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Synthesis of Pyrazoles via Vilsmeier Haack reaction and their pyrazolone, thiazolidinedione derivatives: A comparative study of conventional and microwave routes

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Abstract: Phenyl hydrazine treated with variable acetophenone to give substituted phenyl carbonyl hydrazone compounds, 1-(1-substituted -2-ylethylidene)-2-phenylhydrazine (1a-e). This is undergoing cyclization by using Vilsmeier-Haack reaction and afforded compounds 3-substituted-2-yl-1-phenyl-1H-pyrazole-4-carbaldehyde (2a-e). The reaction of an N,N disubstituted formamide, such as DMF or N-methylformanilide, with acid chlorides, such as phosphoryl chloride or phosgene, leads to the formation of an adduct, this adduct usually referred to as a Vilsmeier Haack reagent. In one path compound 2a-e reflux with pyrazolone and give compound 4-[(3-substituted -2-yl-1-phenyl-1H-pyrazol-4-yl)methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3a-e), in another pathway compounds 2(a-e) react with thiazolidione and give target molecule compounds 5-{[3-(4-substitutedphenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-1,3-thiazolidine-2,4-dione (4a-e). The structures of all the synthesized compounds were supported by spectral and analytical studies.

Keywords: Vielsmeier-Haack reaction, Phenyl hydrazine, Substituted Acetophenone, Pyrazolone, Thiazolidione, Spectral data.

Introduction

In this study, pyrazole, thiazole and their derivative were synthesized using conventional synthesis and microwave assisted synthesis which clearly indicates that synthesis of pyrazole derivatives in microwave afforded better yield in short time via eco-friendly route. Azoles have played a crucial part in the history of heterocyclic chemistry and also been used extensively as important synthons in organic synthesis. Owing to the versatile chemotherapeutical activities of azoles, a significant amount of research activity has been directed towards this class. Pyrazole is a important class of heterocycles due to their synthetic versatility and effective biological activity [1-3].They have been found to possess antifungal [4], antidepressant, anticonvulsant [5-8], anti-inflammatory [9], antibacterial [10-11] andanti-tumor [12], antitubercular [13] and insecticidal [14] properties. Thaizolidinediones serve as basic pharmacophore for various biological profiles i.e. Antidiabetic [15] , Anticancer [16-19], Antimicrobial [20-25] , and Anti-inflammatory [26-27] and so on. Thiazolidinediones have recently received a lot of attention because of their wide range of therapeutic and pharmacological properties. Thiazolidinediones acts by binding to PPARs (Peroxisome Proliferator Activated Receptors) [28], antihyperglycemic activity [29], and antihyperglycemic activity [29-31]. 2,4-thiazolidinediones are one of the most important classes of the anti-HIV activity [32-35]. Recent publications on thiazolidinedione have documented a new class of NNRTIs, 2,3-diaryl-1,3-thiazolidin-4-one

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derivatives, that proved to be highly effective in inhibiting HIV-1 replication at nanomolar concentrations acting as RT inhibitors, from the structure -/activity relationship (SAR) point of view, the anti-HIV activity is strongly dependent on the nature of the substituents at C-2 and N-3 of the thiazolidinone ring [36-37]. Pyrazole and thiazolidinediones containing compounds have practical applications in the agrochemical and medicinal field and the biological activity of its derivatives are well documented [38-40].

Results and discussion

Compound 1a was achieved by treatment with various acetophenone and phenyl hydrazine. The structure of this compound is confirmed by presence of a singlet at δ5.15 due to (N-H) group. Compound 2a is synthesized by a Vielsmeier-Haack reaction of 1a-e. The structures of this compounds were elucidate by IR absorptions at 1670 cm-1 due to the C=O group. The absorption bands associated with other functionalities present all appeared in the expected regions. The 1H NMR spectra of the compound 2a exhibited a sharp singlet at δ 9.59 corresponding to the CHO proton of the pyrazole ring. The N-H proton of 1a was replaced from Vilsmeier Haack reaction. Compounds 3a-e and 4a-e achieved by two different route, in first path the compound 2a condensed with pyrazole and gives final compounds 3a. In another path compound 2a refluxed with thiazolidinedione to achieve targeted molecule (4a). Compound 3a shows the IR spectra of C=O group at 1705 cm-1and 4a displayed absorption band for C=O group at 1710 cm-1. Compound 4a also shows 1H NMR at δ 5.10 of NH group which was present in its precursor. All the synthesized compounds are tested for anti-bacterial and anti-fungal activity.

Rection Scheme

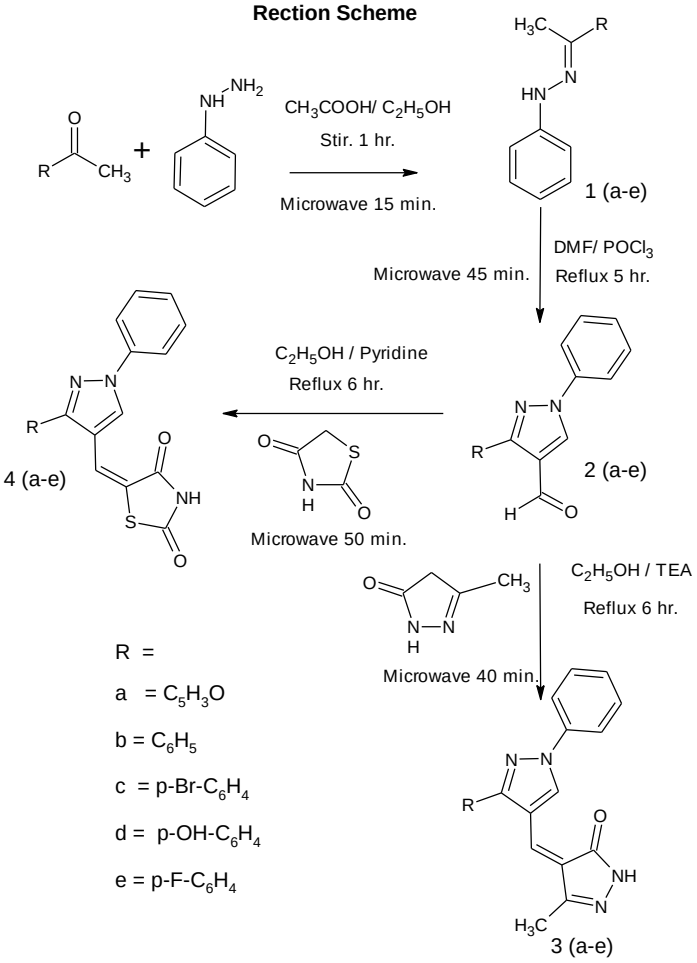

Table I: Physical and analytical data of new synthesized compounds 1a-e, 2a-e, 3a-e and 4a-e:

Com.	Mol.formula	MW	mp °C	Yield (%) Co/mw	(%) of C Found/cal.	(%) of H Found/cal.	(%) of N Found/cal.	(%) of S Found/cal.
1a	$C_{12}H_{12}N_2O$	200	83	70/90	71.28/71.98	6.01/6.04	13.87/13.99	-
1b	$C_{14}H_{14}N_2$	210	92	75/92	79.90/79.97	6.70/6.71	13.30/13.32	-
1c	$C_{14}H_{13}BrN_2$	289	99	74/91	58.20/58.15	4.55/4.53	9.71/9.69	-
1d	$C_{14}H_{14}N_2O$	226	97	76/88	74.29/74.31	6.21/6.24	12.36/12.38	-
1e	$C_{14}H_{13}FN_2$	228	101	72/90	73.65/73.66	5.71/74	12.24/12.27	-
2a	$C_{14}H_{10}N_2O_2$	238	98	75/95	70.55/70.58	4.19/4.23	11.74/11.76	-
2b	$C_{16}H_{12}N_2O$	248	142	74/93	77.37/77.40	4.85/4.87	11.27/11.28	-
2c	$C_{16}H_{11}BrN_2O$	327	145	70/88	58.77/58.74	3.42/3.39	8.58/8.56	-
2d	$C_{16}H_{12}N_2O_2$	264	147	72/85	72.62/72.72	4.49/4.58	10.52/10.62	-
2e	$C_{16}H_{11}FN_2O$	266	149	75/86	72.02/72.17	4.03/4.16	10.40/10.52	-
3a	$C_{18}H_{14}N_4O_2$	318	182	80/90	67.81/67.91	4.35/4.43	17.10/17.60	-
3b	$C_{20}H_{16}N_4O$	328	186	82/92	73.05/73.15	4.79/4.91	16.97/17.06	-
3c	$C_{20}H_{15}BrN_4O$	407	190	80/89	59.01/58.98	3.73/3.71	13.77/13.76	-
3d	$C_{20}H_{16}N_4O_2$	344	188	75/90	69.64/69.76	4.66/4.68	16.20/16.27	-
3e	$C_{20}H_{15}FN_4O$	346	194	74/88	69.28/69.35	4.35/4.37	16.14/16.18	-
4a	$C_{17}H_{11}N_3O_3S$	337	160	75/90	60.42/60.52	3.28/3.29	12.43/12.46	9.48/9.50
4b	$C_{19}H_{13}N_3O_2S$	347	165	76/92	65.60/65.69	3.76/3.77	12.08/12.10	9.22/9.23
4c	$C_{19}H_{12}BrN_3O_2S$	426	169	80/90	53.55/53.53	2.86/2.84	9.88/9.86	7.54/7.52
4d	$C_{19}H_{13}N_3O_3S$	363	167	82/92	62.70/62.80	3.60/3.61	11.54/11.56	8.80/8.82
4e	$C_{19}H_{12}FN_3O_2S$	365	170	81/90	62.36/62.46	3.30/3.31	11.48/11.50	8.75/8.78

Biological activity:

Preliminary antibacterial and antifungal susceptibility tests for all the synthesized compounds 3a-e and 4a-e were performed by using cup and well method [31]. In the present investigation all the synthesized compounds were screened at 200 ppm against various pathogenic strains viz. B. subtilis, S. typhi, P. aeruginosa and E. coli, for antibacterial and A. fumigatus and C. albicans for antifungal activity.

Standard (Std.) drugs used for antibacterial and antifungal activity were Ciprofloxacin and Fluconazole respectively. The screening results have been summarized in Table **II**. It is clear that compound 4a possesses strong activity against B. subtilis, while other compounds 4c and 4d show poor to moderate activity. Compounds 3d exhibit good to strong activity against P. Aeruginosa and, 3b and 3c compounds show moderate activity against bacteria. Similarly compound 3a shows good activity against A. fumigatus fungal strains as compared to standard drugs. Compound 4c gives good activity against C. albicans. Hence, the conclusion can be drawn that synthesized compounds are better antibacterial agents than antifungal.

Table II: Antimicrobial activity of synthesized compounds on 200 ppm 3a-e and 4a-e:

	Zone of inhibition (mm),					
	Antibacterial activity				antifungal activity	
Compd	B. subtilis	E. coli	S. typhi	P. aeruginosa	A. fumigatus	C. Albicans
3a	++	++	++	++	+++	++
3b	++	+	++	++	++	++
3c	++	++	+	++	+	++
3d	+	++	++	++++	++	++
4a	++++	++	+	++	+	+
4b	+++	+	++	+	++	++
4c	++	+	+	++	++	+++
4d	+	+	++	+	+	++
STD_1	+++	+++	++	+++	--	--
STD_2	--	--	--	--	+++	+++

+ = 10-14 (poor activity), ++ =15-18(moderate activity), +++ = 19-22 (good activity), ++++ = 23-26 (strong activity).

Standard:

STD_1 =Ciprofloxacin, STD_2 = Fluconazole,

Conclusion

All the synthesized compounds are tested for anti bacterial and antifungal activity .In the synthesized compound 4a possesses strong activity against B. subtilis, and 3b and 3c compounds show moderate activity against bacteria. Similarly compound 3a shows good activity against A. fumigatus fungal strains as compared to standard drugs.

Experimental

All melting points were determined in open capillary tube and are uncorrected. The IR spectra were recorded on Perkin-Elmer-1800 spectrometer. The 1H NMR spectra ($CDCl_3$) were scanned on a DRX-300 (300 MHz) spectrometer using TMS as internal standard and chemical shifts are expressed in δ, ppm. The mass spectra were recorded on Jeol SX-102 (FAB) spectrometer. Microwave induced reaction were carried out in CATA scientific microwave synthesis system (2450 MHz, catalyst system, INDIA). Purity of synthesized compounds was checked by element analysis and homogeneity was checked by TLC using

silica gel-G, as adsorbent and visualization was accomplished by iodine.

Conventional Synthesis of 1-(1-furan-2-ylethylidene)-2-phenylhydrazine (1a):

The compound Acetyl furan (0.01 M) taken in Dry round bottom flask and added 15 ml ethanol with gla. acetic acid as a catalytic amount. The above solution, Phenyl hydrazine (0.01 M) added drop -wise, the reaction mixture further stirrer for 1 hrs at room temperature. after the completion of reaction indicated by TLC, the shiff base formed which was isolated and recrystallized from ethanol.

Microwave assisted synthesis of 1-(1-furan-2-ylethylidene)-2-phenylhydrazine (1a):

The compound Acetyl furan (0.01 M) taken in Dry round bottom flask and added 15 ml ethanol with glacial acetic acid as a catalytic amount. The reaction mixture was transferred in an Erlenmeyer flask and irradiated under microwave irradiation for 15 min with a time interval of 40 seconds, after the completion of reaction indicated by TLC, the shiff base formed which was isolated and recrystallized from ethanol.

IR (KBr) cm^{-1}: 3346 (N-H str), 3085 (Ar-H, str.), 2875 (CH_3 str.), 1621 (C=N str.), 1520 (N-N); ^{1}H-NMR ($CDCl_3$) δ: 7.01-8.10 (m, 8H, aromatic), 5.15 (s,1H, N-H) 3.21 (s, 1H, CH_3); MS: m/z 200 [M]+., 133, 105, 77, 29.

Similarly, compounds 1b-e were prepared with some change in stirrer time and reaction work up.

(1-phenyl-2-(1-phenylethylidene)hydrazine (1b):

IR (KBr) cm^{-1}: 3351 (N-H str), 3090 (Ar-H, str.), 2880 (CH_3), 1625 (C=N str.), 1523(N-N); ^{1}H-NMR ($CDCl_3$) δ: 7.11-8.19 (m, 10H, Ar-H), 5.21 (s,1H, N-H), 3.27(s, 1H, CH_3); MS: m/z 210 [M]+., 133, 118, 92, 77, 15.

1-[1-(4-bromophenyl)ethylidene]-2-phenylhydrazine (1c):

IR (KBr) cm^{-1}: 3354 (N-H str), 3095 (Ar-H, str.), 2882 (CH_3), 1627 (C=N str.), 1525 (N-N); ^{1}H-NMR ($CDCl_3$) δ: 7.15-8.25 (m, 9H, Ar-H), 5.25 (s, 1H, N-H), 3.32 (s, 1H, CH3); MS: m/z 288 [M]+., 290[M+2]+., 200, 133, 106, 77, 29.

4-[-N-phenylethanehydrazonoyl]phenol(1d):

IR (KBr) cm^{-1}: 3422 (OH str), 3353 (N-H str), 3093 (Ar-H, str.), 2881 (CH_3), 1626 (C=N str.), 1524 (N-N), ^{1}H-NMR ($CDCl_3$) δ: 7.12-8.20 (m, 9H, Ar-H), 5.23 (s,1H, N-H), 3.29 (s, 1H, CH_3), 4.59 (s, 1H, O-H); MS: m/z226 [M]+., 149., 132, 104, 76, 27.

1-[1-(4-fluorophenyl)ethylidene]-2-phenylhydrazine (1e):

IR (KBr) cm^{-1}: 3360 (N-H str), 3095 (Ar-H, str.), 2885 (CH_3), 1630 (C=N str.), 1530 (N-N); ^{1}H-NMR ($CDCl_3$) δ: 7.21-8.30 (m, 9 H, Ar-H), 5.32 (s,1H, N-H), 3.36 (s,1H, CH_3), MS: m/z228[M]+., 151., 95.

Conventional Synthesis of 3-furan-2-yl-1-phenyl-1H-pyrazole-4-carbaldehyde (2a):

1-(1-furan-2-ylethylidene)-2-phenylhydrazine (0.01 mol) was added in mixture of Vilsmeier-Haack reagent (prepared by drop wise addition of 3 ml of $POCl_3$ in ice cooled 25 ml dimethyl formamide) and refluxed for 5 hrs at 600 C. The reaction mixture was poured into ice followed by neutralization using NaOH, and heat 50-600^{o}C, cooled and acidified to pH = 6 by 10 M HCl the solid thus obtained which was filtered and recrystallized from methanol.

Microwave assisted synthesis of 3-furan-2-yl-1-phenyl-1H-pyrazole-4-carbaldehyde (2a):

1-(1-furan-2-ylethylidene)-2-phenylhydrazine (0.01 mol) was added in mixture of Vilsmeier-Haack reagent (prepared by drop wise addition of 3 ml of $POCl_3$ in ice cooled 25 ml dimethyl formamide). The reaction mixture was transferred in an Erlenmeyer flask and reflux irradiated under microwave irradiation at 500 for 45 min. with a time interval of 35 seconds. The reaction mixture was poured into ice followed by neutralization using NaOH, and heat 50-600 C, cooled and acidified to pH = 6 by 10 M HCl the solid thus obtained which was filtered and recrystallized from methanol.

IR (KBr) cm^{-1}: 3034 (Ar-H, str.), 2856, 2720 (CHO, str.), 1670 (C=O, str.), 1604 (C=N str.), 1511 (N-N); ^{1}H NMR ($CDCl_3$) δ: 7.24-7.41 (m, 8H, Ar-H), 6.62 (s, 1H, pyrazole ring), 9.59 (s, 1H, CHO); MS: m/z238 [M]+., 161, 132, 65.

Similarly, compounds 2b-e were prepared with some change in reflux time and reaction work up.

1,3-diphenyl-1H-pyrazole-4-carbaldehyde (2b):

IR (KBr) cm^{-1}: 3080 (Ar-H, str.) , 2820, 2745 (CHO, str.), 1734 (C=O, str.), 1620 (C=N str.), 1521 (C-N), 1507 (N-N); ^{1}H NMR ($CDCl_3$) δ: 7.02-7.94 (m, 10 H, Ar-H), 6.89 (s, 1H, pyrazole ring), 9.64 (s, 1H, CHO); MS: m/z 248 [M]+., 171, 142, 65.

3-(4-bromophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (2c):

IR (KBr) cm^{-1}: 3085 (Ar-H, str.), 2856, 2760 (CHO, str.), 1734 (C=O, str.), 1630 (C=N str.), 1525 (N-N); ^1H NMR ($CDCl_3$) δ: 7.06-7.99 (m, 9 H, Ar-H), 6.94 (s, 1H, pyrazole ring), 9.68 (s, 1H, CHI); MS: m/z 328 [M]+., 330[M+2]+., 247, 170, 141, 65.

3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (2d):

IR (KBr) cm^{-1}: 3081 (Ar-H, str.), 3421(O-H str.), 2840, 2770 (CHO, str.), 1732 (C=O, str.), 1628 (C=N str.), 1523(N-N); ^1H NMR ($CDCl_3$) δ: 7.03-7.96 (m, 9H, Ar-H), 6.92 (s, 1H, pyrazole ring), 9.67 (s, 1H, CHO), 5.23 (s,O-H str.); MS: m/z 264 [M]+., 187, 158, 141, 65.

3-(4-fluorophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (2e):

IR (KBr) cm^{-1}: 3086 (Ar-H, str.), 2890, 2782 (CHO, str.), 1740 (C=O, str.), 1665 (C=N str.), 1528 (N-N); ^1H NMR ($CDCl_3$) δ: 7.16-8.05 (m, 9H, Ar-H), 6.98(s, 1H, pyrazole ring), 9.84 (S, 1H, CHO); MS: m/z 266 [M]+., 189, 160, 141, 65.

Conventional Synthesis of 4-[(3-furan-2-yl-1-phenyl-1H-pyrazol-4-yl)methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3a):

Take a 100 ml two -necked flask and charged 20 ml ethanol and use triethylamine as a catalytic amount than added pyrazolone, Compound 5 (0.001M) and compound 2 (0.001M). The mixture was refluxed for 5-6 hrs. After complete the reaction, the reaction-mixture was poured on crushed ice. The solid obtained was isolated and recrystallized from ethanol.

Microwave assisted Synthesis of 4-[(3-furan-2-yl-1-phenyl-1H-pyrazol-4-yl)methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3a):

Take a 100 ml two -necked flask and charged 20 ml ethanol and use triethylamine as a catalytic amount than added pyrazolone, Compound 5 (0.001M) and compound 2 (0.001M). The reaction mixture was transferred in an Erlenmeyer flask and reflux irradiated under microwave irradiation for 40 min. with a time interval of 20 seconds. After complete the reaction, the reaction-mixture was poured on crushed ice. The solid obtained was isolated and recrystallized from ethanol.

IR (KBr) cm^{-1}: 3346 (N-H, str.), 3050 (Ar-H, str.) 2948 (CH_3, str.), 1705 (C=O, str.), 1661 (C=N str.), 1505 (N-N); ^1H NMR ($CDCl_3$) δ: 7.10-8.10 (m, 8H, Ar-H), 6.41 (s, 1H, C=C-H, pyrazole ring) , 5.91 (s, 1H, C=C-H), 5.10 (s,1H, N-H), 3.11(s,1H, CH_3); MS: m/z 318 [M]+., 241, 226, 211, 132, 65.

Similarly, compounds 3b-e were prepared with some change in stirrer time and reaction work up.

4-[(1,3-diphenyl-1H-pyrazol-4-yl)methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3b):

IR (KBr) cm^{-1}: 3330 (N-H, str.), 3080 (Ar-H, str.), 2957 (CH_3, str.), 1715 (C=O, , str.), 1665 (C=N str.), 1510 (N-N); ^1H NMR ($CDCl_3$) δ: 7.15-8.15 (m, 9 H, Ar-H), 6.50 (s, 1H, C=C-H, pyrazole ring), 5.95 (s, 1H, C=C-H) 5.54 (s,1H, N-H), 3.32 (s,1H, CH_3); MS: m/z 328 [M]+., 251, 236, 221, 142, 65.

4-{[3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3c):

IR (KBr) cm^{-1}: 3334 (N-H, str.), 3082 (Ar-H, str.), 2941(CH_3), 1720 (C=O, str.), 1668 (C=N str.), 1515 (N-N); ^1H NMR ($CDCl_3$) δ: 7.25-8.25 (m, 9H, Ar-H), 6.71 (s, 1H, C=C-H, pyrazole ring), 6.25 (s, 1H, C=C-H), 5.70 (s, 1H, N-H), 3.42 (s, 1H, CH_3); MS: m/z 408 [M]+., 410[M+2]+., 327, 312, 296, 218, 141, 65.

(4-4-{[3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3d):

IR (KBr) cm^{-1}: 3420 (O-H str.), 3331 (N-H, str.), 3080 (Ar-H, str.), 2947 (CH_3, str.), 1710 (C=O, str.), 1667 (C=N str.), 1511 (N-N); ^1H NMR ($CDCl_3$) δ: 7.23-8.21 (m, 9 H, Ar-H), 6.65 (s, 1H, C=C-H pyrazole ring), 6.20 (s, 1H, C=C-H) ,5.65 (s, 1H N-H), 3.39 (s,1H CH_3); MS: m/z 344 [M]+., 267, 251, 236, 158, 141, 65.

4-{[3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-5-methyl-2,4-dihydro-3H-pyrazol-3-one (3e):

IR (KBr) cm^{-1}: 3335 (N-H, str.), 3085 (Ar-H, str.), 2955 (CH_3, str.), 1715 (C=O, str.), 1675 (C=N str.), 1516(N-N); ^1H NMR ($CDCl_3$) δ: 7.27-8.26 (m, 9H, Ar-H), 6.85 (s, 1H, C=C-H, pyrazole ring), 6.35 (s, 1H, C=C-H), 5.80 (s,1H, N-H), 3.50 (s,1H, CH_3); MS: m/z 346 [M]+., 269, 254, 238, 163, 141, 65.

Conventional Synthesis of 5-[(3-furan-2-yl-1-phenyl-1H-pyrazol-4-yl)methylidene]-1,3-thiazolidine-2,4-dione 4a):

Take a 100 ml two -necked flask and charged 20 ml ethanol and use triethylamine as a catalytic amount than added Thiazolidinedione, Compound 6 (0.001M)

and compound 2 (0.001M). The mixture was refluxed for 5-6 hrs. After complete the reaction, the reaction-mixture was poured on crushed ice. The solid obtained was isolated and recrystallized from ethanol or methanol.

Microwave assisted Synthesis of 5-[(3-furan-2-yl-1-phenyl-1H-pyrazol-4-yl)methylidene]-1,3-thiazolidine-2,4-dione (4a):

Take a 100 ml two -necked flask and charged 20 ml ethanol and use triethylamine as a catalytic amount than added Thiazolidinedione, Compound 6 (0.001M) and compound 2 (0.001M). The reaction mixture was transferred in an Erlenmeyer flask and reflux irradiated under microwave irradiation for 50 min. with a time interval of 25 seconds. After complete the reaction, the reaction-mixture was poured on crushed ice. The solid obtained was isolated and recrystallized from ethanol or methanol.

IR (KBr) cm^{-1}: 3326 (N-H, str.), 3090 (Ar-H, str.), 1710 (C=O, str.), 1662 (C=N, str.), 1501(N-N), 1280 (C-S); ^{1}H NMR ($CDCl_3$) δ: 7.02-8.10 (m, 8H, Ar-H), 6.12 (s,1H,C=C-H, pyrazole ring) , 5.12 (s, 1H, C=C-H), 5.10 (s, 1H, N-H); MS: m/z337 [M]+., 260, 244, 228, 132, 65.

Similarly, compounds 4b-e were prepared with some change in stirrer time and reaction work up.

5-[(1,3-diphenyl-1H-pyrazol-4-yl)methylidene]-1,3-thiazolidine-2,4-dione (4b):

IR (KBr) cm^{-1}: 3330 (N-H, str.), 3092 (Ar-H, str.), 1715 (C=O, str.), 1666(C=N, str.), 1504 (N-N), 1285 (C-S, str.); ^{1}H NMR ($CDCl_3$) δ: 7.20-8.30 (m, 10H, Ar-H), 6.30 (s,1H, C=C-H, pyrazole ring) , 5.70 (s, 1H, C=C-H), 5.30 (s,1H, N-H); MS: m/z 347 [M]+., 270, 254, 238, 142, 65.

5-{[3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-1,3-thiazolidine-2,4-dione (4c):

IR (KBr) cm^{-1}: 3335 (N-H, str.), 3094 (Ar-H, str.), 1718 (C=O, str.), 1669 (C=N, str.), 1510 (N-N), 1288 (C-S); ^{1}H NMR ($CDCl_3$) δ: 7.20-8.40 (m, 9H, Ar-H), 6.50 (s, 1H, C=C-H, pyrazole ring), 6.20 (s, 1H, C=C-H), 5.45 (s, 1H, N-H); MS: m/z 427 [M]+., 429 [M+2]+., 346, 269, 253, 237, 141, 65.

5-{[3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-1,3-thiazolidine-2,4-dione (4d):

IR (KBr) cm^{-1}: 3423 (O-H, str.), 3332 (N-H, str.), 1716 (C=O, str.), 1667 (C=N, str.), 1501 (N-N), 1287 (C-S, str.); ^{1}H NMR ($CDCl_3$) δ: 7.20-8.40 (m, 9H, Ar-H), 6.80 (s, 1H, C=C-H, pyrazole ring), 6.20 (s, 1H, C=C-H), 5.70 (s,1H,N-H), 5.25(s,1H, O-H); MS:m/z 363 [M] +, 286, 270, 254, 158, 141, 65.

5-{[3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl]methylidene}-1,3-thiazolidine-2,4-dione (4e):

IR (KBr) cm^{-1}: 3340 (N-H, str.), 1735 (C=O, str.), 1670 (C=N, str.), 1510 (N-N), 1292 (C-S); ^{1}HNMR ($CDCl_3$) δ: 7.30-8.50 (m, 9H, Ar-H,), 6.90 (s,1H,C=CH, pyrazole ring), 6.30 (s, C=C-H), 5.80 (s, 1H, N-H); MS: m/z 365[M+], 288, 272, 256, 160, 141, 65.

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