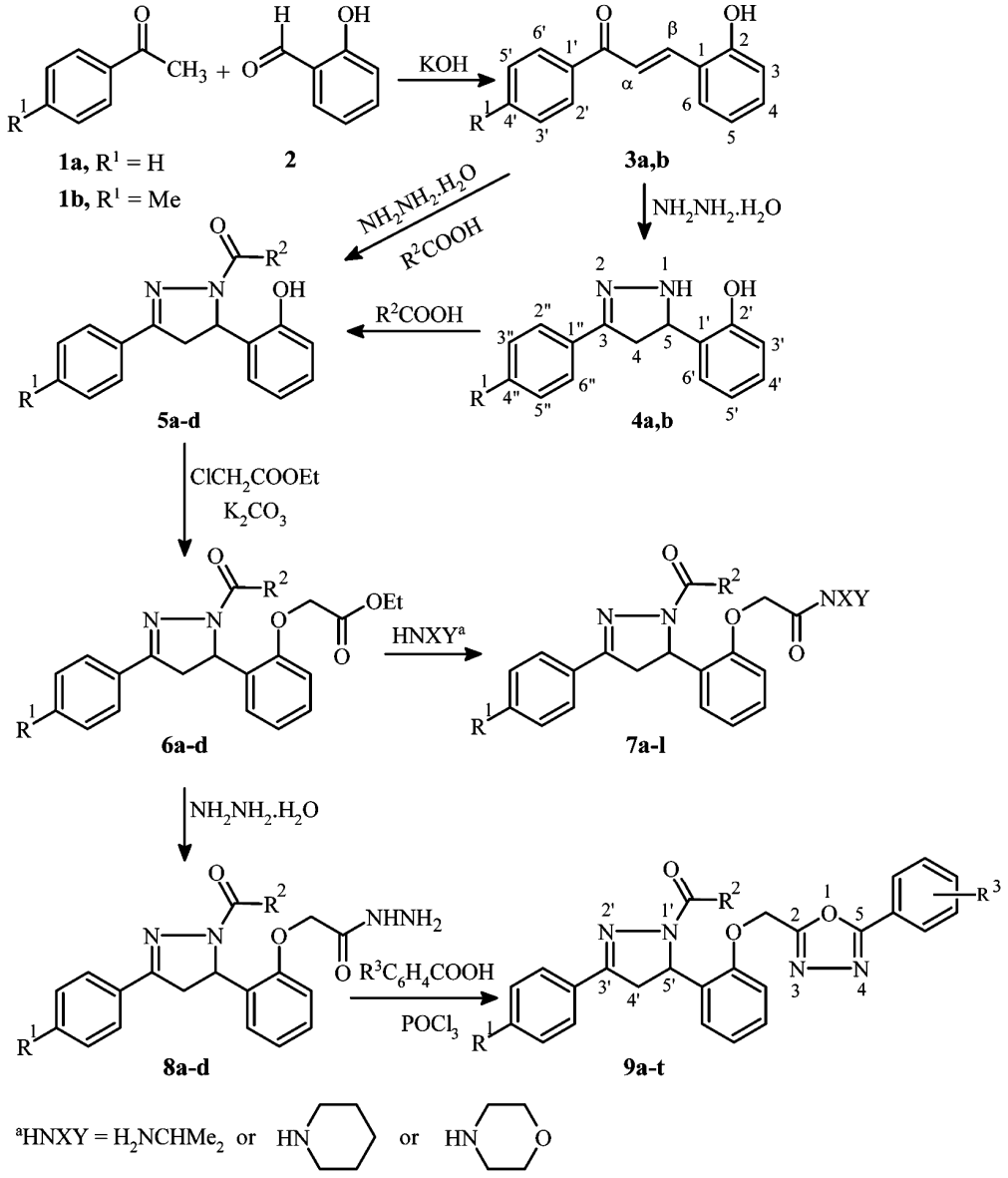


Fig. 1 — Structure of compound **A**, **B** and **9**

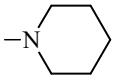
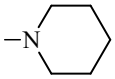
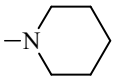
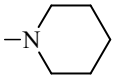
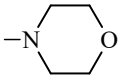
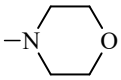
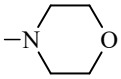
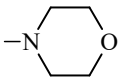
J = 8 and 8 Hz), 6.96 (d, 1H, H-3, J = 8 Hz), 7.21 (ddd, 1H, H-4, J = 2, 8 and 8 Hz), 7.29 (d, 2H, H-3' and H-5', J = 8 Hz), 7.56 (dd, 1H, H-6, J = 2 and 8 Hz), 7.71 (dd, 1H, H-α, J = 16 Hz), 7.93 (dd, 2H, H-2' and H-6', J = 8 Hz), 8.09 (d, 1H, H-β, J = 16 Hz); IR:3125 (OH), 1640 C=O). Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92%. Found C, 80.81; H 6.04.

4,5-Dihydro-5-(2-hydroxyphenyl)-3-phenyl-1*H*-pyrazole (4a): A solution of **3a** (11.2 g, 0.05 mole) in methanol 50 mL was refluxed with hydrazine hydrate (6 mL, excess) for 14 h. The reaction mixture was cooled and poured onto crushed ice with stirring. The solid, thus separated, was filtered, washed with water,



Scheme 1 — Synthesis of pyrzolylphenocmethyloxadizoles

Table 1 — Characterization data and antifungal activity results of 2-[{2-(1-Acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy} methyl]-5-aryl-1,3,4-oxadiazoles and their intermediates

Compd. No.	R^1	R^2	R^3 or NXY	Molecular formula	Yield (%)	m.p. (°C)	MIC (mg L^{-1}) against[a]			
							A. helianthus	*C. falcatum*	*F. oxysporum*	*R. solani*
3a	H	-	-	$C_{15}H_{12}O_2$	80	155	50	50	3.13	25
3b	Me	-	-	$C_{16}H_{14}O_2$	50	160	100	100	50	50
4a	H	-	-	$C_{15}H_{14}N_2O$	84	190	50	100	50	100
4b	Me	-	-	$C_{16}H_{16}N_2O$	80	163	50	100	25	50
5a	H	Me	-	$C_{17}H_{16}N_2O_2$	64[b]	247	100	100	100	100
5b	Me	Me	-	$C_{18}H_{18}N_2O_2$	75[b]	167	100	100	50	50
5c	H	Et	-	$C_{18}H_{18}N_2O_2$	74[b]	216	-	-	-	50
5d	Me	Et	-	$C_{19}H_{20}N_2O_2$	50[b]	90	25	50	100	100
6a	H	Me	-	$C_{21}H_{22}N_2O_4$	80	186	-	-	50	-
6b	Me	Me		$C_{22}H_{24}N_2O_4$	82	105	50	100	25	100
6c	H	Et	-	$C_{22}H_{24}N_2O_4$	67	106	100	-	25	100
6d	Me	Et	-	$C_{23}H_{26}N_2O_4$	53	90	100	100	100	100
7a	H	Me	$NHCHMe_2$	$C_{22}H_{25}N_3O_3$	69	170	100	100	-	100
7b	Me	Me	$NHCHMe_2$	$C_{23}H_{27}N_3O_3$	68	145	50	50	100	-
7c	H	Et	$NHCHMe_2$	$C_{23}H_{27}N_3O_3$	71	145	-	-	-	-
7d	Me	Et	$NHCHMe_2$	$C_{24}H_{29}N_3O_3$	65	135	100	50	100	50
7e	H	Me		$C_{24}H_{27}N_3O_3$	60	127	50	100	-	100
7f	Me	Me		$C_{25}H_{29}N_3O_3$	56	132	100	-	-	100
7g	H	Et		$C_{25}H_{29}N_3O_3$	67	92	100	12·5	6·25	-
7h	Me	Et		$C_{26}H_{31}N_3O_3$	68	120	100	100	100	100
7i	H	Me		$C_{23}H_{25}N_3O_4$	64	118	-	-	-	-
7j	Me	Me		$C_{24}H_{27}N_3O_4$	51	gum	50	-	100	50
7k	H	Et		$C_{24}H_{27}N_3O_4$	66	120	100	100	50	-
7l	Me	Et		$C_{25}H_{29}N_3O_4$	57	181	-	100	100	50
8a	H	Me	-	$C_{19}H_{20}N_4O_3$	68	167	100	100	12·5	-
8b	Me	Me	-	$C_{20}H_{22}N_4O_3$	68	160	-	100	100	100
8c	H	Et	-	$C_{20}H_{22}N_4O_3$	90	175	-	100	100	12·5
8d	Me	Et	-	$C_{21}H_{24}N_4O_3$	60	208	100	100	100	25
9a	H	Me	H	$C_{26}H_{22}N_4O_3$	68	195	100	6·25	100	100
9b	Me	Me	H	$C_{27}H_{24}N_4O_3$	65	220	-	100	100	100
9c	H	Et	H	$C_{27}H_{24}N_3O_3$	60	145	100	100	-	-
9d	Me	Et	H	$C_{28}H_{26}N_4O_3$	65	210	100	100	100	100
9e	H	Me	4-NO_2	$C_{26}H_{21}N_5O_5$	70	111	100	100	100	100
9f	Me	Me	4-NO_2	$C_{27}H_{23}N_5O_5$	68	220	-	100	50	12·5

(*contd.*)

Table 1 — Characterization data and antifungal activity results of 2-[{2-(1-Acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy} methyl]-5-aryl-1,3,4-oxadiazoles and their intermediates

Compd. No.	R^1	R^2	R^3 or NXY	Molecular formula	Yield (%)	m.p. (°C)	MIC (mg L^{-1}) against[a]			
							A. helianthus	*C. falcatum*	*F. oxysporum*	*R. solani*
9i	H	Me	4-Br	$C_{26}H_{21}BrN_4O_3$	68	178	100	50	25	100
9j	Me	Me	4-Br	$C_{27}H_{23}BrN_4O_3$	65	190	100	100	100	100
9k	H	Et	4-Br	$C_{27}H_{23}BrN_4O_3$	70	180	-	100	25	100
9ℓ	Me	Et	4-Br	$C_{28}H_{25}BrN_4O_3$	72	205	-	100	100	6·25
9m	H	Me	4-Cl	$C_{26}H_{21}ClN_4O_3$	72	109	50	100	-	100
9n	Me	Me	4-Cl	$C_{27}H_{23}ClN_4O_3$	65	170	100	12·5	25	100
9o	H	Et	4-Cl	$C_{27}H_{23}ClN_4O_3$	68	164	100	100	50	50
9p	Me	Et	4-Cl	$C_{28}H_{25}ClN_4O_3$	69	170	100	100	100	25
9q	H	Me	3-Cl	$C_{26}H_{21}ClN_4O_3$	75	210	25	-	50	100
9r	Me	Me	3-Cl	$C_{27}H_{23}ClN_4O_3$	70	195	100	100	100	25
9s	H	Et	3-Cl	$C_{27}H_{23}ClN_4O_3$	67	168	-	100	50	100
9t	Me	Et	3-Cl	$C_{28}H_{25}ClN_4O_3$	70	100	100	100	100	12·5
Carbendazim							0·79	-	3.13	0.79

[a]Dash "-" indicates that the compound was inactive upto a tested concentration of 100 mg L^{-1}; [b]Yield described is for method A. Yields obtained using method B for **Va-d** are respectively 72, 80, 68 and 65%, respectively.

dried and recrystallized from methanol to give 10.0 g of **4a**, yield 84%, m.p. 190°C. ^{1}H NMR: 3.13 (dd, 1H, *trans* H-4, J = 14 and 16 Hz), 3.42 (dd, 1H, *cis* H-4, J = 10 and 16 Hz), 4.92 (dd, 1H, H-5, J = 10 and 14 Hz), 6.85 (ddd, 1H, H-5', J = 1, 8 and 8 Hz), 6.92 (dd, 1H, H-3', J = 1 and 8 Hz), 7.06 (dd, 1H, H-6', J = 2 and 8 Hz), 7.22 (ddd, 1H, H-4', J = 2, 8 and 8 Hz), 7.38 – 7.42 (m, 3H, H-3", H-4", and H-5"), 7.65 – 7.69 (m, 2H, H-2" and H-6"); IR: 3000 (br band, OH, NH). Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75·61; H, 5.92; N, 11.76%. Found: C, 75.82; H, 5.92; N, 11.54.

1-Acetyl-4,5-dihydro-5-(2-hydroxyphenyl)-3-(4-methylphenyl)-1*H*-pyrazole (5b): Method A: A solution of **4b** (2.52 g, 0.01 mol) in acetic acid (10 mL) was refluxed for 8 h. The reaction mixture was cooled and poured onto crushed ice with stirring. The separated solid was filtered, washed with water, dried, and recrystallized form methanol to give 2·21 g of **5b,** yield 75%, m.p. 167°C;.^{1}H NMR (10% DMSO-d_6 in $CDCl_3$ v/v): 2.40 (s, 3H, CH_3), 2.41 (s, 3H, $COCH_3$), 3.28 (dd, 1H, *trans* H-4, J = 4 and 18 Hz), 3.72 (dd, 1H, *cis* H-4, J = 12 and 18 Hz), 5.58 (dd, 1H, H-5, J = 4 and 12 Hz), 6.79 [dd (t), 1H, H-5', J = 8 and 8 Hz), 6.90 (d, 1H, H-3', J = 8 Hz), 6.95 (dd, 1H, H-6', J = 2 and 8 Hz), 7.11 (ddd, 1H, H-4', J = 2, 8 and 8 Hz), 7.24 (d, 2H, H-3" and H-5", J = 8 Hz), 7.66 (d, 2H, H-2" and H-6", J = 8 Hz); IR : 3130 (OH), 1620 (C=O). Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52%. Found: C, 73.70; H, 5.92; N 9.18. **Method (B)**: A solution of **3b** (2.38 g, 0.01 mol) in acetic acid (20 mL) was refluxed with hydrazine hydrate (2 mL, excess) for 8 h. The reaction mixture was cooled and worked-up as described in method A to give 2.35g of **5b,** yield 80%, identical in all respects with **5b** prepared using method A.

Ethyl [2-(1-acetyl-4,5-dihydro-3-phenyl-1*H*-pyrazole-5-yl)phenoxy]acetate (6a): A solution of **5a** (2.68 g, 0.01 mol), ethyl chloroacetate (1.22 g, 0.01 mol) in dimethylformamide (20 mL) was stirred with potassium carbonate (1.38 g, 0.01 mol) for 16 h. The reaction mixture was diluted with ice-cold water, the separated solid was filtered, washed thoroughly with water and dried. The product was purified by column chromatography over silica gel using ethyl acetate: hexane mixture as eluent to give 2.92 g of **6a**, yield 80%, m.p. 186°C. ^{1}H NMR: 1.29 (t, 3H, CH_3, J = 7 Hz), 2.47 (s, 3H, $COCH_3$), 3.19 (dd, 1h, *trans* H-4, J = 5 and 18 Hz), 3.77 (dd, 1H, *cis* H-4, J = 12 and 18 Hz), 4.24 (q, 2H, $CO_2CH_2CH_3$, J = 7 Hz), 4.68 (s, 2H, OCH_2), 5.92 (dd, 1H, H-5, J = 5 and 12 Hz), 6.77 (dd, 1H, H-3', J = 1 and 8 Hz), 6.93 (ddd, 1H, H-5', J = 1, 8 and 8), 7.05 (dd, 1H, H-6', J = 2 and 8 Hz), 7.19 (ddd, 1H, H-4', J = 1 and 8 Hz), 7.37-7.41 (m, 3H, H-3", H-4" and H-5"), 7.72-7.75 (m, 2H, H-2" and H-6"); IR: 1730 (ester), 1640 (C=O). Anal. Calcd. for $C_{21}H_{22}N_2O_4$: C, 68·84; H, 6·05; N, 7·65%. Found: C, 68.56; H, 6.09; N, 7.48.

2-[2-(1-Acetyl-4,5-dihydro-3-phenyl-1*H*-pyrazol-5-yl)phenoxy]-N-isopropylacetamide (7a): A

mixture of **6a** (0.37 g, 0.001 mol) and isopropylamine (3 mL, excess) was allowed to stand at room temperature for 240 h. The reaction mixture was then diluted with ice-cold water. The separated solid was filtered, washed with water, dried and recrystallized from methanol to give 0.26 g of **7a**, yield 69%, m.p. 170°C. ^{1}H NMR: 0.99 (d, 3H, CH_3, J = 7 Hz), 1.19 (d, 3H, CH_3, J = 7 Hz), 2.39 (s, 3H, $COCH_3$), 3.23 (dd, 1H, *trans* H-4, J = 5 and 18 Hz), 3.75 (dd, 1H, *cis* H-4, J = 12 and 18 Hz), 4.15 (m, 1H, CH), 4.81 (s, 2H, OCH_2), 6.50 (dd, 1H, H-5, J = 5 and 12 Hz), 6.81 (dd, 1H, H-3', J = 1 and 8 Hz), 6.95 (ddd, 1H, H-5', J = 1, 8 and 8), 7.12 (dd, 1H, H-6', J = 2 and 8 Hz), 7.22 (ddd, 1H, H-4', J = 2, 8 and 8 Hz), 7.45 (m, 3H, H-3", H-4" and H-5"), 7.77 (m, 2H, H-2" and H-6"); Anal. Calcd. for $C_{22}H_{25}N_3O_3$: C, 69.63; H, 6.64; N, 11.07%. Found: C, 69·61; H, 6.45; N, 10.92.

2-[2-(1-Acetyl-4,5-dihydro-3-phenyl-1*H*-pyrazol-5-yl)phenoxy]acetic acid hydrazide (8a). A solution of **6a** (7.32 g, 0.02 mol) in methanol (60 mL) was refluxed with hydrazine hydrate (6 mL, excess) for 12 h. The reaction mixture was cooled and poured onto crushed ice with stirring. The separated solid was filtered, washed with water, dried and recrystallized from methanol to give 4.78 g of **8a**, yield 68%, m.p. 167°C. ^{1}H NMR: 2.40 (s, 3H, $COCH_3$), 3.22 (dd, 1H, *trans* H-4, J = 5 and 18 Hz), 3.77 (dd, 1H, *cis* H-4, J = 11 and 18 Hz), 4.69 (d, 1H, OCH-*H*, J = 16 Hz), 4.76 (d, 1H, OCH-*H*, J = 16 Hz), 6.01 (dd, 1H, H-5, J = 5 and 11 Hz), 6.81 (d, 1H, H-3', J = 8 Hz), 6.95 [dd (t), 1H, H-5', J = 8 and 8), 7.13 (dd, 1H, H-6', J = 1 and 8 Hz), 7.22 (ddd, 1H, H-4', J = 1, 8 and 8 Hz), 7.44 – 7.46 (m, 3H, H-3", H-4" and H-5"), 7.77 – 7.80 (m, 2H, H-2" and H-6"); Anal. Calcd. for $C_{19}H_{20}N_4O_3$: C, 64.76; H, 5.72; N, 15.90%. Found: C, 64.61; H, 5.68; N, 16.04.

2-[{2-(1-Acetyl-4,5-dihydro-3-phenyl-1*H*-pyrazol-5-yl)phenyl}methyl]-5-phenyl-1,3,4-oxadiazole (9a): A mixture of **8a** (0·35 g, 0.001 mol), benzoic acid (0.167 g, 0.001 mol) and phosphoryl chloride (6 mL, excess) was refluxed for 12 h. The reaction mixture was cooled and poured slowly into ice-water with stirring. The precipitated solid was filtered, washed with water, dried and recrystallized from ethanol to give 0·30 g of **9a**, yield 68%, m.p. 195°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6): 2.40 (s, 3H, $COCH_3$), 3.18 (dd, 1H, *trans* H-4', J = 5 and 18 Hz), 3.74 (dd, 1H, *cis* H-4', J = 12 and 18 Hz), 4.58 (d, 1H, OCH-*H*, J = 17 Hz), 5.06 (d, 1H, OCH-*H*, J = 17 Hz), 5.98 (dd, 1H, H-5', J = 5 and 12 Hz); Anal. Calcd. for $C_{26}H_{22}N_4O_3$: C, 71.22; H, 5.06; N, 12.78%. Found: C, 71.04; H, 4.92; N, 12.96.

Bioassay

The compounds were screened for their *in vitro* growth-inhibitory activity against four phytopathogenic fungi namely *Alternaria helianthus, Colletotrichum falcatum, Fusarium oxysporum* and *Rhizoctonia solani*. The cultures were maintained on Czapek's Dox agar slants[21] at 5°C. A standard fungicide, carbendazim (2-methoxycarbamoyl-benzimidazole) was also tested under similar conditions for comparison. Stock solutions of the compounds and standard fungicide at a concentration of 1 mg mL^{-1} were prepared in dimethylsulfoxide. The activity of the compounds against the fungi was carried out using two-fold serial-dilution technique.[6]

Results and Discussion

The starting synthons, 2-hydroxychalkone (**3a**) and 2-hydroxy-4-methylchalkone (**3b**) were prepared by condensation of salicylaldehyde (**2**) with acetophenone (**1a**) and 4-methylacetophenone (**1b**), respectively, in 5.6% methanolic potassium hydroxide at room temperature in good yield (Scheme 1). The compounds **3a,b** were assigned E-configuration because the two olefinic protons H_α and H_β appeared as two AB doublets in ^{1}H NMR spectra with a coupling constant of 16 Hz each.

The cyclization of **3a,b** with hydrazine hydrate in refluxing methanol gave the corresponding 3-aryl-4,5-dihydro-5-(2-hydroxyphenyl)-1*H*-pyrazole (**4a,b**). The first step in this reaction would be nucleophilic attack of hydrazine at carbonyl carbon of chalkone followed by elimination of water leading to the formation of α,β-unsaturated hydrazone which then undergoes intramolecular cyclization at the double bond.[17] However, the possibility of alternative mechanism could not be ruled out[18]. In the ^{1}H NMR spectra of **4a,b**, the two geminal protons at C-4, adjacent to a chiral centre at C-5 showed magnetic non-equivalence and, therefore, appeared at different chemical shifts. These were assigned on the basis of their chemical shifts[19] rather than on the basis of their coupling constants with the proton at C-5, because coupling constants in such compounds are known to be influenced by the nature of N-1 substituents.[20] Accordingly, the one resonating at higher field was

assigned *trans* C-4 H and the one resonating at lower field was assigned *cis* C-4 H with respect to C-5 H.

The dihydropyrazoles **4a,b** were acylated to the corresponding 1-acyl derivatives 5**a-d** by refluxing the former in acetic or propionic acids. The 1-acyl-4,5-dihydropyrazoles 5**a-d** were also prepared directly from **3a,b** in a single step by refluxing these with hydrazine hydrate in acetic or propionic acids. The C-4 and C-5 protons also displayed characteristic chemical shifts and coupling constants in their ^{1}H NMR spectra.[19].

Alkylation of **5a-d** with ethyl chloroacetate in presence of potassium carbonate in dimethylformamide at room temperature gave the corresponding ethyl 2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy]acetates (**6a-d**) in good yield. Besides the characteristic signals for protons at C-4 and C-5, a triplet and a quartet for CH_3 and CH_2 with a coupling constant of 7 Hz each and a singlet for OCH_2 were also observed in their ^{1}H NMR spectra.

Aminolysis of the esters **6a-d** with isopropylamine, piperidine and morpholine yielded the corresponding 2-[2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy]-N-isopropylacetamides (**7a-d**), 1-[{2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy}-acetyl]-piperidines (**7e-h**), and 4-[{2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxyacetyl]morpholines (**7i-ℓ**), respectively. The two methyl groups of isopropyl moiety in N-isopropylacetamide derivatives **7a-d** showed unusual magnetic nonequivalence and appeared as two doublets by coupling with methine proton each with a coupling constant of 7 Hz.

Hydrazinolysis of esters **VIa-d** with hydrazine hydrate in refluxing methanol furnished the corresponding 2-[2-(1-acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy]acetic acid hydrazides (**8a-d**) in good yields. In these compounds, the OCH_2 protons were found magnetically nonequivalent and appeared as AB doublets in their ^{1}H NMR spectra with geminal coupling constants of 16 Hz each besides other expected signals.

Refluxing of hydrazides (**8a-d**) with five different substituted benzoic acids in phosphoryl chloride yielded the corresponding title compounds, 2-[{2-(1-Acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy}-methyl]-5-aryl-1,3,4-oxadiazoles (**IXa-t**). The compounds displayed expected spectral and analytical data.

The antifungal screening data presented in Table 1 indicates that many of the compounds **3-9** were active against the fungi tested at varying concentrations. The most active compound against *A. helianthus* were found to be **5d**, and **9q** which prevented its growth at a concentration of 25 mg litre^{-1}. The compounds **3a, 4a,b, 6b, 7b,e,j** and **9m** were found effective at a concentration of 50 mg litre^{-1}. The remaining other compounds were toxic at 100 mg litre^{-1} except **5c, 6a, 7c,i,ℓ, 8b,c, 9b,f,,h,k,ℓ** and **9s** which were ineffective upto this concentration.

C. falcatum was found most sensitive to **9a** which inhibited its growth at 6.25 mg litre^{-1} concentration. The compounds **7g** and **9n** were active at 12.5 mg L^{-1} while compounds **3a, 5d, 7b,d,** and **9i** were active at 50 mg L^{-1} concentrations. The compounds **5c, 6a, 7c,f,i,j** and **9q** were inactive and remaining compounds were active against *C. falcatum* at 100 mg L^{-1} concentration.

The compound **3a, 7g** and **8a** were active against *F. oxysporum* at concentrations as low as 3.13, 6.25 and 12.5 mg L^{-1}, respectively. The compounds **4b, 6b,c, 9i,k,** and **9n** at 25 mg L^{-1} and compounds **3b, 4a, 5b, 6a, 7k, 9f,o,q** and **9s** at 50 mg L^{-1} concentrations also registered their activity against this fungus. Majority of the remaining compounds were active at 100 mg L^{-1} concentration except **5c, 7a,c,e,f,i, 9c,h,** and **9m** which were unable to prevent its growth upto 100 mg L^{-1} concentration.

The most toxic compound against *R. solani was* found to be **9ℓ** (MIC 6.25 mg L^{-1}) followed by **8c, 9f,h** and **9t** (MIC 12.5 mg L^{-1}). The compounds **8d, 9p** and **9r** were found active against this fungus at 25 mg litre^{-1} while **3b, 4b, 5b,c, 7d,j,ℓ** and **9o** at 50 mg L^{-1} concentrations. Except the compounds **6a, 7b,c, g,i,k, 8a** and **9c** which were inactive upto a concentration of 100 mg L^{-1}, all remaining compounds were active at this concentration.

Though none of the compounds could surpass the activity of carbendazim, however, the promising activity shown by some of the compounds may offer a suitable lead for synthesis of more active compounds by further structural modifications. The mixed pattern of activity results also did not allow us to draw structure activity correlations.

Conclusion

2-[{2-(1-Acyl-3-aryl-4,5-dihydro-1*H*-pyrazol-5-yl)phenoxy}methyl]-5-aryl-1,3,4-oxadiazoles and related compounds were synthesized, characterized and evaluated for their *in vitro* growth-inhibitory activity against four fungal pests, *A. helianthus, C. falcatum, F. oxysporum* and *R. solani*. Many of the compounds have

displayed promising activity at different concentrations ranging from 3.13 – 100 mg L^{-1}.

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