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NOTE

Synthesis of various pharma based pyrido[2,3-*d*]pyrimidine as well as pyrido[1,2-*a*]pyrimidine and their antimicrobial activities

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Abstract : 4-Amino-7-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-5-(substitutedphenyl)-1*H*-pyrido[2,3-*d*]pyrimidine-2-one (4a-j), 4-amino-7-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-5-(substitutedphenyl)-1*H*-pyrido[2,3-*d*]pyrimidine-2-thione (5a-j), 4-thioureido-7-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-5-(substitutedphenyl)-1*H*-pyrido[2,3-*d*]pyrimidine-2-thione (6a-j), 2-methyl-7-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-5-(substitutedphenyl)-3*H*-pyrido[2,3-*d*]pyrimidine-4-one (7a-j) and 4-methyl-5-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-2-oxo-7-(substitutedphenyl)-2*H*-pyrido[1,2-*a*]pyrimidine-8-carbonitrile (8a-j) have been synthesized by the reaction of 2-amino-6-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-4-(substitutedphenyl)pyridine-3-carbonitrile (3) with urea, thiourea, ammonium thiocyanate, acetic anhydride and ethylacetoacetate respectively. These compounds have been screened for their antibacterial and antifungal activities against different microorganisms. The structures of novel synthesized compounds have been established on the basis of elemental analysis, ^{1}H NMR and IR spectral data.

Keywords : Pyrimidine, synthesis, antimicrobial activities.

Introduction

The increasing importance of pyrimidine and its derivatives as intermediates for the synthesis of biologically active[1,2] compounds. Pyrimidines and fused pyrimidines, being an integral part of DNA and RNA, play an essential role in several biological processes and have considerable chemical and pharmacological importance. Diverse biological properties have been shown to be associated with numerous fused pyrimidines, including antiallergic[3], hypnotic[4], anti-inflammatory[5], antiviral[6] and plant bactericidal[7] effects. Pyrimidine derivatives, a constituent unit of nucleobases[8], are useful in drug discovery. Recently, it has been proved that pyrimidine and fused heterocyclic pyrimidine nucleus are potent antiviral agents[9].

The synthesis of pyridopyrimidine and their derivatives is of high interest in organic chemistry, because of their biological and pharmacological activities. The pyridopyrimidine functionality has also been used for the development of biologically interesting molecules[10]. Earlier reported procedures for the synthesis of pyridopyrimidines typically involved a multistep-approach[11]. Pyridopyrimidines were reported to be used as a cytotoxic agents and apoptosis inducers[12], adenosine kinase inhibitors[13,14], inhibitors of pneumocystis carinii, toxoplasma gondii, mycobacterium dihydrofolate reductase[15] and anti-tumor[16], antiviral[17] and antimicrobial[18] activities.

Results and discussion

The starting compounds 2-amino-6-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-4-(substitutedphenyl)-pyridine-3-carbonitrile (3) have been synthesized by refluxing 1-{4′-[(4″-methylpiperazinyl)diazenyl]phenyl}-3-(substitutedphenyl)prop-2-en-1-one (2), malononitrile and ammonium acetate. Further, it reacted with urea, thiourea, ammonium thiocynate, acetic anhydride and ethylacetoacetate to give **4a-j**, **5a-j**, **6a-j**, **7a-j** and **8a-j** respectively.

The structures were established through IR and ^{1}H NMR spectral data. In IR spectra of **4a-j**, significant bands were appeared at 3232 (-NH), 3336 (-NH_2) and 1680 cm^{-1} (C=O). In ^{1}H NMR spectra of these compounds revealed signals at δ 8.0 (-NH) and 7.4 (-NH_2), and the other signals in their expected positions. In IR spectra of

5a-j significant bands exhibited at 3319 (-NH), 3579 (-NH_2) and 1168 cm^{-1} (C=S). In ^1H NMR spectra of these compounds structure was evident by appearance of signal at δ 8.17 (-NH) and 7.42 (-NH_2), and other signals in their expected positions. IR spectrum of **6a-j** showed bands at 3215 (-NH), 3336 (-NH_2) and 1178 cm^{-1} (C=S). ^1H NMR spectra revealed signals at δ 9.0 (-NH) and 9.2 (-NH_2), and other signals in their expected positions. In the IR spectra of **7a-j**, significant bands appeared at 3215 (-NH), 1598 (C=O) and 2945 cm^{-1} (-CH_3). The ^1H NMR spectra of these compounds show signals at δ 10.0 (-NH), 2.5 (-CH_3) and other signals at expected positions. The IR spectra of **8a-j** showed absorption bands at 2206 (-CN) and 1600 cm^{-1} (C=O). In the ^1H NMR spectra, these compounds showed signal at δ 2.6 (-CH_3) beside the other signals in their expected positions. All the compounds were tested for their effect on the growth of microbial cultures at concentration level ranging from 128–512 μg/mL on different organisms.

Antibacterial activity : All the compounds were tested for *in vitro* screening against Gram-positive *Staphylococcus aureus* and Gram-negative *E. coli* and *Pseudomonas aeruginosa*. The minimum inhibitory concentration (MIC) was determined using tube dilution method according to the standard procedure[19] at three-test concentrations 128, 256, 512 μg/mL. Inoculums of standard suspension (0.1 mL of the test organism strain which contains 10^6 bacilli/mL) were added. The tubes were incubated at 37 °C for 48 h and then examined for the presence or absence of growth of the organism. The lowest concentration, which showed no visible growth, was taken as an end point minimum inhibitory concentration (MIC). The MIC level of compounds against these organisms are given in Table 2.

An examination of the data reveals that almost all the compounds showed antimicrobial activity in good to moderate range.

Antifungal activity : The antifungal activity of compounds has been assayed *in vitro* at a concentration of 128, 256 and 512 μg/mL against *Candida albicans*, which were maintained on nutrient agar slants, and were stored at 4 °C. None of the compounds was found to possess better activity than the fungicide Dithane-M 45 (Table 2).

Table 1. Characterization data of the compounds

Compd.	R	M.p. (°C)	Mol. formula	Mol. wt.	Yield (%)	(%) N Calcd.	(%) N Found
4a	4-OCH_3	193	$C_{25}H_{26}O_2N_8$	470	59	23.81	23.86
4b	-H	188	$C_{24}H_{24}ON_8$	440	60	25.44	25.46
4c	2-Cl	171	$C_{24}H_{23}ON_8Cl$	475	55	23.59	23.60
4d	3-Cl	181	$C_{24}H_{23}ON_8Cl$	475	52	23.59	23.62
4e	4-Cl	189	$C_{24}H_{23}ON_8Cl$	475	58	23.59	23.64
4f	4-$N(CH_3)_2$	>300	$C_{26}H_{29}ON_{10}$	483	62	26.07	26.11
4g	3-NO_2	280	$C_{24}H_{23}O_3N_9$	485	60	25.97	25.99
4h	2-OH	>300	$C_{24}H_{24}O_2N_8$	457	68	24.55	24.60
4i	3-OCH_3, 4-OH	>300	$C_{25}H_{27}O_3N_8$	486	64	23.03	23.07
4j	3-OCH_3, 4-OCH_3	>300	$C_{26}H_{29}O_3N_8$	500	60	22.39	22.43
5a	4-OCH_3	228	$C_{25}H_{26}ON_8S$	486	62	23.03	23.08
5b	-H	216	$C_{24}H_{24}N_8S$	456	57	24.54	24.58
5c	2-Cl	219	$C_{24}H_{23}N_8SCl$	491	64	22.82	22.85
5d	3-Cl	191	$C_{24}H_{23}N_8SCl$	491	50	22.82	22.86
5e	4-Cl	168	$C_{24}H_{23}N_8SCl$	491	60	22.82	22.87
5f	4-$N(CH_3)_2$	211(d)	$C_{24}H_{29}N_{10}S$	500	66	25.23	25.27
5g	3-NO_2	284	$C_{24}H_{23}O_2N_9S$	501	60	25.13	25.17
5h	2-OH	>300	$C_{24}H_{23}ON_8S$	472	65	23.71	23.76

Table-1 (contd.)

5i	3-OCH_3, 4-OH	>300	$C_{25}H_{26}O_2N_8S$	502	54	22.30	22.35
5j	3-OCH_3, 4-OCH_3	>300	$C_{26}H_{29}O_2N_8S$	517	58	21.69	21.73
6a	4-OCH_3	220	$C_{26}H_{27}ON_9S_2$	546	66	23.10	23.14
6b	-H	235	$C_{25}H_{25}N_9S_2$	516	71	24.45	24.49
6c	2-Cl	245(d)	$C_{25}H_{24}N_9S_2Cl$	550	66	22.92	22.96
6d	3-Cl	>300	$C_{25}H_{24}N_9S_2Cl$	550	60	22.92	22.97
6e	4-Cl	>300	$C_{25}H_{24}N_9S_2Cl$	550	69	22.92	22.94
6f	-$NH(CH_3)_2$	>300	$C_{27}H_{30}N_{10}S_2$	559	70	25.07	25.12
6g	3-NO_2	>300	$C_{25}H_{24}O_2N_{10}S_2$	561	74	24.98	25.01
6h	2-OH	205	$C_{25}H_{24}ON_9S_2$	532	58	23.71	23.77
6i	3-OCH_3, 4-OH	250	$C_{26}H_{27}O_2N_9S_2$	562	65	22.44	22.48
6j	3-OCH_3, 4-OCH_3	212	$C_{27}H_{29}O_2N_9S_2$	576	59	21.90	21.95
7a	4-OCH_3	228	$C_{26}H_{27}O_2N_7$	469	65	20.88	20.92
7b	-H	239	$C_{25}H_{25}ON_7$	439	67	22.31	22.35
7c	2-Cl	202	$C_{25}H_{24}ON_7Cl$	474	60	20.69	20.72
7d	3-Cl	298	$C_{25}H_{24}ON_7Cl$	474	63	20.69	20.75
7e	4-Cl	236	$C_{25}H_{24}ON_7Cl$	474	60	20.69	20.74
7f	4-$N(CH_3)_2$	>300	$C_{27}H_{30}ON_8$	482	63	23.22	23.27
7g	3-NO_2	>300	$C_{25}H_{24}O_3N_8$	484	61	23.13	23.16
7h	2-OH	>300	$C_{25}H_{25}O_2N_7$	455	60	21.52	21.57
7i	3-OCH_3, 4-OH	284	$C_{26}H_{28}O_3N_7$	485	66	20.19	20.23
7j	3-OCH_3, 4-OCH_3	294	$C_{27}H_{30}O_3N_7$	499	61	19.63	19.66
8a	4-OCH_3	227	$C_{28}H_{27}O_2N_7$	493	56	19.87	19.90
8b	-H	213	$C_{27}H_{25}ON_7$	463	59	21.15	21.22
8c	2-Cl	197	$C_{27}H_{24}ON_7Cl$	498	64	19.69	19.72
8d	3-Cl	226	$C_{27}H_{24}ON_7Cl$	498	55	19.69	19.76
8e	4-Cl	215	$C_{27}H_{24}ON_7Cl$	498	61	19.69	19.74
8f	4-$N(CH_3)_2$	174	$C_{29}H_{30}ON_8$	507	64	22.12	22.16
8g	3-NO_2	>300	$C_{27}H_{24}O_3N_8$	508	55	22.03	22.08
8h	2-OH	183	$C_{27}H_{25}O_2N_7$	479	57	20.45	20.48
8i	3-OCH_3, 4-OH	165	$C_{28}H_{27}O_3N_7$	509	52	19.24	19.29
8j	3-OCH_3, 4-OCH_3	>300	$C_{29}H_{29}O_3N_7$	523	55	18.73	18.77

Table 2. Antimicrobial activity of the compounds

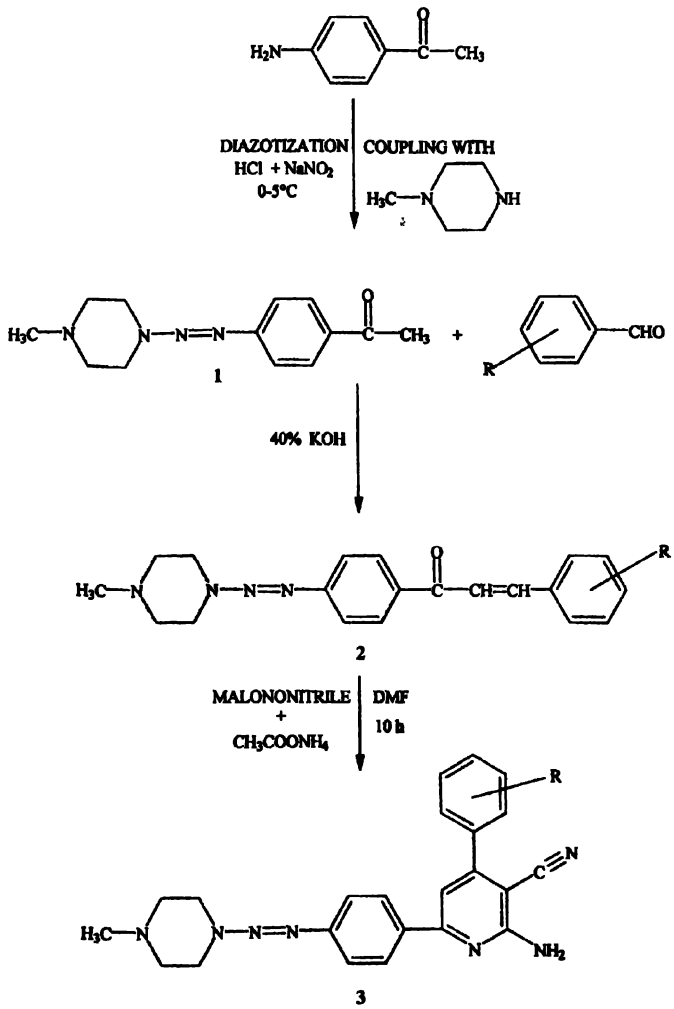
The compounds were tested by tube dilution method at three test concentration 128, 256 and 512 µg/mL against two Gram-negative and a Gram-positive bacteria and yeast. The following results were obtained

	E. coli			*P. aeruginosa*			*S. aureus*			*C. albicans*		
	128	256	512	128	256	512	128	256	512	128	256	512
4a	-	+	+	-	+	+	-	-	+	-	+	+
4b	-	+	++	-	++	++	-	+	++	-	-	-
4c	-	++	++	-	++	+++	-	++	+++	-	-	+
4d	-	++	+++	-	+++	+++	-	+++	+++	-	+	+
4e	-	++	+++	-	++	+++	-	++	+++	-	-	-
4f	-	++	++	-	+	++	-	++	++	-	-	-
4g	-	+	+	-	+	++	-	+	++	-	-	-
4h	-	+	++	-	++	++	-	++	++	-	-	-

Table-2 (contd.)

4i	-	+	++	-	+	++	-	+	++	-	-	-
4j	-	++	++	-	++	+++	-	++	++	-	-	+
5a	-	+	+	-	+	+	-	+	+	-	-	+
5b	-	+	++	-	+	++	-	+	++	-	-	-
5c	-	+++	+++	-	+++	+++	-	+++	+++	-	-	-
5d	-	++	+++	-	++	++	-	++	++	-	+	+
5e	-	+++	+++	-	++	+++	-	++	+++	-	-	-
5f	-	+	++	-	+	++	-	+	++	-	-	-
5g	-	-	+	-	+	+	-	+	+	-	-	-
5h	-	+	+	-	+	++	-	+	++	-	-	-
5i	-	+	++	-	+	++	-	+	++	-	-	-
5j	-	+	++	-	+	++	-	-	++	-	-	+
6a	-	-	+	-	+	+	-	-	+	-	+	+
6b	-	+	++	-	++	++	-	+	++	-	-	-
6c	-	++	+++	-	++	+++	-	++	++	-	-	+
6d	-	++	+++	-	+++	+++	-	+++	+++	-	+	+
6e	-	++	+++	-	++	+++	-	++	+++	-	-	-
6f	-	+	++	-	+	++	-	++	++	-	-	-
6g	-	+	+	-	+	+	-	+	++	-	-	-
6h	-	+	++	-	++	++	-	++	++	-	-	-
6i	-	+	++	-	+	++	-	+	++	-	-	-
6j	-	++	++	-	++	+++	-	++	++	-	-	+
7a	-	+	++	-	+	++	-	++	++	-	-	+
7b	-	+	++	-	+	++	-	+	-	-	-	-
7c	-	++	+++	-	++	+++	-	++	+++	-	-	-
7d	-	++	+++	-	++	++	-	++	++	-	+	+
7e	-	++	+++	-	++	+++	-	++	+++	-	-	-
7f	-	+	++	-	+	++	-	+	++	-	-	-
7g	-	-	+	-	+	+	-	-	+	-	-	-
7h	-	+	+	-	+	++	-	+	++	-	-	-
7i	-	+	++	-	+	++	-	++	++	-	-	-
7j	-	+	++	-	+	++	-	-	++	-	-	+
8a	-	-	+	-	+	++	-	+	++	-	-	-
8b	-	+	++	-	+	++	-	+	++	-	-	-
8c	-	++	++	-	++	+++	-	++	+++	-	-	+
8d	-	++	++	-	+	++	-	++	+++	-	-	-
8e	-	++	+++	-	++	+++	-	++	+++	-	-	-
8f	-	+	+	-	+	++	-	+	++	-	-	-
8g	-	-	+	-	-	+	-	-	+	-	-	-
8h	-	+	+	-	++	++	-	+	++	-	-	-
8i	-	+	+	-	+	++	-	+	++	-	-	-
8j	-	+	++	-	+	++	-	++	++	-	-	+
Streptomycin	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	-	-
Dithane-M 45	-	-	-	-	-	-	-	-	-	-	++++	++++

(-) = < 6 mm, (+) = 7-10 mm, (++) = 11-15 mm, (+++) = 16-21 mm, (++++) = 22-28 mm.



1

2

3

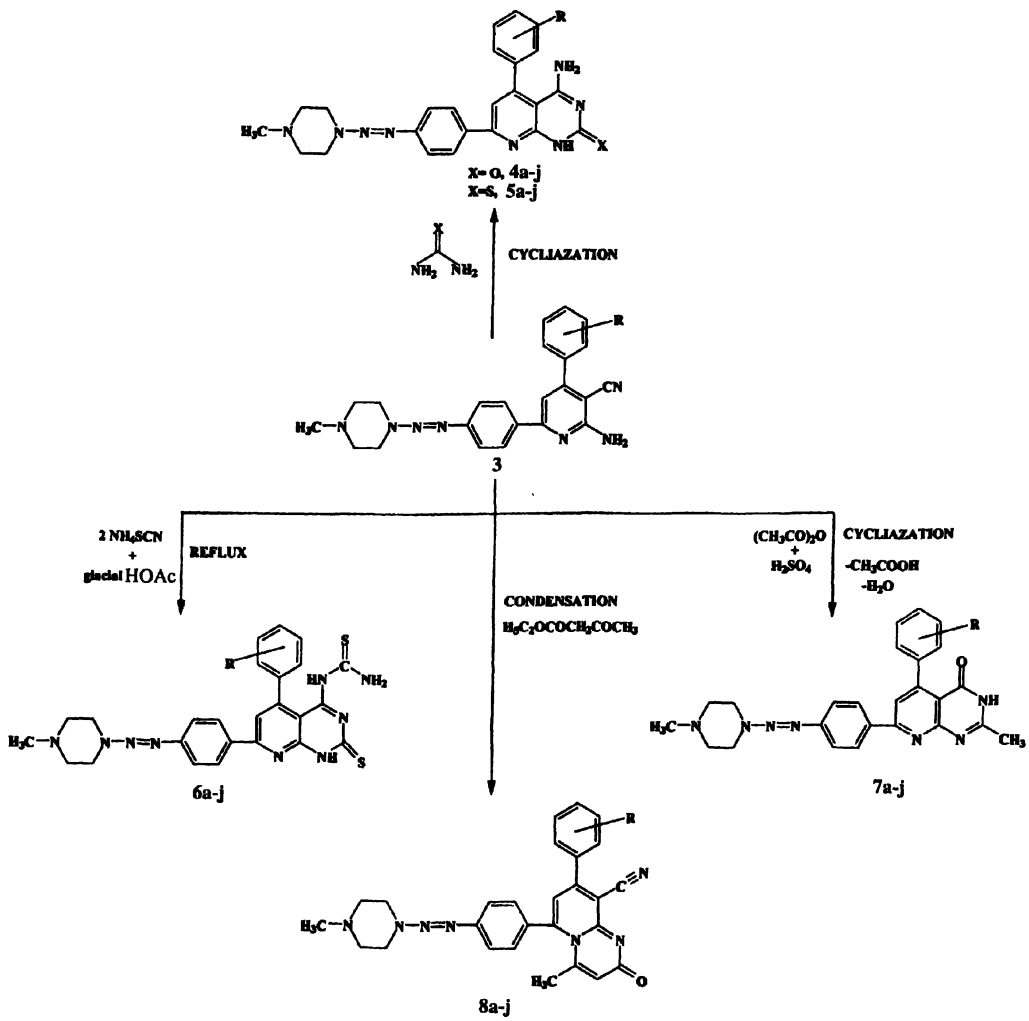
	R		R
a	4-OCH_3	f	4-$N(CH_3)_2$
b	-H	g	3-NO_2
c	2-Cl	h	2-OH
d	3-Cl	i	3-OCH_3, 4-OH
e	4-Cl	j	3,4-di-OCH_3

Scheme 1

Experimental

Melting points were taken in open capillaries and are uncorrected. The purity of compounds was checked by TLC on silica gel 'G' coated glass plates. IR spectra were recorded in KBr on Shimadzu FTIR spectrophotometer, ^1H NMR spectra ($CDCl_3$) were recorded on Brucker Avance-II-400 spectrometer using TMS as internal standard.

Synthesis of 1-{4'-[(4''-methylpiperazinyl)diazenyl)]-phenyl}-3 (substitutedphenyl)prop-2-en-1-one (2) : A mix-



	R		R
a	4-OCH_3	f	4-$N(CH_3)_2$
b	-H	g	3-NO_2
c	2-Cl	h	2-OH
d	3-Cl	i	3-OCH_3, 4-OH
e	4-Cl	j	3,4-di-OCH_3

Scheme 2

ture of *p*-aminoacetophenone and concn. HCl was warmed on water bath to make clear solution. Then it was cooled at 0–5 °C and solution of $NaNO_2$, was added to it, until the starch iodide paper becomes blue black. The mixture was stirred for one hour. After diazotization was completed, *N*-methylpiperazin (0.01 mol) solution in NaOH was added in the above mentioned solution with constant stirring. The pH of the reaction mixture was maintained

at 7–8 by the simultaneous addition of sodium carbonate solution. The resulting solid was filtered, washed with cold water and dried (yield 65–70%).

To a solution of 1-{4''-[(4''-methylpiperazinyl)-diazenyl]phenyl}ethan-1-one (**1**) (0.01 mol) in KOH, various substituted aldehyde (0.01 mol) was added portionwise with constant stirring. The mixture was stirred for 2 h, then the contents were poured into crushed ice and concn. HCl was added. The separated product was filtered and crystallized from ethanol (yield 65–79%).

Synthesis of 2-amino-6-{4'-[(4''-methylpiperazinyl)-diazenyl]-phenyl}-4-(substitutedphenyl)pyridine-3-carbonitrile (**3**) : A mixture of **2** (0.01 mol), malononitrile (0.01 mol) and ammonium acetate (0.08 mol) in DMF was refluxed for 10 h and then allowed to stand at room temperature. The contents were then poured into crushed ice with constant stirring. The solid, thus obtained, was washed with water and recrystallized from DMF-ethanol (1 : 10) (yield 60–71%).

Synthesis of 4-amino-7-{4'-[(4''-methylpiperazinyl)-diazenyl]phenyl}-5-(substitutedphenyl)-1H-pyrido[2,3-d]-pyrimidine-2-one (**4a-j**) : A mixture of **3** (0.01 mol) and urea (0.02 mol) was heated under reflux at 120–130 °C for 6 h. After completion of the reaction, the reaction mixture was poured in crushed ice. The product thus obtained was filtered, washed with water and recrystallized from DMF-ethanol (1 : 10) (yield 52–68%).

(**4b**) : IR (KBr) : 3336 (-NH_2), 3232 (-NH), 2924 (-CH_3), 1680 (C=O), 1631 cm^{-1} (N=N); ^1H NMR of compound **4a** : δ 8.14 (2H, d, *J* 8.0 Hz, C-H), 8.00 (1H, s, N-H), 7.95 (1H, s, C-H, (pyrido-pyrimidine ring)), 7.75 (2H, d, *J* 8.0 Hz, C-H), 7.63 (2H, d, *J* 8.4 Hz, C-H), 7.40 (2H, s, -NH_2), 6.62 (2H, d, *J* 8.4 Hz, C-H), 3.40 (3H, s, O-CH_3), 2.70 (3H, s, CH_3-N), 2.80–3.20 (4H, m, -CH_2-N), 2.20–2.50 (4H, m, -N-CH_2).

Synthesis of 4-amino-7-{4'-[(4''-methylpiperazinyl)-diazenyljphenyl}-5-(substitutedphenyl)-1H-pyrido[2,3-d]-pyrimidine-2-thione (**5a-j**) : A homogenous-grind mixture of **3** (0.01 mol) and thiourea (0.02 mol) was heated under reflux at 120–130 °C for 6 h. After completion of the reaction, the reaction mixture was poured into crushed ice. The product thus obtained was filtered, washed with water and recrystallized from DMF-ethanol (1 : 10) (yield 50–66%).

(**5b**) : IR (KBr) : 3579 (-NH_2), 3319 (-NH), 2924 (-CH_3), 1598 (N=N), 1168 cm^{-1} (C=S); ^1H NMR of compound **5a** : δ 8.17 (1H, s, N-H), 8.12 (2H, d, *J* 8.0 Hz, C-H), 7.95 (1H, s, C-H, (pyrido-pyrimidine ring)), 7.76 (2H, d, *J* 8.0 Hz, C-H), 7.28 (2H, d, *J* 8.7 Hz, C-H), 7.42 (2H, s, -NH_2), 6.60 (2H, d, *J* 8.4 Hz, C-H), 3.35 (3H, s, O-CH_3), 2.72 (3H, s, CH_3-N), 2.80–3.20 (4H, m, -CH_2-N), 2.20–2.50 (4H, m, -N-CH_2).

Synthesis of 4-thioureido-7-{4'-[(4''-methylpiperazinyl) diazenyl]phenyl}-5-(substitutedphenyl)-1H-pyrido[2,3-d]pyrimidine-2-thione (**6a-j**) : A mixture of **3** (0.01 mol) and ammonium thiocyanate (0.03 mol) in glacial acetic acid (15 mL) was heated under reflux at 130–140 °C for 10 h. The solid that separated on cooling and dilution with water was filtered off and purified by boiling several times with ethanol. Product thus obtained, was dried and recrystallized from DMF-ethanol (1 : 10) (yield 58–74%).

(**6b**) : IR (KBr) : 3336 (-NH_2), 3215 (-NH), 2929 (-CH_3), 1600 (N=N), 1178 cm^{-1} (C=S); ^1H NMR of compound **6b** : δ 9.20 (2H, s, -NH_2), 9.00 (2H, s, N-H), 7.99 (2H, d, *J* 8.0 Hz, C-H), 7.85 (1H, s, C-H, (pyrido-pyrimidine ring)), 7.63 (2H, d, *J* 8.0 Hz, C-H), 7.00–7.80 (5H, m, Ar-H), 2.50–3.00 (4H, m, -CH_2-N), 2.10 (3H, s, CH_3-N), 1.20–2.00 (4H, m, -N-CH_2).

Synthesis of 2-methyl-7-[4'-{(4''-methylpiperazinyl)-diazenyl]-phenyl}-5-(substitutedphenyl)-3H-pyrido[2,3-d]pyrimidine-4-one (**7a-j**) : A mixture of **3** (0.01 mol), acetic anhydride (0.03 mol) and H_2SO_4 (0.5 mL) was heated under reflux for 4 h. The resulting residual mass was cooled, poured into crushed ice, filtered, washed with water and recrystallized from ethanol (yield 59–67%).

(**7c**) : IR (KBr) : 3215 (-NH), 2945 (-CH_3), 1598 (C=O), 1546 (N=N), 765 cm^{-1} (C-Cl); ^1H NMR of compound **7b** : δ 10.00 (2H, s, N-H), 8.00 (2H, d, *J* 8.0 Hz, C-H), 7.91 (1H, s, C-H, (pyrido-pyrimidine ring)), 7.65 (2H, d, *J* 8.0 Hz, C-H), 7.00–7.80 (5H, m, Ar-H), 2.52–3.00 (4H, m, -CH_2-N), 2.50 (3H, s, -CH_3), 2.15 (3H, s, CH_3-N), 1.20–2.00 (4H, m, -N-CH_2).

Synthesis of 4-methyl-5-{4'-[(4''-methylpiperazinyl)-diazenyl]phenyl}-5-oxo-7-(substitutedphenyl)-4-methyl-2H-pyrido[1,2-a]pyrimidine-8-carbonitrile (**8a-j**) : A mixture of **3** (0.01 mol) and ethylacetoacetate (0.02 mol) was heated under reflux at 180 °C for 5 h. The oil obtained was washed with diluted NaOH solution and precipitated

by adding ethanol. The solid so obtained was filtered and recrystallized from DMF-ethanol (1 : 10) (yield 51–64%).

(8c) : IR (KBr) : 2908 ($-CH_3$), 2206 (-CN), 1600 (C=O), 1546 (N=N), 765 cm^{-1} (C-Cl); ^1H NMR of compound **8a** : δ 8.10 (2H, d, *J* 8.0 Hz, C-H,), 7.70 (1H, s, C-H, (pyrido-pyrimidine ring)), 7.63 (2H, d, *J* 6.8 Hz, C-H), 7.47 (2H, d, *J* 6.8 Hz, C-H), 7.37 (1H, s, C-H), 6.61 (2H, d, *J* 8.0 Hz, C-H), 3.40 (3H, s, O-CH_3), 2.60 (3H, s, $-CH_3$), 2.60–3.00 (4H, m, $-CH_2-N$), 2.10 (3H, s, CH_3-N), 1.20–2.00 (4H, m, $-N-CH_2$).

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