Synthesis of Some New 6,8-Disubstituted 7,8-Dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines and 6,7,8-Trisubstituted Pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine Derivatives

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Cyclization of 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **4** with excess of 85% hydrazine hydrate afforded the 3-amino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine **5**, which can react with appropriate Mannich base derivatives **13a-c** and chalcones **27a,b** to yield the corresponding 6,8-disubstituted 7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines **15a-c** and **30a,b**, respectively. On the other hand, the 6,7,8-trisubstituted pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine derivatives **8a-g, 20a-e, 36** and **38** were obtained by treatment of compound **5** with appropriate 1,3-diketones **6a-g**, 3-dimethylamino-1-(substituted)prop-2-enones **18a-e**, 3-aminocrotononitrile **3**, and ethoxymethylenemalononitrile **37** under acidic condition, respectively.

Keywords: 5-Cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine; 3-Amino-6-phenylpyrazolo-[3,4-d]pyrimidine; 6,8-Disubstituted 7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines; 6,7,8-Trisubstituted pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines.

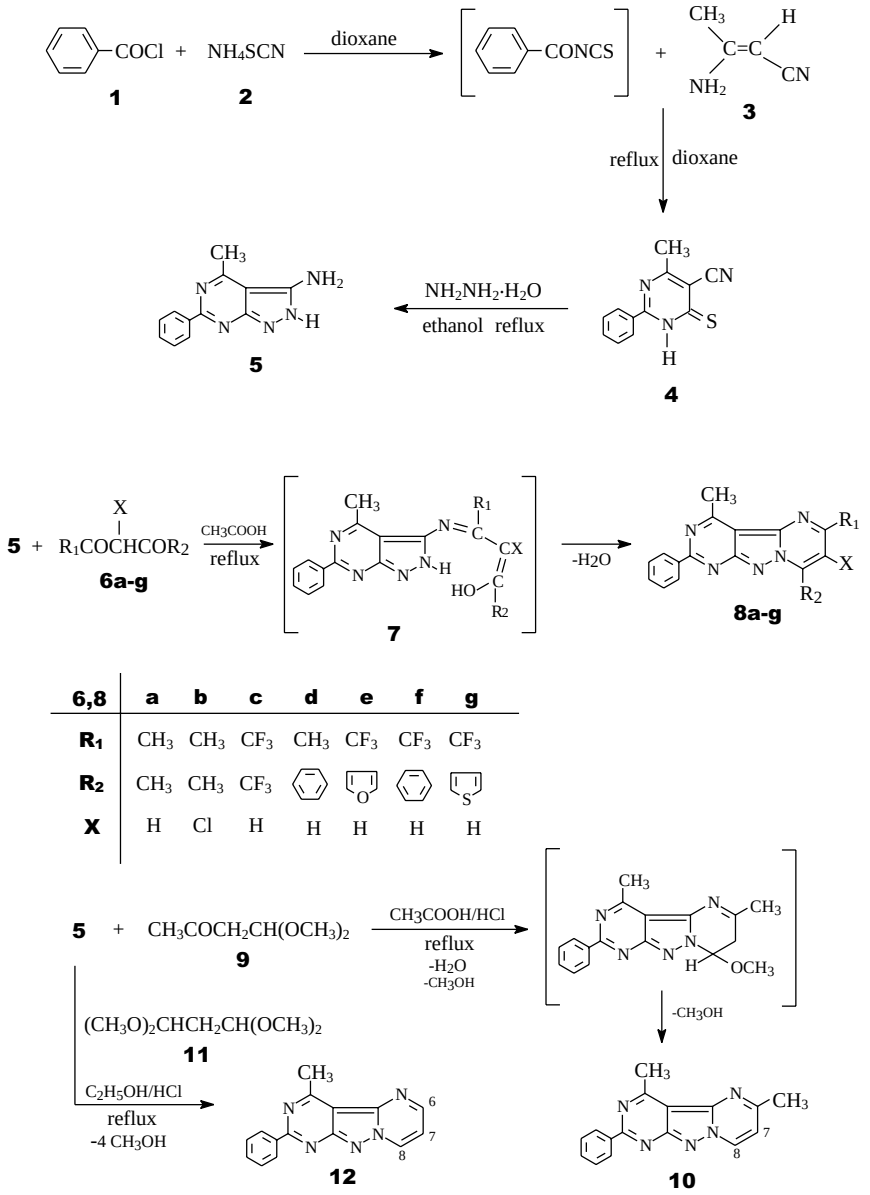
INTRODUCTION

Some pyrazole derivatives possess biological and pharmacological activites[1-8] and also find application in dyes.[9-10] The interesting biological activities reported for pyrazolo-[1,5-a]pyrimidines have stimulated chemists to develop the chemistry of this class of compounds.[11-14] Robins and coworkers reported that certain 3-substituted pyrazolo[1,5-a]pyrimidines inhibit the metabolism schistosomiasis in snails.[15-16] Preliminary tests of some 2-aminopyrazolo[1,5-a]pyrimidines showed strong antischistosomiasis.[17-18] In view of these it was considered of interest to synthesize some new pyrazolo[1,5-a]pyrimidine derivatives. The most common methods for the preparation of pyrazolo[1,5-a]pyrimidine derivatives are cyclocondensations of 5-aminopyrazoles with β-bifunctional reagents.[19-20] Hussein[21] et al. have recently described the synthesis of 6-amino-7-substituted pyrazolo[1,5-a]pyrimidines from arylidenemalononitrile with 5-amino-4-cyano-3-phenylpyrazole. The 7-(4-chlorophenyl)-2-substituted-1H-pyrazolo[1,5-a]pyrimidines[22] also have been prepared from 5-amino-3-phenyl-1H-pyrazole with 3-(4-chlorophenyl)-2-(N,N-dimethylamino)-methylene-3-oxopropanenitrile. Although a number of papers have been published concerning the synthesis of pyrazolo[1,5-a]pyrimidine derivatives, those containing a triheterocyclic system of pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines have not yet been reported. In a preceding paper[23] we have described the synthesis of 3-(2-amino-5,7-disubstituted-pyrazolo[1,5-a]-pyrimidine-3-yl)azo-thieno[2,3-b]pyridines from 3-amino-2-cyano-thieno[2,3-b]pyridine. In continuation of our studies, we report here the synthesis of some new 6,8-disubstituted 7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines and 6,7,8-trisubstituted pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines by making use of 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **4** as the starting material.

RESULTS AND DISCUSSION

The required compound 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **4** was prepared by treating benzoylisothiocyanate with 3-aminocrotononitrile **3** in refluxing dioxane.[24] The reaction of thioxopyrimidine **4** with excess of 85% hydrazine hydrate in refluxing ethanol for 24 h gave the corresponding 3-amino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine **5** (Scheme I). The structure of **5** was established by examining spectral data and elemental analysis. The IR spectrum of compound **5** indicated the absence of the C≡N and C=S absorption bands, and contains the characteristic absorption bands at 3424, 3307 cm^{-1} for the NH_2 group and at 3213 cm^{-1} for the NH group. The ^1H NMR spec-

Scheme I



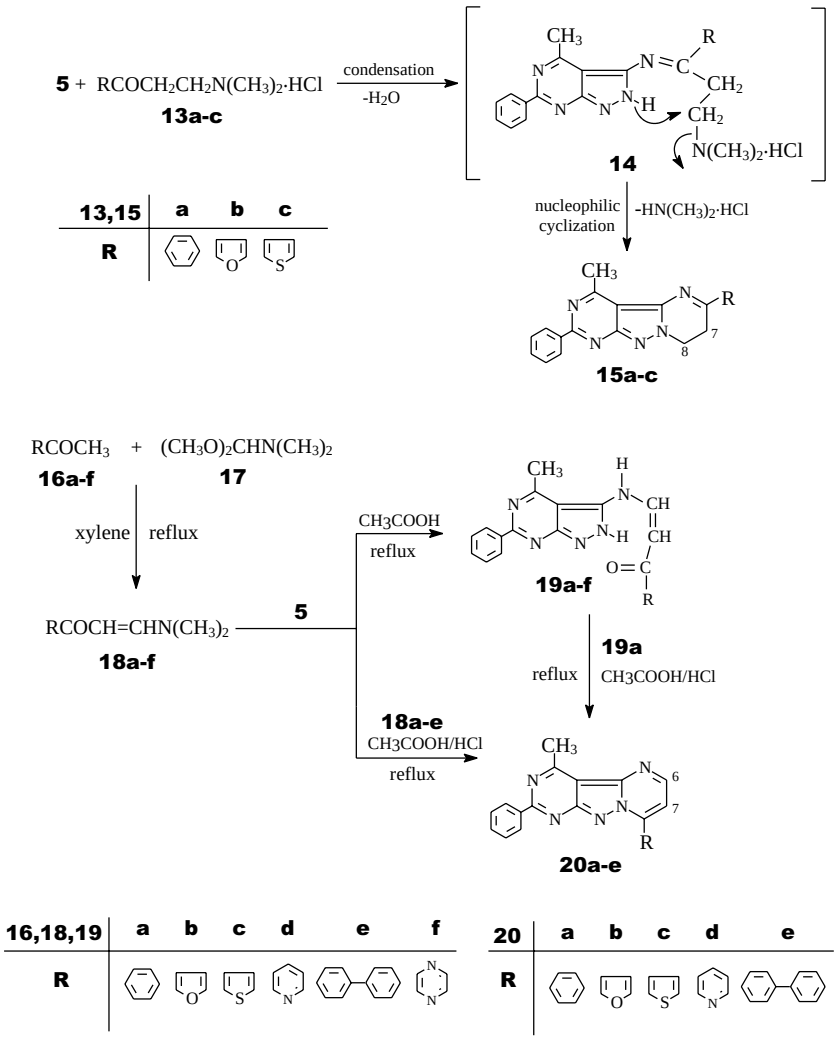
trum (DMSO-d_6) showed a broad singlet at δ 5.62 (2H, br) assigned to the NH_2 protons, a broad singlet at δ 12.44 (H, br) assigned to the NH proton and a multiplet at δ 8.43-7.48 (5H, m) assigned to the phenyl protons. The reaction of **5** with appropriate 1,3-diketones **6a-g** in refluxing glacial acetic acid yielded the corresponding 4-methyl-6,7,8-trisubstituted-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines **8a-g** (Scheme I). The reaction probably involves the condensation of the 3-NH_2 of the pyrazolo[3,4-d]pyrimidine ring with the carbonyl group, followed by dehydration, and subsequent cyclization with loss of water.[25-27] The IR spectra of compounds **8a-g** indicated the absence of the NH_2 and NH groups. The ^{1}H NMR spectra ($CDCl_3$) of compounds **8a** and **8c-g** revealed a singlet at δ 8.71-6.91 (1H, s), which were readily assigned to the hydrogen attached at C_7 of the pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively.

Under similar reaction conditions, condensation of compound **5** with 4,4-dimethoxy-2-butanone **9** in refluxing glacial acetic acid/hydrochloride afforded 4,6-dimethyl-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine **10**. We propose that the first step of the mechanism involves the condensation of the 3-NH_2 of the pyrazolo[3,4-d]pyrimidine ring with the carbonyl group, followed by dehydration, and subsequent nucleophilic cyclization with the loss of methanol[28]

(Scheme I). The ^{1}H NMR spectrum (DMSO-d_6) of compound **10** revealed two doublets at δ 7.14 (1H, d) and 8.80 (1H, d) assigned to the 7-H and 8-H of pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively. In addition, 4-dimethyl-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine **12** was also obtained from the reaction of compound **5** with malonaldehydebis(dimethylacetal) **11** under acidic condition. The ^{1}H NMR spectrum (DMSO-d_6) of compound **12** displayed signals at δ 7.55-7.52 (1H, m), 8.87 (1H, d) and 9.27 (1H, d), which were readily assigned to the hydrogen attached at C_7, C_8 and C_6 of the pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively.

On the other hand, when compound **5** and Mannich bases **13a-c** were heated at 200 °C in the absence of solvent they produced the corresponding 6-substituted-4-methyl-2-phenyl-7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines **15a-c** (Scheme II). Compounds **15a-c** were assumed to be formed via condensation of the 3-NH_2 of the pyrazolo-[3,4-d]pyrimidine ring with the carbonyl group, followed by dehydration, and subsequent nucleophilic cyclization with loss of N,N-dimethylamine hydrochloride.[28-30] The structures of compounds **15a-c** were established on the basis of their elemental analysis and spectral data. The ^{1}H NMR spectra (DMSO-d_6 or $CDCl_3$) revealed triplets at δ 3.53 (2H, t) and δ 4.63 (2H, t) for compound **15a**, at δ 3.31 (2H, t) and δ 4.57 (2H, t) for compound **15b** and at δ 3.36 (2H, t) and δ 4.55 (2H, t) for compound **15c**. These triplets were assigned to the methylene protons at the 7- and 8-position of the pyrimido-[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively. Compound **15b** showed signals at δ 6.61 (1H, m), 7.23 (1H, d) and 7.65 (1H, d), which were assigned to the protons of furyl moiety. Compound **15c** also showed signals at δ 7.10 (1H, m) and

Scheme II



7.61 (2H, m) assigned to the protons of thienyl moiety.

Furthermore, the reactions of compound **5** with enaminones **18a-f** were also investigated. Thus, it has been found that compound **5** with 3-dimethylamino-1-phenylprop-2-enone **18a** in refluxing glacial acetic acid gave a pale yellow product of molecular formula $C_{21}H_{17}N_5O$ (31% yield, mp 277 °C). Spectroscopic analyses revealed that 3-(1-phenylprop-2-enone-3-yl)amino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine **19a** was obtained (Scheme II). The IR spectrum of the reaction product showed the characteristic absorption band at 3125 cm^{-1} for the NH group and at 1630 cm^{-1} for the carbonyl group (C=O). The ^1H NMR spectrum (DMSO-d_6) of the reaction product, which showed two doublets at δ 6.38 (1H, d) and 7.88 (1H, d) assigned to the -CH=CH- of 1-phenylprop-2-enone moiety, and two signals at δ 12.58 (1H, s) and 13.51 (1H, br) assigned to the NH proton, was also confirmed by the mass spectrum *m/z* 355 (M^+) (Table 4). Under similar reaction condition, treatment of compound **5** with enaminones **18b-f** afforded the corresponding 3-(1-substituted-prop-2-enone-3-yl)amino-pyrazolo[3,4-d]pyrimidines **19b-f**, respectively (Scheme II).

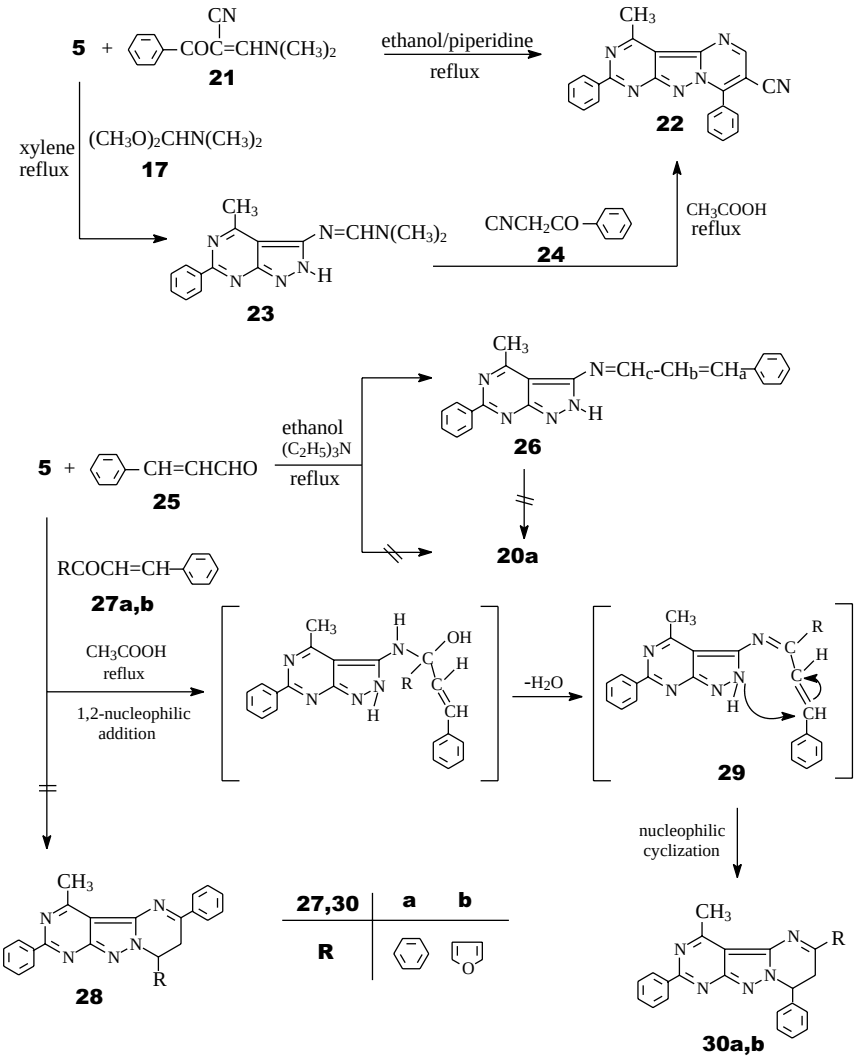
On the other hand, the compound **5** could be cyclized with enaminones **18a-e** under different conditions to form cyclic compounds. Thus, the reaction of compound **5** with enaminone **18a** in refluxing glacial acetic acid/hydrochloride (1:1) afforded the 2,8-diphenyl-pyrimido[2,3:4,3]pyrazolo-[1,5-a]pyrimidine **20a**. The mass spectrum showed a peak at *m/z* 337 (M^+, 100). The formation of compound **20a** would involve an initial nucleophilic substitution of the exocyclic amino group in compound **5** to the activated double bond in enaminone **18a** to form the compound **19a**, which then undergoes cyclization and aromatization via loss of water affording the final product **20a**. Elnagdi et al.[31-32] have also reported an analogous reaction in their papers. The structure of compound **20a** was further confirmed from an independent synthesis of compound **20a** by the reacting of compound **19a** in glacial acetic acid/hydrochloride (1:1) under reflux to afford a product identical in all respects (mp., mixed mp., TLC and spectra) (Scheme II). Also, compound **5** reacted with enaminones **18b-e** to yield products **20b-e** under the same reaction condition. The IR spectra of compounds **20a-e** showed absence of the NH and C=O absorption bands, indicating the formation of cyclic compounds. In addition, the structures of compounds **20a-e** were supported by the ^1H NMR spectra (DMSO-d_6 or CF_3COOD), which revealed two downfield doublets at δ 8.25-7.91 (1H, d) and δ 9.11-8.98 (1H, d) assigned to the 7-H and 6-H of the pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively.

Next, reaction of compound **5** with 2-cyano-3-dimethylamino-1-phenylprop-2-enone **21** in refluxing ethanol in the presence of catalytic amounts of piperidine afforded the 7-cyano-4-methyl-2,8-diphenylpyrimido[2,3:4,3]pyrazolo-[1,5-a]pyrimidine **22** (Scheme III). The structure of compound **22** was confirmed on the basis of its elemental analysis, spectral data, and an independent synthesis by reacting an equimolar amount of 3-N,N-dimethylaminomethyleneamino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine **23** with benzoylacetonitrile **24** in glacial acetic acid under reflux. The IR spectrum of compound **22** showed the characteristic absorption band at 2220 cm^{-1} for the C≡N group. In addition, the structure was supported by the ^1H NMR spectrum (DMSO-d_6), which showed the expected proton signal at δ 9.11 (1H, s) assigned to the 6-H of pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring and a multiplet at δ 7.91-7.30 (10H, m) assigned to the phenyl protons.

Moreover, attempted preparation of compound **20a** via condensation of compound **5** with cinnamaldehyde **25** failed. Only 4-methyl-2-phenyl-3-(cinnamylideneamino)-pyrazolo-[3,4-d]pyrimidine **26** was obtained (Scheme III). The IR spectrum of compound **26** showed the characteristic absorption band at 3124 cm^{-1} for the NH group. The ^1H NMR spectrum (DMSO-d_6) of compound **26** showed signals at δ 8.92 (1H, d) and 9.67 (1H, d), which were assigned to the proton H_a and H_c of cinnamylidene moiety, respectively, and a multiplet at δ 8.48-7.30 (11H, m) assigned to the phenyl-H and H_b of the cinnamylidene moiety. The spectrum also revealed a broad singlet at 11.5 (1H, br) assigned to the NH proton. Attempted cyclization of **26** into compound **20a** also failed. Furthermore, the reaction of compound **5** with chalcones **27a,b** in refluxing glacial acetic acid gave the corresponding 6-substituted 2,8-diphenyl-4-methyl-7,8-dihydropyrimido-[2,3:4,3]pyrazolo[1,5-a]pyrimidines **30a,b** rather than the compound **28** (Scheme III). The formation of **30a,b** can be explained by the reaction pathway depicted in Scheme III. The mechanism involves 1,2-nucleophilic addition of 3-amino of pyrazolo[3,4-d]pyrimidine ring to the carbonyl group, followed by dehydration and subsequent nucleophilic cyclization.[28] The ^1H NMR spectrum (DMSO-d_6) of compounds **30a,b** revealed a doublet at δ 6.92 (2H, d) and 7.10 (2H, d) assigned to the methylene protons at the 7-position of the pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine ring, respectively.

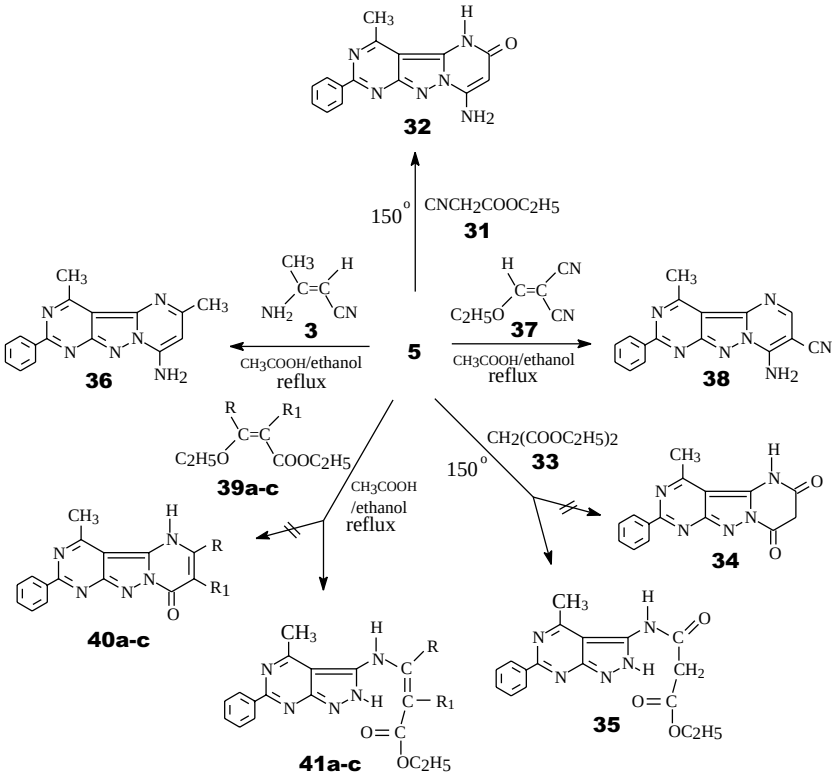
On the other hand, heating of compound **5** with excess of ethyl cyanoacetate **31** at 150 °C afforded the 8-amino-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidin-6(5*H*)-one **32** (Scheme IV). However, treatment of compound **5** with

Scheme III



malonic acid diethyl ester **33** under the same reaction conditions, gave the major product ethyl 2-[(4-methyl-6-phenylpyrazolo[3,4-d]pyrimidinyl-3-yl)amido]ethanoate **35**, instead of the expected compound **34**, as evidenced by analytical and spectral data. The structure of compound **35** was assigned by its IR specturm [ν 3224 cm^{-1} (NH) and 1740 (CO) cm^{-1}] and mass spectrum (*m/z* 339), confirmed by the satisfactory elemental analysis. In particular, the ^{1}H NMR spectrum (CF_3COOD) revealed a methylene (δ 3.42 (2H, s)) and ethoxycarbonyl (δ 1.50 (3H, t) and 4.53 (2H, q)) groups. Moreover, when compound **5** was treated with 3-aminocrotononitrile **3** and ethoxymethylenemalononitrile **37** in glacial acetic acid/ethanol to give the corresponding 6- and 7-substituted 8-amino-2-phenylpyrimido[2,3:4,3]pyrazolo-[1,5-a]pyrimidine **36** and **38**, respectively. Nevertheless, when compound **5** was reacting with appropriate alkylethoxymethylenes **39a-c** under the same reaction conditions, the compounds **41a-c** were smoothly obtained, rather than the expected compounds **40a-c** (Scheme IV). Evidence for the structure of compounds **41a-c** included the IR spectrum, which revealed a strong absorption band at 3226-3217 cm^{-1} for the NH group and contains the characteristic absorption band at 1700-1654 cm^{-1} for the C=O group. The ^{1}H NMR spectrum (DMSO-d_6) of compounds **41a,b** revealed a triplet at δ 1.31, 1.28 (3H, t) and a quartet at δ 4.30, 4.27 (2H, q) assigned to the ethyl group (CH_2CH_3), and a broad singlet at 13.43, 13.95 assigned for the NH group, respectively. Also, the ^{1}H NMR spectrum (DMSO-d_6) of compounds **41c** revealed two triplets at δ 1.31-1.23 (6H, m) and two quartets at δ 4.14 (2H, q) and 4.25 (2H, q) assigned to the two ethyl

Scheme IV



39,41	a	b	c
R	H	CH_3	H
R_1	CN	CN	$COOC_2H_5$

groups, also confirmed by the mass spectrum *m/z* 395 (M^+).

In conclusion, 3-amino-4-methyl-6-phenylpyrazolo-[3,4-d]pyrimidine **5** has been shown to be a useful building block for the synthesis of some new 6,8-disubstituted 7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines **15a-c** and **30a,b**. The 6,7,8-trisubstituted pyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine derivatives **8a-g**, **20a-e**, **36** and **38** were also prepared from compound **5**.

EXPERIMENTAL SECTION

All melting points were determined in a capillary tube and are uncorrected. The IR spectra were recorded on potassium bromide pellets on a JASCO FTIR-3 spectrometer. The ^{1}H NMR spectra were obtained on a Bruker AM-300WB FT-NMR spectrometer and chemical shifts are expressed in δ ppm using TMS as an internal standard. Electron impact mass spectra were obtained at 70 eV by using a Finnigan Mat TSQ-46C spectrometer. Microanalyses for C, H, and N were performed on a Perkin-Elmer 240 elemental analyzer. N,N-Dimethyl-2-substitutedethylamine hydrochloride **13a,b**,[28] 3-dimethylamino-1-(substituted)prop-2-enones **18a-c**[33] and chalcones **28a,b**[28] were prepared according to the literature.

5-Cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine (4)

To a suspension of ammonium thiocyanate (7.60 g, 0.1 mol) in dry dioxane (100 mL), benzoyl chloride (14 g, 0.1 mol) was added. The reaction mixture was refluxed for 5 mim., then treated with 3-aminocrotononitrile (8.20 g, 0.1 mol). The reaction mixture was refluxed for 2 h and poured into ice water. The solid product was collected by filtration, washed with water and recrystallized from ethanol to give 17 g of yellow needle crystals (74% yield), mp 212 °C; IR: ν 2225 (CN), 1200 (C=S) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.50

(3H, s, CH_3), 2.90 (1H, s, NH), 8.11-8.08, 7.66-7.51 (5H, m, phenyl-H); MS: 227 (M^+).

Anal. Calcd. for $C_{12}H_9N_3S$: C, 63.43; H, 3.96; N, 18.50. Found: C, 63.40; H, 4.00; N, 18.60%.

3-Amino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine (5)

A mixture of thioxopyrimidine **4** (2.27 g, 0.01 mol) and hydrazine hydrate (4 mL, 85% solution 0.04 mol) was refluxed in absolute ethanol (10 mL) for 24 h. After cooling, the resulting solid product was collected by filtration, washed with water, and the crude product recrystallized from ethanol to give 1.5 g of pale yellow needles (67% yield), mp 194 °C; IR: ν 3424, 3307 (NH_2), 3213 (NH) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.78 (3H, s, CH_3), 5.62 (2H, br, NH_2), 8.43-7.48 (5H, m, phenyl-H), 12.44 (1H, br, NH); MS: 225 (M^+, 100), 210 (25), 196 (8), 170 (8), 154 (2), 128 (1), 122 (23), 104 (21), 93 (9), 77 (19), 52 (5).

Anal. Calcd. for $C_{12}H_{11}N_5$: C, 64.00; H, 4.92; N, 31.09. Found: C, 64.00; H, 4.90; N, 31.09%.

General procedure of 4-methyl-6,7,8-trisubstituted-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines (8a-g)

A mixture of compound **5** (0.50 g, 2.2 mmol) and appropriate 1,3-diketones **6a-g** (2.3 mmol) was refluxed in glacial acetic acid (5 mL) for 10 h. A crystalline solid was obtained on cooling. It was recrystallized from an appropriate solvent. The physical constants and spectral data of compounds **8a-g** are recorded in Tables 1, 2.

4-Methyl-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine (10)

This compound was synthesized from compound **5** (0.50 g, 2.2 mmol) and 4,4-dimethoxy-2-butanone **9** (0.68 g, 2.2 mmol) in a manner similar to that described for the preparation of **8a**. It was recrystallized from ethanol to give 0.46 g of pink needles (76% yield), mp 275 °C; ^1H NMR (DMSO-d_6): δ 2.93 (3H, s, CH_3), 3.12 (3H, s, CH_3), 7.14 (1H, d, J = 1.0 Hz, 7-H), 8.65-8.60 (5H, m, phenyl-H), 8.80 (1H, d, J = 1.0 Hz, 8-H); MS: 275 (M^+, 100), 260 (60), 233 (6), 207 (1), 172 (6), 157 (5), 137 (12), 103 (12), 79 (4), 77 (18), 51 (6).

Anal. Calcd. for $C_{16}H_{13}N_5$: C, 69.82; H, 4.73; N, 25.45. Found: C, 69.85; H, 4.70; N, 25.46%.

4-Methyl-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine (12)

To a mixture of compound **5** (0.50 g, 2.2 mmol) and malonaldehydebis(dimethylacetal) **11** (0.37 g, 2.2 mmol) in ethanol (5 mL), a few drops of hydrochloride was added. The reaction mixture was refluxed for 10 h. A crystalline solid was obtained on cooling. It was recrystallized from ethanol/acetic acid to give 0.31 g of pale yellow needles (53% yield), mp 261 °C; ^1H NMR (DMSO-d_6): δ 3.12 (3H, s, CH_3), 7.55-7.52 (1H, m, 7-H), 8.52, 7.44-7.43 (5H, m, phenyl-H), 8.87 (1H, d, J = 1.0, Hz, 8-H), 9.27 (1H, d, J = 1.0, Hz, 6-H);

Table 1. Physical and Analytical Data of Compounds **8a-g**

Compound	R_1	R_2	X	Yield % (recrystallization solvent)	Mp °C	Molecular Formula	Element Analysis (%) Calcd/Found C	H	N
8a	CH_3	CH_3	H	69 glacial acetic acid	272	$C_{17}H_{15}N_5$	70.59 70.46	5.20 5.55	24.22 24.22
8b	CH_3	CH_3	Cl	83 ethanol/chloroform	280	$C_{17}H_{14}ClN_5$	63.06 63.16	4.33 4.58	21.64 21.32
8c	CF_3	CF_3	H	56 acetone	245	$C_{17}H_9F_6N_5$	51.38 51.32	2.27 2.31	17.63 17.40
8d	CH_3	phenyl	H	85 DMF/H_2O	308	$C_{22}H_{19}N_5$	75.21 75.12	5.41 5.36	19.94 19.99
8e	CF_3	furyl	H	51 DMF/ethanol	177	$C_{20}H_{12}F_3N_5O$	69.53 69.52	3.31 3.32	18.27 18.30
8f	CF_3	phenyl	H	45 DMF/H_2O	319	$C_{22}H_{14}F_3N_5$	65.18 65.18	3.45 3.52	17.28 17.22
8g	CF_3	thienyl	H	32 DMF/ethanol	229	$C_{20}H_{12}F_3N_5S$	58.39 58.41	2.91 2.89	17.03 17.11

Table 2. Spectral Data of Compounds **8a-g**

Compound	MS (M^+)	^{1}H NMR ($CDCl_3$) δ (ppm)
8a	289	2.61 (3H, s, CH_3), 2.85 (3H, s, CH_3), 3.07 (3H, s, CH_3), 6.91 (1H, s, 7-H), 8.65-8.63, 7.44-7.42 (5H, m, phenyl-H).
8b	323.5	2.73 (3H, s, CH_3), 3.05 (3H, s, CH_3), 3.08 (3H, s, CH_3), 8.63, 7.47 (5H, m, phenyl-H).
8c	397	3.24 (3H, s, CH_3), 8.69-8.68, 7.49 (5H, m, phenyl-H), 7.96 (1H, s, 7-H).
8d	351	2.77 (6H, s, 4,6-CH_3), 7.78 (1H, s, 7-H), 8.18-8.03, 7.56-7.51 (10H, m, phenyl-H).[a]
8e	395	2.77 (3H, s, CH_3), 6.74 (1H, m, 4-H of furyl-H), 8.35-8.33, 7.52-7.49 (5H, m, phenyl-H), 7.81 (1H, d, *J* = 1.0 Hz, 3-H of furyl-H), 8.01 (1H, d, *J* = 1.0 Hz, 5-H of furyl-H), 8.39 (1H, s, 7-H).
8f	405	2.08 (3H, s, CH_3), 8.10-7.81, 7.58-7.29 (10H, m, phenyl-H), 8.28 (1H, s, 7-H).
8g	441	2.78 (3H, s, CH_3), 7.20-7.18 (1H, m, 4-H of thienyl-H), 8.21-8.19, 8.00-7.96 (5H, m, phenyl-H), 7.43 (1H, d, *J* = 1.5 Hz, 3-H of thienyl-H), 7.44 (1H, d, *J* = 1.5 Hz, 5-H of thienyl-H), 8.71 (1H, s, 7-H).

[a] ^{1}H NMR in CF_3COOD

MS: 261 (M^+, 100), 246 (52), 219 (8), 193 (1), 158 (2), 143 (10), 130 (15), 116 (10), 103 (12), 91 (7), 77 (18), 51 (9).

Anal. Calcd. for $C_{15}H_{11}N_5$: C, 68.97; H, 4.21; N, 26.82. Found: C, 68.95; H, 4.20; N, 26.66%.

N,N-Dimethyl-2-thenoylethylamine Hydrochloride (13c)

This compound was synthesized according to a literature report.[28] It was recrystallized from 95% ethanol to give 3.82 g of colorless needles (58% yield), mp 184 °C; IR: ν 1652 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.78 (6H, s, $N(CH_3)_2$), 3.57-3.37 (4H, m, CH_2CH_2), 7.29 (1H, dd, *J* = 1.0, 1.0 Hz, 4-H of thienyl), 8.08 (2H, m, 3-H, 5-H of thienyl); MS: 219.5 (M^+).

Anal. Calcd. for $C_9H_{14}NClOS$: C, 49.20; H, 6.37; N, 31.09. Found: C, 49.40; H, 6.80; N, 31.22%.

2,6-Diphenyl-4-methyl-7,8-dihydropyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidine (15a)

A mixture of compound **5** (0.30 g, 1.3 mmol) and N,N-dimethyl-2-benzoylethylamine hydrochloride **13a** (0.29 g, 1.36 mmol) was heated at 200 °C for ten minutes. The reaction mixture was left to cool then triturated with ethanol. The solid product, so formed, was collected by filtration and recrystallized from dioxane/DMF to give 0.27 g of yellow needles (60% yield), mp 310 °C; ^{1}H NMR (DMSO-d_6): δ 2.97 (3H, s, CH_3), 3.53 (2H, t, *J* = 3.0 Hz, 7-H), 4.63 (2H, t, *J* = 3.0 Hz, 8-H), 8.48-7.96, 7.66-7.49 (10H, m, phenyl-H); MS: 339 (M^+, 100), 324 (45), 296 (5), 235 (4), 210 (6), 169 (8), 153 (5), 115 (13), 103 (25), 77 (18), 51 (3).

Anal. Calcd. for $C_{21}H_{17}N_5$: C, 74.33; H, 5.01; N, 20.65. Found: C, 74.21; H, 4.96; N, 20.66%.

6-Furyl-4-methyl-2-phenyl-7,8-dihydropyrimido[2,3:4,3]-pyrazolo[1,5-a]pyrimidine (15b)

This compound was synthesized from compound **5** (0.30 g, 1.3 mmol) and N,N-dimethyl-2-furoylethylamine hydrochloride **13b** (0.28 g, 1.36 mmol) in a manner similar to that described for the preparation of **15a**. It was recrystallized from THF/DMF to give 0.23 g of yellow needles (53% yield), mp 270 °C; ^{1}H NMR ($CDCl_3$): δ 2.97 (3H, s, CH_3), 3.31 (2H, t, *J* = 2.0 Hz, 7-H), 4.57 (2H, t, *J* = 2.0 Hz, 8-H), 6.61 (1H, m, 4-H of furyl), 7.23 (1H, d, *J* = 1.0 Hz, 3-H of furyl), 7.65 (1H, d, *J* = 1.0 Hz, 5-H of furyl), 8.56-8.54, 7.44-7.42 (5H, m, phenyl-H); MS: 329 (M^+, 100) 314 (38), 300 (5), 236 (3), 209 (2), 183 (3), 153 (8), 104 (6), 93 (11), 77 (22), 65 (9).

Anal. Calcd. for $C_{19}H_{15}N_5O$: C, 69.30; H, 4.56; N, 21.27. Found: C, 69.55; H, 4.50; N, 21.66%.

4-Methyl-2-phenyl-6-thienyl-7,8-dihydropyrimido[2,3:4,3]-pyrazolo[1,5-a]pyrimidine (15c)

This compound was synthesized from compound **5** (0.30 g, 1.3 mmol) and N,N-dimethyl-2-thenoylethylamine

hydrochloride **13c** (0.30 g, 1.36 mmol) in a manner similar to that described for the preparation of **15a**. It was recrystallized from THF/DMF to give 0.27 g of yellow needles (59% yield), mp 292 °C; ^{1}H NMR (DMSO-d_6): δ 2.91 (3H, s, CH_3), 3.36 (2H, t, *J* = 2.0 Hz, 7-H), 4.55 (2H, t, *J* = 2.0 Hz, 8-H), 7.10 (1H, m, 4-H of thienyl), 7.61 (2H, m, 3-H ,5-H of thienyl), 8.48-8.46, 7.38-7.36 (5H, m, phenyl-H); MS: 345 (M^+, 100), 330 (31), 302 (2), 236 (3), 199 (2), 172 (14), 109 (40), 77 (22), 65 (7), 51 (5).

Anal. Calcd. for $C_{19}H_{15}N_5S$: C, 66.08; H, 4.34; N, 20.29. Found: C, 66.15; H, 4.30; N, 20.26%.

3-Dimethylamino-1-(4-pyridyl)prop-2-enone (18d)

To a solution of 4-acetylpyridine **16d** (1.21 g, 0.01 mol) in dry xylene (10 mL), dimethylformamide dimethylacetal (1.20 g, 0.01 mol) was added. The reaction was heated under reflux for 6 h. The solvent was removed by evaporation under reduced pressure and the remainder was left to cool. The solid product so formed was collected by filtration, washed with petroleum ether (bp 40-60 °C), and the crude product recrystallized from ethanol to give 1.53 g (87% yield) of **18d**, mp 89 °C; IR: ν 1640 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.84 (6H, s, $N(CH_3)_2$), 5.56 (1H, d, *J* = 3.0 Hz, 2-H), 7.59 (2H, d, *J* = 1.0 Hz, 3-H, 5-H of pyridyl), 7.75 (1H, d, *J* = 3.0 Hz, 3-H), 8.59 (2H, d, *J* = 1.0 Hz, 2-H, 6-H of pyridyl); MS: 176 (M^+).

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.18; H, 6.81; N, 15.90. Found: C, 68.23; H, 6.80; N, 16.01%.

3-Dimethylamino-1-(4-biphenyl)prop-2-enone (18e)

This compound was synthesized from 4-acetylbiphenyl **16e** (1.96 g, 0.01 mol) and dimethylformamide dimethylacetal (1.20 g, 0.01 mol) in a manner similar to that described for the preparation of **18d**. It was recrystallized from ethanol to give 1.53 g (61% yield) of **18e**, mp 101 °C; IR: ν 1680 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.62 (6H, s, $N(CH_3)_2$), 5.75 (1H, d, *J* = 3.0 Hz, 2-H), 7.82 (1H, d, *J* = 4.0 Hz, 3-H), 8.02-7.95, 7.68-7.60, 7.47-7.33 (9H, m, biphenyl-H); MS: 251 (M^+).

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.27; H, 6.77; N, 5.57. Found: C, 81.23; H, 6.80; N, 5.51%.

3-Dimethylamino-1-(2-pyrazinyl)prop-2-enone (18f)

This compound was synthesized from 2-acetylpyrazine **16f** (1.22 g, 0.01 mol) and dimethylformamide dimethyl-

Table 3. Physical and Analytical Data of Compounds **19a-f** and **20a-e**

Compound	R_1	Yield %	Mp °C	Molecular Formula	Element Analysis (%) Calcd/Found		
					C	H	N
19a	phenyl	31	277	$C_{21}H_{17}N_5O$	70.98	4.79	19.72
					70.98	4.71	19.81
19b	furyl	37	269	$C_{19}H_{15}N_5O_2$	66.09	4.35	20.29
					66.08	4.32	20.36
19c	thienyl	52	229	$C_{19}H_{15}N_5OS$	63.16	4.16	19.39
					63.46	4.26	19.65
19d	pyridyl	51	261	$C_{20}H_{16}N_6O$	67.41	4.49	23.60
					67.51	4.44	23.59
19e	biphenyl	37	297	$C_{27}H_{21}N_5O$	75.17	4.87	16.24
					75.14	4.92	16.33
19f	Pyrazinyl	35	253	$C_{19}H_{15}N_7O$	63.87	4.20	27.45
					63.46	4.19	27.55
20a	phenyl	82	257	$C_{21}H_{15}N_5$	74.77	4.45	20.77
					74.46	4.55	20.33
20b	furyl	95	271	$C_{19}H_{13}N_5O$	69.72	3.97	21.40
					69.79	3.58	21.32
20c	thienyl	98	281	$C_{19}H_{13}N_5S$	66.47	3.79	20.40
					66.32	3.80	20.40
20d	pyridyl	82	270	$C_{20}H_{14}N_6$	71.00	4.14	24.85
					71.12	4.16	24.99
20e	biphenyl	60	350	$C_{27}H_{19}N_5$	78.45	4.60	16.95
					78.52	4.78	16.95

Table 4. Spectral Data of Compounds **19a-f** and **20a-e**

Compound	MS (M^+)	IR (KBr) ν (cm^{-1})	^{1}H NMR (DMSO-d_6) δ (ppm)
19a	355(77), 338(18), 278 (15), 250(100), 223(19), 210(10), 177(5), 153(8), 131(10), 105(61), 77(83), 51(13).	3125 (NH), 1630 (C=O)	2.99 (3H, s, CH_3), 6.38 (1H, d, J = 2.0 Hz, =CH-), 7.88 (1H, d, J = 2.0 Hz, -CH=), 8.46-7.52 (10H, m, phenyl-H), 12.58 (1H, s, NH), 13.51 (1H, br, NH).
19b	345(100), 327(19), 316(94), 299(51), 288(7), 262(7), 250(93), 225(28), 210(16), 196(7), 158(4), 131(4), 104(61), 77(38), 66(22), 51(12).	3120 (NH), 1629 (C=O)	2.94 (3H, s, CH_3), 6.13 (1H, d, J = 2.0 Hz, =CH-), 6.70-6.69 (1H, m, 4-H of furyl), 7.20 (1H, d, J = 1.0 Hz, -CH=), 7.38 (1H, d, J = 1.0 Hz, 3-H of furyl), 8.00-7.93, 7.51-7.48 (6H, m, phenyl-H and 5-H of furyl), 12.30 (1H, s, NH), 13.48 (1H, br, NH).
19c	361(78), 344(10), 328(18), 277(6), 250(100), 222(14), 210(7), 196(3), 153(5), 137(4), 111(61), 104(30), 77(18), 66(8), 51(4).	3122 (NH), 1627 (C=O)	2.94 (3H, s, CH_3), 6.25 (1H, d, J = 2.0 Hz, =CH-), 7.23-7.21 (1H, m, 4-H of thienyl), 7.74 (1H, d, J = 1.0 Hz, -CH=), 7.99-7.92, 7.52-7.51 (6H, m, phenyl-H and 3-H of thienyl), 7.89 (1H, d, J = 1.0 Hz, 5-H of thienyl), 12.24 (1H, s, NH), 13.48 (1H, br, NH).
19d	356(65), 337(22), 327(18), 278(39), 250(100), 237(42), 223(18), 210(10), 178(17), 153(8), 147(17), 118(8), 104(56), 77(47), 66(11), 51(26).	3125 (NH), 1663 (C=O)	2.98 (3H, s, CH_3), 6.38 (1H, d, J = 2.0 Hz, =CH-), 7.71 (1H, d, J = 2.0 Hz, -CH=), 8.14-8.10, 7.87-7.52 (7H, m, phenyl-H and 3, 5-H of pyridyl), 8.75 (2H, d, J = 1.0 Hz, 2, 6-H of pyridyl), 12.58 (1H, s, NH), 13.58 (1H, br, NH).
19e	331(75), 412(32), 388 (2), 354(7), 278(9), 250 (188), 237(17), 225(22), 210(10), 181(60), 153(100), 127(9), 104(38), 77(30), 66(10), 51(6).	3124 (NH), 1628 (C=O)	3.19 (3H, s, CH_3), 8.13-7.20 (15H, m, phenyl-H, and =CH-), 7.84 (1H, d, J = 1.0 Hz, -CH=).[a]
19f	357(83), 339(42), 328 (5), 303(10), 285(18), 278(74), 250(100), 237 (78), 225(16), 210(18), 182(8), 153(9), 133(17), 120(20), 104(61), 79 (65), 66(15), 52(28).	3128 (NH), 1636 (C=O)	3.02 (3H, s, CH_3), 7.88 (1H, d, J = 1.0 Hz, =CH-), 8.64-8.43 (5H, m, phenyl-H), 9.49 (1H, s, 5-H of pyrazinyl), 10.05 (1H, d, J = 1.0 Hz, -CH=), 10.33 (1H, d, J = 1.0 Hz, 6-H of pyrazinyl), 10.51 (1H, d, J = 1.0 Hz, 3-H of pyrazinyl).[a]
20a	337(100), 322(4), 295(1), 244(5), 231(15), 206(4), 180(2), 153(2),103(2), 77(1), 52(2).		3.15 (3H, s, CH_3), 7.71-7.67, 7.56-7.53 (5H, m, phenyl-H), 8.57-8.52, 8.27-8.22 (5H, m, phenyl-H), 7.91 (1H, d, J = 2.4 Hz, 7-H), 9.06 (1H, d, J = 2.4 Hz, 6-H).
20b	337(100), 312(62), 299(13), 272(2), 231(2), 209(5), 194(7), 181(4), 163(6), 154(10), 129(3), 103(3), 77(11), 52(5).		3.12 (3H, s, CH_3), 7.00-6.97 (1H, m, 4-H of furyl), 8.54-8.50, 7.59-7.55 (5H, m, phenyl-H), 8.03 (1H, d, J = 2.5 Hz, 7-H), 8.25 (1H, d, J = 1.0 Hz, 3-H of furyl), 8.36 (1H, d, J = 1.8 Hz, 5-H of furyl), 9.00 (1H, d, J = 2.6 Hz, 6-H).
20c	343(100), 328(20), 301(3), 275(1), 239(6), 198(7), 171(15), 146(6), 121(8), 109(8), 77(16), 52(4).		3.12 (3H, s, CH_3), 7.47-7.43 (1H, m, 4-H of thienyl), 8.58-8.53, 7.59-7.55 (5H, m, phenyl-H), 8.25 (1H, d, J = 3.0 Hz, 7-H), 8.40 (1H, d, J = 2.6 Hz, 3-H of thienyl), 8.69 (1H, d, J = 2.6 Hz, 5-H of thienyl), 8.98 (1H, d, J = 2.6 Hz, 6-H).
20d	338(100), 323(9), 285(2), 245(1), 234(13), 207(9), 180(8), 166(5), 129(10), 104(20), 77(22), 52(11).		3.14 (3H, s, CH_3), 8.59-8.54, 7.56-7.53 (5H, m, phenyl-H), 8.03 (1H, d, J = 2.8 Hz, 7-H), 8.26 (2H, d, J = 3.0 Hz, 3, 5-H of pyridyl), 8.95 (2H, d, J = 3.0 Hz, 2, 6-H of pyridyl), 9.11 (1H, d, J = 2.4 Hz, 6-H).
20e	413(100), 384(1), 336(11), 282(4), 233(34), 204(9), 152(1).		2.29 (3H, s, CH_3), 8.28-8.24, 8.03-7.50 (14H, m, phenyl-H), 8.10 (1H, d, J = 2.5 Hz, 7-H), 9.11 (1H, d, J = 2.5 Hz, 6-H).[a]

[a] ^{1}H NMR in CF_3COOD

acetal (1.20 g, 0.01 mol) in a manner similar to that described for the preparation of **18d**. It was recrystallized from ethanol to give 1.24 g (73% yield) of **18f**, mp 138 °C; IR: ν 1637 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.95 (6H, s, $N(CH_3)_2$), 6.31 (1H, d, J = 3.0 Hz, 2-H), 7.88 (1H, d, J = 3.0 Hz, 3-H), 8.51 (1H, d, J = 1.0 Hz, 5-H of pyrazinyl), 8.59 (1H, d, J = 1.0 Hz, 6-H of pyrazinyl), 9.27 (1H, s, 3-H of pyrazinyl); MS: 177 (M^+).

Anal. Calcd. for $C_9H_{11}N_3O$: C, 61.01; H, 6.21; N, 23.72. Found: C, 61.03; H, 6.21; N, 23.70%.

General procedure of 3-(1-substituted prop-2-enone-3-yl)amino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidines (19a-f)

A mixture of compound **5** (0.30 g, 1.33 mmol) and 3-dimethylamino-1-(substituted)prop-2-enones **18a-f** (1.33 mmol) in glacial acetic acid (10 mL) was refluxed with stirring for 10 h. The reaction mixture was cooled. The resulting solid product was collected by filtration and recrystallized from DMF/ethanol. The physical constants and spectral data of compounds **19a-f** are recorded in Tables 3, 4.

General procedure of 4-methyl-8-substituted-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidines (20a-e)

A mixture of compound **5** (0.30 g, 1.33 mmol) and 3-dimethylamino-1-(substituted)prop-2-enones **18a-e** (1.33 mmol) in glacial acetic acid/hydrochloride (1:1 10 mL) was refluxed with stirring for 10 h. The reaction mixture was cooled. The resulting solid product was collected by filtration and recrystallized from DMF/ethanol. The physical constants and spectral data of compounds **20a-e** are recorded in Tables 3, 4.

2-Cyano-3-dimethylamino-1-phenylprop-2-enone (21)

To a suspension of benzoylacetonitrile (1.80 g, 0.01 mol) in dry xylene (10 mL), dimethylformamide dimethylacetal (1.20 g, 0.01 mol) was added. The reaction mixture was refluxed for 6 h. The solvent was removed by evaporation under reduced pressure and the remainder was left to cool. The yellowish solid product so formed was collected by filtration, washed with petroleum ether (bp 40-60 °C) and dried. Recrystallization from ethanol afforded 1.92 g of yellow needles (96% yield), mp 96 °C; IR: ν 2192 (CN), 1700 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.38 (6H, s, $N(CH_3)_2$), 7.42-7.29 (5H, m, phenyl), 7.84 (1H, s, olefinic CH); MS: 200 (M^+).

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.00; H, 6.00; N, 14.00. Found: C, 72.23; H, 6.10; N, 14.11%.

7-Cyano-4-methyl-2,8-diphenylpyrimido[2,3:4,3]pyrazolo-[1,5-a]pyrimidine (22)

Method A

To a mixture of compound **5** (0.46 g, 2.0 mmol) and compound **21** (0.40 g, 2.0 mmol) in ethanol (10 mL), a few drops of piperidine was added. The reaction mixture was refluxed for 6 h. The resulting solid product was collected by filtration and recrystallized from DMF/ethanol to give 0.21 g of yellow needles (29% yield), mp > 340 °C; IR: ν 2220 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.13 (3H, s, CH_3), 7.91-7.30 (10H, m, phenyl-H), 9.11 (1H, s, 6-H); MS: 362 (M^+).

Anal. Calcd. for $C_{22}H_{14}N_6$: C, 72.92; H, 3.86; N, 23.20. Found: C, 72.84; H, 3.94; N, 23.36%.

Method B

To a solution of benzoylacetonitrile **24** (0.15 g, 1.0 mmol) in glacial acetic acid (5 mL), 3-N,N-dimethylaminomethylene-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine **23** (0.28 g, 1.0 mmol) was added. The reaction mixture was refluxed for 6 h, and then allowed to stand overnight. The resulting solid product was collected by filtration and recrystallized to give 0.16 g (45% yield).

3-N,N-Dimethylaminomethyleneamino-4-methyl-6-phenylpyrazolo[3,4-d]pyrimidine (23)

This compound was synthesized from compound **5** (2.25 g, 0.01 mol) and dimethylformamide dimethylacetal **17** (1.20 g, 0.01 mol) in a manner similar to that described for the preparation of **18d**. It was recrystallized from ethanol to give 2.30 g (82% yield) of **24**, mp 235 °C; IR: ν 3210 (NH) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.84 (3H, s, CH_3), 3.02 (6H, s, $N(CH_3)_2$), 8.44-8.43, 7.50-7.49 (5H, m, phenyl-H), 8.26 (1H, s, -N=CH), 12.86 (1H, s, NH); MS: 280 (M^+, 100), 265 (12), 252 (15), 238 (38), 224 (23), 210 (15), 197 (5), 153 (5), 121 (3). 104 (25), 83 (3), 77 (15), 57 (8), 51 (4).

Anal. Calcd. for $C_{15}H_{16}N_6$: C, 64.28; H, 5.71; N, 30.00. Found: C, 64.23; H, 5.40; N, 30.25%.

4-Methyl-2-phenyl-3-(cinnamylideneamino)-pyrazolo[3,4-d]pyrimidine (26)

To a mixture of compound **5** (0.30 g, 1.33 mmol) and cinnamaldehyde **25** (0.18 g, 1.33 mmol) in ethanol (5 mL), a few drops of triethylamine was added. The reaction mixture was refluxed for 5 h. The resulting solid product was collected by filtration and recrystallized from ethanol to give 0.24 g (53% yield) of **26**, mp 239 °C; IR: ν 3124 (NH) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.90 (3H, s, CH_3), 8.48-8.38, 7.75-7.30 (11H, m, CH_b and phenyl-H), 8.92 (1H, d, J = 3.0 Hz, CH_a), 9.67 (1H, d, J = 2.0 Hz, CH_c), 11.5 (1H, br, NH); MS:

339(M^+, 100), 297 (4), 262 (76), 235 (2), 225 (12), 210 (10), 192 (3), 169 (12), 140 (5), 115 (39), 77 (21), 66 (4).

Anal. Calcd. for $C_{21}H_{17}N_5$: C, 74.33; H, 5.01; N, 20.64. Found: C, 74.54; H, 5.20; N, 20.61%.

4-Methyl-2,6,8-triphenyl-7,8-dihydropyrimido[2,3:4,3]-pyrazolo[1,5-a]pyrimidine (30a)

To a solution of compound **5** (0.30 g, 1.33 mmol) in glacial acetic acid (10 mL), chalcone **27a** (0.28 g, 1.33 mmol) was added. The reaction mixture was refluxed for 10 h. The solvent was removed by evaporation under reduced pressure and the remainder was left to cool. The solid product so formed was collected by filtration, and washed with ether. Recrystallization from DMF/ethanol gave 0.21 g (38% yield) of **30a**, mp 285 °C; ^{1}H NMR (DMSO-d_6): δ 3.08 (3H, s, CH_3), 6.92 (2H, d, J = 1.0 Hz, 7-H), 8.52-8.17, 7.71-7.25 (16H, m, phenyl-H); MS: 415 (M^+, 100), 402 (2), 338 (8), 314 (38), 282 (6), 236 (5), 206 (31), 153 (14), 115 (10), 104 (46), 77 (38), 51 (7).

Anal. Calcd. for $C_{27}H_{21}N_5$: C, 78.07; H, 5.06; N, 16.86. Found: C, 78.03; H, 5.10; N, 16.66%.

6-Furyl-4-methyl-2,8-diphenyl-7,8-dihydropyrimido-[2,3:4,3]pyrazolo[1,5-a]pyrimidine (30b)

This compound was synthesized from compound **5** (0.30 g, 1.33 mmol) and 1-phenyl-3-(2-furyl)-2-propen-1-one **27b** (0.26 g, 1.33 mmol) in a manner similar to that described for the preparation of **30a**. It was recrystallized from DMF/THF to give 2.80 g (52% yield) of **30b**, mp 279 °C; ^{1}H NMR (DMSO-d_6): δ 2.98 (3H, s, CH_3), 6.78 (1H, m, 4-H of furyl), 7.10 (2H, d, J = 2.0 Hz, 7-H), 8.08-8.06, 7.85-7.30 (11H, m, phenyl-H), 8.48 (2H, m, 3-H, 5-H of furyl); MS: 405 (M^+, 100), 376 (15), 328 (28), 311 (15), 244 (4), 196 (9), 181 (22), 40), 93 (22), 77 (19), 65 (13), 51 (4).

Anal. Calcd. for $C_{25}H_{19}N_5O$: C, 74.07; H, 4.69; N, 17.28. Found: C, 74.22; H, 4.40; N, 17.25%.

8-Amino-4-methyl-2-phenylpyrimido[2,3:4,3]pyrazolo[1,5-a]pyrimidin-6(5*H*)-one (32)

A mixture of compound **5** (0.30 g, 1.33 mmol) and ethyl cyanoacetate **31** (1.0 g, 8.8 mmol) was heated at 150 °C with stirring for 2 h. The reaction mixture was diluted with ethanol. The solid product so formed was collected by filtration and washed with ether. Recrystallization from DMF/ethanol to give 0.36 g (93% yield) of **32**, mp > 350 °C; IR: ν 3424, 3236 (NH_2), 3124 (NH), 1678 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.93 (3H, s, CH_3), 4.05 (2H, br, NH_2), 7.94 (1H, s, 7-H), 8.52-8.45, 7.54-7.48 (5H, m, phenyl-H), 13.84 (1H, br, NH); MS: 292 (M^+).

Anal. Calcd. for $C_{15}H_{12}N_6O$: C, 61.64; H, 4.11; N, 28.76. Found: C, 61.56; H, 4.11; N, 28.66%.

Ethyl 2-[(4-methyl-6-phenylpyrazolo[3,4-d]pyrimidinyl-3-yl)amido]ethanoate (35)

This compound was synthesized from compound **5** (0.30 g, 1.33 mmol) and malonic acid diethyl ester **33** (1.4 g, 8.8 mmol) in a manner similar to that described for the preparation of **32**. It was recrystallized from ethanol to give 0.28 g (62% yield) of **35**, mp 308 °C; IR: ν 3224 (NH), 1740 (CO) cm^{-1}; ^{1}H NMR (CF_3COOD): δ 1.50 (3H, t, J = 2.0 Hz, CH_3), 2.33 (3H, s, CH_3), 3.42 (2H, s, CH_2), 4.53 (2H, q, J = 3.0 Hz, CH_2), 8.33-7.78 (5H, m, phenyl-H); MS: 339 (M^+, 38), 294 (6), 252 (5), 225 (100), 210 (5), 170 (1), 104 (3).

Anal. Calcd. for $C_{17}H_{17}N_5O_3$: C, 60.17; H, 5.01; N, 20.64. Found: C, 60.25; H, 5.01; N, 20.56%.

8-Amino-4,6-dimethyl-2-phenylpyrimido[2,3:4,3]pyrazolo-[1,5-a]pyrimidine (36)

To a mixture of compound **5** (0.30 g, 1.33 mmol) and 3-aminocrotononitrile **3** (0.12 g, 1.35 mmol) in ethanol (5 mL), a few drops of glacial acetic acid was added. The reaction mixture was refluxed for 6 h. The resulting solid product was collected by filtration and recrystallized from DMF/ethanol to give 0.16 g (42% yield) of **36**, mp 337 °C; IR: ν 3412, 3308 (NH_2) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.55 (3H, s, CH_3), 2.98 (3H, s, CH_3), 6.54 (1H, s, 7-H), 8.55-8.50, 7.55-7.50 (5H, m, phenyl-H), 8.20 (2H, br, NH_2); MS: 290 (M^+).

Anal. Calcd. for $C_{16}H_{14}N_6$: C, 66.20; H, 4.82; N, 28.96. Found: C, 66.25; H, 4.90; N, 29.01%.

8-Amino-7-cyano-4-methyl-2-phenylpyrimido[2,3:4,3]-pyrazolo[1,5-a]pyrimidine (38)

This compound was synthesized from compound **5** (0.30 g, 1.33 mmol) and ethoxymethylenemalononitrile **37** (0.23 g, 1.35 mmol) in a manner similar to that described for the preparation of **36**. It was recrystallized from DMF/ethanol to give 0.21 g (53% yield) of **38**, mp > 350 °C; IR: ν 3434, 3325 (NH_2), 2220 (CN) cm^{-1}; ^{1}H NMR (CF_3COOD): δ 2.96 (3H, s, CH_3), 8.54-8.40 (5H, m, phenyl-H), 8.56 (2H, br, NH_2), 9.78 (1H, s, 6-H); MS: 301 (M^+).

Anal. Calcd. for $C_{16}H_{11}N_7$: C, 63.78; H, 3.65; N, 32.55. Found: C, 63.92; H, 3.31; N, 32.66%.

Ethyl (4-methyl-6-phenylpyrazolo[3,4-d]pyrimidinyl-3-yl)aminomethylenecyanoacetate (41a)

To a mixture of compound **5** (0.30 g, 1.33 mmol) and

ethoxymethylenecyanoacetate **39a** (0.23 g, 1.33 mmol) in ethanol (5 mL), a few drops of glacial acetic acid was added. The reaction mixture was refluxed for 7 h. The resulting solid product was collected by filtration and recrystallized from ethanol to give 0.35 g (75% yield) of **41a**, mp 268 °C; IR: ν 3217 (NH), 2226 (CN), 1683 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.31 (3H, t, *J* = 8.3 Hz, CH_3), 2.82 (3H, s, CH_3), 4.30 (2H, q, *J* = 6.9 Hz, CH_2), 8.47-8.40, 7.45-7.40 (5H, m, phenyl-H), 8.30 (1H, s, -CH=C), 11.17 (1H, s, NH), 13.43 (1H, br, NH); MS: 348 (M^+).

Anal. Calcd. for $C_{18}H_{16}N_6O_2$: C, 62.06; H, 4.60; N, 24.13. Found: C, 62.33; H, 4.52; N, 24.26%.

Ethyl (4-methyl-6-phenylpyrazolo[3,4-d]pyrimidinyl-3-yl)aminomethylmethylenecyanoacetate (41b)

This compound was synthesized from compound **5** (0.30 g, 1.33 mmol) and methylethoxymethylenecyanoacetate **39b** (0.25 g, 1.33 mmol) in a manner similar to that described for the preparation of **41a**. It was recrystallized from ethanol to give 0.29 g (60% yield) of **35**, mp 271 °C; IR: ν 3218 (NH), 2212 (CN), 1669 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.28 (3H, t, *J* = 1.8 Hz, CH_3), 2.47 (3H, s, CH_3), 2.83 (3H, s, CH_3), 4.27 (2H, q, *J* = 1.8 Hz, CH_2), 8.46, 7.55-7.53 (5H, m, phenyl-H), 11.83 (1H, br, NH), 13.95 (1H, br, NH); MS: 362 (M^+).

Anal. Calcd. for $C_{19}H_{18}N_6O_2$: C, 62.98; H, 4.97; N, 23.20. Found: C, 62.70; H, 5.01; N, 23.26%.

Diethyl (4-methyl-6-phenylpyrazolo[3,4-d]pyrimidinyl-3-yl)aminomethylenemalonate (41c)

This compound was synthesized from compound **5** (0.30 g, 1.33 mmol) and ethoxymethylenemalonic acid diethyl ester **39c** (0.29 g, 1.33 mmol) in a manner similar to that described for the preparation of **41a**. It was recrystallized from ethanol to give 0.45 g (85% yield) of **41c**, mp 258 °C; IR: ν 3226 (NH), 1700, 1654 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.31-1.23 (6H, m, CH_3), 2.84 (3H, s, CH_3), 4.14 (2H, q, *J* = 3.0 Hz, CH_2), 4.25 (2H, q, *J* = 2.7 Hz, CH_2), 8.76 (1H, s, CH=C), 8.74-8.38, 7.41-7.38 (5H, m, phenyl-H), 11.33 (1H, s, NH), 13.27 (1H, br, NH); MS: 395 (M^+).

Anal. Calcd. for $C_{20}H_{21}N_5O_4$: C, 60.75; H, 5.31; N, 17.72. Found: C, 60.70; H, 5.41; N, 17.66%.

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