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Convenient synthesis, characterization of some novel subs-tituted 3-methyl-2-pyrazoline-5-ones and substituted 3,5-dimethyl pyrazoles

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ABSTRACT

Some of the pyrazolones and pyrazoles bearing different functional groups, substituted pyrazolones were synthesized by the condensation reaction of newly synthesized substituted thiosemicarbazide (1a, 2a) with substituted ethyl aceto hydrazone (a_1-g_1) in the presence of glacial acetic acid as a catalyst, they are coloured solid, having high melting points. Substituted pyrazoles have been synthesized by the condensation of newly synthesized substituted thiosemicarbazide (1a, 2a) with substituted phenyl benzene-azo acetyl acetone hydrazone (a_2 - i_2) and glacial acetic acid used as a medium in all condensation reactions. The constitution of the newly synthesized substituted pyrazolones and substituted pyrazoles are characterized by their physical properties, elemental analysis, spectral studies like IR.

Key words: Substituted Thiosemicarbazides, Pyrazolones, Pyrazoles, GAA, Synthesis, Characterization, Spectral Analysis.

INTRODUCTION

Pyrazolones belong to the group of heterocycles that have been attracting attention for last few decades due to their wide range of bioligical activities[1]. These heterocycles are of great interest to medicinal chemists for molecular manipulation and biologist for further pharmacological evaluation. Pyrazolones and their derivatives are important biological agents and a significant amount of research activity has been directed towards this class of compounds. In particular they are used as antitumor[2], antibacterial[3], anti-fungal[4], antiviral[5], insecticidal[6] agents. Pyrazolone have also been found anti-inflammatory[7], antidia-betic[8], analgesic[9] properties. Derivatives of pyra-zolone have also been found to possess various biological activities including anti-hyperglycemic[10], antitumor necrosis factor activity[11].

Pyrazoles have been found to be associated with wide range of biological activities like anti-inflammatory[12]. Some substituted pyrazoles and their derivatives have been reported as antibacterial[13], fungicidal[14], antidiuretic[15] and anticancer[16] properties.

Keeping these mentioned properties in view in continuation of our previous work[17-22], in the present paper the author is synthesized some new novel substituted 2-pyrazoline-5-ones and substituted 3,5-dimethyl pyrazoles bearing chloro, methoxy, methyl functional groups.

EXPERIMENTAL

Material and Methods

All the melting points are taken in open capillary tubes and are uncorrected. All the

chemicals were used for the synthesis are of analytical grade were obtained from Sigma-Aldrich Company. Purity of the newly synthesized compounds was checked by TLC using silica-gel-coated Al-Plates (Merck). IR spectra of the newly synthesized compounds were recorded on Perkin - Elmer spectrum RX-1 FT-IR spectrophotometer using Kbr pallatisation technique in cm^{-1} at ST. John's College Agra.

General method for the synthesis of substi-tuted thiosemicarbazide (1a, 2a)

To the substituted amine (3-Cl-4-OCH_3, 2-OCH_3-5-CH_3; 0.1 mole) in ammonia (20 ml) with distilled water, then add carbon disulphide (7.6 ml) with absolute ethanol (20 ml) and the contents was stirr vigorously for about 45 minutes, the solution of sodium carbonate (5.3 gm) and monochloro acetic acid (9.5 gm) in distilled water (40 ml) was added to it followed by the addition of hydrazine hydrate 99% (6 ml), then refluxed for 30-45 minutes on steam-bath, cooling the contents, thus the resulting product obtained, recrystallized with absolute ethanol.

General method for the synthesis of ethyl 2,3-dioxobutyrate-2(substituted)phenyl hydrazono (a_1-g_1)

To the substituted aniline (0.025 mole) diazotised by adding concentrated HCl (8 ml) with (7 ml) of distilled water at 0^OC maintained temperature in an ice-bath, aqueous solution of Sodium Nitrite (0.025 mole) was added to it, then the prepared diazonium salt solution was added slowly drop-wise in to the cold solution of Sodium acetate (0.12 mole) and ethyl aceto acetate (0.025 mole) in ethanol (25 ml) at 0^OC dissolved with distilled water. The resulting solid product started separating out, filtered, washed with cold water, recrystallized with absolute ethanol .

General procedure for the synthesis of substituted 3-methyl-2-pyrazoline-5-one (1b-1j,2b 2d)

To (1a, 2a; 0.001 mole) dissolved in absolute ethanol (10 ml) and (a_1-g_1; 0.001 mole) was added with the catalyst glacial acetic acid and then the reaction mixture was refluxed for 4-5 hours, thus the resulting solid product was obtained during the refluxing, filtered, recrystalli-zed from ethanol 99%.

General method for the synthesis of substituted phenyl benzeneazo acetyl acetone (a_2-i_2)

To the substituted aniline (0.025 mole) was diazotised by adding together with con. HCl (8 ml) and dis. water (7ml) at 0^OC in an ice-bath, the cooled aqueous solution of $NaNO_2$ (0.025 mole) was added drop-wise to it, the diazonium salt solution was added drop-wise in to the solution of Sodium acetate (0.12 mole) and acetyl acetone (0.025 mole) in ethanol (20 ml) at 0^OC, thus the resulting solid was separated out, filtered, washed with cold dis. water, recrystallized with hot ethanol 99%.

General procedure for the synthesis of substituted 3,5-dimethyl pyrazole (3a-3i)

To (1a,1b; 0.001 mole) dissolved in absolute ethanol (10 ml) and (a_2-i_2 ; 0.001 mole) was added, in the presence of glacial acetic acid 4-5 dropes, refluxed the reaction mixture for 3-4 hours, cooling, filtered, the resulting solid was recrystallized by absolute ethanol.

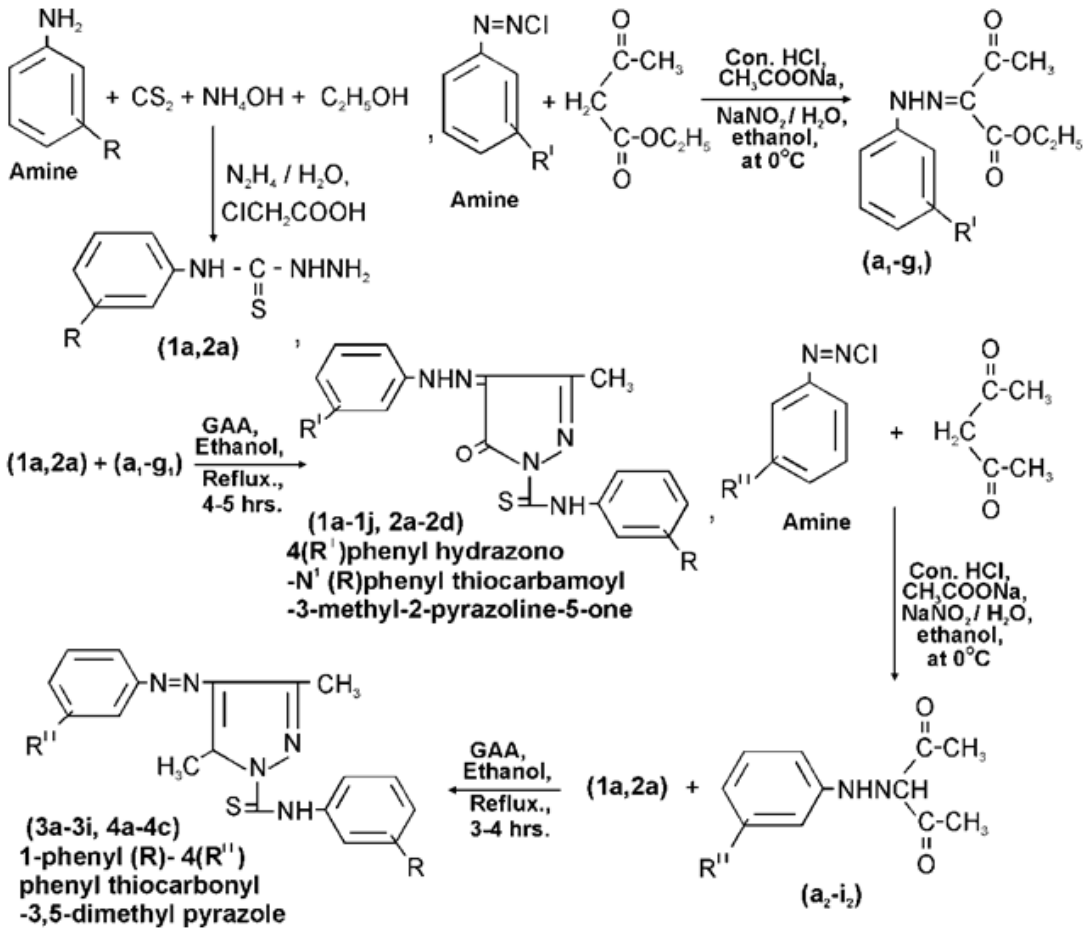
RESULTS AND DISCUSSION

The infrared spectrum of newly synthesized compounds have been recorded in the frequency region 4000-500 cm^{-1} are mentioned in the Table-2. The IR spectrum of compounds(1b,1d-1f,2a,2d) shows -NH stretching vibrations in the region 3414.7-3469.5 cm^{-1}, stretching vibrations in the region 2345.5-2368.0 cm^{-1} indicates CH=N, stretching vibrations in the region 1636.6-1638.4 cm^{-1} reveals -C=N, absorption in the range 17 34.3-1736.4 cm^{-1} confirm aromatic C=O, 1376.2-1384.6 cm^{-1} (-C=S str.), 1522.6-1547.3 cm^{-1} (pyrazolone ring N-N str.), while stretching vibr-ations in the range 1419.7-1439.7 cm^{-1} indicates —CH_3 group, absorption in the range 668.4-672.0 cm^{-1} confirming the mono substitution. All of the above observations are lent support to the assigned structure of compounds (1b,1d-1f,2b,2d) and other compounds (1c,1g-1f,2c).

The IR spectrum of newly synthesized compounds (3c,3d,3f,3i,4b) shows absorption in the region 3413.0-3416.4 cm^{-1} indicates -NH, 1636.7-1637.9 cm^{-1} (-C=N str.), absorption in the range 1725.8-1736.4 cm^{-1} confirm the presence of lactone C=O, 1330.7-1353.7 cm^{-1} (C=S str.), 1458.9-1474.2 cm^{-1} indicates -N=N str., absorp-tion in the range

Table 1: Physical and Analytical data of newly synthesized compounds

codes	Molecular Formula	Molecular Weight	Yield %	M.P 0°C	% Analytical data C cal.%	(found)	H cal.%	(found)	N cal.%	(found)	S cal.%	(found)	colour
1a	$C_8H_{10}N_3S_1O_1Cl_1$	231.65	74.68	178°	41.47	(41.48)	4.35	(4.37)	18.14	(18.18)	13.81	(13.84)	dirty spice
2a	$C_6H_{13}N_3S_1O_1$	211.23	49.23	160°	51.17	(51.19)	6.20	(6.22)	19.89	(19.93)	15.15	(15.18)	crystalline white
1b	$C_{19}H_{18}N_5S_1O_2Cl_1$	415.85	54.69	154°	54.87	(54.86)	4.36	(4.35)	16.84	(16.88)	07.69	(07.71)	deep orange
1c	$C_{19}H_{18}N_5S_1O_3Cl_1$	431.85	53.33	148°	52.84	(52.86)	4.20	(4.22)	16.21	(16.25)	07.41	(07.42)	dark sunrise
1d	$C_{18}H_{15}N_5S_1O_2Cl_1F_1$	419.82	55.40	157°	51.49	(51.51)	3.60	(3.62)	16.68	(16.72)	07.62	(07.65)	orange
1e	$C_{18}H_{15}N_5S_1O_2Cl_1Br_1$	480.73	65.25	154°	44.97	(44.99)	3.14	(3.16)	14.56	(14.59)	06.65	(06.68)	deep orange
1f	$C_{20}H_{20}N_5S_1O_3Cl_1$	445.88	56.18	164°	53.87	(53.88)	4.52	(4.54)	15.70	(15.73)	07.17	(07.19)	dull sunrise
1g	$C_{18}H_{14}N_5S_1O_2Cl_3$	470.72	47.94	147°	45.92	(45.93)	2.99	(3.00)	14.87	(14.90)	06.79	(06.81)	orange
1h	$C_{20}H_{20}N_5S_1O_3Cl_1$	445.88	57.17	157°	53.87	(53.88)	4.52	(4.54)	15.70	(15.75)	07.17	(07.21)	dark sunrise
1i	$C_{19}H_{14}N_5S_1O_2Cl_2F_3$	504.28	40.56	182°	45.25	(45.26)	2.79	(2.80)	13.88	(13.90)	06.34	(06.37)	lemon yellow
1j	$C_{19}H_{14}N_5S_1O_2Cl_2$	447.28	49.12	163°	51.02	(51.03)	3.15	(3.17)	15.66	(15.70)	07.15	(07.18)	dull sunrise
2b	$C_{19}H_{18}N_5S_1O_2Cl_1$	415.85	50.90	141°	54.87	(54.88)	4.36	(4.37)	16.84	(16.88)	07.69	(07.71)	crystalline orange
2c	$C_{19}H_{18}N_5S_1O_2Br_1$	460.31	59.73	130°	49.57	(49.58)	3.94	(3.96)	15.21	(15.25)	06.95	(06.98)	sporty yellow
2d	$C_{21}H_{23}N_5S_1O_3$	425.46	57.05	151°	59.28	(59.30)	5.44	(5.42)	16.46	(16.49)	07.52	(07.54)	orange
3a	$C_{19}H_{17}N_5S_1O_2Cl_1$	414.84	46.05	177°	55.01	(55.03)	4.13	(4.14)	16.88	(16.91)	07.71	(07.73)	dirty limon
3b	$C_{20}H_{20}N_5S_1O_2Cl_1$	429.88	54.34	181°	55.88	(55.89)	4.67	(4.68)	16.29	(16.34)	07.44	(07.47)	deep limon
3c	$C_{20}H_{20}N_5S_1O_3Cl_1$	445.88	51.82	166°	53.87	(53.88)	4.52	(4.53)	15.70	(15.75)	07.17	(07.19)	light heena
3d	$C_{19}H_{17}N_5S_1O_2Cl_1F_1$	433.84	55.63	174°	52.60	(52.62)	3.95	(3.97)	16.14	(16.16)	07.37	(07.39)	light sugarcane
3e	$C_{19}H_{17}N_5S_1O_2Cl_1Br_1$	494.76	57.99	182°	46.12	(46.14)	3.46	(3.48)	14.15	(14.18)	06.46	(06.48)	limon
3f	$C_{21}H_{22}N_5S_1O_3Cl_1$	459.91	50.52	175°	54.84	(54.82)	4.82	(4.81)	15.22	(15.26)	06.96	(06.94)	shining limon
3g	$C_{21}H_{22}N_5S_1O_3Cl_1$	459.91	47.18	177°	54.84	(54.85)	4.82	(4.80)	15.22	(15.27)	06.96	(06.98)	wild yellow
3h	$C_{19}H_{16}N_5S_1O_2Cl_3$	484.75	43.45	202°	47.07	(47.05)	3.32	(3.30)	14.44	(14.42)	06.60	(06.63)	deep limon
3i	$C_{20}H_{16}N_5S_1O_2Cl_2F_3$	518.30	40.22	183°	46.34	(46.36)	3.11	(3.09)	13.51	(13.54)	06.17	(06.19)	off white
4a	$C_{20}H_{20}N_5S_1O_2F_1$	413.42	63.97	186°	58.10	(58.11)	4.87	(4.88)	16.94	(16.99)	07.74	(07.76)	light brazen gold
4b	$C_{20}H_{20}N_5S_1O_2Br_1$	474.34	67.70	178°	50.64	(50.65)	4.25	(4.27)	14.76	(14.79)	06.74	(06.77)	brazen gold
4c	$C_{21}H_{23}N_5S_1O_2$	409.46	72.49	171°	61.60	(61.62)	5.66	(5.67)	17.10	(17.14)	07.81	(07.83)	light gold rush



1500.4-1515.7 cm^{-1} confirming (pyrazole ring -N-N str.), -CH_3 group is confirm by the stretching vibrations in the range 1417.3-1440.1 cm^{-1}, while absorption in the range 644.9-671.0 cm^{-1} confirm the mono substitution.

Above observations of these compounds are lent support to the assigned structure of compounds (3c,3d,3f,3i,4b) and other compounds (3a,3b,3e,3g-3h,4a,4c).

Table 2: Characterization (IR in ν cm^{-1}) data of newly synthesized compounds

codes	-NH cm^{-1} stretching	CH=N cm^{-1} stretching	C=N cm^{-1} stretching	C=O cm^{-1} stretching	C=S cm^{-1} stretching	N=N cm^{-1} stretching	N-N cm^{-1} stretching	CH_3 cm^{-1} stretching	mono subs.
1b	3448.2	2361.5	1636.6	1734.3	1375.4	-	1522.6	1419.7	668.4
1d	3414.7	2364.4	1638.0	1736.1	1376.3	-	1534.1	1430.0	669.5
1e	3414.8	2345.5	1638.2	1736.4	1374.9	-	1547.3	1438.5	672.0
1f	3448.8	2365.6	1638.3	1736.2	1384.4	-	1542.7	1439.7	670.0
2b	3415.0	2368.0	1638.4	1736.3	1376.2	-	1533.9	1430.2	669.9
2d	3469.5	2363.5	1637.1	1735.4	1384.6	-	1539.6	1438.0	668.9
3c	3416.4	-	1637.6	1725.8	1343.4	1459.1	1500.5	1440.1	668.6
3d	3415.1	-	1637.9	1736.0	1341.6	1460.1	1500.4	1439.3	669.0
3f	3413.0	-	1636.7	1734.4	1353.5	1474.2	1515.7	1417.3	644.9
3i	3414.7	-	1638.2	1736.4	1330.7	1461.1	1501.2	1429.9	671.0
4b	3415.2	-	1637.4	1735.5	1353.7	1458.9	1510.0	1420.1	669.0

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