

Novel synthesis and spectral characterization of some new substituted pyrazolones and isoxazolone

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ABSTRACT

A Series of some new substituted pyrazolone derivatives containing different functional groups have been synthesized by the condensation reaction of 2-methoxy-5-methyl ethyl aceto hydrazone (1a) and different substituted phenyl malonamic acid hydrazides (2a-2k) in presence of glacial acetic acid as a catalyst, substituted isoxazolone (4a) have been synthesized by the condensation of 2-methoxy-5-methyl ethyl aceto hydrazone (1a) and hydroxylamine hydrochloride with sodium acetate. The constitution of the synthesized compounds are characterized by their elemental analysis, spectral studies like IR.

Key words: Ethyl Acetohydrazone, Acid hydrazides, Glacial acetic acid, Condensation, Spectral data.

INTRODUCTION

The chemistry and pharmacology of pyrazolone derivatives have been of great inter-est because they possess various biological activities viz: antibacterial¹, antifungal², antiviral³, anticancer⁴, insecticidal⁵ and effective antibacterial⁶ agents. Pyrazolone derivatives are also effective against the metabolism Schistosomiasis in Snails and they have been possess significant biological properties^{7,8}. Pyrazolone are still least explored compounds for anti-inflammatory and analgesic profile. The Isoxazolone belong to an important structural group found in a variety of anti-convulsants⁹, antivirals¹⁰ and analgesics¹¹. Many papers have been published by various workers describing the synthesis of pyrazolone and isoxazolone derivatives in our laboratory¹²⁻¹⁶. Therefore in present work we have synthesized a series of some new substituted pyrazolone derivatives using substituted ethyl aceto hydrazone

with substituted acid hydrazides in presence of glacial acetic acid, substituted isoxazolone are synthesized by substituted ethyl aceto hydrazone and hydroxylamine hydrochloride with sodium acetate.

EXPERIMENTAL

Material

All the melting points were determined on Electro-thermal apparatus in open capillary tubes and were uncorrected. All the chemicals used in the synthesis were obtained from Sigma-Aldrich Company. The IR spectra (KBr-disc) were recorded on Perkin-Elmer spectrum RX-1 FT-IR spectrophotometer at Central Drug Research Institute (CDRI), Lucknow. All synthesized compounds were recrystallised by absolute ethanol. The purities of compounds were checked on silica-gel-coated Al plates (E-Merck). The identity of Newly synthesized compounds was confirm by melting

points, molecular weight, molecular formula, colour, yield%, IR spectral data.

The physical and analytical observations of all synthesized compounds are recorded in Table-1 and their IR spectral data are recorded in Table-2.

Synthesis of ethyl 2,3-dioxobutyrate 2-(2-methoxy-5-methyl)phenyl hydrazone (1a) To primary amine (0.025 mole) was diazotised with concentrated HCl (8ml) and water (7ml) at 0°C-2°C then added the cooled aqueous solution of sodium nitrite to it, after that treated with a well cooled mixture of Sodium acetate(0.12 mole) and ethyl aceto acetate(0.025 mole) in ethanol(25 ml) dissolved in minimum quantity of water.A resulting precipitate of 2-methoxy-5-methyl benzeneazo ethyl aceto acetate started separating out immediately and was collected, washed with cold water.This was recrystallised with hot ethyl alcohol, yield 74.17%. Synthesis of malon (R) anilic acid hydrazide (2a-2k)

To substituted aniline (0.025 mole) and diethyl malonate (0.05 mole) was added with

dimethyl formamide and refluxed for about 45-60 minutes, after that ethanol (20 ml) was added to it , the filtrate was concentrated over water-bath , hydrazine hydrate 99% with ethanol (20 ml) was added to it , the solid thus obtained, after some time recrystallised with absolute ethanol and was identified malon (R) anilic acid hydrazide (2a-2k).

General procedure for the synthesis of 4(2-methoxy-5-methyl)-phenyl hydrazone-N' (R) amino malonyl-3-methyl pyrazolone (3a-3k)

A mixture of (1a;0.001 mole) dissolved in ethanol (10 ml) and (2a-2k;0.001 mole) in glacial acetic acid (3-4 drops) was refluxed for 4-5 hours, the resulting solid was obtained during refluxing, filtered, this was recrystallised from absolute ethanol 99%.General procedure for the synthesis of 3-methyl-4-(2-methoxy-5-methyl phenyl hydrazone)-isoxazolone (4a)

A mixture of (1a;0.001 mole) in excess of ethanol, aqueous solution of hydroxylamine hydrochloride (0.01 mole) dissolved in minimum quantity of water , refluxed for about 4 hours, the resulting product was obtained as crystals on cooling , recrystallised from absolute ethanol 99%.

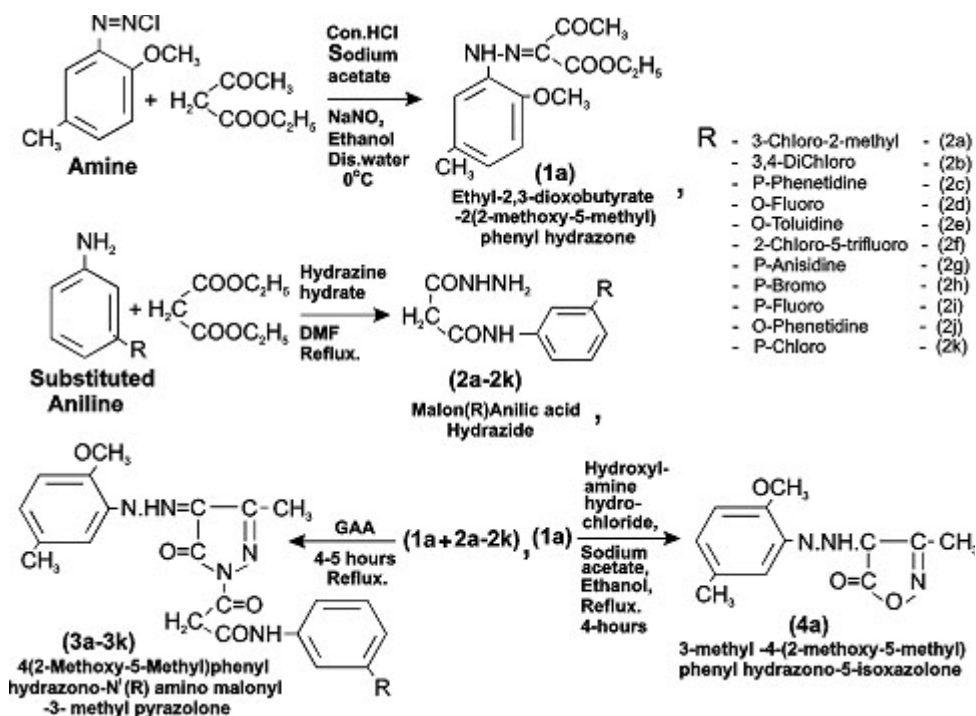


Table 1: Physical and Analytical data of synthesized compounds (1a,2a-2k,3a-3k,4a)

S. Compounds No. code	Molecular Formula	Molecular Weight	Melting Point °C	Yield %	Colour	% Analytical data				
						C cal.%	H cal.%	N cal.%		
1 1a	C ₁₄ H ₁₉ N ₃ O ₄	279.32	92	74.17	sunrise	60.20	6.85	6.87	10.03	10.07
2 2a	C ₁₆ H ₂₃ N ₃ O ₂ Cl ₁	241.68	108	51.46	crystalline white	49.69	5.00	5.01	17.38	17.40
3 2b	C ₁₆ H ₂₃ N ₃ O ₂ Cl ₂	262.11	142	54.38	sugared nut	41.24	3.46	3.48	16.03	16.06
4 2c	C ₁₁ H ₁₅ N ₃ O ₃	237.26	123	40.31	off white	55.68	6.37	6.39	17.71	17.75
5 2d	C ₉ H ₁₃ N ₃ O ₂ F ₁	211.20	89	35.06	white pebble	51.18	4.77	4.78	19.89	19.91
6 2e	C ₁₀ H ₁₃ N ₃ O ₂	207.23	94	32.59	magnolia	57.96	6.32	6.30	20.28	20.29
7 2f	C ₁₀ H ₁₃ N ₃ O ₂ ClF ₃	295.66	135	44.82	cream carress white	40.62	3.07	3.08	14.21	14.25
8 2g	C ₁₀ H ₁₃ N ₃ O ₃	223.24	119	47.15	light coffee	53.80	5.87	5.89	21.50	21.54
9 2h	C ₁₂ H ₁₇ N ₃ O ₂ Br ₁	272.12	124	43.56	morning white	47.59	3.70	3.71	15.44	15.47
10 2i	C ₁₂ H ₁₇ N ₃ O ₂ F ₁	211.20	105	39.37	peach orange	51.18	4.77	4.79	19.89	19.93
11 2j	C ₁₁ H ₁₅ N ₃ O ₃	237.26	134	37.23	crystalline white	55.68	6.37	6.38	17.71	17.74
12 2k	C ₁₃ H ₁₇ N ₃ O ₂ Cl ₁	227.66	166	48.94	crystalline corel white	47.48	4.42	4.44	18.46	18.49
13 3a	C ₂₂ H ₃₄ N ₃ O ₂ Cl ₁	457.93	246	42.99	orange frost	57.69	5.28	5.29	15.29	15.31
14 3b	C ₂₁ H ₃₁ N ₃ O ₂ Cl ₂	478.35	254	47.50	light royal ivory	52.73	4.42	4.45	14.64	14.67
15 3c	C ₂₃ H ₃₇ N ₃ O ₅	453.51	248	58.52	light wheat sprig	60.91	6.00	6.02	15.44	15.48
16 3d	C ₂₁ H ₂₇ N ₃ O ₄ F ₁	427.44	230	38.36	light maize stalk	59.00	5.18	5.19	16.37	16.39
17 3e	C ₂₂ H ₃₅ N ₃ O ₄	423.48	241	35.39	light yellow	62.40	5.95	5.96	16.54	16.57
18 3f	C ₂₂ H ₃₁ N ₃ O ₄ Cl ₁ F ₃	511.91	244	37.21	light yelloweish	51.62	4.13	4.14	13.68	13.72
19 3g	C ₂₂ H ₃₅ N ₃ O ₅	439.48	247	58.16	ivory	60.12	5.73	5.75	15.93	15.96
20 3h	C ₂₁ H ₂₇ N ₃ O ₄ Br ₁	488.36	244	51.54	light caseablanca	51.65	4.54	4.56	14.34	14.38
21 3i	C ₂₁ H ₂₇ N ₃ O ₄ F ₁	427.44	229	32.45	off white	59.00	5.18	5.20	16.37	16.40
22 3j	C ₂₃ H ₃₇ N ₃ O ₅	453.51	261	47.48	royal ivory	60.91	6.00	6.01	15.44	15.47
23 3k	C ₂₁ H ₂₇ N ₃ O ₄ Cl ₁	443.90	259	56.41	off white	56.82	4.99	5.01	15.77	15.82
24 4a	C ₁₂ H ₁₅ N ₃ O ₃	249.27	124	32.77	dark oranguish	57.82	6.06	6.08	16.86	16.89

RESULTS AND DISCUSSION

The IR Spectra of prepared compounds have been recorded in the frequency region 4000-450 cm^{-1} these spectral observations are mentioned in the Table - 2. The literature survey reveals that all of the newly synthesized compounds are Novel. The Infra-red spectrum of 4-(2-methoxy-5-methyl) phenyl hydrazono-N¹ (R) amino malonyl-3-methyl pyrazolone^{3a-3h} showed Absorption in the range 1664.0-1653.0 cm^{-1} confirm the presence of aromatic C=O stretching vibrations, absorption in the range 3297.1-3189.1 cm^{-1} reveals the N-H

stretching, absorption in the range 3051.9-3047.8 cm^{-1} indicated the presence of aromatic -CH, -N=CH stretching vibrations were obtained between the range 2366.6-2365.3 cm^{-1} while absorption at 1598.8-1590.3 cm^{-1} reveals C=N stretching, N-N stretching vibrations were obtained between 1497.6-1486.8 cm^{-1} and absorption at 1241.4-1232.5 cm^{-1} confirm the presence of C-N, absorption in the range 1432.1-1411.9 cm^{-1} reveals the -CH₃ stretching vibrations. The above observations are lent support to the structures of compounds 3a-3h and other compounds (3i-3k).

Table-2: IR Absorption bands

Compound No.	Ar CH Cm^{-1} stretching	NH Cm^{-1} stretching	N=CH Cm^{-1} stretching	C=N Cm^{-1} stretching	Ar C=O Cm^{-1} stretching	C-N Cm^{-1} stretching	N-N Cm^{-1} stretching	CH ₃ Cm^{-1} stretching
3a	3051.1	3291.7	2366.3	1592.3	1653.0	1236.8	1497.6	1432.1
3b	3050.4	3294.2	2365.6	1593.0	1664.0	1232.5	1495.7	1430.0
3c	3051.2	3292.5	2365.5	1590.6	1653.4	1236.2	1497.1	1429.0
3d	3048.7	3290.6	2366.4	1593.0	1655.5	1233.8	1491.2	-
3e	3049.4	-	2366.4	1598.3	1657.0	1232.9	1486.8	1431.0
3f	3047.8	3189.1	2365.3	1598.8	1656.3	1233.6	1489.6	1426.7
3g	3051.9	3297.1	2366.5	1590.3	1654.9	1241.4	1495.4	1411.9
3h	3050.0	3295.0	2366.6	1591.8	1654.3	1234.5	1493.5	1428.0
4a	-	-	2362.6	1562.5	1707.9	-	1498.0	1430.5

The IR Spectrum of 3-methyl-4-(2-methoxy-5-methyl phenyl hydrazono)-isoxazolone^{4a} showed absorption at 2362.6 cm^{-1} reveals N=CH, C=N stretching vibrations were obtained at 1562.5 cm^{-1} while absorption at 1707.9 cm^{-1} Indicate the presence of aromatic C=O group, absorption at 1498.0 cm^{-1} reveals the N-N stretching vibrations, absorption at 1430.5 cm^{-1} indicating the presence

of CH₃ stretching vibrations. These characters are lent support to the structure of compound **4a**.

Thus IR Spectra of all substituted pyrazolones and isoxazolone indicating the absorption spectrum was in agreement with the assigned structures, colouring properties, pyrazolones were found to possess higher melting points.

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