Synthesis of some novel pyrazolo[3,4-*d*]pyrimidine derivatives

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Abstract

Reaction of ethyl imidates derived from *N*-aryl-5-amino-4-cyanopyrazoles with amines or arylhydrazines gave only 4-substituted pyrazolo[3,4-*d*]pyrimidines, resulting from cyclization followed by Dimroth rearrangement. From the reaction with arylhydrazines, a mixture of the hydrazines and their oxidized forms, the azo products, was obtained. This was proven by an independent synthesis starting from the corresponding 4-chloropyrazolo[3,4-*d*]pyrimidines as starting material. The structures of the compounds obtained were confirmed by mass spectrometry, ^{1}H and ^{13}C NMR.

Keywords: Cyanopyrazoles, pyrazolo[3,4-*d*]pyrimidines, Dimroth rearrangement

Introduction

In recent years, pyrazolopyrimidines and related fused heterocycles have been identified as bioactive molecules. They are known to function as CNS (Central Nervous System) depressants,[1] neuroleptic agents,[2] and as tuberculostatic[3]. Pyrazolo[3,4-*d*]pyrimidines were identified as a general class of adenosine receptors.[4,5] Moreover, fluorinated compounds find much importance in the pharmaceutical field.[6] The introduction of a CF_3 group provides compounds with increased lipophylicity and activity when compared to their non-fluorinated analogues. The trifluoromethyl substituted compounds have been reported to possess biological activity as herbicides, fungicides,[7] analgesic, antipyretic, and inhibitors for platelet aggregation.[8]

We have concentrated our attention on *ortho*-aminocyanopyrazoles and their derivatives as inhibitors of xanthine oxidase.[9] With the objective of synthesizing members of this class of compounds we started from the key intermediates **2a**–**d** (ethyl *N*-4-cyano-1-(4-substituted)-1*H*-pyrazol-5-ylformimidate). These compounds are readily prepared from the N_1-substituted-5-amino-4-cyanopyrazoles **1** (Scheme 1) and react with arylhydrazine derivatives to produce pyrazolo[3,4-d]pyrimidines. The antifungal activity of these new heterocycles is currently being evaluated.

Results and Discussion

The 5-amino-1-substitutedpyrazole-4-carbonitrile **1** were reacted with triethylorthoformate to give the corresponding ethoxymethylene amino derivatives **2** which are the key compounds for the preparation of pyrazolo[3,4-*d*]pyrimidine derivatives. Reaction of **2** with hydrazine hydrate was known to produce 4-imino-pyrazolo[3,4-*d*]pyrimidines[10] **3** with mp 236-238 ºC [Lit.[10] mp 235ºC]. When **2** was reacted with phenylhydrazine derivatives under reflux, rather than yielding **4** as expected, two products were isolated as white and orange solids respectively. Based on spectroscopic data, as described below, to these compounds were assigned structures **5** and **6**, respectively.

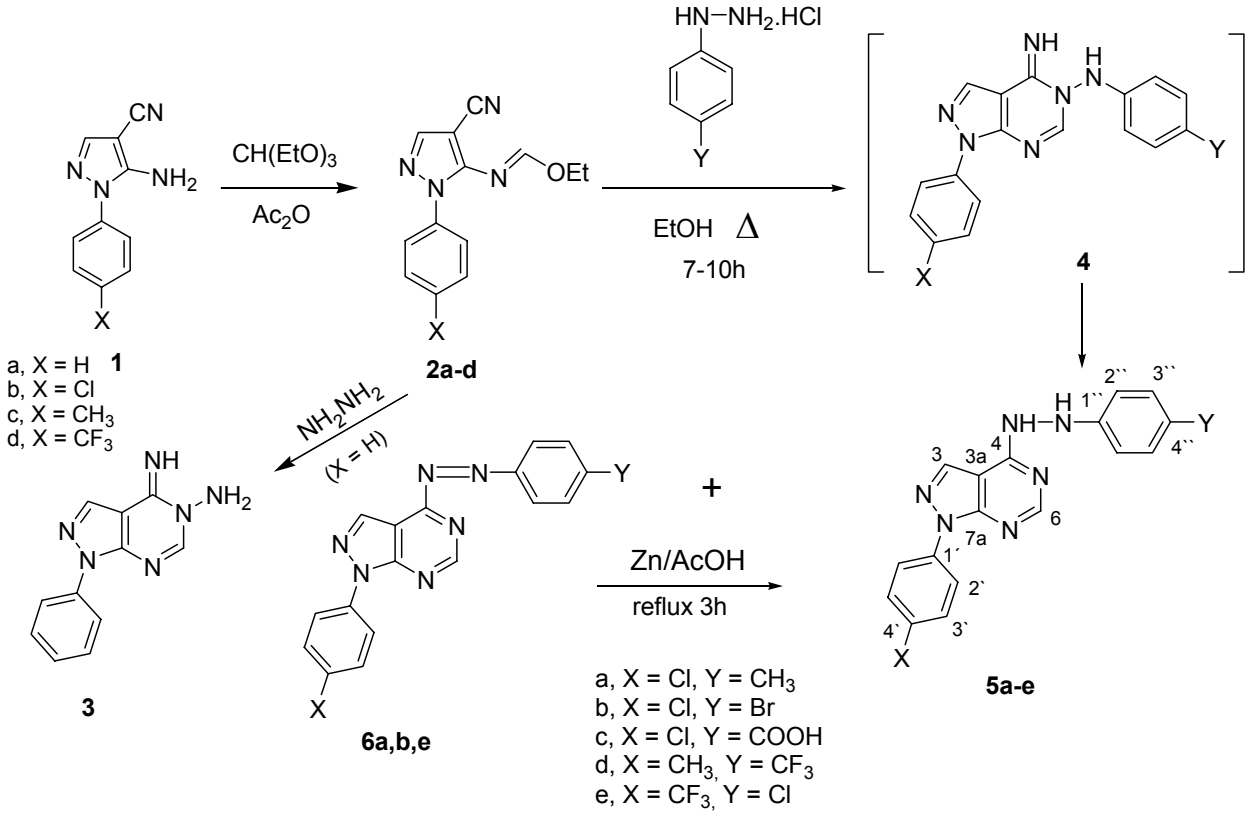
Several experiments were performed with different starting substituted pyrazoles, **1**, varying the reaction time, Table 1. A mixture of both compounds, **5** and **6**, was obtained and their proportion depended on the reaction time, longer heating time yielding mainly compounds **6** (entries 1, 2 and 5 versus 6, 7 and 8).

The NMR spectrum of the white solid showed all the expected signals for two *para*-substituted phenyl rings, two C-H singlets and two NH singlets, which could also agree with structure **4** in view of the previously reported results with hydrazine hydrate.[10]

No NH signals were found in the proton NMR of the orange solid. This absence suggested that the oxidized form of the hydrazine was present**.** We are therefore led to propose structures **5** for the hydrazine form and **6** for the azo form; the rearrangement of **4** to **5** could be due to Dimroth rearrangement.[11,12] Mass spectrometry confirmed the molecular weight of compounds **6**. The structure of compound **4** was excluded based on NMR data. The one dimensional, ^{1}H NMR of compound **5a** showed all the expected signals for aromatic protons and two singlets at 10.04 and 8.34 for the two NH protons, and this was not sufficient to differentiate between structures **4a** and **5a**. For this reason, we obtained the HMQC and HMBC NMR spectra and made an unambiguous assignment in the ^{1}H and ^{13}C NMR spectrum (see experimental part).

In the HMBC spectrum, we observed an intense correlation peak between NH at 8.34 and carbon signals at 112.4 (C-2``, 6``), 145.6 (C-1``) and 161.0 ppm (C-4) which is characteristic only for structure **5a** but not for **4a**, because no correlation peak between the NH and C-6 was observed.

To confirm the structure of compounds **5** an independent route was followed reacting 4-chloropyrazolopyrimidine **7**, mp 139-140 ºC [Lit.[14] mp 138-139 ºC], with *p*-tolylhydrazine, and the products isolated were the pyrazolo[3,4-*d*]pyrimidines **5a** (25%) and **6a** (54%) whose spectral characteristics were completely coincident with the samples obtained before (Scheme 2).



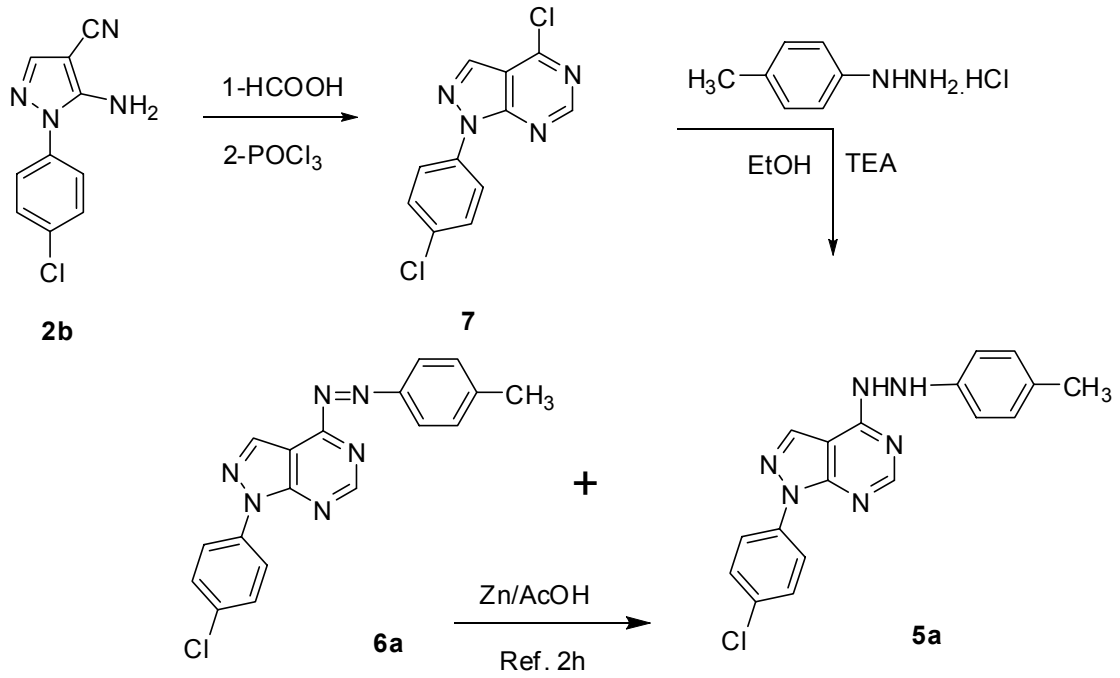
Scheme 1

Table 1. Preparation of compounds **5** and **6**

Entry			Reaction time (hr)	Yield (%)	
	X	Y		Hydrazine **5**	Azo **6**
1	Cl	CH_3	4	72 (5a)	20 (6a)
2	Cl	Br	4	68 (5b)	22 (6b)
3	Cl	COOH	4	55 (5c)	*
4	CH_3	CF_3	4	61 (5d)	*
5	CF_3	Cl	4	70 (5e)	21 (6e)
6	Cl	CH_3	7-10	10 (5a)	77 (6a)
7	Cl	Br	7-10	15 (5b)	56 (6b)
8	CF_3	Cl	7-10	18 (5e)	70 (6e)

* The azo form was not isolated.

Moreover, compound **5a** could be converted to compound **6a** by long reflux in ethanolic triethylamine solution and compounds **6** were reduced by zinc in acetic acid to afford compounds **5**. These results also prove the correct structures of compounds **5** and **6** as suggested in scheme 1.



Scheme 2

It seemed of interest to study the analogous reactions of ethoxymethylene amino derivatives **2** with amines. In this case, we considered that the presence of the amidine moiety may ensure the possibility of closure of the pyrimidine ring, resulting in novel derivatives of pyrazolo[3,4-*d*]pyrimidine of significant interest for biological study, since such compounds are substituted analogues of the well-known drug allopurinol.[13]

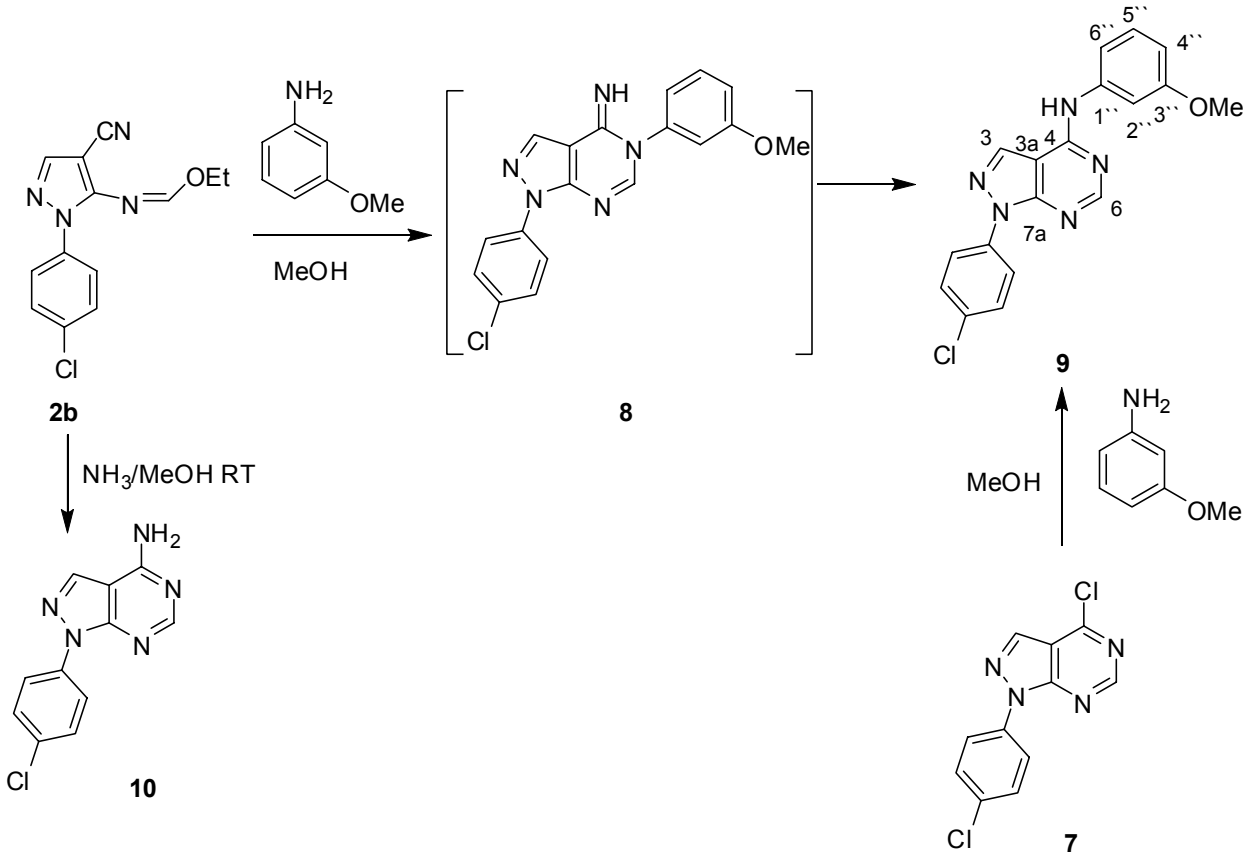
As the amines for studying their reactions with the amidine **2b**, we selected the relatively low-basicity *m*-anisidine and the more basic ammonia.

Heating ethoxymethylene amino derivatives **2b** with amines led to the formation of pyrazolo[3,4-*d*]pyrimidines **9** and **10**. The rates of these reactions differ quite significantly. In order for the process to go to completion (TLC), it was necessary to stir the reaction mixture for 3 h in methanol at RT. A reaction time of 14 h in refluxing methanol was required for the least basic *m*-anisidine to react to completion. Again the reaction of **2b** (X = Cl) with *m*-anisidine afforded the Dimroth rearrangement product **9** via the intermediate **8** (Scheme 3). The reaction of pyrazole **2b** with ammonia led exclusively to the 4-aminopyrazolo[3,4-*d*]pyrimidine derivative **10** with mp 280-282 ºC [Lit. [14] mp 284 ºC].

The alternative structure **8** was excluded based on NMR data. The one-dimensional ^{1}H NMR spectrum, showed all the expected signals with protons 3 and 6 overlapping in a sharp singlet at 8.54 ppm (integrating for two protons) and a sharp NH signal at 10.19 ppm.

In the HMBC spectrum, we observe an intense correlation peak for the NH proton with the peaks at 107.2 (C-2``) and 113.5 ppm (C-6``) which is characteristic only of structure **9** but not for **8**, where the indicated proton and carbon atoms are separated by five bonds.

The structure of compounds **9** could also be confirmed by reaction of 4-chloropyrazolopyrimidine **7** with *m*-anisidine (Scheme 3).



Scheme 3

In conclusion reaction of various monosubstituted hydrazines with ethyl *N*-4-cyano-1-(4-substituted)-1*H*-pyrazol-5-ylformimidate **2** yields a mixture of the Dimroth rearrangement products, **5**, together with their oxidized forms **6**. The proportion of **5** and **6** depends on the reaction time; longer heating yielding mainly compounds **6**. Reduction of compounds **6** afforded the corresponding hydrazinyl derivatives **5**. Reaction of compound **2** with *m*-anisidine afforded only the Dimroth rearrangement product **9**.

Experimental Section

General Procedures. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. IR spectra were registered on a Perkin Elmer FTIR-1600. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.4 MHz) spectra were recorded on a Varian Unity Plus Spectrometer. Double resonance, HMQC and HMBC experiments were carried out for complete assignment of

proton and carbon signals in the NMR spectra, whenever possible. High resolution mass spectra were obtained on a AutoSpec E spectrometer. Elemental analyses were obtained on a Leco CHNS-932 instrument. Compounds **3**, **7** and **10** were prepared by known methods.[10,14]

General procedure for preparation of 2a-e

A mixture of 5-amino-4-cyano-1-substituted pyrazole (0.2 mol), triethylorthoformate (20 ml) and acetic anhydride (20 ml) was heated under reflux for 7 h and then evaporated under reduced pressure. The residue was treated with ethanol and the solid product so formed was collected by filtration, washed with ethanol and crystallized from EtOH-H_2O.

Ethyl *N*-(4-cyano-1-phenyl-1*H*-pyrazol-5-yl)formimidate (2a). Yield (82%), white solid, mp 56-57 ^oC (EtOH-H_2O); ^1H NMR (DMSO-d_6) δ = 1.37 (t, 3H, *J* = 7.5Hz, CH_3), 4.45 (q, 2H, *J* = 7.5Hz, CH_2), 7.47-7.63 (m, 5H, Ar-H), 7.83 (s, 1H, pyrazole-H), 8.39 (s, 1H, HC=N). Anal. Calcd: C, 64.99; H, 5.03; N, 23.32; Found: C, 64.85; H, 5.09; N, 23.57.

Ethyl *N*-[1-(4-chlorophenyl)-4-cyano-1*H*-pyrazol-5-yl]formimidate (2b). Yield (78%), white solid, mp 69-70 ^oC (EtOH-H_2O); ^1H NMR ($CDCl_3$) δ = 1.37 (t, 3H, *J* = 7.5Hz, CH_3), 4.34 (q, 2H, *J* = 7.5 Hz, CH_2), 7.47 (d, 2H, *J* = 9Hz, Ar-H), 8.14 (d, 2H, *J* = 9Hz, Ar-H), 8.20 (s, 1H, pyrazole-H), 8.42 (s, 1H, HC=N). Anal. Cald for $C_{13}H_{11}ClN_4O$: C, 56.84; H, 4.04; N, 20.40. Found: C, 56.58; H, 4.03; N, 20.10.

Ethyl *N*-[4-cyano-1-(*p*-tolyl)-1*H*-pyrazol-5-yl]formimidate (2c). Yield (75%), white solid, mp 82-84 ^oC (EtOH-H_2O); ^1H NMR ($CDCl_3$) δ = 1.37 (t, 3H, *J* = 7.5Hz, CH_3), 2.40 (s, 3H, CH_3), 4.34 (q, 2H, *J* = 7.5 Hz, CH_2), 7.24 (d, 2H, *J* = 9Hz, Ar-H), 7.50 (d, 2H, *J* = 9Hz, Ar-H), 7.80 (s, 1H, pyrazole-H), 8.38 (s, 1H, HC=N). MS (EI) *m/z* 254 (M^+, 100), 226(12), 225(20), 209(23), 198(76), 197(20), 91(10). Anal. Cald for $C_{14}H_{14}N_4O$: C, 66.13; H, 5.55; N, 22.03. Found: C, 66.29; H, 5.50; N, 22.09.

Ethyl *N*-{4-cyano-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-5-yl}formimidate (2d). Yield (74%), yellowish white solid, mp 92-94 ^oC (EtOH-H_2O); IR = 2227 (CN), 1630 (C=N); ^1H NMR ($CDCl_3$) δ = 1.30 (t, 3H, *J* = 7.5Hz, CH_3), 4.32 (q, 2H, *J* = 7.5 Hz, CH_2), 7.88-7.95 (m, 4H, Ar-H), 8.24 (s, 1H, pyrazole-H), 8.57 (s, 1H, HC=N). Anal. Cald for $C_{14}H_{11}F_3N_4O$: C, 54.55; H, 3.60; N, 18.18. Found: C, 54.61; H, 3.67; N, 18.07.

Reaction with phenylhydrazine derivatives

Method A. Reaction of ethyl *N*-4-cyano-1-(4-substitutedphenyl)-1*H*-pyrazol-5-yl formimidate

To a solution of pyrazol-5-ylformimidate (0.1 mol) in ethanol (20 ml), phenylhydrazine derivative (0.1 mol) was added (a catalytic amount of triethylamine was added in the case of phenylhydrazine HCl). The reaction mixture was heated under reflux for 7-10 h. The orange precipitate formed after cooling was filtered off, dried and recrystallized from ethanol to afford the oxidized product as an orange solid (except for entries 3 and 4, table 1, where no orange solid precipitated on cooling). The mother liquor was poured onto ice and the solid formed was filtered off and crystallized from EtOH to produce the hydrazinyl product as a white powder.

Method B. Reaction of 1-(4-chlorophenyl)-4-chloropyrazolo[3,4-*d*]pyrimidine with phenyl hydrazine derivatives

To a solution of 4-chloropyrazolo[3,4-*d*]pyrimidine (0.1 mol) in ethanol (20 ml) was added the phenylhydrazine derivative (0.1 mol) and a catalytic amount of triethylamine. The reaction mixture was heated under reflux for 7 h**.** It was followed the same work up as mentioned above.

1-(4-Chlorophenyl)-4-(2-*p*-tolylhydrazinyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine (5a). Yield (72%), white solid, mp 234-235 ^{o}C (EtOH); ^{1}H NMR (DMSO-d_6) δ = 2.17(s, 3H, CH_3), 6.70 (d, 2H, *J* = 9Hz, H-2" and 6"), 7.01 (d, 2H, *J* = 9Hz, H-3" and 5"), 7.60 (d, 2H, *J* = 9Hz, H-3' and 5'), 8.09 (s, 1H, H-3), 8.20 (d, 2H, *J* = 9Hz, H-2' and 6'), 8.34 (s, 1H, NH), 8.40 (s, 1H, H-6), 10.04 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ = 20.2 (CH_3), 99.7 (C-3a), 112.4 (C-2``), 122.1 (C-2`), 128.2 (C-4``), 129.2 (C-3`), 129.7 (C-3``), 130.2 (C-4`), 136.0 (C-3), 137.6 (C-1`), 145.6 (C-1``), 154.0 (C-7a), 156.2 (C-6), 161.0 (C-4). MS (EI) = 352 (M^{+}, ^{37}Cl, 2.8%), 350 (M^{+}, ^{35}Cl, 7%), 247(18), 245(100), 107(30), 106(52). Anal. Calcd for $C_{18}H_{15}ClN_6$: C, 61.63; H, 4.31; N, 23.96. Found: C, 61.41; H, 4.19; N, 23.96.

4-[2-(4-Bromophenyl)hydrazinyl]-1-(4-chlorophenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine (5b). Yield (68%), white solid, mp 191-192 ^{o}C (EtOH)**;** ^{1}H NMR ($CDCl_3$) δ = 6.19 (s, 1H, NH), 6.84 (d, 2H, *J* = 9Hz, Ar-H), 7.40 (d, 2H, *J* = 9Hz, Ar-H), 7.47 (d, 2H, *J* = 9Hz, Ar-H), 7.67 (brs, 1H, NH), 8.16 (d, 2H, *J* = 9Hz, Ar-H), 8.23 (s, 1H, H-3), 8.40 (s, 1H, H-6). Anal. Calcd for $C_{17}H_{12}BrClN_6$: C, 49.12; H, 2.91; N, 20.22. Found : C, 49.40; H, 3.10; N, 19.91.

4-{2-[1-(4-Chlorophenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl]hydrazinyl}benzoic acid (5c). Yield (55%), white solid, mp 284-286 ^{o}C (EtOH-DMF); ^{1}H NMR (DMSO-d_6) δ = 6.85 (d, 2H, *J* = 9Hz, Ar-H), 7.59 (d, 2H, *J* = 9Hz, Ar-H), 7.80 (d, 2H, *J* = 9Hz, Ar-H), 8.04 (s, 1H, H-3), 8.21 (d, 2H, *J* = 9Hz, Ar-H), 8.44 (s, 1H, H-6), 9.12 (s, 1H, NH), 10.26 (brs, 1H, NH), 12.18 (brs, 1H, COOH). MS (FB^{+})= 382 ((M^{+},^{37}Cl, 8%), 380(M^{+},^{35}Cl, 17%). Anal. Cald for $C_{18}H_{13}ClN_6O_2$ ½ H_2O: C, 55.53; H, 3.59; N, 21.59. Found: C, 55.71; H, 3.88; N 21.54.

1-*p*-Tolyl-4-{2-[4-(trifluoromethyl)phenyl]hydrazinyl}-1*H*-pyrazolo[3,4-*d*]pyrimidine (5d). Yield (61%), white solid, mp 224-225 ^{o}C (EtOH); ^{1}H NMR ($CDCl_3$) δ = 2.40 (s, 3H, CH_3), 6.52 (s, 1H, NH), 6.99 (d, 2H, *J* = 9Hz, Ar-H), 7.31 (d, 2H, *J* = 9Hz, Ar-H), 7.54 (d, 2H, *J* = 9Hz, Ar-H), 7.97 (d, 2H, *J* = 9Hz, Ar-H), 8.09 (brs, 1H, NH), 8.14 (s, 1H, H-3), 8.42 (s, 1H, H-6). MS(FB+) = 386($(M+2)^{+}$, 22%), 385 ($(M+1)^{+}$, 100%), 384 (M^{+}, 54%). Anal. Calcd for $C_{19}H_{15}F_3N_6$: C, 59.37; H, 3.93; N, 21.87. Found: C, 59.31; H, 4.00; N, 21.68.

4-[2-(4-Chlorophenylhydrazinyl)]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*d*]pyrimidine (5e). Yield (70%), white solid, mp 199-200 ^{o}C (EtOH); ^{1}H NMR ($CDCl_3$) δ = 6.20 (s, 1H, NH), 6.89 (d, 2H, *J* = 9Hz, Ar-H), 7.25 (d, 2H, *J* = 9Hz, Ar-H), 7.75 (brs, 1H, NH), 7.77 (d, 2H, *J* = 9Hz, Ar-H), 8.26 (s, 1H, H-3), 8.42 (d, 2H, *J* = 9Hz, Ar-H), 8.46 (s, 1H, H-6). Anal. Calcd for $C_{18}H_{12}ClF_3N_6$: C, 53.41; H, 2.99; N, 20.76. Found: C, 53.86; H, 3.18; N, 20.46.

1-(4-Chlorophenyl)-4-(*p*-tolyldiazenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine (6a). Yield (77%), orange solid, mp 204-205 ^{o}C (EtOH); ^{1}H NMR ($CDCl_3$) δ = 2.52 (s, 3H, CH_3), 7.44 (d, 2H, *J* = 9Hz, Ar-H), 7.55 (d, 2H, *J* = 9Hz, Ar-H), 8.12 (d, 2H, *J* = 9Hz, Ar-H), 8.29 (d, 2H, *J* = 9Hz, Ar-

H), 8.66 (s, 1H, H-3), 9.28 (s, 1H, H-6). Anal. Calcd for $C_{18}H_{13}ClN_6$: C, 61.98; H, 3.76; Cl, 10.16; N, 24.09. Found: C, 61.90; H, 4.02; N, 23.72.

4-[(4-Bromophenyl)diazenyl]-1-(4-chlorophenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine (6b). Yield (56%), orange solid, mp 330-332 ^{o}C (EtOH); ^{1}H NMR ($CDCl_3$) δ = 7.57 (d, 2H, *J* = 9Hz, Ar-H), 7.80 (d, 2H, *J* = 9Hz, Ar-H), 8.09 (d, 2H, *J* = 9Hz, Ar-H), 8.29 (d, 2H, *J* = 9Hz, Ar-H), 8.63 (s, 1H, H-3), 9.30 (s, 1H, H-6). Anal. Calcd for $C_{17}H_{10}BrClN_6$: C, 49.36; H, 2.44; N, 20.32. Found: C, 49.29; H, 2.59; N 19.94.

4-[(4-Chlorophenyl)diazenyl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*d*]pyrimidine (6e). Yield (70%), orange solid, mp 204-205 ^{o}C (EtOH); ^{1}H NMR ($CDCl_3$) δ = 7.64 (d, 2H, *J* = 9Hz, H-2" and 6"), 7.86 (d, 2H, *J* = 8.7 Hz, H-3' and 5'), 8.17 (d, 2H, *J* = 8.4 Hz, H-3" and 5"), 8.56 (d, 2H, *J* = 8.7 Hz, H-2´and 6'), 8.67 (s, 1H, H-3), 9.33 (s, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ = 105.4 (C-3a), 121.1 (C-2` and C-6'), 122.09 and 125.70 (right hand side of q, ^{1}J= 272 Hz, CF_3), 125.5 (C-3`` and C-5"), 128.75 (q, $^{2}J$= 24,5 Hz, C-4') 126.4 (q, $^{3}J$= 4Hz, C-3' and C-5'), 130.0 (C-2`` and C-6"), 135.6 (C-3), 140.8 (C-1" or C-4"), 141.2 (C-1'), 150.9 (C-1" or C-4"), 155.8 (C-7a), 156.4 (C-6), 161.9 (C-4). MS(FB+) = 405 ((M $^{+}$, ^{37}Cl, 16,7%), 403(M^{+}, ^{35}Cl, 35.5%). Anal. Calcd for $C_{18}H_{10}ClF_3N_6$: C, 53.68; H, 2.50; N, 20.87. Found: C, 53.50; H, 2.66; N 20.60.

Reduction of diazenyl derivatives to hydrazinyl derivatives, with Zn/AcOH (conversion of compounds 6 to 5)

To a solution of diazenyl derivatives **6** (0.1 mol) in glacial acetic acid (25 ml), Zn dust (2 g) was added. The reaction mixture was refluxed for 2 h during which time the color turned to pale yellow. The reaction mixture was filtered while hot, left to cool to RT and then poured onto crushed ice (25 g). The precipitated solid was collected by filtration and recrystalized from $CHCl_3$ to afford the corresponding hydrazinyl derivative which was found identical in all respects with that obtained from the above reaction (TLC, mp, NMR). (**5a**, 74 % yield, **5b**, 58 %yield, **5e,** 65 % yield).

Reactions with *m*-anisidine

Method A. To a solution of pyrazol-5-ylformimidate (0.1 mol) in methanol (20 ml) was added *m*-anisidine (0.1 mol). The reaction mixture was heated under reflux for 14 h. The precipitate formed after cooling overnight was filtered off and dried and recrystallized from ethanol (77% yield).

Method B. To a solution of 4-chloropyrazolo[3,4-*d*]pyrimidine (0.1 mol) in methanol (20 ml) was added *m*-anisidine (0.1 mol). The reaction mixture was refluxed for 5 h. The precipitate formed during reflux was filtered off and found identical in all respect with that obtained from method A (85 %).

1-(4-Chlorophenyl)-*N*-(3-methoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-amine (9). Yield (77%), pale yellow solid, mp 215-217 ^{o}C (EtOH); ^{1}H NMR (DMSO-d_6) δ = 3.77 (s, 3H, OCH_3), 6.72 (dd, 1H, *J* = 8.4, 2.7 Hz, Ar-H), 7.29 (t, 1H, *J* = 8 Hz, Ar-H), 7.42 (d, 1H, *J* = 8 Hz, Ar-H), 7.54 (t, 1H, *J* = 2.1 Hz, Ar-H), 7.61 (d, 2H, *J* = 9Hz, Ar-H), 8.24 (d, 2H, *J* = 9Hz, Ar-H), 8.54 (s,

2H, H-3, H-6), 10.19 (s, 1H, NH); ^{13}C NMR (DMSO) δ =55.1 (OCH_3), 102,6 (C-3a), 107.2 (C-2``), 109.0 (C-4``), 113.5 (C-6``), 122.0 (C-2`), 129.2 (C-3`), 129.5 (C-5``), 130.3 (C-4`), 134.1 (C-3), 137.6 (C-1`), 140.0 (C-1``), 153.1 (C-7a), 154.5 (C-4), 156.2 (C-6), 159.5 (C-3``). MS (EI)= 353 ((M^+, ^{37}Cl, 7%), 352 (M^+-1, ^{37}Cl, 22%), 351 (M^+, ^{35}Cl, 35%), 350 (M^+-1, ^{35}Cl, 100%). Anal. Calcd for $C_{18}H_{14}ClN_5O$: C, 61.46; H, 4.01; N, 19.91. Found: C, 61.15; H, 4.35; N 19.78.

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