Synthesis and Reactions of 2-Amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile [1]

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2-Amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**1**) obtained by the reaction of 4-(1-iminoethyl)-3-methyl-1-phenyl-2-pyrazolin-5-one with benzylidenemalononitrile, was reacted with triethyl orthoformate followed by hydrazine hydrate, acetic anhydride, acetyl chloride, alkyl halides, benzoyl chloride, sulphuric acid followed by formamide, phenyl isothiocyanate, carbon disulphide followed by ethyl iodide, formamide, trichloroacetonitrile, nitrous acid, giving new oxopyrazolinylpyridines (**2,3,5,6,8,9,10**) and related pyridopyrimidines (**11**-**17**) and pyridotriazine (**18**).

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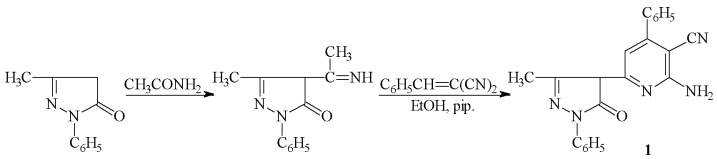
As a continuation of our previous work [2,3] about the chemistry of 5-pyrazolone derivatives and their wide applications in different industrial, biological and medicinal fields [4-6], we report in this paper the synthesis of oxopyrazolinylpyridines and some related pyridopyrimidines and pyridotriazine. For this purpose 2-amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**1**) was prepared by the reaction of 4-(1-iminoethyl)-3-methyl-1-phenyl-2-pyrazolin-5-one [7] with benzylidenemalononitrile in ethanol in the presence of piperidine as a catalyst (Scheme 1).

Scheme 1

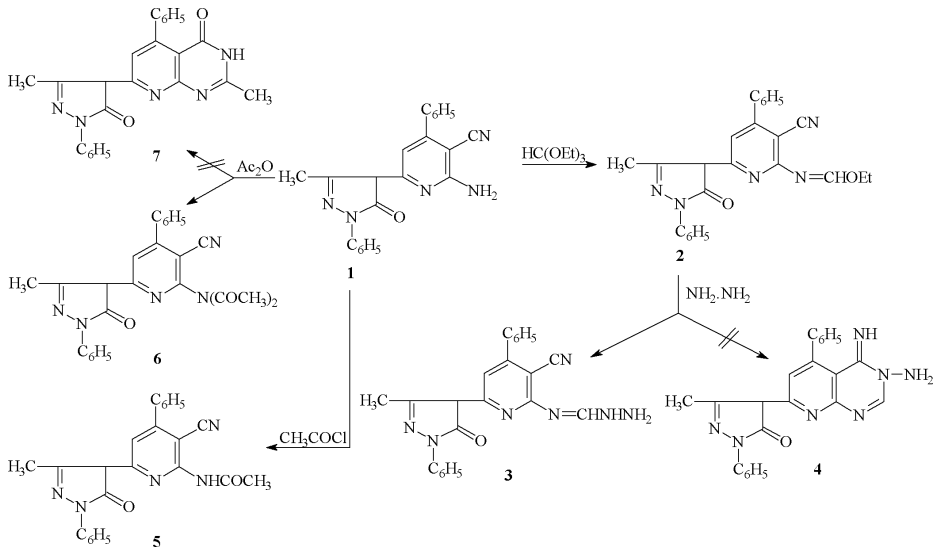


The *o*-aminonitrile function of **1** was exploited to synthesize some new oxopyrazolinylpyridines and related pyridopyrimidines and pyridotriazine. Thus, the reaction of **1** with excess triethyl orthoformate led to the formation of 2-(ethoxymethyleneamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**2**), whose reaction with hydrazine hydrate gave 2-(hydrazinomethyleneamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**3**). Attempts to cyclize **3** by refluxing in ethanol containing piperidine and/or pyridine to afford **4** were unsuccessful.

The reaction of compound **1** with acetic anhydride provided two products, which were identified as 2-acetylamino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**5**) and 2-diacetylamino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**6**), however the cyclized compound **7** was not obtained.

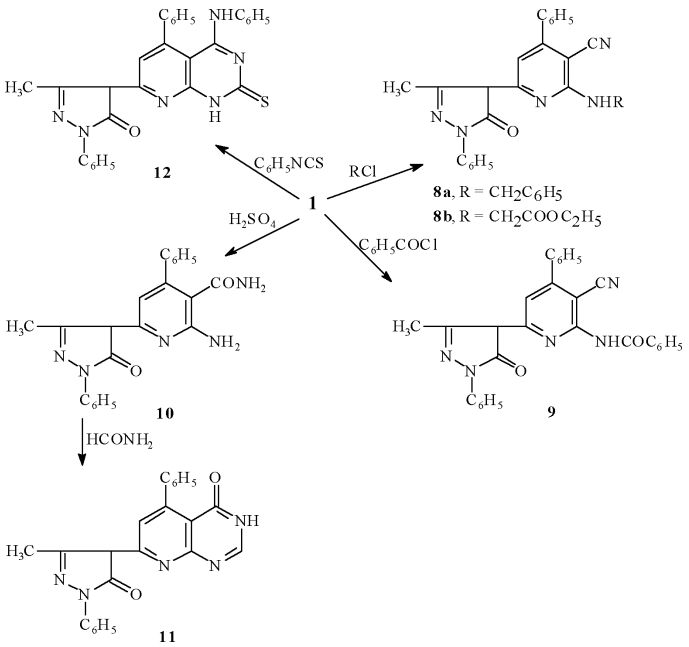
Compound **5** was also prepared by an alternative route *via* the reaction of **1** with acetyl chloride in the presence of pyridine as a catalyst (Scheme 2).

Scheme 2

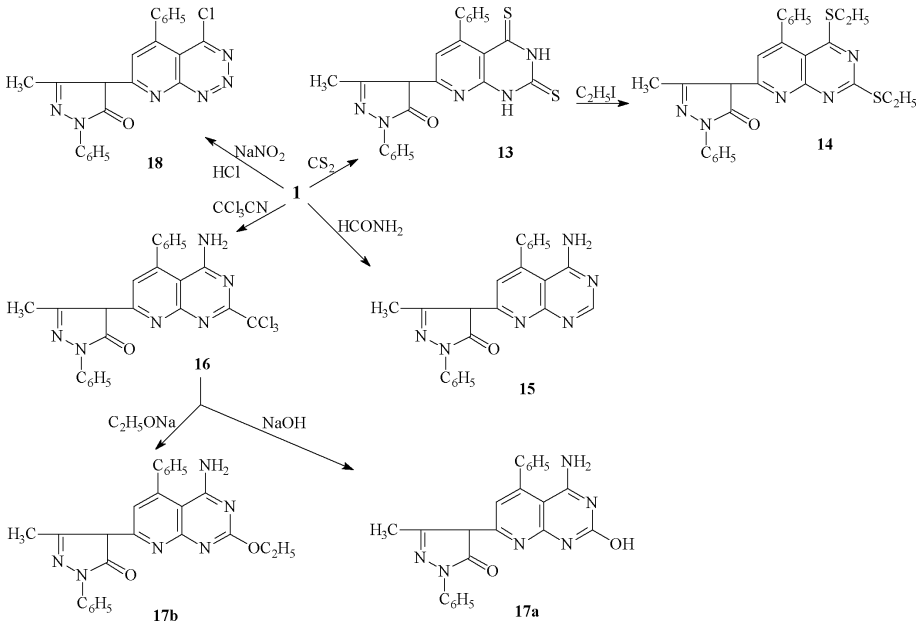


Treatment of **1** with benzylchloride or ethyl chloroacetate led to the formation of 2-(benzylamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**8a**) or ethyl 2-[3-cyano-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridin-2-yl]aminoacetate (**8b**) respectively, while benzoylation of the amino group of **1** produced *N*-[3-cyano-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridin-2-yl]benzamide (**9**). Moreover, hydrolysis of **1** with concentrated sulphuric acid gave 2-amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carboxamide (**10**). Treatment of **10** with formamide afforded 7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (**11**), while the reaction of **1** with phenyl isothiocyanate in pyridine provided 4-phenylamino-7-(3-methyl-5-oxo-1-phenyl-2-

Scheme 3



Scheme 4



pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine-2(1*H*)-thione (**12**) (Scheme 3).

Carbon disulphide reacted with **1** in alcoholic sodium hydroxide solution to give 7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dithione (**13**), which on subsequent alkylation with ethyl iodide afforded 2,4-bis(ethylmercapto)-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido-[2,3-*d*]pyrimidine (**14**), while reaction of **1** with formamide gave 4-amino-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**15**).

Also, reaction of trichloroacetonitrile with **1** in refluxing toluene in the presence of a catalytic amount of piperidine yields 4-amino-2-trichloromethyl-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**16**). The trichloromethyl moiety in **16** could be substituted by hydroxyl group on refluxing with aqueous sodium hydroxide solution and by ethoxy group on boiling with sodium ethoxide in ethanol solution giving 4-amino-2-(hydroxy)- and 2-(ethoxy)-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidines (**17a,b**) respectively. Reaction of nitrous acid with **1** under ordinary conditions afforded 4-chloro-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*][1,2,3]-triazine (**18**) (Scheme 4).

The structures of new compounds were confirmed on the basis of elemental analyses as well as spectral data (IR, ^{1}H-NMR and MS).

Table I

Physical Properties and Elemental Analyses of the Prepared Compounds

Compound	M.P. °C	Yield %	Molecular Formula(M.Wt)	Elemental Analyses Calcd/Found %C	%H	%N	%S	%Cl
1	280-282	40	$C_{22}H_{17}N_5O$	71.93	4.63	19.07		
			(367)	72.01	4.90	18.75	-	-
2	138-140	85	$C_{25}H_{21}N_5O_2$	70.92	4.96	16.55		
			(423)	71.00	4.80	16.33	-	-
3	173-175	60	$C_{23}H_{19}N_7O$	67.48	4.65	23.96		
			(409)	67.35	4.50	23.75	-	-
5	318-320	90	$C_{24}H_{19}N_5O_2$	70.42	4.65	17.11		
			(409)	70.78	4.48	17.12	-	-
6	170-172	80	$C_{26}H_{21}N_5O_3$	69.18	4.66	15.52		
			(451)	69.00	4.27	15.35	-	-
8a	149-150	73	$C_{29}H_{23}N_5O$	76.15	5.03	15.32		
			(457)	76.00	5.10	15.15	-	-
8b	338-340	45	$C_{26}H_{23}N_5O_3$	68.87	5.08	15.45		
			(453)	68.75	5.20	14.50	-	-
9	244-245	85	$C_{29}H_{21}N_5O_2$	73.89	4.46	14.86		
			(471)	73.66	4.50	14.90	-	-
10	250-252	60	$C_{22}H_{19}N_5O_2$	68.57	4.94	18.18		
			(385)	69.75	4.65	17.90	-	-
11	178-180	70	$C_{23}H_{17}N_5O_2$	69.87	4.30	17.72		
			(395)	69.55	4.45	17.85	-	-
12	168-170	75	$C_{29}H_{22}N_6OS$	69.32	4.38	16.73	6.37	
			(502)	69.00	4.50	16.70	6.25	-
13	>360	90	$C_{23}H_{17}N_5OS_2$	62.30	3.84	15.80	14.45	
			(443)	62.25	3.75	15.75	14.75	-
14	193-195	87	$C_{27}H_{25}N_5OS_2$	64.93	5.01	14.03	12.83	
			(499)	64.65	5.20	14.00	12.90	-
15	309-310	95	$C_{23}H_{18}N_6O$	70.05	4.57	21.32		
			(394)	69.98	4.35	21.50	-	-
16	338-340	95	$C_{24}H_{17}N_6OCl_3$	56.30	3.32	16.42		20.82
			(511.5)	56.40	2.97	16.50	-	20.95
17a	>360	60	$C_{23}H_{18}N_6O_2$	67.32	4.39	20.49		
			(410)	67.11	4.35	20.70	-	-
17b	>385	55	$C_{25}H_{22}N_6O_2$	68.49	5.02	19.18		
			(438)	68.30	5.12	19.25	-	-
18	>360	60	$C_{22}H_{15}N_6OCl$	63.69	3.62	20.27		8.56
			(414.5)	63.50	3.60	20.30	-	8.85

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were run on a pye-unicam SP 3-100 spectrophotometer using KBr disc technique (ν_{amx} in cm^{-1}). ^{1}H-NMR spectra were recorded on JNM-FT 400-lambda series, chemical shifts are given in ppm (δ-scale), and MS spectra were run on JEOL JMS 600 spectrophotometer. Yields, melting points, and analytical data of all reported compounds are given in Table I.

2-Amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**1**).

A mixture of 4-(1-iminoethyl)-3-methyl-1-phenyl-2-pyrazolin-5-one [7] (7.0 g, 0.03 mol) and benzylidene malononitrile (5.0 g, 0.03 mol) was heated under reflux for 3 hours in ethanol (50 mL) and a few drops of piperidine. The solid thus precipitated was collected and washed several times with ethanol and recrystallized from dioxane as yellow needles. The IR (KBr): υ 3400, 3300 cm^{-1} (NH_2), 2200 (C≡N), 1620 (C=O) (the lower frequency is due to the enol form of 5-pyrazolone) [8]. ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 6.54 (s, 1H, H-4, pyrazolone), 7.11-7.68 (m, 10H, arom-H), 8.00 (s, 1H, H-5, pyridine) and 8.40 (s, 2H, NH_2).

2-(Ethoxymethyleneamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**2**).

Compound **1** (1.0 g, 0.0028 mol) in excess triethyl orthoformate (10 mL) was refluxed for 5 hours. The reaction mixture was cooled and triturated with cold ethanol, the product was separated, collected by filtration, washed with petroleum ether (40-60 °C) and recrystallized from ethanol. The IR spectrum showed disappearance of the bands attributable to (NH_2) group, but showed bands at 2200 cm^{-1} (C≡N), 1620 (C=O); ^{1}H-NMR ($CDCl_3$): δ 1.45 (t, 3H, CH_2CH_3), 2.60 (s, 3H, CH_3), 4.55 (q, 2H, CH_2CH_3), 7.26 (s, 1H, H-4, pyrazolone), 7.31-7.69 (m, 10H, arom-H), 7.72 (s, 1H, H-5, pyridine), 8.67 (s, 1H, CHOEt); MS, m/z (%): 423 (M^+, 42), 422 (100), 408 (23), 395 (18), 394 (17), 367 (23), 366 (17), 348 (14), 347 (59).

2-(Hydrazinomethyleneamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**3**).

To a solution of **2** (0.2 g, 0.0005 mol) in dioxane (15 mL) was added hydrazine hydrate (5 mL), the reaction mixture was stirred for 0.5 hours, solid product was isolated during stirring collected by filtration, dried, and recrystallized from methanol. The IR (KBr): υ 3450, 3300, 3200 cm^{-1} (NH_2, NH), 2200 (C≡N), 1620 (C=O); ^{1}H-NMR ($CDCl_3$): δ 2.60 (s, 3H, CH_3), 5.40 (s, 2H, NH_2), 7.20 (s, 1H, NH), 7.30 (s, 1H, CH=N), 7.37 (s, 1H, H-4, pyrazolone), 7.41-7.71 (m, 10H, arom-H), 7.79 (s, 1H, H-5, pyridine); MS, m/z (%): 409 (M^+, 14), 395 (28), 394 (100), 393 (25), 379 (50), 366 (43).

2-(Acetylamino) and 2-(Diacetylamino)-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**5,6**).

Compound **1** (0.5 g, 0.0014 mol) was refluxed with acetic anhydride (5 mL) for 3 hours. The reaction mixture was cooled and then poured into cold water (100 mL), then the product was precipitated, collected and recrystallized from benzene to give yellow needles of **5**. The filtrate was concentrated under reduced pressure, then the solid obtained was filtered off, washed with petroleum ether (40-60 °C) and recrystallized from benzene to give **6** as colourless needles.

Compound **5** has IR (KBr): υ 3250 cm^{-1} (NH), 2200 (C≡N), 1700 (C=O of acetyl group), 1600 (C=O) of pyrazolone); ^{1}H-NMR (DMSO-d_6): δ 2.69 (s, 3H, CH_3), 2.94 (s, 3H, $COCH_3$), 7.72 (s, 1H, H-4, pyrazolone), 7.42-8.14 (m, 10H, arom-H), 8.27 (s, 1H, pyridine), 11.24 (s, 1H, NH); MS, m/z (%): 410 (29), 409 (M^+, 100), 368 (24), 367 (92).

Compound **6** has IR (KBr): υ 2220 cm^{-1} (C≡N), 1720 (C=O) of $(COCH_3)_2$, 1680 (C=O of pyrazolone); ^{1}H-NMR ($CDCl_3$): δ 2.40 (s, 6H, $N(COCH_3)_2$), 2.60 (s, 3H, CH_3), 7.20 (s, 1H, H-4, pyrazolone), 7.40-7.58 (m, 10H, arom-H), 7.66 (s, 1H, H-5, pyridine); MS, m/z (%): 452 (19), 451 (M^+, 61), 410 (40), 409 (100), 391 (18), 368 (15), 367 (58).

An Alternative Route for the Preparation of **5**.

Compound **1** (0.5 g, 0.0014 mol) was refluxed with acetyl chloride (5 mL) in pyridine (10 mL) for 3 hours. The reaction mixture was cooled and poured into cold water, then the solid product was separated, filtered off, and recrystallized from benzene to give yellow needles of **5**. It was found that the compound **5** was identical in all aspects (mp, mixed mp, IR, ^{1}H-NMR and MS) with that prepared from **1** with acetic anhydride.

2-Benzylamino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carbonitrile (**8a**) and Ethyl 2-[3-Cyano-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridin-2-yl]aminoacetate (**8b**).

General Procedure.

A mixture of **1** (0.0014 mol) and benzyl chloride and/or ethyl chloroacetate (5 mL) was refluxed for 2 hours, then the reaction mixture was allowed to cool. The reaction product was triturated with petroleum ether (40-60 °C) several times, then collected by filtration, and recrystallized from the proper solvent indicated below.

Compound **8a** was crystallized from benzene, IR (KBr): υ 3370 cm^{-1} (NH), 2200 (C≡N), 1650 (CO); ^{1}H-NMR ($CDCl_3$): δ 2.33 (s, 3H, CH_3), 4.65 (s, 2H, CH_2), 5.30 (s, 1H, NH), 7.30 (s, 1H, H-4, pyrazolone), 7.42-7.86 (m, 15H, arom-H), 8.10 (s, 1H, H-5, pyridine); MS, m/z (%): 457 (M^+, 43), 456 (95), 455 (32).

Compound **8b** was crystallized from ethanol, IR (KBr): υ 3350 cm^{-1} (NH), 2210 (C≡N), 1650 (C=O of ester group), 1620 (C=O of pyrazolone); ^{1}H-NMR ($CDCl_3$): δ 1.60 (t, 3H, CH_2CH_3), 2.50 (s, 3H, CH_3), 3.00 (s, 2H, CH_2), 4.20 (q, 2H, CH_2CH_3), 5.60 (s, 1H, NH), 7.00 (s, 1H, H-4, pyrazolone), 7.30-7.69 (m, 10H, arom-H), 7.80 (s, 1H, H-5, pyridine); MS, m/z (%): 453 (M^+, 43).

N-[3-Cyano-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridin-2-yl]benzamide (**9**).

A mixture of **1** (0.5 g, 0.0014 mol) and benzoyl chloride (5 mL) was refluxed for 2 hours, then allowed to cool and treated with petroleum ether (60-80 °C) (50 mL), whereby petroleum ether was decanted, the solid product was separated, collected by filtration, and washed with petroleum ether (60-80 °C) several times, dried, and recrystallized from ethanol to give **9** as brown crystals. The IR (KBr): υ 3400 cm^{-1} (NH), 2200 (C≡N), 1750 (C=O of benzoyl), 1695 (C=O of pyrazolone). ^{1}H-NMR (DMSO-d_6): δ 2.33 (s, 3H, CH_3), 7.35 (s, 1H, H-4, pyrazolone), 7.43-7.69 (m, 15H, arom-H), 7.79 (s, 1H, H-5, pyridine), 8.14 (s, 1H, NH); MS, m/z (%): 471 (M^+, 38), 470 (43), 453 (16), 452 (100).

2-Amino-6-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-4-phenylpyridine-3-carboxamide (**10**).

Concentrated sulphuric acid (30 mL) was cooled to 20 °C and **1** (2.5 g, 0.007 mol) was added with stirring so that the temperature

did not raise above 40 °C. The addition of **1** took 0.5 hour, the solution was stirred at room temperature for 4 hours. The sulphuric acid solution was then poured with stirring into a mixture of 500 mL of water and ice and the solution left overnight in the refrigerator, then the product was precipitated, collected by filtration and washed free of excess sulphuric acid, dried, and then recrystallized from toluene. The IR (KBr): υ 3400-3300 cm^{-1} (NH_2, $CONH_2$), 1620 (C=O). ^{1}H-NMR (DMSO-d_6): δ 2.33 (s, 3H, CH_3), 6.40 (s, 2H, NH_2), 7.06 (s, 1H, H-4, pyrazolone), 7.34-7.51 (m, 10H, arom-H), 7.72 (s, 1H, H-5, pyridine), 8.05 (s, 2H, $CONH_2$); MS, m/z (%): 386 (26), 385 (M^+, 100), 369 (16), 368 (64).

7-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido-[2,3-*d*]pyrimidin-4(3*H*)-one (**11**).

Compound **10** (0.5 g, 0.0013 mol) and 15 mL of formamide were heated at 180-190 °C for 45 minutes, then the reaction mixture was cooled whereby brown precipitate formed, was collected by filtration, dried, and recystallized from ethanol. The IR (KBr): υ 3400 cm^{-1} (NH), 1685 (CONH), 1620 (C=O of pyrazolone). ^{1}H-NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), 6.40 (s, 1H, NH), 7.06 (s, 1H, H-4, pyrazolone), 7.32-7.50 (m, 10H, arom-H), 7.60 (s, 1H, H-5, pyridine), 7.70 (s, 1H, H-2, pyrimidine); MS, m/z (%): 396 (26), 395 (M^+, 90), 394 (94), 377 (80), 368 (89), 369 (26), 343 (24), 342 (100).

4-Phenylamino-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine-2(1*H*)-thione (**12**).

Compound **1** (0.5 g, 0.0014 mol) was dissolved in pyridine (5 mL), phenyl isothiocyanate (0.2 mL, 0.0015 mol) was added to the above solution. The reaction mixture was refluxed for 6 hours, and then cooled, whereby reddish brown crystals were separated out, collected by filtration, dried and recrystallized from ethanol. The IR (KBr): υ 3400 cm^{-1} (NH), 1600 (C=O), 1240 (C=S) and no band at 2200 cm^{-1} for (C≡N); ^{1}H-NMR (DMSO-d_6): δ 2.34 (s, 3H, CH_3), 6.79 (s, 1H, H-4, pyrazolone), 7.10-7.79 (m, 15H, arom-H), 8.04 (s, 1H, H-5, pyridine), 8.55 (s, 1H, NH), 9.81 (s, 1H, SH).

7-(3-Methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido-[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dithione (**13**).

Compound **1** (1.0 g, 0.0028 mol) was dissolved in 10% alcoholic sodium hydroxide solution (5 mL), and then refluxed with excess carbon disulphide on a water bath for 8 hours. During the reflux time fresh carbon disulphide was added (two times), then the product was separated, collected by filtration, and recrystallized from acetic acid as deep red crystals. The IR (KBr): υ 3400, 3280 cm^{-1} (2 NH), 1600 (C=O), and no band at 2220 cm^{-1} for (C≡N); ^{1}H-NMR (DMSO-d_6): δ 2.3 (s, 3H, CH_3), 6.99 (s, 1H, H-4, pyrazolone), 7.11-7.49 (m, 10H, arom-H), 7.55 (s, 1H, H-5, pyridine), 8.04 (s, 2H, 2 NH); MS, m/z (%): 443 (M^+, 24).

2,4-Bis(ethylmercapto)-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**14**).

Compound **13** (0.5 g, 0.0011 mol) was refluxed with ethyl iodide (2 mL, 0.018 mol) in ethanol (20 mL) in the presence of anhydrous sodium acetate (2.0 g) for 2 hours. The colour of the reaction mixture changed from red to brown, then the brown product was precipitated, collected by filtration, and recrystallized from dioxane as deep brown crystals. The IR (KBr): υ 1650 (C=O), no bands for NH, ^{1}H-NMR ($CDC1_3$): δ 1.15 (t, 3H, CH_2CH_3), 1.42 (t, 3H, CH_2CH_3), 2.43 (s, 3H, CH_3), 2.97 (q, 2H, CH_2CH_3), 3.20 (q, 2H, CH_2CH_3), 6.99 (s, 1H, H-4, pyrazolone), 7.11-7.55 (m, 10H, arom-H), 8.03 (s, 1H, H-5, pyridine); MS, m/z (%): 500 (14), 499 (M^+, 33), 498 (100).

4-Amino-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**15**).

A mixture of **1** (0.5 g, 0.0014 mol) and formamide (5 mL) was refluxed for 1 hour. On cooling, the product was precipitated, collected by filtration, and washed several times with cold ethanol and recrystallized from ethanol as deep violet crystals. The IR spectrum did not exhibit any band attributable to (C≡N) but showed bands at 3400, 3300 cm^{-1} (NH_2), 1620 (C=O); ^{1}H-NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 7.05 (s, 1H, H-4, pyrazolone), 7.13-7.61 (m, 10H, arom-H), 8.03 (s, 1H, H-5, pyridine), 8.40 (s, 2H, NH_2); MS, m/z (%): 395 (27), 394 (M^+, 100), 393 (9), 367 (7), 261 (17).

4-Amino-2-trichloromethyl-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**16**).

A mixture of **1** (1.0 g, 0.0028 mol) and trichloroacetonitrile (0.4 mL, 0.003 mol) was refluxed in dry toluene with a catalytic amount of piperidine for 0.5 hour. The product, which was separated during the reflux, was filtered off, dried and recrystallized from ethanol. The IR (KBr): υ 3450, 3300 cm^{-1} (NH_2), 1600 (C=O) and no band for (C≡N) at 2200 cm^{-1} 780 (C-Cl); ^{1}H-NMR (DMSO-d_6): δ 2.39 (s, 3H, CH_3), 5.24 (s, br, 1H, NH), 7.11 (s, 1H, H-5, pyrazolone), 7.36-7.62 (m, 10H, arom-H), 8.00 (s, 1H, H-5, pyridine); MS, m/z (%): 511.5 (M^+, 40).

4-Amino-2-hydroxy-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**17a**).

Compound **16** (0.25 g, 0.001 mol) was heated with aqueous sodium hydroxide solution (0.5 g NaOH, 5 mL H_2O) for 0.5 hour, then the product was obtained, collected by filtration, and recrystallized from aqueous ethanol. The IR (KBr): υ br. band at 3000-3300 (OH, NH_2), 1600 cm^{-1} (C=O) and no band at 780 for C-Cl; ^{1}H-NMR ($CDCl_3$): 2.38 (s, 3H, CH_3), 5.35 (s, 2H, NH_2), 6.90 (s, 1H, H-4, pyrazolone), 7.13-7.42 (m, 10H, arom-H), 7.50 (s, 1H, H-5, pyridine), 8.50 (s, 1H, OH); MS, m/z (%): 410 (M^+, 15).

4-Amino-2-ethoxy-7-(3-mehtyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*]pyrimidine (**17b**).

A mixture of **16** (0.25 g, 0.001 mol) and sodium ethoxide solution (0.1 g Na/10 mL absoulte ethanol) was refluxed for 0.5 hour. After cooling, the precipitated solid was collected by filtration and recrystallized from dioxane. The IR (KBr): υ 3460, 3360 cm^{-1} (NH_2), 1680 (C=O); ^{1}H-NMR (DMSO-d_6): δ 1.50-1.70 (t, 3H, CH_2CH_3), 2.35 (s, 3H, CH_3), 3.45 (q, 2H, CH_2CH_3), 6.95 (s, 2H, NH_2), 7.20 (s, 1H, H-4, pyrazolone), 7.35-7.69 (m, 10H, arom-H), 7.80 (s, 1H, H-5, pyridine); MS, m/z (%): 438 (M^+, 16).

4-Chloro-7-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-yl)-5-phenylpyrido[2,3-*d*][1,2,3]triazine (**18**).

To a cold solution of **1** (0.5 g, 0.0014 mol) in hydrochloric acid (2 mL) added a solution of sodium nitrite (0.15 g, 0.002 mol) in 5 mL of water with stirring in ice-bath (at 5 °C), after the complete addition of sodium nitrite solution the product was separated, collected by filtration, and recrystallized from ethanol to give **18**. The IR (KBr): υ 1620 cm^{-1} (C=O) and disappearance of the band attributed to (C≡N); ^{1}H-NMR ($CDC1_3$): δ 2.30 (s, 3H, CH_3),

7.30 (s, 1H, H-5, pyrazolone), 7.42-7.79 (m, 10H, arom-H), 8.10 (s, 1H, H-5, pyridine); MS, m/z (%): 414 (M^+, 30).

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