

Novel and efficient synthesis and spectral evaluation of certain new substituted pyrazolones

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ABSTRACT

Series of some new substituted pyrazolones have been synthesized by condensation of the acid hydrazide with different ethylaceto hydrazones in the presence of glacial acetic acid. Characterisation of new compounds has been done by means of spectral data and elemental analysis.

Keywords : Pyrazolone, spectral evaluation, glacial acetic acid, condensation.

INTRODUCTION

Pyrazolones as a class of heterocyclic compounds have been studied extensively for the past several years because of their broad spectrum of biological activity and variety of medicinal applications. However, pyrazolones are still least explored compounds for anti-inflammatory and analgesic profile. Substituted pyrazolones have been reported as bacteriostatic¹, fungicidal², analgesic³, anti-coagulant⁴, anti-rheumatic⁵ and germicidal⁶ activities. Pyrazolones have also been found to possess anti-inflammatory⁷ and anti-bacterial activity⁸. Several substituted pyrazolones and their derivatives have been prepared in our laboratory⁹⁻¹⁴.

So in the present work we have synthesized a series of new pyrazolones. The synthesis involves condensation of synthesized acid hydrazide and ethyl aceto hydrazones in presence of glacial acetic acid.

EXPERIMENTAL

Material

The melting points were determined in open capillary and were uncorrected. All chemicals

used in the synthesis were obtained from Sigma-Aldrich Company. All the Novel synthesized compounds were recrystallised by absolute ethanol. The purity of compounds were checked on silica-gel-coated Al plates (Merck), by using 10% (benzene / methanol) for pyrazolones. The IR spectra (KBr-disc) were recorded on Perkin-Elmer spectrum RX-1 FT-IR at St. John's College, Agra.

The Identity of all newly synthesized compounds was confirmed by melting-point, molecular formula, molecular weight, elemental analysis, IR spectral data. All of these are recorded in Table-1.

Synthesis of malon (3-chloro-4-methoxy) anilic acid hydrazide (1)

To the primary amine (0.025 mole), diethyl malonate (0.05 mole) was added with dimethyl formamide as a catalyst and refluxed for 45-60 minutes, after cooling, ethanol (20 ml) was added, and the filtrate was concentrated over a water-bath, after some time add ethanol (20 ml) and hydrazine hydrate 99%. The mixture was set a side and the solid separated was recrystallised by absolute ethanol and was identified malon (3-chloro-4-methoxy) anilic acid hydrazide (1).

Table 1 : Physical and Analytical data of synthesized compounds

C.No.	Compound Name	Molecular Weight	Molecular Formula	C cal.	Found	H cal.	Found	N cal.	Found	Colour	M.P. (°C)	Yield %
1.	Malon (3-Cl-4-OCH ₃) Anilic Acid Hydrazide	257.68	C ₁₆ H ₁₂ N ₂ O ₃ Cl	46.61	46.65	4.69	4.70	16.30	16.33	White	158°	56.30
2.	Ethyl- (R') 2 (2-Cl-5tri Fluoro Methyl) Phenyl hydrazone	337.72	C ₁₆ H ₁₃ O ₃ N ₂ ClF ₃	45.23	45.26	3.88	3.90	08.29	8.32	Pinkish Yellow	96°	64.65
3.	Ethyl- (R') 2 (2-OC ₂ H ₅) Phenyl hydrazone	279.31	C ₁₄ H ₁₆ O ₂ N ₂	60.26	60.29	6.85	6.88	10.03	10.05	Thar Desert	76°	62.60
4.	Ethyl- (R') 2 (2,5 DiChloro) Phenyl hydrazone	304.16	C ₁₂ H ₁₃ N ₂ O ₂ Cl ₂	47.38	47.42	4.30	4.32	9.21	9.24	Pinkish	84°	68.61
5.	Ethyl- (R') 2 (4-Fluoro) Phenyl hydrazone	205.25	C ₁₂ H ₁₄ N ₂ O ₂ F	70.21	70.25	6.87	6.89	13.64	13.65	Earth Red	62°	69.64
6.	Ethyl- (R') 2 (2-OCH ₃) Phenyl hydrazone	265.29	C ₁₃ H ₁₇ N ₂ O ₄	58.86	58.82	6.45	6.46	10.56	10.57	Light Yellow	75°	60.17
7.	Ethyl- (R') 2 (4-Br) Phenyl hydrazone	314.17	C ₁₂ H ₁₄ N ₂ O ₂ Br	45.87	45.92	4.49	4.51	8.91	8.93	Lemon Yellow	67°	71.34
8.	Ethyl- (R') 2 (3-Chloro) Phenyl hydrazone	234.25	C ₁₂ H ₁₄ N ₂ O ₂	61.52	61.54	6.02	6.03	11.96	11.95	Earth Red	59°	66.04
9.	Ethyl- (R') 2 (3-Cl-2CH ₃) Phenyl hydrazone	283.74	C ₁₆ H ₁₈ N ₂ O ₂ Cl	55.02	55.03	5.68	5.70	9.87	9.89	Dirty Yellow	61°	54.44
10.	Ethyl- (R') 2 (2-CH ₃) Phenyl hydrazone	249.29	C ₁₃ H ₁₇ N ₂ O ₂	62.63	62.66	6.87	6.89	11.23	11.26	Light Yellow	59°	56.43
11.	Ethyl- (R') 2 (2,4 (CH ₃) ₂) Phenyl hydrazone	263.31	C ₁₄ H ₁₈ N ₂ O ₂	63.86	63.90	7.27	7.24	10.64	10.65	Dark Yellow	93°	55.70
12.	Ethyl- (R') 2 (3,5 (CH ₃) ₂) Phenyl hydrazone	263.31	C ₁₄ H ₁₈ N ₂ O ₂	63.86	63.88	7.27	7.28	10.64	10.61	Orange	68°	62.23
13.	Ethyl- (R') 2 (2,5 (CH ₃) ₂) Phenyl hydrazone	263.31	C ₁₄ H ₁₈ N ₂ O ₂	63.86	63.87	7.27	7.26	10.64	10.60	Yellow	56°	54.99
14.	4 - (2Cl 5 F,Methyl) Phenyl hydrazono - R ²	532.33	C ₂₁ H ₁₆ N ₂ O ₂ Cl ₂ F ₅	47.38	47.41	3.40	3.41	13.15	13.18	Lemon Yellow	235°	58.58
15.	4 - (2-OC ₂ H ₅) Phenyl hydrazono - R ²	473.92	C ₂₂ H ₂₄ N ₂ O ₂ Cl	55.75	55.78	5.10	5.11	14.77	14.79	Dark Yellow	230°	60.63
16.	4 - (2,5-DiChloro) Phenyl hydrazono - R ²	498.77	C ₂₀ H ₁₆ N ₂ O ₂ Cl ₂	48.16	48.19	3.63	3.64	14.04	14.07	Thar Desert	219°	63.80
17.	4 - (4-Fluoro) Phenyl hydrazono - R ²	447.87	C ₂₀ H ₁₆ N ₂ O ₂ ClF	53.63	53.67	4.27	4.29	15.63	15.64	Sporty Yellow	239°	66.45
18.	4 - (2-OCH ₃) Phenyl hydrazono - R ²	459.90	C ₂₁ H ₂₂ N ₂ O ₂ Cl	54.84	54.88	4.82	4.84	15.23	15.25	Light Yellow	221°	54.98
19.	4 - (4-Br) Phenyl hydrazono - R ²	508.78	C ₂₀ H ₁₆ N ₂ O ₂ ClBr	47.21	47.22	3.76	3.77	13.76	13.78	Light Yellow	247°	63.04
20.	4 - (3-Chloro) Phenyl hydrazono - R ²	464.32	C ₂₀ H ₁₆ N ₂ O ₂ Cl	51.73	51.75	4.12	4.15	15.08	15.09	Light Yellow	240°	51.93
21.	4 - (3-Cl-2CH ₃) Phenyl hydrazono - R ²	478.35	C ₂₁ H ₂₁ N ₂ O ₂ Cl	52.72	52.76	4.42	4.44	14.64	14.67	Dark Yellow	234°	61.11
22.	4 - (2-CH ₃) Phenyl hydrazono - R ²	443.90	C ₂₁ H ₂₂ N ₂ O ₂ Cl	56.82	56.84	4.99	4.98	15.77	15.78	Dirty Yellow	248°	64.62
23.	4 - (2,4 - (CH ₃) ₂) Phenyl hydrazono - R ²	457.93	C ₂₂ H ₂₄ N ₂ O ₂ Cl	57.70	57.68	5.28	5.26	15.29	15.28	Light Yellow	238°	62.69
24.	4 - (3,5 - (CH ₃) ₂) Phenyl hydrazono - R ²	457.93	C ₂₂ H ₂₄ N ₂ O ₂ Cl	57.70	57.66	5.28	5.29	15.29	15.30	Light Yellow	245°	56.92
25.	4 - (2,5-(CH ₃) ₂) Phenyl hydrazono - R ²	457.93	C ₂₂ H ₂₄ N ₂ O ₂ Cl	57.70	57.67	5.28	5.27	15.29	15.27	Dirty Yellow	241°	54.80

R¹=2,3-dioxobutylateR²=N' (3-Chloro-4-Methoxy) amino malonyl-3-methyl pyrazolone

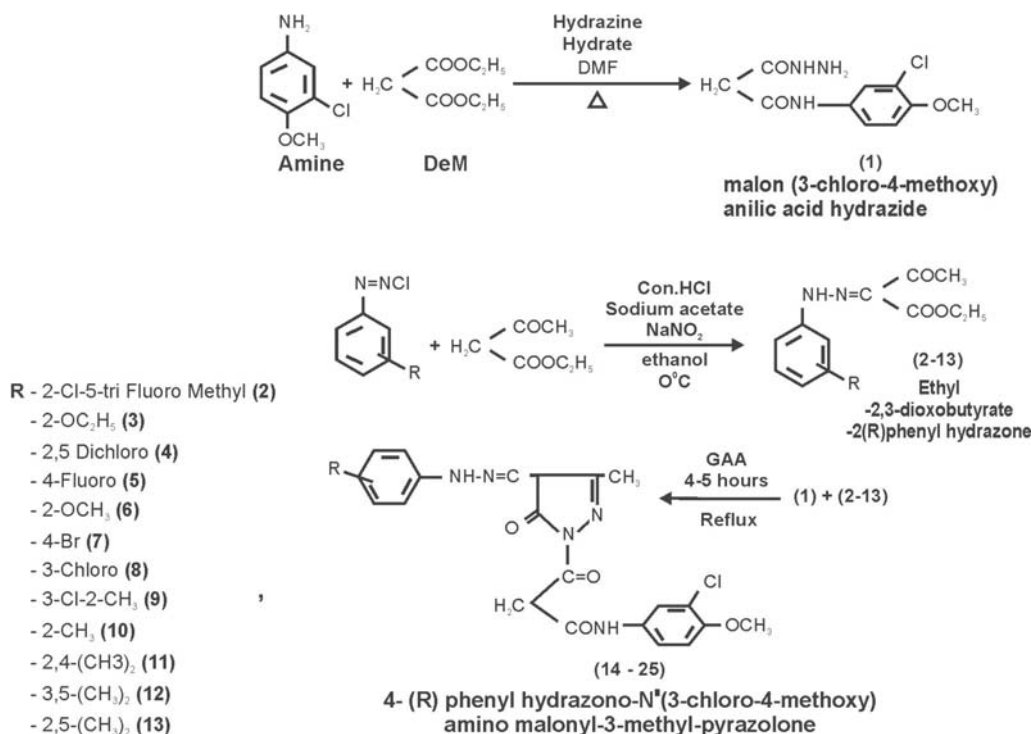


Table 2 : IR Absorption Bands

Compound No.	Ar CH cm ⁻¹ Stretching	NH cm ⁻¹ Stretching	N=CH cm ⁻¹ Stretching	C=N cm ⁻¹ Stretching	ArC=O cm ⁻¹ Stretching	C-N cm ⁻¹ Stretching	N-N cm ⁻¹ Stretching	C-Cl cm ⁻¹ Stretching	CH ₃ cm ⁻¹ Stretching
13.	3020	3431	2362	1589.9	1665	1214.9	1526	669	1425
14.	3020.6	3402	2361	1590	1664	1215.8	1527	670	1427
15.	3020.00	3421	2361.8	1582	1662	1215	1528	669	1426
16.	3020.5	3436	2361.7	1595	1663	1215.4	1525	670	1425
17.	3020.8	3419	2362	1582	1648	1215	1527	669	1424
18.	3020	3441	2361	1585	1653	1215.9	1530	670	1427.9
19.	2922	3401	2359.8	1586	1642	1218	1523	666	1426
20.	3020.6	3432	2361.5	1590.7	1662	1215.5	1527	670	1427

Synthesis of ethyl 2,3-dioxobutyrate 2-(R) phenyl hydrazone (2-13)

To the substituted aniline (0.025 mole) was diazotized by adding concentrated HCl (8 ml) and water (7 ml) cooled at 0°C in an ice-bath, then a cold aqueous solution of sodium nitrite (0.025 mole) was added to it. The ready diazonium salt solution was added slowly dropwise into the cooled solution

of sodium acetate (0.12 mole) and ethyl acetoacetate (0.025 mole) in (25 ml) ethanol. The solid was separated, filtered, washed with cold water and recrystallised with hot ethanol.

General method for the synthesis of substituted pyrazolone (14-25)

To (1; 0.001 mole) dissolved in absolute

ethanol (15 ml) and (2-12 ; 0.001 mole) was added and refluxed for 4-5 hours in presence of 3-4 drops of glacial acetic acid. The resulting solid obtained during refluxing was cooled, filtered and was recrystallised with hot absolute ethanol several times.

RESULTS AND DISCUSSION

The IR spectra of the newly synthesized compounds have been recorded in the frequency region 4000-450 cm^{-1} , these are recorded in Table-2.

The IR (KBr) spectrum of 4(R)phenyl hydrazono-N' (3-chloro-4-methoxy) amino malonyl-3-methyl-pyrazolone 13-20 shows absorption at 1665-1642 cm^{-1} indicating-C=O stretching vibrations, absorption in the range 3441-3401 cm^{-1} reveals -NH stretching vibrations,-C=N stretching

vibrations were obtained between 1595-1582 cm^{-1} and absorption at 3020.8-2922 cm^{-1} stretching vibrations confirms the aromatic character of-CH, absorption at 1427.9-1424 cm^{-1} indicating-CH₃ stretching vibrations, absorption in the range 1530-1523 cm^{-1} show-N-N stretching vibrations, and absorption at 1218-1214.9 cm^{-1} stretching vibrations confirms the-C-N, absorption at 670-666 cm^{-1} reveals-C-Cl stretching vibrations.

The above observations are agreed with the assigned structure of compounds no. 13-20 and other compounds (21-25).

The pyrazolones were found to possess higher melting points, shows the thermal stability. The study reveals absorption spectrum was in agreement with the assigned structure and colouring properties.

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