Oriental Journal of Chemistry Vol. **26**(3), 1167-1170 (2010)

An efficient route for the synthesis, characterization of some new novel substituted pyrazoles

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(Received: April 15, 2010; Accepted: May 20, 2010)

ABSTRACT

An efficient synthesis of some newly substituted pyrazoles (3a-3r) have been synthesized by the condensation reactions of malon (3-chloro-4-methoxy) phenyl anilic acid hydrazide (1a) with different substituted phenyl benzeneazo acetyl acetone hydrazones(2a-2r) and glacial acetic acid being used as a catalyst in the all condensation reactions. The newly synthesized substituted pyrazoles structures have been established on the basis of their m.p, colour, analytical data, spectral analysis viz: I.R.

Key words: Synthesis, subs. hydrazide, subs. acetyl hydrazones, GAA, pyrazoles, spectral analysis.

INTRODUCTION

Pyrazoles are well known nitrogen containing five member heterocyclic compounds and various procedures have been deployed for their synthesis. Pyrazole derivatives possess important pharmacological activities and there fore they are useful materials in drug research. Pyrazole derivatives are used as analgesic[1], anti-inflammatory[2], anti-fedant[3] agents. Some of the pyrazole derivatives are reported to possess anti-HIV[4], antitumor[5], anti–inflammatory[6], and anti-depressant properties[7]. It also finds applications as dye stuffs, analytical reagents and agro chemicals[8]. Pyrazole have also been found to possess anti-cancer[9], antidiabetic[10], biological activities[11].

They are being used as psychopharmacologi cal agents[12], pain relief agent, amino and hydro xy pyrazoles have been used as cholinesterase inhibitors[13], fluorine containing pyrazole derivatives are also reported to possess anti- cancer and antiviral activity[14]. In the light of these facts and in continuation of our previous work[15] we have synthesized some new novel substituted pyrazoles. A large number of subs. Pyrazoles and their derivatives have been prepared in our laboratory by various workers[16-19].

EXPERIMENTAL

Material and Methods

The melting points of the newly synthesized compounds were determined in open capillary tubes and were uncorrected . TLC was used to moniter the progress of the reaction . The IR spectra were recorded on Perkin-Elmer spectrum RX-1 FT-IR spectrophotometer by using Kbr disc method at St. John's College Agra. All the used chemicals in the synthesis were obtained from Sigma-Aldrich Company.

The analytical and physical data, molecular weight, molecular formula, m.p, colour , yield% of the newly synthesized compounds are recorded in the Table-1 and spectral analysis are recorded in the Table-2.

General procedure for the synthesis of malon (3-chloro-4-methoxy) phenyl anilic acid hydrazide (1a)

To the substituted amine (3-chloro-4-methoxy ; 0.025 mole), freshly distilled diethyl malonate (0.05 mole) was added with condensing agent di-methyl formamide and then the mix. was refluxed for about 50-60 minutes, ethanol 20 ml was added to it and then concentrated the mixture over the boiling water-bath, and then it is treated with hydrazine hydrate 99% and ethyl alcohol (20 ml), thus the obtained solid was recrystallized by hot ethanol, was identified to be (1a).

General procedure for the synthesis of substituted phenyl benzeneazo acetyl acetone hydrazones (2a-2r)

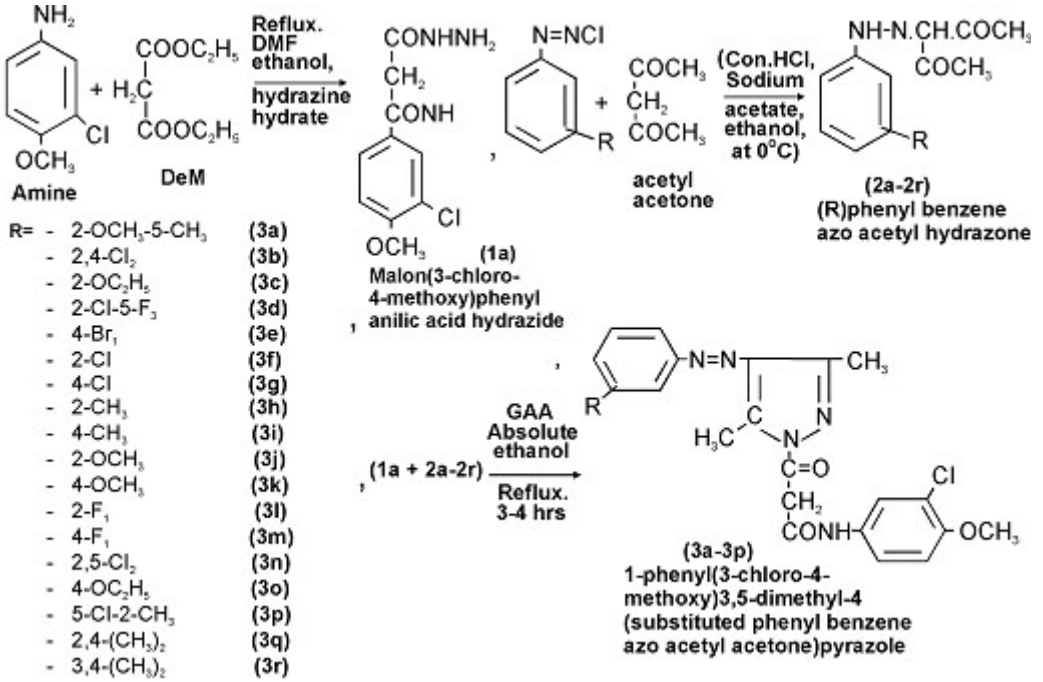
To the substituted aniline (0.025 mole) was diazotised by adding concentrated HCl (8 ml) with dis. water (6 ml) at maintained temperature 0°C - 2°C, then add cooled aqueous solution of $NaNO_2$ (0.025 mole) drop-wise to it, then the diazotised salt solution was added slowly drop - wise in the cooled solution of sodium acetate (0.12 mole) and acetyl acetone (0.025 mole) in ethanol (20 ml), thus the solid was separated out, filtered, washed with cold water, recrystallized with hot ethanol 99%.

General procedure for the synthesis of substituted pyrazole (3a-3r)

To (1a; 0.001 mole) dissolved in absolute ethanol (10 ml) and (2a-2r ; 0.001 mole) was added in equimolar (1:1) quantity and then refluxed for about 3-4 hours in the presence of catalyst GAA 4-5 drops, cooling, filtered, and thus the obtained solid was recrystallized by absolute ethanol 99%.

The infrared spectra of the newly synthesized substituted pyrazoles have been recorded in the frequency region 4000-500 cm^{-1}, are mentioned in the Table 2.

The IR spectra of compounds 1-phenyl-(3-chloro-4-methoxy)3,5-dimethyl-4(substituted phenylbenzene azo acetyl acetone)pyrazole [3a-3e] shows the stretching vibrations in the range 3294.4 - 32 20.0 cm^{-1} represents -NH, stretching vibrations at 3052.3-3021.0 cm^{-1} indicating -CH, stretching vibrations in the range 1653.1-1648.2 cm^{-1} reveals the aromatic C=O, stretching vibrations in the range



R= - 2-OCH_3-5-CH_3 (3a)
- 2,4-Cl_2 (3b)
- 2-OC_2H_5 (3c)
- 2-Cl-5-F_3 (3d)
- 4-Br_1 (3e)
- 2-Cl (3f)
- 4-Cl (3g)
- 2-CH_3 (3h)
- 4-CH_3 (3i)
- 2-OCH_3 (3j)
- 4-OCH_3 (3k)
- 2-F_1 (3l)
- 4-F_1 (3m)
- 2,5-Cl_2 (3n)
- 4-OC_2H_5 (3o)
- 5-Cl-2-CH_3 (3p)
- 2,4-$(CH_3)_2$ (3q)
- 3,4-$(CH_3)_2$ (3r)

Table 1: Physical and Analytical data of Newly Synthesized Compounds (3a-3r)

codes	Molecular Formula	Molecular Weight	% Analytical data C % cal.% (found)	H% cal.% (found)	N% cal.% (found)	M.P °C	Yield %	Colour
1a.	$C_{10}H_{12}N_3O_3Cl_1$	257.68	46.61 (46.65)	4.69 (4.70)	16.30 (16.33)	158°	56.30	white
3a.	$C_{23}H_{25}N_5O_4Cl_1$	470.95	58.65 (58.67)	5.35 (5.33)	14.87 (14.91)	246°	54.74	garlic pod
3b.	$C_{21}H_{19}N_5O_3Cl_3$	495.79	50.87 (50.89)	3.86 (3.87)	14.12 (14.14)	242°	49.52	sugared nut
3c.	$C_{23}H_{25}N_5O_4Cl_1$	470.95	58.65 (58.67)	5.35 (5.33)	14.87 (14.88)	253°	55.92	summer sprinkle
3d.	$C_{22}H_{19}N_5O_3Cl_2F_3$	529.34	49.92 (49.94)	3.61 (3.63)	13.23 (13.26)	257°	45.74	dark sugared nut
3e.	$C_{21}H_{20}N_5O_3Cl_1Br_1$	505.82	49.86 (49.89)	3.98 (3.99)	13.84 (13.88)	254°	61.89	sugared nut
3f.	$C_{21}H_{20}N_5O_3Cl_2$	461.34	54.67 (54.68)	4.36 (4.34)	15.18 (15.21)	241°	59.07	dirty royal ivory
3g.	$C_{21}H_{20}N_5O_3Cl_2$	461.34	54.67 (54.69)	4.36 (4.37)	15.18 (15.23)	253°	53.22	light corel shell
3h.	$C_{22}H_{23}N_5O_3Cl_1$	440.92	59.92 (59.93)	5.25 (5.23)	15.18 (15.22)	238°	53.78	summer sprinkle
3i.	$C_{22}H_{23}N_5O_3Cl_1$	440.92	59.92 (59.94)	5.25 (5.26)	15.18 (15.20)	249°	60.08	light wild yellow
3j.	$C_{22}H_{23}N_5O_4Cl_1$	456.92	57.83 (57.84)	5.07 (5.06)	15.32 (15.35)	249°	55.84	magnolia light
3k.	$C_{22}H_{23}N_5O_4Cl_1$	456.92	57.83 (57.86)	5.07 (5.08)	15.32 (15.36)	251°	52.43	off white
3l.	$C_{21}H_{20}N_5O_3Cl_1F_1$	444.88	56.69 (56.71)	4.53 (4.51)	15.74 (15.76)	244°	61.25	light cream
3m.	$C_{21}H_{20}N_5O_3Cl_1F_1$	444.88	56.69 (56.72)	4.53 (4.55)	15.74 (15.78)	247°	67.70	light royal ivory
3n.	$C_{21}H_{19}N_5O_3Cl_3$	495.79	50.87 (50.88)	3.86 (3.88)	14.12 (14.16)	248°	55.93	cream caress
3o.	$C_{23}H_{25}N_5O_4Cl_1$	470.95	58.65 (58.66)	5.35 (5.36)	14.87 (14.90)	255°	51.58	wheat sprig
3p.	$C_{22}H_{22}N_5O_3Cl_2$	475.37	55.58 (55.60)	4.66 (4.68)	14.73 (14.76)	247°	56.27	off white
3q.	$C_{23}H_{25}N_5O_3Cl_1$	454.96	60.72 (60.74)	5.53 (5.54)	15.39 (15.41)	256°	54.89	light cream
3r.	$C_{23}H_{25}N_5O_3Cl_1$	454.96	60.72 (60.73)	5.53 (5.52)	15.39 (15.42)	259°	49.79	light jasmine

Table 2: IR Absorption Bands

S. No.	Codes	-NH cm^{-1} stretching	-CH cm^{-1} stretching	Ar C=O cm^{-1} stretching	C=C cm^{-1} stretching	C-N cm^{-1} stretching	N-N cm^{-1} stretching	$-CH_3 cm^{-1}$ stretching	mono substi.
1.	3a	3280.0	3021.0	1649.8	1594.2	1238.2	1500.0	1386.2	669.0
2.	3b	3294.4	3051.9	1650.3	1591.1	1235.1	1500.8	1425.7	671.3
3.	3c	3290.0	3052.3	1653.1	1592.6	1235.5	1501.5	1421.0	674.5
4.	3d	3292.9	3051.1	1651.1	1591.5	1235.5	1500.1	1427.5	671.0
5.	3e	3220.0	3050.0	1648.2	1593.1	1236.4	1501.0	1420.5	670.0

of 1238.2-1235.1 cm^{-1} indicates C-N, absorption at 1501.5-1500.00 cm^{-1} indicates the presence of -N-N, absorption in the range 1427.5-1386.2 cm^{-1} represents the CH_3 group, absorption in the range 674.5-669.00 cm^{-1} are show the mono substitution ring. The above absorption spectrum are lent support to the assigned structures of newly synthesized compounds 3a-3e and other compounds (3f-3r).

Thus the IR spectra of the compounds indicateng the absorption spectrum was in agreement with the assigned structures. Substituted pyrazoles are stable solids, which are rather springly soluble in common solvents, with high melting point, they are also have characteristic colour.

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