5-(1-Pyrrolyl)-2-phenylthieno[2,3-*d*]pyrimidine as Building Block in Heterocyclic Synthesis: Novel Synthesis of Some Pyrazoles, Pyrimidines, Imidazo[1,2-*a*]pyrimidines, Pyrazolo[1,5-*a*]pyrimidines, Pyrido-(pyrimido)pyrazolo[1,5-*a*]pyrimidines, 1,2,4-Triazolo[1,5-*a*]pyrimidine and a 1,2,3,4-Tetrazolo[1,5-*a*]pyrimidine Derivative

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Treatment of enaminone derivative 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** with appropriate hydrazine compounds **2a,b** in refluxing ethanol afforded the corresponding 6-(1-substituted-pyrazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidines **3a,b**. Cyclization of enaminone derivative **1** with appropriate guanidine compounds **13a-c** in the presence of a basic catalyst yields the corresponding 6-(2-substituted-pyrmidin-6-yl)-2-phenylthieno[2,3-*d*]pyrimidines **15a-c**. The compound **15c** can be cyclized with appropriate α-halogenocarbonyl compounds **16a-d** to afford the corresponding 6-(2-substituted-imidazo[1,2-*a*]pyrimidin-7-yl)-2-phenylthieno[2,3-*d*]pyrimidines **17a-d**. On the other hand, the pyrazolo[1,5-*a*]pyrimidines **20a-c**, pyrido(pyrimido)[2,3:4,3]pyrazolo[1,5-*a*]pyrimidines **22a-c**, pyrido[4,5:4,3]pyrazolo[1,5-*a*]pyrimidine **24**, 1,2,4-triazolo[1,5-*a*]pyrimidine **26a**, and 1,2,3,4-tetrazolo[1,5-*a*]pyrimidine derivative **26b** were also obtained by the intramolecular cyclization of enaminone derivative **1** with appropriate 5(3)-amino-pyrazole derivatives **18a-c**, **21a-c**, **23**, 3-amino-1,2,4-triazole **25a** and 5-amino-*1H*-tetrazole **25b** under acid conditions, respectively.

Keywords: Pyrrolothieno[2,3-*d*]pyrimidine; Pyrazoles; Pyrimidines; Imidazo[1,2-*a*]pyrimidines; Pyrazolo[1,5-*a*]pyrimidines; Pyrido(pyrimido)pyrazolo[1,5-*a*]pyrimidines; 1,2,4-Triazolo[1,5-*a*]pyrimidine; 1,2,3,4-Tetrazolo[1,5-*a*]pyrimidine derivatives.

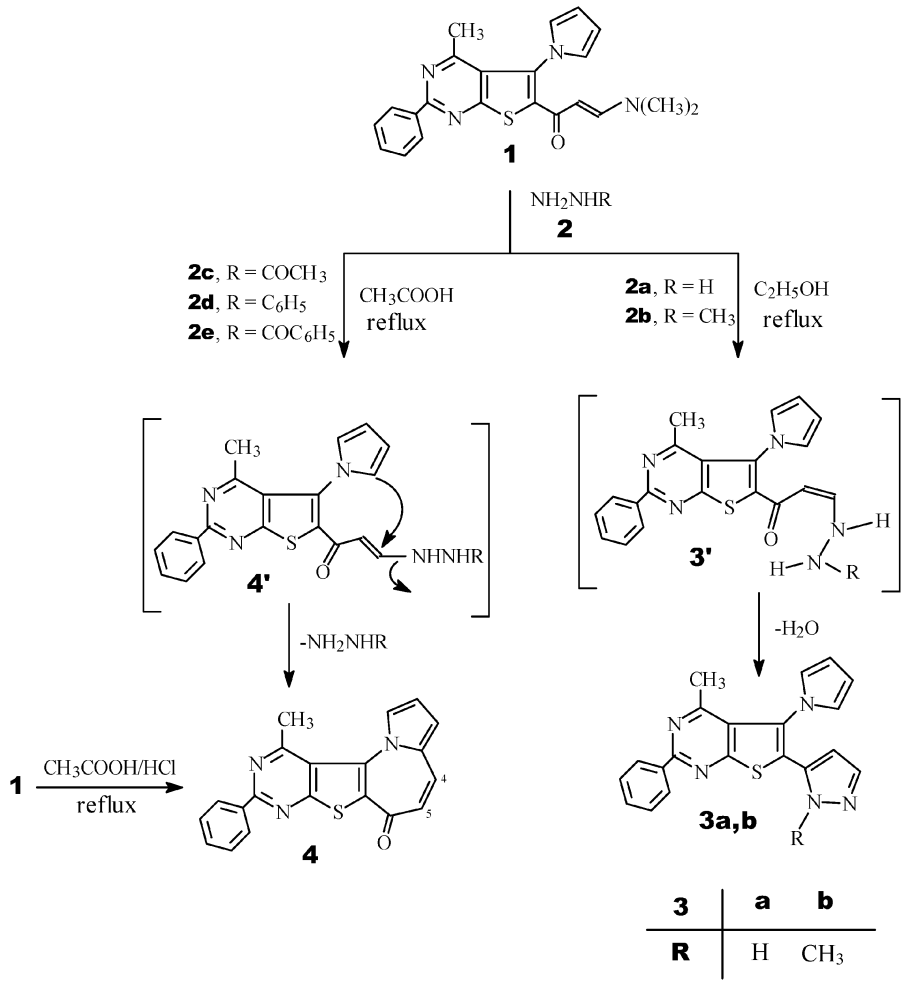
INTRODUCTION

The considerable biological and medicinal activity of fused thienopyrimidines have stimulated much research in this field.[1-8] The incorporation of two moieties increases biological activity of both and thus it was of value to synthesize some new heterocyclic derivatives having two moieties in the same molecules. Our research has been devoted to the development of new classes of heterocycle systems which incorporate the pyrrolothienopyrimidine moiety in the hope that they may be biologically active. In preceding papers[9,10] we have described the synthesis of pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidines, pyrido[3',2':4,5]thieno[2,3-*e*]-1,2,4-triazolo[1,5-*c*]pyrimidines and pyrimido-[2,3:4,3]pyrazolo[1,5-*a*]pyrimidines. More recently, a series of Schiff's bases, chalcones, pyridines, pyridin-2(1H)-ones and 2H-pyran-2-one derivatives containing a 5-(1-pyrrolyl)-4-methyl-2-phenyl-thieno[2,3-*d*]pyrimidine moiety were reported from our laboratory.[11] In continuation of our studies, we report herein the use of enaminone derivative 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** for the synthesis of various pyrazoles, pyrimidines, imidazo[1,2-*a*]-pyrimidines, pyrazolo[1,5-*a*]pyrimidines, pyrido(pyrimido)-[2,3:4,3]pyrazolo[1,5-*a*]pyrimidines, pyrido[4,5:4,3]pyrazolo[1,5-*a*]pyrimidine 1,2,4-triazolo[1,5-*a*]pyrimidine, and a 1,2,3,4-tetrazolo[1,5-*a*]pyrimidine derivative incorporating a 5-(1-pyrrolyl)-4-methyl-2-phenyl-thieno[2,3-*d*]pyrimidine moiety.

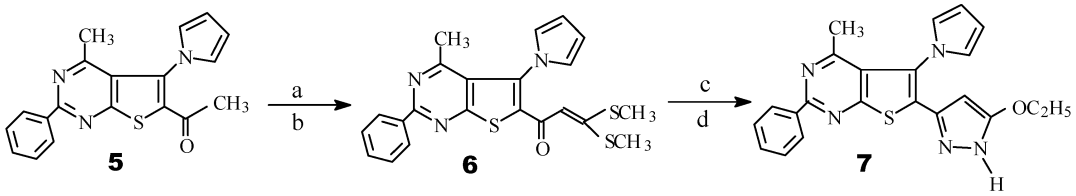
RESULTS AND DISCUSSION

All relevant reactions are depicted in Schemes I-III. 6-(3-Dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1**, which is required as a starting material, was prepared as previously reported.[11] Several pyrrolothienopyrimidines substituted at position-6 with different heterocyclic residues were obtained *via* treatment of enaminone derivative **1** with different reagents.

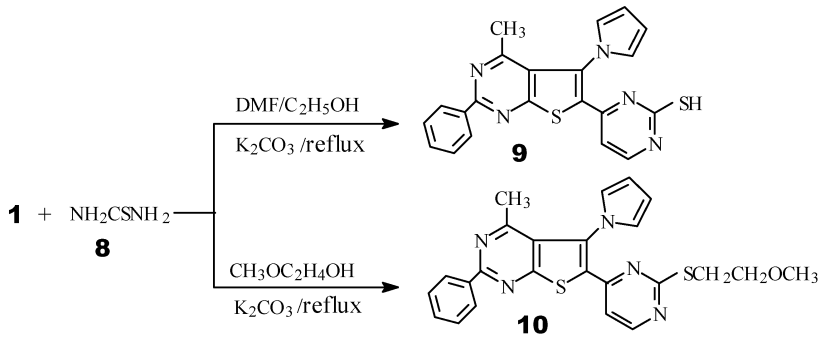
Scheme I



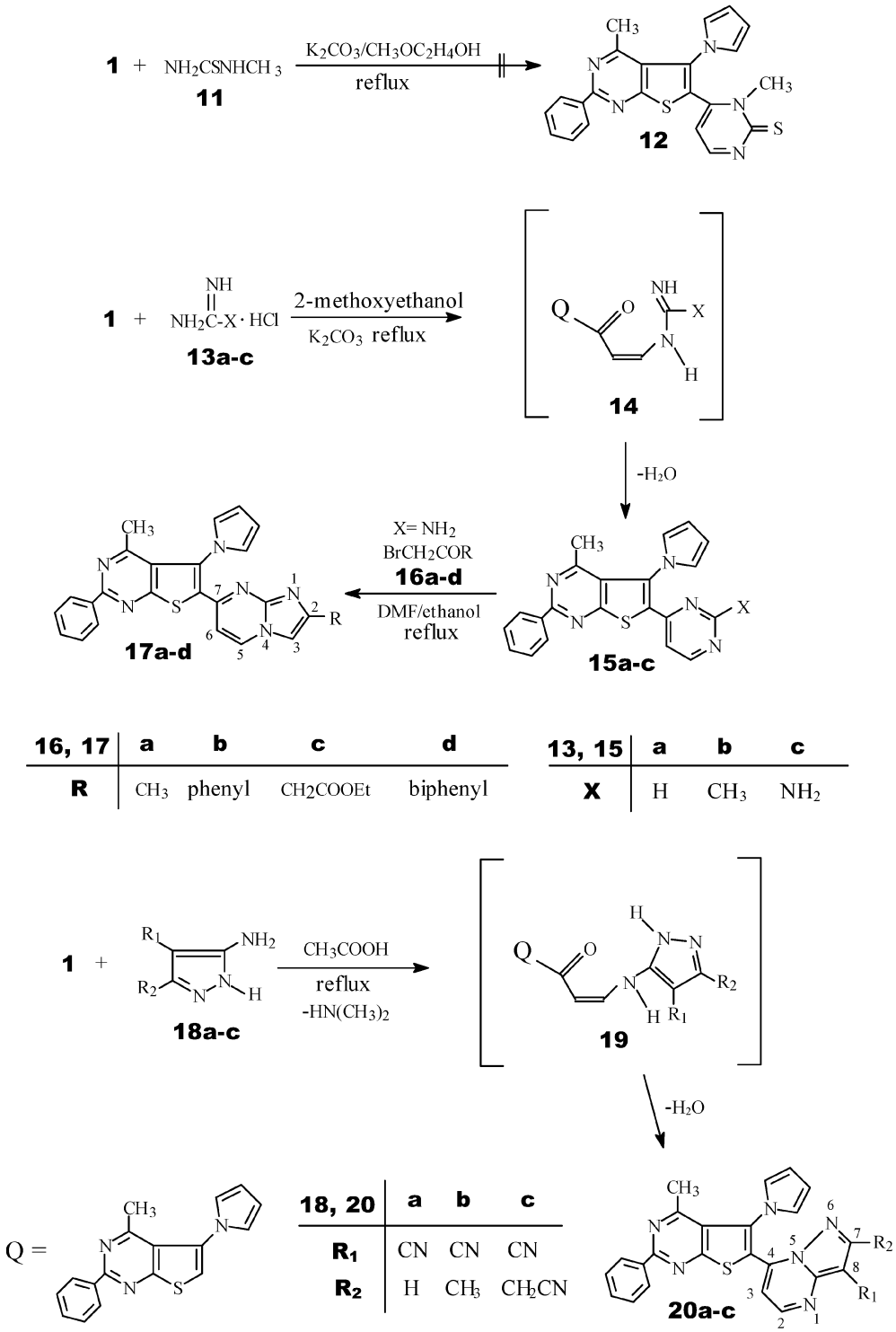
Scheme II



Reagents : a. CS_2/DMF; b. CH_3I; c. C_2H_5ONa ; d. $NH_2NH_2.H_2O$



Scheme III



Thus, reaction of 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** with appropriate hydrazine compounds **2a,b** in refluxing ethanol afforded the corresponding 6-(1-substituted-pyrazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidines **3a,b** (Scheme I). The structures of **3a,b** were established on the basis of their elemental analysis and spectral data. The IR spectra of compounds **3a,b** indicated the absence of the C=O group

absorption band, indicating the formation of pyrazole derivatives **3a,b**. In addition, the ^{1}H NMR spectra ($CDCl_3$) of compounds **3a,b** revealed two doublets at δ 5.27-5.15 (1H, d) and 7.73-7.22 (1H, d), which were readily assigned to the hydrogen attached at C_4 and C_3 of the pyrazole ring, respectively. The formation of compounds **3a,b** would involve an initial addition of the amino group in hydrazine compounds **2a,b** to the activated double bond in enaminone derivative **1**, followed by deamination, to form the intermediate **3'**, which then undergoes cyclization and aromatization *via* loss of water[17] affording the final products **3a,b**. Nevertheless, the enaminone derivative **1** was cyclized with hydrazine compound **2c-e** under different conditions to form a tetracyclic compound. Thus, it has been found that enaminone derivative **1** with hydrazine compound **2c** in refluxing glacial acetic acid gave the 11-methyl-6-oxo-9-phenyl-pyrimido[3',2':4,5]thieno[2,3-*f*]pyrrolo[1,2-*a*]azepine **4** (Scheme I). The oxopyrimido[3',2':4,5]thieno[2,3-*f*]pyrrolo[1,2-*a*]azepine **4** was assumed to be formed *via* addition of an amino group in hydrazine compound **2c** to the activated double bond in enaminone derivative **1**, followed by deamination, to form the intermediate **4'**, which followed by dehydration, and subsequent nucleophilic cyclization with loss of hydrazine compound affords the final product **4**. The IR spectra of compound **4** indicated the characteristic absorption band at 1710 cm^{-1} for the C=O group. In particular, the ^{1}H NMR spectra ($CDCl_3$) of compound **4** revealed four doublets at δ 6.44 (1H, d), 6.92 (1H, d), 7.47 (1H, d) and 7.50 (1H, d) which were readily assigned to the hydrogen attached at C_3, C_4, C_5, and C_1 of the oxopyrimido[3',2':4,5]thieno[2,3-*f*]pyrrolo[1,2-*a*]azepine ring, respectively, and a triplet at δ 6.69 (1H, t) assigned to the hydrogen attached at C_2 of the oxopyrimido[3',2':4,5]-thieno[2,3-*f*]pyrrolo[1,2-*a*]azepine ring, was also confirmed by the mass spectrum *m/z* 343 (M^+, 52). The structure of compound **4** was further confirmed from an independent synthesis of compound **4** by the reacting of enaminone derivative **1** in glacial acetic acid/hydrochloride (1:1) under reflux to afford a product indentical in all respects (mp., mixed mp., TLC and spectra). Also, enaminone derivative **1** reacted with **2d-e** to yield product **4** under the same reaction conditions.

Furthermore, the 6-(5-ethoxy-pyrazol-3-yl)-2-phenylthieno[2,3-*d*]pyrimidine **7** was obtained by treatment of 6-(3,3-bis(methylthio)-2-propen-1-one)-2-phenylthieno-[2,3-*d*]pyrimidine **6** in refluxing ethanol in the presence of an equimolar amount of sodium ethoxide and hydrazine hydrate (Scheme II). Junjappa et al.[12] have also reported an analogous reaction in their papers. The α-ketoketene dithioacetal derivative **6** was prepared from compound **5**[11] following the method in the literature.[13] The structure of pyrazole derivative **7** was established on the basis of their elemental analysis and spectral data. The ^{1}H NMR spectra ($CDCl_3$) of compound **7** revealed an ethoxycarbonyl (δ 1.28 (3H, s) and 4.02 (2H, q)) groups and a singlet at δ 5.51 (1H, s) assigned to the hydrogen attached at C_4 of the pyrazole ring, was also confirmed by the mass spectrum *m/z* 401 (M^+, 35). The mass fragmentation pattern of compound **7** showed the presence of the ion peaks $[M\text{-}CH_3]^+$ at *m/z* 386, $[M\text{-}CH_2CH_3]^+$ at *m/z* 372 and $[M\text{-}OCH_2CH_3]^+$ at *m/z* 356.

Next, reaction of enaminone derivative **1** with thiourea **8** in refluxing DMF/ethanol in the presence of excess anhydrous potassium carbonate afforded the 6-(2-mercapto-pyrimidin-6-yl)-2-phenylthieno[2,3-*d*]pyrimidine **9** (Scheme II). The ^{1}H NMR spectra ($DMSO\text{-}d_6$) of compound **9** revealed two doublets at δ 5.12 (1H, d) and 7.88 (1H, d) which were readily assigned to the hydrogen attached at C_5 and C_4 of the pyrimidine ring, respectively, and a singlet at δ 3.07 (1H, s) assigned to the -SH attached at C_2 of the pyrimidine ring was also confirmed by the mass spectrum *m/z* 401 (M^+, 100). Nevertheless, when enaminone derivative **1** was reacting with thiourea **8** under similar reaction conditions, except that DMF/ethanol was replaced by 2-methoxyethanol to give the 6-(2-methoxyethylthio-pyrimidin-6-yl)- 2-phenylthieno[2,3-*d*]pyrimidine **10**. The structure of pyrimidine derivative **10** was established on the basis of their elemental analysis and spectral data. The ^{1}H NMR spectra ($CDCl_3$) of compound **10** revealed two triplets at δ 4.60 (2H, t) and 3.84 (2H, t) which were readily assigned to the $-SCH_2CH_2-$ protones and a singlet at δ 2.28 (3H, s) assigned to the methoxy protones was also confirmed by the mass spectrum *m/z* 459 (M^+, 10). The mass fragmentation pattern of compound **10** showed the presence of the ion peaks $[M\text{-}CH_3]^+$ at *m/z* 444, $[M\text{-}OCH_3]^+$ at *m/z* 428, $[M\text{-}CH_2OCH_3]^+$ at *m/z* 414, $[M\text{-}CH_2CH_2OCH_3]^+$ at *m/z* 400 and $[M\text{-}SCH_2CH_2OCH_3]^+$ at *m/z* 368. Under the same reaction conditions, reaction of enaminone derivative **1** with methylthiourea **11** did not produce the desired compound **12**, but led only to the recovery of starting material (Scheme III).

On the other hand, the study was extended to investigate the behavior of enaminone derivative **1** with different nucleophiles like guanidine and aminopyrazole derivatives

with a view to synthesizing various heterocyclic ring systems. Intramolecular cyclization of enaminone derivative **1** gave different products depending on reaction conditions. Thus, treatment of enaminone derivative **1** with guanidine compound **13a-c** in refluxing 2-methoxyethanol in the presence of excess anhydrous potassium carbonate afforded the corresponding 6-(2-substituted-pyrimidin-6-yl)-2-phenylthieno[2,3-*d*]pyrimidine **15a-c** (Scheme III). The structures of pyrimidine derivatives **15a-c** were established on the basis of their elemental analysis and spectral data. The ^{1}H NMR spectra ($CDCl_3$) of compound **15a** revealed two doublets at δ 6.10 (1H, d) and 7.75 (1H, d) which were readily assigned to the hydrogen attached at C_5 and C_4 of the pyrimidine ring, respectively, and a singlet at δ 9.20 (1H, s) assigned to the hydrogen attached at C_2 of the pyrimidine ring. The formation of compound **15** would involve an initial addition of the amino group in compound **13** to the activated double bond in enaminone derivative **1**, followed by deamination, to form the compound **14**, which then undergoes intramolecule cyclization *via* loss of water affording the final product **15a**. The ^{1}H NMR spectra of compound **15b-c** are similar to compound **15a**. Furthermore, when aminopyrimidine derivative **15c** was allowed to cyclocondensate with appropriate α-halogenocarbonyl compounds **16a-c** under reflux in DMF/ethanol, it afforded the corresponding 6-(2-substituted-imidazo[1,2-*a*]pyrimidin-7-yl)-2-phenylthieno[2,3-*d*]pyramidines **17a-d**. The ^{1}H NMR spectra ($CDCl_3$) of compound **17a-c** revealed two doublets at δ 5.58-5.40 (1H, d) and 8.13-8.01 (1H, d) which were readily assigned to the hydrogen attached at C_6 and C_5 of the imidazo[1,2-*b*]pyrimidine ring, respectively, and a singlet at δ 6.92-6.60 (1H, s) was assigned to the hydrogen at C_3 of the imidazo[1,2-*b*]pyrimidine ring. Compound **17c** revealed a methylene (δ 5.19 (2H, s)) and ethoxycarbonyl (δ 1.27 (3H, t) and 4.25 (2H, q)) groups.

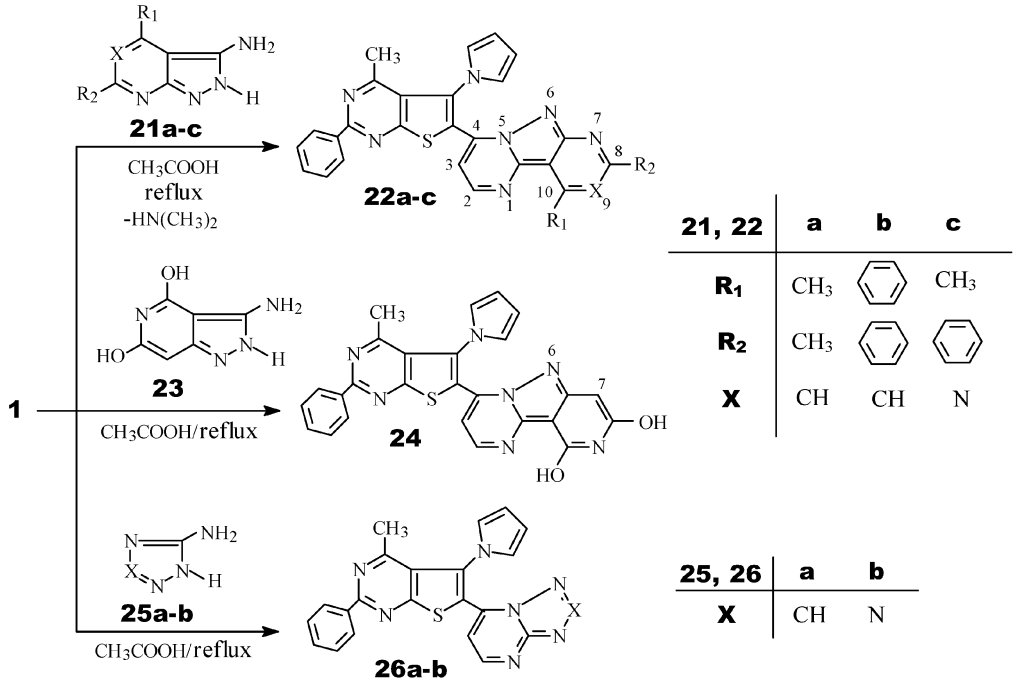
On the other hand, the 6-[(7,8-disubstituted)-pyrazolo-[1,5-*a*]pyrimidin-4-yl]-2-phenylthieno[2,3-*d*]pyramidine derivatives **20a-c** were obtained by intramolecular cyclization of enaminone derivative **1** with 5-amino-3,4-disubstituted-pyrazoles **18a-c** in refluxing glacial acetic acid (Scheme III). Abu Elmaati et al.[16] have also reported an analogous reaction in their papers. The mechanisms of compounds **20a-c** are similar to compound **15a-c**. The IR spectra of compounds **20a-c** indicated the characteristic absorption bands at 2205-2194 cm^{-1} for the C≡N group. The ^{1}H NMR spectra of compound **20a-c** revealed two doublets at δ 6.62-5.65 (1H, d) and 8.84-8.63 (1H, d) which were readily assigned to the hydrogen attached at C_3 and C_2 of the pyrazolo[1,5-*a*]pyrimidine ring, respectively. In addition, compound **20a** and **20c** revealed a sharp singlet at δ 8.74 (1H, s) and at δ 4.60 (2H, s), which were assigned to the hydrogen and the $CNCH_2$- protons at C_7 of the pyrazolo[1,5-*a*]pyrimidine ring, respectively. Finally, under the same reaction conditions, cyclocondensation of the enaminone derivative **1** with 3-amino-4,6-disubstituted-pyrazolo[3,4-*d*]pyridine derivatives **21a-b**, 3-amino-4-methyl-6-phenyl-pyrazolo[3,4-*d*]pyrimidine **21c**, 3-amino-4,6-dihydroxy-pyrazolo[4,3-c]pyridine **23**, 3-amino-1,2,4-triazole **25a** and 5-amino-1*H*-tetrazole **25b** afforded the corresponding pyrido(pyrimido)[2,3:4,3]pyrazolo[1,5-*a*]pyrimidines **22a-c**, pyrido[4,5:4,3]pyrazolo[1,5-*a*]pyrimidine **24**, 1,2,4-triazolo[1,5-*a*]pyrimidine **26a**, and 1,2,3,4-tetrazolo[1,5-*a*]pyrimidine derivative **26b**, respectively (Scheme IV). The structures of compounds **22a-c**, **24** and **26a,b** were established on the basis of their elemental analysis and spectral data. The ^{1}H NMR (CF_3COOD) spectra of compound **22a** revealed two doublets at δ 7.36 (1H, d) and 8.28 (1H, d) which were readily assigned to the hydrogen attached at C_3 and C_2 of the pyrido[2,3:4,3]pyrazolo[1,5-*a*]pyramidine ring and a sharp singlet at δ 7.46 (1H, s), which was assigned to the hydrogen at C_9 of the pyrido-[2,3:4,3]pyrazolo[1,5-*a*]pyramidine ring.

In conclusion, 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** has been shown to be a useful building block for the synthesis of some new pyrazoles, pyrimidines, imidazo[1,2-*b*]pyrimidines, pyrazolo[1,5-a]pyrimidines, pyrido(pyrimido)-pyrazolo[1,5-*a*]pyrimidine derivatives, 1,2,4-triazolo[1,5-*a*]pyrimidine, and 1,2,3,4-tetrazolo[1,5-*a*]pyrimidine derivative.

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

Scheme IV



C, H, and N were performed on a Perkin-Elmer 240 elemental analyzer. 5-Amino-3,4-disubstituted-pyrazoles **18a-c**, 3-amino-4,6-disubstituted-pyrazolo[3,4-*d*]pyridine derivatives **21a-b**, 3-amion-4-methyl-6-phenyl-pyrazolo-[3,4-*d*]pyrimidine **21c**, and 3-amino-4,6-dihydroxy-pyrazolo[4,3-*c*]pyridine **23** were prepared following the methods in the literature,[14,10,15] respectively.

6-(Pyrazol-5-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno-[2,3-*d*]pyrimidine (3a)

A mixture of 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** (0.39 g, 1 mmol) and an excess of hydrazine hydrate **2a** (4 mL, 85% solution 4 mmol) was refluxed in absolute ethanol (10 mL) for 7 h. After cooling, the resulting solid product was collected by filtration, washed with water and recrystallized from ethanol to give 0.28 g of gray white crystals (78% yield), mp 279 °C; IR: ν 3224 (NH) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.14 (3H, s, CH_3), 5.15 (1H, d, J = 1.0 Hz, 4-H of pyrazole), 6.42 (2H, t, 3,4-H of pyrrolyl), 7.03 (2H, t, 2,5-H of pyrrolyl), 7.73 (1H, d, J = 1.0 Hz, 3-H of pyrazole), 8.47-8.45, 7.53-7.52 (5H, m, phenyl-H), 13.29 (1H, s, NH); MS: 357 (M^+, 100), 329 (8), 315 (4), 253 (6), 226 (8), 185 (5), 111 (5), 103 (17), 77 (13).

Anal. Calcd. for $C_{20}H_{15}N_5S$: C, 67.22; H, 4.20; N, 19.60. Found: C, 67.13; H, 4.23; N, 19.77%.

6-(1-Methyl-pyrazol-5-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (3b)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and methylhydrazine **2b** (0.05 g, 1 mmol) in a manner similar to that described for the preparation of **3a**. It was recrystallized from ethanol/THF to give 0.36 g of yellow crystals (98% yield), mp 148 °C; ^1H NMR ($CDCl_3$): δ 2.25 (3H, s, CH_3), 3.93 (3H, s, N-CH_3), 5.27 (1H, d, J = 1.0 Hz, 4-H of pyrazole), 6.46 (2H, t, 3,4-H of pyrrolyl), 6.81 (2H, t, 2,5-H of pyrrolyl), 7.22 (1H, d, J = 1.0 Hz, 3-H of pyrazole), 8.55-8.53, 7.52-7.49 (5H, m, phenyl-H); MS: 371 (M^+, 100), 357 (8), 302 (3), 253 (3), 226 (10), 198 (7), 143 (3), 125 (11), 103 (44), 77 (30), 51 (7).

Anal. Calcd. for $C_{21}H_{17}N_5S$: C, 67.92; H, 4.58; N, 18.86. Found: C, 67.88; H, 4.52; N, 18.59%.

11-Methyl-6-oxo-9-phenyl-pyrimido[3',2':4,5]thieno-[2,3-*f*]pyrrolo[1,2-*a*]azepine (4)

Method A

A mixture of 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** (0.39 g, 1 mmol) and acetyl hydrazine **2c** (0.08 g, 1 mmol) was refluxed in glacial acid (8 mL) for 12 h. After cooling, the resulting solid product was collected by filtration, washed with water and recrystallized from ethanol to give 0.18 g of greenish yellow crystals (52% yield), mp 189 °C; IR: ν

1710 (CO) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.66 (3H, s, CH_3), 6.44 (1H, d, *J* = 1.8 Hz, 3-H of pyrimidothienopyrroloazepine), 6.69 (1H, t, *J* = 1.24 Hz, 2-H of pyrimidothienopyrroloazepine), 6.92 (1H, d, *J* = 1.0 Hz, 4-H of pyrimidothienopyrroloazepine), 7.47 (1H, d, *J* = 1.3 Hz, 5-H of pyrimidothienopyrroloazepine), 7.50 (1H, d, *J* = 1.0 Hz, 1-H of pyrimidothienopyrroloazepine), 8.60-8.58, 7.55-7.54 (5H, m, phenyl-H); MS: 343 (M^+, 52), 315 (100), 288 (1), 223 (7), 211 (58), 179 (18), 153 (9), 140 (4), 103 (34), 77 (29), 51 (9).

Anal. Calcd. for $C_{20}H_{13}N_3OS$: C, 69.97; H, 3.79; N, 12.24. Found: C, 70.10; H, 3.90; N, 12.36%.

Method B

A mixture of 6-(3-dimethylamino-acryloyl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine **1** (0.39 g, 1 mmol) and acetyl hydrazine **2c** (0.08 g, 1 mmol) was refluxed in glacial acid/HCl (10 mL) for 4 h. The mixture was poured into ice-water, and the precipitated product was collected by filtration, washed with water, and the crude product recrystallized to give 0.25 g (74% yield).

6-(3,3-Bis(methylthio)-2-propen-1-one)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (6)

This compound was prepared following the methods in the literature.[13] It was recrystallized from acetone/THF to give 3.09 g of yellow crystals (93% yield), mp 90 °C; IR: ν 1701 (CO) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.17 (3H, s, SCH_3), 2.20 (3H, s, SCH_3), 2.28 (3H, s, CH_3), 6.47 (2H, m, 3,4-H of pyrrolyl), 6.87 (2H, m, 2,5-H of pyrrolyl), 7.46 (1H, s, COCH=), 8.57-8.54, 7.52-7.46 (5H, m, phenyl-H); MS: 437 (M^+, 16), 422 (10), 390 (50), 375 (6), 343 (4), 333 (100), 318 (29), 290 (32), 244 (5), 223 (7), 184 (22), 160 (18), 107 (10), 103 (62), 91 (50), 77 (43), 51 (12).

Anal. Calcd. for $C_{22}H_{19}N_3OS_3$: C, 60.41; H, 4.34; N, 9.61. Found: C, 60.55; H, 4.52; N, 9.59%.

6-(5-Ethoxy-pyrazol-3-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (7)

A mixture of compound **6** (0.44 g, 1 mmol) and sodium ethoxide (0.07 g, 1 mmol) in refluxing ethanol (10 mL) for 15 minutes and hydrazine hydrate (10 mL) was added. The mixture was refluxed for 6 h and poured into ice-water, acidified with hydrochloric acid and the precipitated product was collected by filtration, washed with water, and the crude product recrystallized from chloroform/ethanol to give 0.38 g of pale yellow crystals (94% yield), mp 103 °C; ^1H NMR ($CDCl_3$): δ 1.28 (3H, t, *J* = 2.1 Hz, CH_3), 2.11 (3H, s, CH_3), 4.02 (2H, q, *J* = 2.0 Hz, OCH_2), 5.51 (1H, s, 4-H of pyrazole), 6.40 (2H, m 3,4-H of pyrrolyl), 6.82 (2H, m, 2,5-H of pyrrolyl), 8.55-8.51, 7.51-7.45 (5H, m, phenyl-H), 8.62 (1H, br, NH); MS: 401 (M^+, 35), 386 (4), 372 (10), 356 (5), 347 (32), 330 (100), 316 (18), 304 (10), 290 (34), 251 (5), 226 (10), 185 (12), 160 (8), 129 (5), 103 (40), 77 (37), 51 (10).

Anal. Calcd. for $C_{22}H_{19}N_5OS$: C, 65.83; H, 4.74; N, 17.45. Found: C, 65.56; H, 4.72; N, 17.32%.

6-(2-Mercapto-pyrimidin-6-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (9)

A mixture of compound **1** (0.39 g, 1 mmol), thiourea **8** (0.08 g, 1 mmol) and excess anhydrous potassium carbonate (0.28 g, 2 mmol) was refluxed in DMF/ethanol (10 mL) for 20 h and poured into ice-water, acidified with hydrochloric acid and the precipitated product was collected by filtration, washed with water, and the crude product recrystallized from chloroform/ethanol to give 0.16 g of yellowish brown crystals (40% yield), mp > 300 °C; ^1H NMR (DMSO-d_6): δ 2.1 (3H, s, CH_3), 3.07 (1H, s, SH), 5.12 (1H, d, *J* = 1.0 Hz, 5-H of pyrimidinyl), 6.47 (2H, m, 3,4-H of pyrrolyl), 7.13 (2H, m, 2,5-H of pyrrolyl), 7.88 (1H, d, *J* = 1.0 Hz, 4-H of pyrimidinyl), 8.48-8.45, 7.55-7.54 (5H, m, phenyl-H); MS: 401 (M^+, 100).

Anal. Calcd. for $C_{21}H_{15}N_5S_2$: C, 62.84; H, 3.74; N, 17.45. Found: C, 62.53; H, 3.42; N, 17.68%.

6-(2-Methoxyethylthio-pyrimidin-6-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (10)

A mixture of compound **1** (0.39 g, 1 mmol), thiourea **8** (0.08 g, 1 mmol) and excess anhydrous potassium carbonate (0.28 g, 2.0 mmol) was refluxed in 2-methoxyethanol (10 mL) for 20 h and poured into ice-water, acidified with hydrochloric acid and the precipitated product was collected by filtration, washed with water, and the crude product recrystallized from ethanol/THF to give 0.41 g of pale yellow crystals (90% yield), mp 165 °C; ^1H NMR ($CDCl_3$): δ 2.28 (3H, s, OCH_3), 3.47 (3H, s, CH_3), 3.84 (2H, t, *J* = 1.0 Hz, CH_2), 4.60 (2H, t, *J* = 1.0 Hz, CH_2), 5.83 (1H, d, *J* = 1.0 Hz, 5-H of pyrimidinyl), 6.54 (2H, t, 3,4-H of pyrrolyl), 6.82 (2H, t, 2,5-H of pyrrolyl), 8.35 (1H, d, *J* = 1.0 Hz, 4-H of pyrimidinyl), 8.57-8.53, 7.52-7.50 (5H, m, phenyl-H); MS: 459 (M^+, 10), 444 (100), 428 (2), 414 (8), 400 (16), 368 (36), 356 (68), 343 (59), 313 (12), 291 (56), 238 (4),

211 (5), 160 (4), 77 (14).

Anal. Calcd. for $C_{24}H_{21}N_5OS_2$: C, 62.74; H, 4.57; N, 15.25. Found: C, 62.69; H, 4.60; N, 15.48%.

6-(Pyrimidin-6-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (15a)

A mixture of compound **1** (0.39 g, 1 mmol), formamidine hydrochloride **13a** (0.08 g, 1 mmol) and excess anhydrous potassium carbonate (0.28 g, 2.0 mmol) was refluxed in 2-methoxyethanol (10 mL) for 24 h. After cooling, the resulting solid product was collected by filtration, washed with ethanol and water, and the crude product recrystallized from from THF/ethanol to give 0.32 g of yellow crystals (86% yield), mp 242 °C; ^{1}H NMR ($CDCl_3$): δ 2.29 (3H, s, CH_3), 6.10 (1H, d, J = 1.0 Hz, 5-H of pyrimidinyl), 6.56 (2H, t, 3,4-H of pyrrolyl), 6.84 (2H, t, 2,5-H of pyrrolyl), 7.75 (1H, d, J = 1.2 Hz, 4-H of pyrimidinyl), 8.57-8.53, 7.52-7.48 (5H, m, phenyl-H), 9.20 (1H, s, 2-H of pyrimidinyl); MS: 369 (M^+, 100), 343 (10), 336 (5), 289 (16), 265 (10), 238 (11), 211 (10), 185 (14), 142 (6), 104 (36), 160 (4), 77 (33).

Anal. Calcd. for $C_{21}H_{15}N_5S$: C, 68.29; H, 4.06; N, 18.97. Found: C, 68.33; H, 4.26; N, 18.88%.

6-(2-Methyl-pyrimidin-6-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (15b)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and acetamidine hydrochloride **13b** (0.10 g, 1.0 mmol) in a manner similar to that described for the preparation of **15a**. It was recrystallized from ethanol/THF to give 0.29 g of pale yellow crystals (75% yield), mp 265 °C; ^{1}H NMR ($CDCl_3$): δ 2.25 (3H, s, CH_3), 2.74 (3H, s, CH_3), 5.90 (1H, d, J = 2.0 Hz, 5-H of pyrimidinyl), 6.53 (2H, t, 3,4-H of pyrrolyl), 6.84 (2H, t, 2,5-H of pyrrolyl), 8.42 (1H, d, J = 1.0 Hz, 4-H of pyrimidinyl), 8.54-8.52, 7.49-7.48 (5H, m, phenyl-H); MS: 383 (M^+, 100), 368 (1), 340 (4), 289 (4), 238 (4), 211 (7), 192 (11), 171 (4), 104 (5), 93 (7), 77 (4).

Anal. Calcd. for $C_{22}H_{17}N_5S$: C, 68.93; H, 4.44; N, 18.27. Found: C, 68.73; H, 4.30; N, 18.38%.

6-(2-Amino-pyrimidin-6-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (15c)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and guanidine hydrochloride **13c** (0.10 g, 1.0 mmol) in a manner similar to that described for the preparation of **15a**. It was recrystallized from ethanol/THF to give 0.33 g of yellow crystals (87% yield), mp 288 °C; IR: ν 3243 (NH_2) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.70 (3H, s, CH_3), 6.02 (1H, d, J = 2.0 Hz, 5-H of pyrimidinyl), 6.77 (2H, t, 3,4-H of pyrrolyl), 6.96 (2H, t, 2,5-H of pyrrolyl), 8.21 (1H, d, J = 1.0 Hz, 4-H of pyrimidinyl), 8.34-8.33, 7.86-7.77 (5H, m, phenyl-H); MS: 384 (M^+, 100), 368 (11), 350 (12), 342 (10), 315 (5), 290 (9), 238 (2), 211 (4), 192 (10), 178 (15), 103 (5), 77 (6).

Anal. Calcd. for $C_{21}H_{16}N_6S$: C, 65.62; H, 4.17; N, 21.87. Found: C, 65.73; H, 4.30; N, 21.79%.

6-(2-Methyl-imidazo[1,2-*a*]pyrimidin-7-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (17a)

A mixture of compound **15c** (0.38 g, 1 mmol) and chloroacetone **16a** (0.1 g, 1 mmol) in DMF/ethanol (10 mL) was refluxed overnight and then evaporated to dryness under reduced pressure. The residue was washed with ether and recrystallized from ethanol/THF to give 0.35 g of greenish yellow crystals (82% yield), mp 260 °C; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): δ 2.14 (3H, s, CH_3), 2.50 (3H, s, CH_3), 5.40 (1H, d, J = 1.0 Hz, 6-H of imidazopyrimidinyl), 6.42 (2H, t, 3,4-H of pyrrolyl), 6.60 (1H, s, 3-H of imidazopyrimidinyl), 6.90 (2H, t, 2,5-H of pyrrolyl), 8.01 (1H, d, J = 1.0 Hz, 5-H of imidazopyrimidinyl), 8.47-8.45, 7.46-7.45 (5H, m, phenyl-H); MS: 422 (M^+, 10), 384 (100), 343 (5), 290 (8), 238 (3), 211 (7), 178 (10), 104 (4), 77 (5).

Anal. Calcd. for $C_{24}H_{18}N_6S$: C, 68.24; H, 4.26; N, 19.90. Found: C, 68.33; H, 4.13; N, 20.11%.

6-(2-Phenyl-imidazo[1,2-*a*]pyrimidin-7-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (17b)

This compound was synthesized from compound **15c** (0.38 g, 1 mmol) and 2-bromoacetophenone **16b** (0.20 g, 1 mmol) in a manner similar to that described for the preparation of **17a**. It was recrystallized from ethanol/THF to give 0.37 g of yellow crystals (77% yield), mp 276 °C; ^{1}H NMR (DMSO-d_6): δ 2.18 (3H, s, CH_3), 5.41 (1H, d, J = 1.0 Hz, 6-H of imidazopyrimidinyl), 6.47 (2H, t, 3,4-H of pyrrolyl), 6.92 (1H, s, 3-H of imidazopyrimidinyl), 7.11 (2H, t, 2,5-H of pyrrolyl), 8.13 (1H, d, J = 1.0 Hz, 5-H of imidazopyrimidinyl), 8.50-8.47, 7.57-7.55 (5H, m, phenyl-H); MS: 484 (M^+,100), 451 (100), 380 (2), 353 (3), 250 (2), 242 (38), 169 (6), 116 (6), 77 (7).

Anal. Calcd. for $C_{29}H_{20}N_6S$: C, 71.90; H, 4.13; N, 17.35. Found: C, 71.99; H, 4.25; N, 17.48%.

6-(2-Carbethoxymethyl-imidazo[1,2-*a*]pyrimidin-7-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (17c)

This compound was synthesized from compound **15c** (0.38 g, 1 mmol) and 4-chloroacetoacetic acid ethyl ester **16c** (0.17 g, 1 mmol) in a manner similar to that described for the preparation of **17a**. It was recrystallized from ethanol/THF to give 0.21 g of brown crystals (43% yield), mp 181 °C; IR: ν 1711 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.27 (3H, t, J = 1.5 Hz, CH_3), 2.24 (3H, s, CH_3), 4.25 (2H, q, J = 1.5 Hz, OCH_2), 5.19 (1H, s, CH_2), 5.58 (1H, d, J = 1.0 Hz, 6-H of imidazopyrimidinyl), 6.50 (2H, t, 3,4-H of pyrrolyl), 6.61 (1H, s, 3-H of imidazopyrimidinyl), 6.82 (2H, t, 2,5-H of pyrrolyl), 8.11 (1H, d, J = 1.0 Hz, 5-H of imidazopyrimidinyl), 8.55-8.53, 7.50 (5H, m, phenyl-H); MS: 494 (M^+, 10), 477 (1), 422 (2), 412 (6), 384 (100), 3692 (8), 341 (7), 315 (4), 290 (7), 211 (4), 179 (7), 119 (3), 104 (6), 83 (7), 77 (12).

Anal. Calcd. for $C_{27}H_{22}N_6O_2S$: C, 65.59; H, 4.45; N, 17.00. Found: C, 65.71; H, 4.29; N, 17.18%.

6-(2-Biphenyl-imidazo[1,2-*a*]pyrimidin-7-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (17d)

This compound was synthesized from compound **15c** (0.38 g, 1 mmol) and 2-bromo-4′-phenylacetophenone **16d** (0.28 g, 1 mmol) in a manner similar to that described for the preparation of **17a**. It was recrystallized from ethanol/THF to give 0.21 g of deep yellow crystals (38% yield), mp 304 °C; ^1H NMR (DMSO-d_6 + $CDCl_3$): δ 2.15 (3H, s, CH_3), 5.43 (1H, d, J = 1.0 Hz, 6-H of imidazopyrimidinyl), 6.46 (2H, t, 3,4-H of pyrrolyl), 6.77 (1H, s, 3-H of imidazopyrimidinyl), 6.90 (2H, t, 2,5-H of pyrrolyl), 8.47-8.42, 8.02-7.37 (15H, m, 5-H of imidazopyrimidinyl and phenyl-H); MS: 560 (M^+, 100), 483 (1), 425 (1), 397 (9), 384 (4), 280 (20), 192 (3), 181 (9), 152 (10), 77 (7).

Anal. Calcd. for $C_{35}H_{24}N_6S$: C, 75.00; H, 4.28; N, 15.00. Found: C, 75.38; H, 4.19; N, 15.28%.

6-(8-Cyano-pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (20a)

A mixture of compound **1** (0.39 g, 1 mmol) and 5-amino-4-cyano-pyrazole **18a** (0.1 g, 1 mmol) was refluxed in glacial acid (8 mL) for 12 h. After cooling, the resulting solid product was collected by filtration, washed with water and recrystallized from DMF/glacial acid to give 0.29 g of light yellow crystals (67% yield), mp 275 °C; IR: ν 2194 (C≡N) cm^{-1} ;^1H NMR (CF_3COOD): δ 2.35 (3H, s, CH_3), 6.62 (1H, d, J = 1.0 Hz, 3-H of pyrazolopyrimidinyl), 6.74 (2H, t, 3,4-H of pyrrolyl), 6.92 (2H, t, 2,5-H of pyrrolyl), 8.34-8.27, 7.83-7.66 (5H, m, phenyl-H), 8.74 (1H, s, 7-H of pyrazolopyrimidinyl), 8.84 (1H, d, J = 1.0 Hz, 2-H of pyrazolopyrimidinyl); MS: 433 (M^+, 36), 407 (1), 367 (1), 312 (5), 288 (16), 236 (7), 211 (15), 185 (5), 119 (20), 104 (100), 77 (79).

Anal. Calcd. for $C_{24}H_{15}N_7S$: C, 66.51; H, 3.46; N, 22.63. Found: C, 66.33; H, 3.33; N, 22.49%.

6-(8-Cyano-7-methyl-pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (20b)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 5-amino-4-cyano-3-methyl-pyrazole **18b** (0.11 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/glacial acid to give 0.29 g of light yellow crystals (65% yield), mp 320 °C; IR: ν 2195 (C≡N) cm^{-1}; ^1H NMR (CF_3COOD): δ 2.42 (3H, s, CH_3), 2.64 (3H, s, CH_3), 6.61 (1H, d, J = 1.0 Hz, 3-H of pyrazolopyrimidinyl), 6.94 (2H, t, 3,4-H of pyrrolyl), 6.98 (2H, t, 2,5-H of pyrrolyl), 8.41-8.33, 7.90-7.74 (5H, m, phenyl-H), 8.83 (1H, d, J = 1.0 Hz, 2-H of pyrazolopyrimidinyl); MS: 447 (M^+, 36), 432 (2), 406 (2), 326 (5), 288 (10), 223 (8), 211 (14), 185 (6), 142 (5), 133 (16), 104 (100), 77 (72).

Anal. Calcd. for $C_{25}H_{17}N_7S$: C, 67.11; H, 3.80; N, 21.92. Found: C, 67.26; H, 3.99; N, 22.01%.

6-(8-Cyano-7-cyanomethyl-pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (20c)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 5-amino-3-cyanomethyl-4-cyano-pyrazole **18c** (0.13 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/ethanol to give 0.21 g of brownish yellow crystals (45% yield), mp 230 °C; IR: ν 2205 (C≡N) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.30 (3H, s, CH_3), 4.60 (2H, s, CH_2), 5.65 (1H, d, J = 1.0 Hz, 3-H of pyrazolopyrimidinyl), 6.46 (2H, t, 3,4-H of pyrrolyl), 7.07 (2H, t, 2,5-H of pyrrolyl), 8.51-8.49, 7.51-7.48 (5H, m, phenyl-H), 8.63 (1H, d, J = 1.0 Hz, 2-H of pyrazolopyrimidinyl); MS: 472 (M^+, 100), 447 (4), 432 (18), 421 (3), 406 (4), 368 (2), 326 (10), 315 (22), 290 (50), 275 (9), 236 (22), 211 (24), 179 (18), 131 (12), 103 (61), 77 (64).

Anal. Calcd. for $C_{26}H_{16}N_8S$: C, 66.10; H, 3.39; N,

23.72. Found: C, 66.26; H, 3.59; N, 23.47%.

6-(8,10-Dimethyl-pyrido[2,3:4,3]pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (22a)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 3-amino-4,6-dimethyl-pyrazolo[3,4-*b*]pyridine **21a** (0.23 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/glacial acid to give 0.41 g of orange crystals (85% yield), mp 294 °C; ^{1}H NMR (CF_3COOD): δ 2.91 (3H, s, CH_3), 2.99 (3H, s, CH_3), 3.05 (3H, s, CH_3), 6.82 (2H, t, 3,4-H of pyrrolyl), 7.02 (2H, t, 2,5-H of pyrrolyl), 7.36 (1H, d, J = 1.0 Hz, 3-H of pyridopyrazolopyrimidinyl), 7.46 (1H, s, 9-H of pyridopyrazolopyrimidinyl), 8.28 (1H, d, J = 1.5 Hz, 2-H of pyridopyrazolopyrimidinyl), 8.37-8.35, 7.74-7.66 (5H, m, phenyl-H); MS: 487 (M^+, 6), 421 (2), 344 (2), 322 (12), 315 (5), 215 (3), 187 (8), 173 (16), 162 (100), 119 (10), 77 (10).

Anal. Calcd. for $C_{28}H_{21}N_7S$: C, 68.99; H, 4.31; N, 20.12. Found: C, 69.18; H, 4.06; N, 20.01%.

6-(8,10-Diphenyl-pyrido[2,3:4,3]pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]-pyrimidine (22b)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 3-amino-4,6-diphenyl-pyrazolo[3,4-*b*]pyridine **21b** (0.35 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/glacial acid to give 0.43 g of light yellow crystals (71% yield), mp 340 °C; ^{1}H NMR (CF_3COOD): δ 2.82 (3H, s, CH_3), 6.78 (2H, t, 3,4-H of pyrrolyl), 7.07 (2H, t, 2,5-H of pyrrolyl), 7.37 (1H, d, J = 1.0 Hz, 3-H of pyridopyrazolopyrimidinyl), 8.17 (1H, d, J = 1.0 Hz, 2-H of pyridopyrazolopyrimidinyl), 8.40-8.37, 8.15-7.16 (16H, m, 9-H of pyridopyrazolopyrimidinyl and phenyl-H); MS: 611 (M^+, 10), 545 (2), 343 (3), 333 (12), 286 (100), 257 (15), 128 (11), 103 (16), 77 (10), 51 (16).

Anal. Calcd. for $C_{38}H_{25}N_7S$: C, 74.63; H, 4.09; N, 16.04. Found: C, 74.33; H, 3.91; N, 16.11%.

6-(10-Methyl-8-phenyl-pyrimido[2,3:4,3]pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (22c)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 3-amino-4-methyl-6-phenyl-pyrazolo[3,4-*d*]pyrimidine **21c** (0.23 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/glacial acid to give 0.43 g of light yellow crystals (78% yield), mp 315 °C; ^{1}H NMR (CF_3COOD): δ 2.88 (3H, s, CH_3), 3.31 (3H, s, CH_3), 6.63 (2H, m, 3,4-H of pyrrolyl), 6.91 (2H, m, 2,5-H of pyrrolyl), 7.25 (1H, d, J = 1.0 Hz, 3-H of pyrimidopyrazolopyrimidinyl), 8.15 (1H, d, J = 1.0 Hz, 2-H of pyrimidopyrazolopyrimidinyl), 8.22-8.20, 8.07-7.51 (10H, m, phenyl-H); MS: 550 (M^+, 8), 484 (4), 344 (72), 315 (15), 237 (6), 225 (100), 160 (2), 103 (12), 77 (6).

Anal. Calcd. for $C_{32}H_{22}N_8S$: C, 69.82; H, 4.00; N, 20.36. Found: C, 69.98; H, 4.26; N, 20.21%.

6-(8,10-Dihydroxy-pyrido[4,5:4,3]pyrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (24)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 3-amino-4,6-dihydroxy-pyrazolo-[4,3-*c*]pyridine **23** (0.17 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from DMF/glacial acid to give 0.42 g of brown crystals (86% yield), mp > 330 °C; IR: ν 3350 (OH) cm^{-1}; ^{1}H NMR (CF_3COOD): δ 2.70 (3H, s, CH_3), 6.52 (2H, m, 3,4-H of pyrrolyl), 6.87 (2H, m, 2,5-H of pyrrolyl), 7.19 (1H, d, J = 1.0 Hz, 3-H of pyridopyrazolopyrimidinyl), 7.84-7.81, 7.72-7.69 (6H, m, 7-H of pyridopyrazolopyrimidinyl and phenyl-H), 8.39 (1H, d, J = 1.0 Hz, 2-H of pyridopyrazolopyrimidinyl); MS: 491 (M^+, 68), 474 (33), 402 (2), 392 (6), 343 (20), 315 (45), 288 (68), 236 (15), 224 (68), 211 (32), 166 (26), 153 (18), 104 (98), 77 (100).

Anal. Calcd. for $C_{26}H_{17}N_7O_2S$: C, 63.54; H, 3.46; N, 19.96. Found: C, 63.42; H, 3.26; N, 20.11%.

6-(1,2,4-Triazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (26a)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 3-amino-1,2,4-triazole **25a** (0.10 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from ethanol/chloroform to give 0.25 g of yellow crystals (62% yield), mp 217 °C; ^{1}H NMR ($CDCl_3$): δ 2.38 (3H, s, CH_3), 6.12 (1H, d, J = 1.0 Hz, 3-H of triazolopyrimidinyl), 6.56 (2H, m, 3,4-H of pyrrolyl), 6.84 (2H, m, 2,5-H of pyrrolyl), 7.49 (1H, s, 7-H of triazolopyrimidinyl), 8.54 (1H, d, J = 1.0 Hz, 2-H of triazolopyrimidinyl), 8.63-8.61, 7.53-7.51 (5H, m, phenyl-H); MS: 409 (M^+, 100), 387 (76), 371 (30), 340 (28), 331 (18), 290 (38), 275 (6), 211 (6), 204 (12), 194 (11), 128 (4),

104 (11), 98 (31), 77 (13).

Anal. Calcd. for $C_{22}H_{15}N_7S$: C, 64.54; H, 3.66; N, 23.96. Found: C, 64.42; H, 3.36; N, 24.21%.

6-(1,2,3,4-Tetrazolo[1,5-*a*]pyrimidin-4-yl)-5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine (26b)

This compound was synthesized from compound **1** (0.39 g, 1 mmol) and 5-amino-1*H*-tetrazole **25b** (0.09 g, 1 mmol) in a manner similar to that described for the preparation of **20a**. It was recrystallized from ethanol/chloroform to give 0.25 g of pale yellow crystals (62% yield), mp 186 °C; MS: 410 (M^+, 100).

Anal. Calcd. for $C_{21}H_{14}N_8S$: C, 61.46; H, 3.41; N, 27.31. Found: C, 61.42; H, 3.36; N, 27.01%.

ACKNOWLEDGEMENT

We are grateful to the Nanya Institute of Technology for financial support.

REFERENCES

1. Brown, D. J.; Katritzky, A. R.; Rees, C. W. In *Comprehensive Heterocyclic Chemistry*; Vol. 3, Boulton, A. J.; McKillop, A., Eds.; 1984, p 57.
2. Dave, C. G.; Shah, P. R.; Dave, K. C.; Patel, V. J. *J. Indian Chem. Soc*. **1989**, *66*, 48.
3. (a) Bousquet, E.; Romero, G.; Guerrera, F.; Caruso, A.; Roxas, M. A. *Farmaco Ed. Sci.* **1985**, *40*, 869. (b) Bousquet, E.; Guerrera, F.; Siracusa, N. A.; Caruso, A.; Roxas, M. A. *Farmaco Ed. Sci.* **1984**, *39*, 110.
4. Vieweg, H.; Leistner, S.; Wagner, G.; Boehm, N.; Krasset, U.; Grupe, R.; Lohmann, D.; Loban, G., East German Patent DD **1988**, 257830.; *Chem. Abstr.* **1989**, *110*, 95262p.
5. (a) Chaykovsky, M.; Lin, M.; Rosowsky, A.; Modest, E. J. *J. Med. Chem*. **1973**, *10*, 188. (b) Elsager, E. F.; Jacob, P.; Werbel, L. M. *J. Heterocycl. Chem*. **1972**, *9*, 775.
6. Madding, G. D.; Thompson, M. D. *J. Heterocycl. Chem*. **1987**, *24*, 581.
7. Cheng, C. C. In *Progress in Medicinal Chemistry*; Vol 25, Ellis, G. P.; West, G. B., Eds.; Elsevier Science Publisher B. V. 1000 AE Amsterdam The Netherlands, 1989; p 35.
8. Shishoo, C. J.; Devani, M. B.; Bhadti, V. S. Indian Patent **1983**, 151; *Chem. Abstr.* **1984**, *100*, 209858p.
9. Ho, Y. W. *J. Chin. Chem. Soc*. **2001**, *48*, 1163.
10. Ho, Y. W.; Yao, C. T. *J. Chin. Chem. Soc*. **2003**, *50*, 283.
11. Ho, Y. W.; Yao, W. H. *J. Chin. Chem. Soc*. **2005**, *52*, 313.
12. Chauhan, S. M. S.; Junjappa, H. *Synthesis* **1975**, 798.
13. Chauhan, S. M. S.; Junjappa, H. *Tetrahedron* **1976**, *32*, 1779.
14. Cheng, C. C.; Robins, R. K. *J. Am. Chem. Soc.* **1956**, *78*, 1240.
15. Taylor, E. C.; Hartke, K. S. *J. Am. Chem. Soc.* **1959**, *81*, 2452.
16. El-Taweel, F. M. A.; Abu Elmaati, T. M. *J. Chin. Chem. Soc*. **2002**, *49*, 1051.
17. Dawood, Kamal M.; Farag, Ahmad M.; Ragab, Eman A. *J. Chin. Chem. Soc*. **2004**, *51*, 853.