HETEROCYCLES, Vol. 92, No. 8, 2016, pp. 1397 - 1414. © 2016 The Japan Institute of Heterocyclic Chemistry
Received, 14th March, 2016, Accepted, 31st May, 2016, Published online, 9th June, 2016
DOI: 10.3987/COM-16-13467

A SIMPLE AND CONVENIENT SYNTHESIS OF ISOLATED FUSED HETEROCYCLES BASED ON: 6-PHENYL-2-THIOXO-2,3-DIHYDROPYRIMIDIN-4(5*H*)-ONE AND 5-ACETYL-6-PHENYL-2-THIOXO-2,3-DIHYDROPYRIMIDIN-4(5*H*)-ONE

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Abstract – The reaction of 6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **1** with acetyl chloride in acetic anhydride in the presence of sodium acetate afforded 5-acetyl-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **2** which reacted with bromine, hydrazine hydrate, phenylhydrazine, cyanothioacetamide, aldehydes and (malononitrile/sulfur) to give 2-thioxo-2,3-dihydropyrimidine derivatives **4, 7a,b, 8, 10** and **11** respectively. In the present investigation 6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **1** was reacted with chloroacetyl chloride to yield the corresponding compound **13**. Compound **1** was reacted with some electrophilic reagents such as (benzylidene-cyanothioacetamide derivatives, 2-cyano-2-cyclopentylethanethioamide, 2-cyano-2-cyclohexyl-ethanethioamide and aromatic diazonium salts) to give compounds **23, 27a,b** and **35** respectively. The newly synthesized heterocycles were characterized on the basis of their chemical properties and spectral data.

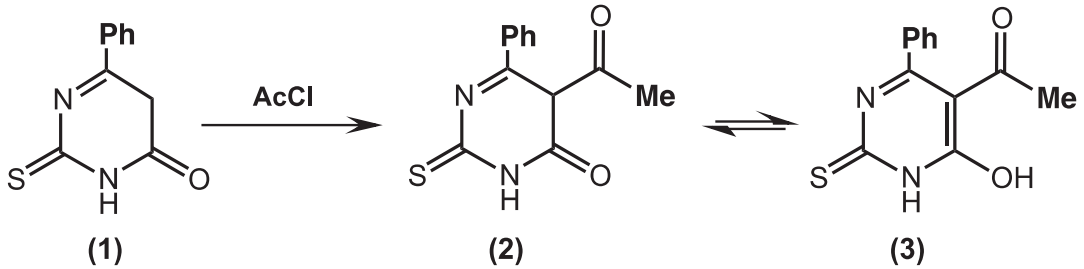
INTRODUCTION

Heterocyclic compounds have drawn special attention in organic chemistry because of their abundance in natural products and their diverse biological properties.[1] Pyrimidine and its derivatives have been recognized as important heterocyclic compounds due to their variety of chemical and biological significance to medicinal chemistry.[2-4] As antiviral,[5] antibacterial,[6] antimalarial,[7] antihypertensive[8] and anti-inflammatory[9] agents. In addition, pyrimidine derivatives form the basis of a large number of pharmacological products with anticancer and tein kinase inhibitory activity.[10] Many substituted pyrimidine rings play an important role as analgesic, antipyretic also as pesticides, herbicides, plant growth

regulators and organic calcium channel modulators.[11-17] In continuation of our search of new compounds with anticipated biological activity, we aimed to obtain new compounds of the fused thiophene system, with similar therapeutic properties and other noteworthy chemical and biological activities.

RESULTS AND DISCUSSION

The key intermediate 5-acetyl-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **2** was prepared in good yield from the reaction of 6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one **1** with acetyl chloride in acetic anhydride and sodium acetate at reflux temperature. The infrared spectrum of compound **2** revealed absorption bands at 3318, 3046, 1698 and 1374 cm^{-1} for amino, aromatic, carbonyl and thiocarbonyl function groups, respectively. ^{1}H-NMR spectrum of compound **2** showed the following signals at δ 3.36 (s, 3H, CH_3), 3.84 (s, 1H, CH), 7.31-7.72 (m, 5H, aromatic H), 10.62 (s, 1H, NH); ^{13}C-NMR spectrum of compound **2** showed the following signals at δ 27.0, 56.3, 127.1, 127.1, 127.1, 127.1, 130.1, 133.1, 160, 170.1, 179.1, 200. Also, its mass spectrum showed a molecular ion peak at *m/z* 246 (M^+).[18]

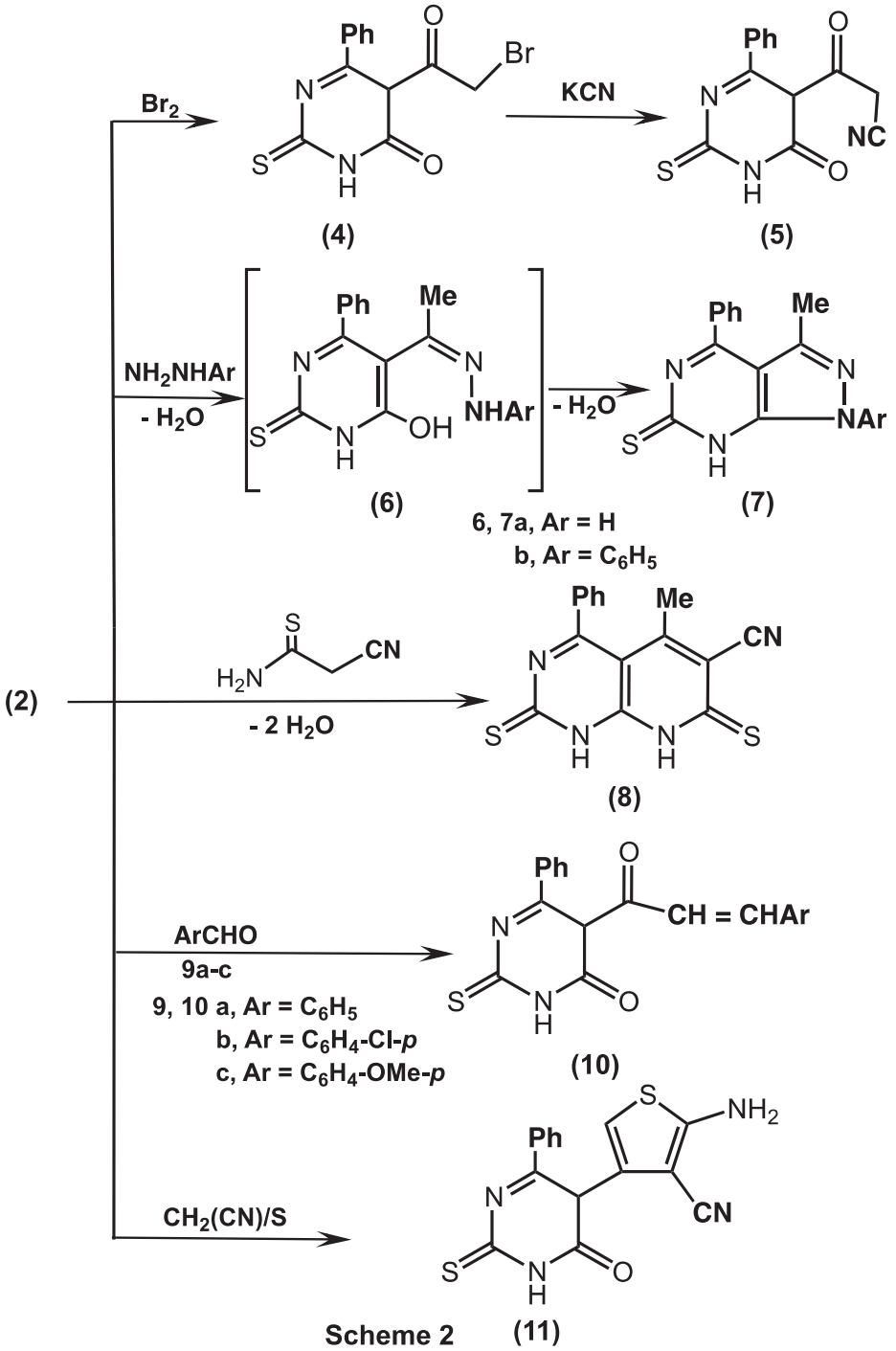


(1) **(2)** **(3)**

Scheme 1

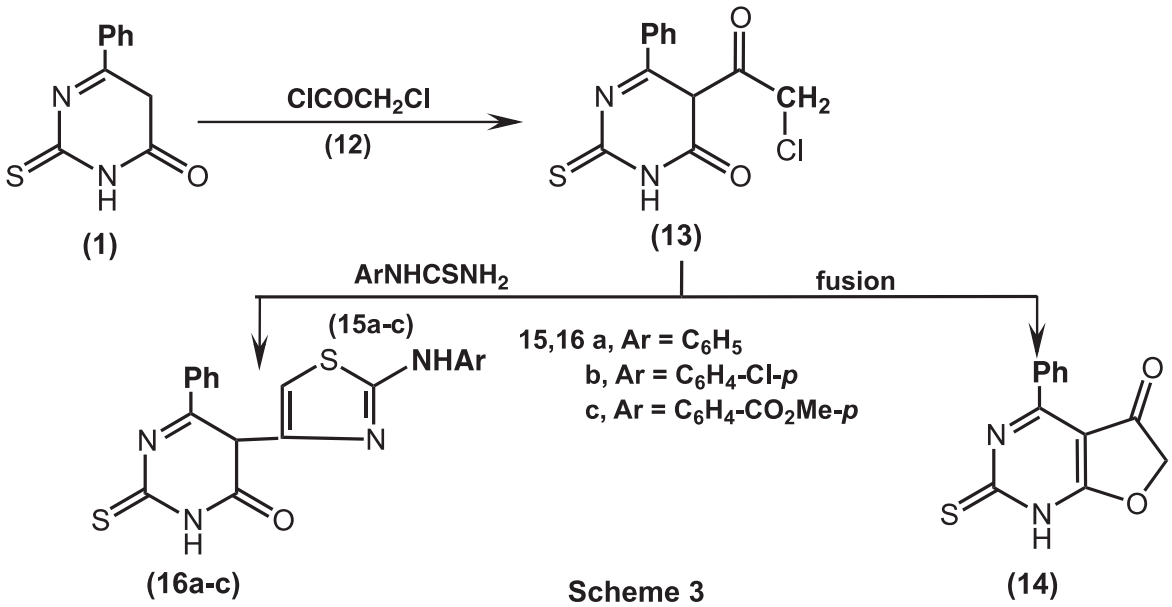
Bromination of 5-acetyl-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **2** with bromine in acetic acid gave 5-(2-bromoacetyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **4**. The structure of compound **4** was established through microanalysis, IR, ^{1}H-NMR, mass spectral data and chemical reactivity. So, acetonitrile derivative **5** was prepared in excellent yield by reaction of compound **4** with potassium cyanide in aqueous ethanol. The structure of compound **5** was characterized by analytical and spectral data. The IR spectrum of compound **5** showed bands 3388 (NH), 2225 (CN), 1694, 1637 (2CO) cm^{-1}, ^{1}H-NMR spectrum of compound **5** in DMSO-d_6 revealed signals at δ 3.84 (s, 1H, CH), 4.10 (s, 2H, CH_2), 7.23-7.75 (m, 5H, aromatic H), 10.62 (s ,1H, NH). Its mass spectrum showed a molecular ion peak *m/z* at 271 (M^+) with a base peak at 116 and other significant peaks appeared at 197 (86%), 218 (79%) and 262 (89%).[19,20] Treatment of compound **2** with hydrazine hydrate afforded 3-methyl-4-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6-(7*H*)-thione **7a** which was established by the disappearance of two carbonyl group in the infrared spectrum. Its ^{1}H-NMR spectrum showed a singlet signal at δ 2.27 ppm assigned for the methyl group and at δ 10.65, 10.80 ppm assigned for 2NH groups. The mass spectrum revealed a molecular ion peak at *m/z* 244 (M^++2) corresponding to the molecular formula

$C_{12}H_{10}N_4S$. Similarly, when compound **2** was treated with phenylhydrazine in ethanolic solution afforded compounds **7b**. The structure of compound **7b** was proved by analytical and spectral data. Cyclocondensation of compound **2** with cyanothioacetamide in pyridine solution yielded the 5-methyl-4-phenyl-2,7-dithioxo-1,2,7,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile **8** in good yield. The structure of compound **8** was confirmed on the basis of its analytical and spectral data. So, the IR spectrum showed the disappearance of carbonyl group and showed absorption bands at 3327, 3177 cm^{-1} due to 2NH groups in addition to the absorption band at 2206 cm^{-1} which can be assigned to CN group. Its ^{1}H-NMR spectrum in DMSO-d_6 displayed signals characteristic for amino, methyl and aromatic protons, the mass spectrum of compound **8** is in agreement with the proposed structure. An equimolar quantity of aromatic aldehydes **9a-c** and methyl ketone **2** react in the presence of sodium hydroxide to give chalcones derivatives by cross aldol condensation reaction. The structures of the synthesized compounds were confirmed by IR, ^{1}H-NMR and mass spectra. The IR spectrum of compound **10a** as example was characterized by disappearance of methyl group and showed an absorption bands at 1629 cm^{-1} due to the carbonyl group. Its ^{1}H-NMR spectrum in DMSO-d_6 revealed signals at δ 3.43 (s, 1H, CH), 5.44 (br s, 1H, CH-olefinic), 6.86 (br s, 1H, CH-olefinic),7.19-7.87 (m, 11H, aromatic H and NH). The mass spectrums of compound **10a-c** are in agreement with the proposed structure.[21-23] In addition to this the behaviour of thioxo-2,3-dihydropyrimidin-4(5*H*)-one derivative **2** toward active methylene reagent and elemental sulfur was also investigated. Thus, compound **2** reacted with a mixture of malononitrile and elemental sulfur to afford the thiophene derivative **11** (Scheme 2). Assignment of structure **11** for the reaction product was based on its compatible spectroscopic data. Thus, its IR spectrum showed absorption band at 3428, 3320 cm^{-1} for NH_2, 3212 cm^{-1} for NH and 2204 cm^{-1} for CN group.[24] 5-(2-Chloroacetyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **13** was obtained by treatment of compound **1** with chloroacetyl chloride in dry toluene. The structure of the newly synthesized compound was confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectra. Compound **13** underwent an intramolecular heterocyclization, upon boiling in toluene to afford 4-phenyl-2-thioxo-1,2-dihydrofuro[2,3-*d*]pyrimidin-5(6*H*)-one **14**. The mass spectrum of compound **14** is in agreement with the proposed structure. On the other hand, when respective aryl amines were treated with ammonium thiocyanate under acidic conditions. It led to the formation of substitution arylthioureas **15a-c**.[25]



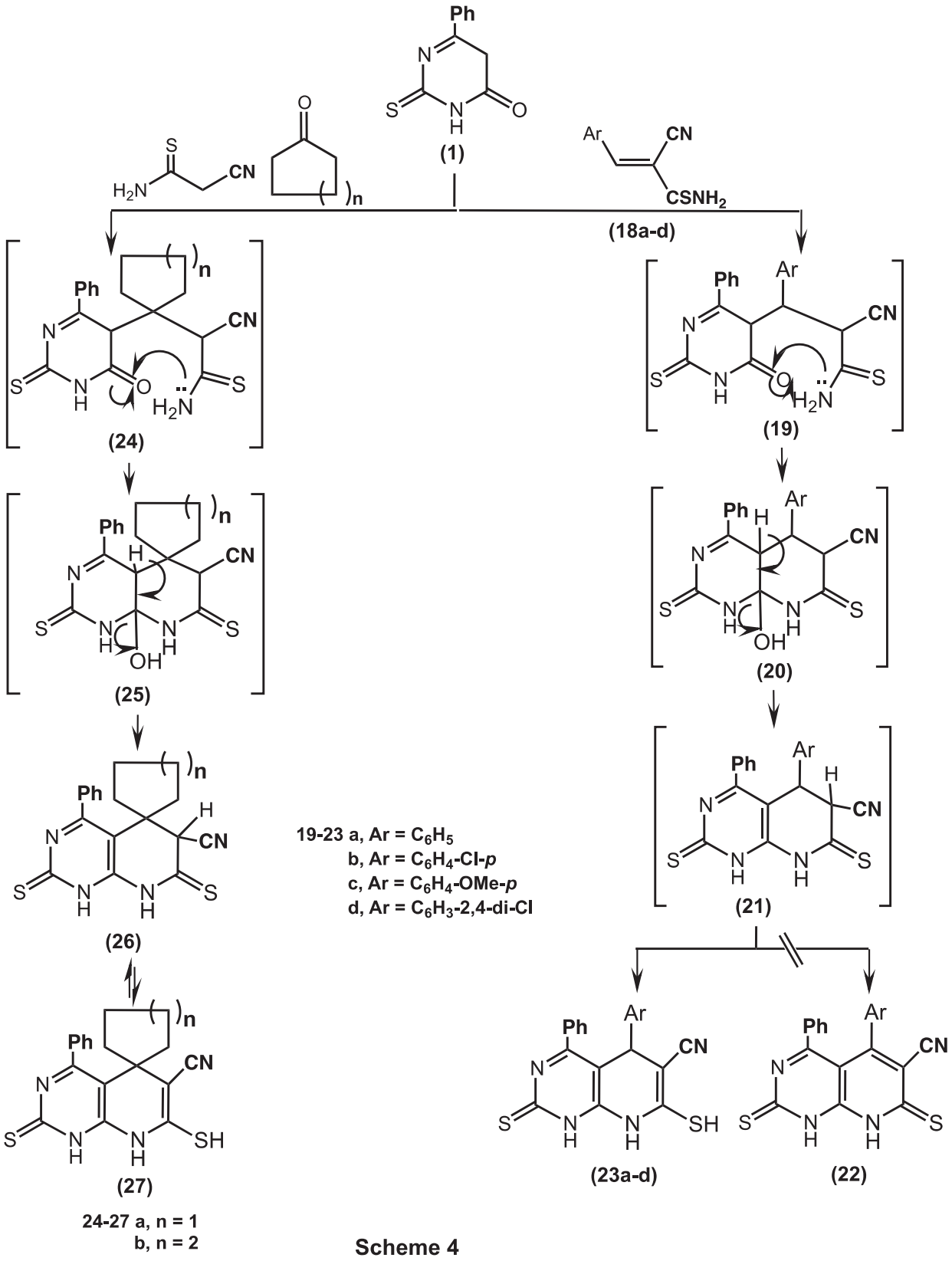
Scheme 2

Compound **13** and **15a-c** were refluxed in dry acetone for 12 h to afford 2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one derivatives **16a-c**. All the synthesized compounds were characterized by IR, ^{1}H-NMR and mass spectra. The IR spectrum of compound **16a** as example showed bands at 3417, 3343 cm^{-1} for 2NH and band at 1675 cm^{-1} for carbonyl group. ^{1}H-NMR spectra showed the following signals at δ 3.98 (s, 1H, CH), 5.44 (s, 1H, CH-thiazole), 7.17-7.60 (m, 10H, aromatic H), 9.00-9.80 (hump, 2H, 2NH) (Scheme 3).



Scheme 3

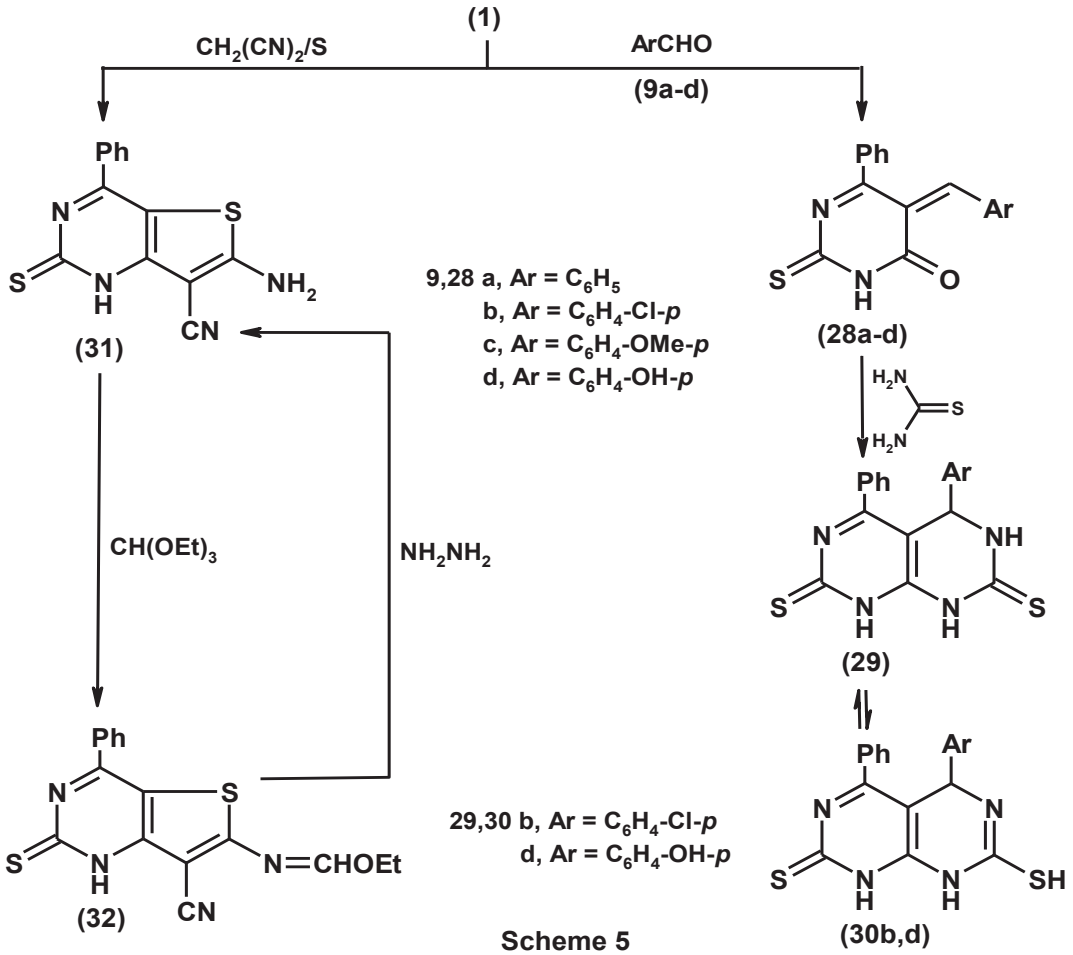
The active methylene group in pyrimidinethione derivative **1** was exploited to synthesize novel tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile **23a-d** and pyrido[2,3-*d*]pyrimidine-6'-carbonitrile **27a,b** derivatives through its reaction with some electrophiles. Thus, the tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile **23a-d** derivatives were obtained in quantitative yield from the reaction of **1** with arylidene-cyanothioacetamide **18a-d** in ethanolic piperidine. Compounds were confirmed on the basis of the spectroscopic analysis. Thus, IR spectrum of compound **23a** as revealed the presence of characteristic bands for amino and cyano functional groups. In addition, the ^{1}H-NMR spectrum of compound **23a** in DMSO-d_6 revealed the absence of methylene moiety. The of compound **23a** was supported by its mass spectrum which revealed molecular ion peak at *m/z* 374 (M^+). The expected pyrimidine **22** formations was ruled out on the basis of analytical and spectral data.[26] Similarly, cyclocondensation of 6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one **1** with cyclopentanone or cyclohexanone and cyanothioacetamide (1:1:1 molar ratio) afforded pyrido[2,3-*d*]pyrimidine-6'-carbonitrile of type **27a,b**. Compounds **27a,b** were confirmed based on the spectroscopic data. Thus, the infrared spectrum of **27a** showed 2NH at 3354, 3215 cm^{-1} and CN at 2198 cm^{-1}. Mass spectrum of **27a** showed amolecular ion peak at *m/z* 354 (M^++2) with a base peak at *m/z* 84.[27] Condensation of compound **1** with aromatic aldehydes **9a-d** in ethanol at reflux temperature in the of potassium hydroxide produced the 2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one derivatives **28a-d**. The structure of the isolated product **28a-d** was verified by elemental analysis and spectroscopic methods IR, ^{1}H-NMR and mass spectra.[28]



Scheme 4

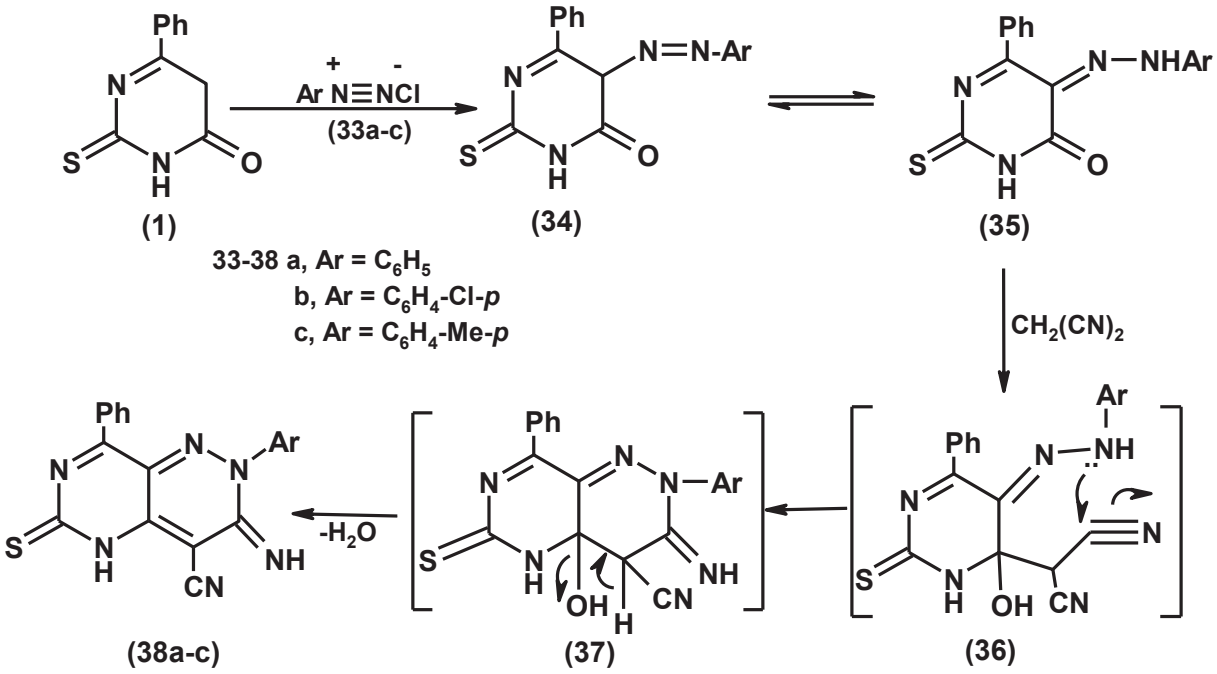
Compounds **28b,d** were reacted with thiourea in ethanol in the presence of potassium hydroxide to yield dihydropyrimido[4,5-*d*]pyrimidine-2(1*H*)-thione derivatives **30b,d**. The structures of all products **30b,d**

were established on the basis of IR, ^{1}H-NMR, mass and elemental analysis.[29,30] Our intention was extended to prepare pyrimidine derivatives with incorporating an active amino heterocyclic moiety. Thus, 6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one **1** reacted with equimolar amounts of malononitrile and elemental sulfur in dioxane/TEA solution to afford in 69% yield the corresponding 6-amino-4-phenyl-2-thioxo-1,2-dihydrthieno[3,2-*d*]pyrimidine-7-carbonitrile **31**. The structure of **31** was established through microanalysis, IR, ^{1}H-NMR and mass spectral data. The IR spectrum of compound **31** revealed the existence of absorption band at 2211 cm^{-1} corresponding to the CN group. The ^{1}H-NMR spectrum of compound **31** revealed the presence of singlet signals for the NH_2 group at δ 12.10 ppm. The mass spectra showed molecular ion peak at *m/z* 284 (M^+) besides a base peak at *m/z* 128. Refluxing of compound **31** with triethyl orthoformate in the presence of acetic anhydride yielded the ethoxymethylene amino derivatives **32**. The IR spectrum of **32** showed bands at 3316 (NH), 2930 (CH-aliph), 2218 (CN) and 1620 cm^{-1} (C=N), the ^{1}H-NMR spectrum of **32** in $CDCl_3$ revealed signals at δ 1.36 (t, 3H, CH_3), 4.39 (q, 2H, CH_2), 6.98-8.02 (m, 6H, aromatic H and CH-olefinic), 12.75 (s, 1H, NH). Attempts cyclization of **32** using hydrazine aiming at preparation of a series of fused pyrimidines failed and afforded the thienopyrimidine **31** in a quantitive yield.[27, 31, 32]



Scheme 5

Compound **1** could be readily coupled with aryldiazonium salts to yield the corresponding arylazo derivatives **34a-c** or isomeric structure **35**. The structure of **35a-c** were established through microanalysis, IR, ^{1}H-NMR, mass spectra and its chemical reactivity of this molecule to active methylene reagent. So, treatment of compounds **35a-c** with malononitrile without solvent in the presence of ammonium acetate afforded pyrimido[5,4-*c*]pyridazine-4-carbonitrile derivatives **38a-c** in quantitative yield. The structures of **38a-c** were established through elemental analysis and spectral data. The IR spectrum of **38a** as example showed bands at 3328, 3181 (2NH), 2195 cm^{-1} (CN). Its ^{1}H-NMR spectrum in $CDCl_3$ exhibited signals at δ 6.95-7.93 (m, 12H, aromatic H and 2NH), mass spectrum of **38a** showed a molecular ion peak *m/z* at 358 (M^++2) corresponding to the molecular formula $C_{19}H_{12}N_6S$.[33, 34]



Scheme 6

EXPERIMENTAL

All melting points were measured using Akofler Block instrument and are uncorrected. IR spectra (KBr) were recorded on a FTIR 5300 spectrometer (υ, cm^{-1}). The ^{1}H-NMR spectra were recorded in DMSO-d_6, $CDCl_3$ at 300 MHz on a Varian Gemini NMR. 1000 EX mass spectrometer at 70 eV. The purity of synthesized compounds was checked by Thin layer chromatography TLC (aluminum sheets) using n-hexane, EtOAc (9:1, V/V, 7:3 V/V) eluent. Elemental analyses were carried out by the Microanalytical Research Center, Faculty of Science, Cairo University.

Preparation of compound (2). A mixture of pyrimidinethione derivatives **1** (0.01 mol) and acetyl chloride (0.01 mol) in acetic anhydride and sodium acetate was heated under reflux for 9 h. The reaction

mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **2**.

5-Acetyl-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (2). It was obtained as yellow crystals from EtOH; yield (85%); Mp 140-142 ºC; IR (KBr) ν cm^{-1} 3318 (NH), 3046 (CH-arom), 1698 (CO), 1374 (C=S); ^{1}H-NMR (DMSO-d_6) δ 3.36 (s, 3H, CH_3), 3.84 (s, 1H, CH), 7.31-7.72 (m, 5H, aromatic H), 10.62 (s, 1H, NH); ^{13}C NMR δ 27.0, 56.3, 127.1, 127.1, 127.1, 127.1, 130.1, 133.1, 160, 170.1, 179.1, 200; MS: *m/z* (%) 246 (M^+). Anal. Calcd for $C_{12}H_{10}N_2O_2S$ (246): C, 58.52; H, 4.09; N, 11.37. Found: C, 58.53; H, 4.10; N, 11.38%.

Preparation of compound (4). To a hot solution (60 ºC) of **2** (0.01 mol) in acetic acid (40 mL), bromine (0.01 mol) in acetic acid (10 mL) was added dropwise with stirring for 10 min. The reaction mixture was allowed to attain room temperature and was poured into ice/water, the formed solid product was collected by filtration and crystallized from the proper solvent to give **4**.

5-(2-Bromoacetyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (4). It was obtained as yellow crystals from EtOH; yield (59%); Mp 200-202 ºC; IR (KBr) ν cm^{-1} 3259 (NH), 3077 (CH-arom), 2985 (CH-aliph), 1658, 1641 (2CO); ^{1}H-NMR (DMSO-d_6) δ 3.60 (s, 1H, CH), 4.18 (s, 2H, CH_2), 6.12-7.00 (m, 5H, aromatic H), 8.97 (s, 1H, NH); MS: *m/z* (%) 325 (M^++1). Anal. Calcd for $C_{12}H_9BrN_2O_2S$ (324): C, 44.32; H, 2.79; N, 8.61. Found: C, 44.33; H, 2.81; N, 8.62%.

Preparation of compound (5). To a hot solution (50 ºC) of **4** (0.01 mol) in EtOH (40 mL), a solution (in 5 mL water) of potassium cyanide (0.01 mol) was added dropwise. The reaction mixture was left at room temperature for 4 h with stirring. The solid product, formed upon pouring into ice/water containing HCl (to pH 6) was collected by filtration and crystallized from the proper solvent to give **5**.

3-Oxo-3-(6-oxo-4-phenyl-2-thioxo-1,2,5,6-tetrahydropyrimidin-5-yl)propanenitrile (5). It was obtained as white crystals from EtOH; yield (80%); Mp 150-152 ºC; IR (KBr) ν cm^{-1} 3388 (NH), 2225 (CN), 1694, 1637(2CO); ^{1}H-NMR (DMSO-d_6) δ 3.84 (s, 1H, CH), 4.10 (s, 2H, CH_2), 7.23-7.75 (m, 5H, aromatic-H), 10.62 (s, 1H, NH); MS: *m/z* (%) 271 (M^+). Anal. Calcd for $C_{13}H_9N_3O_2S$ (271): C, 57.55; H, 3.34; N, 15.49. Found: C, 57.56; H, 3.35; N, 15.51%.

Preparation of compound (7a). A mixture of dihydropyrimidinone derivative **2** (0.01 mol) and hydrazine hydrate (3 mL) in EtOH was heated under reflux for 12 h. The reaction mixture was allowed to cool. The separated solid was filtered, washed with EtOH and crystallized from the proper solvent to give **7a**.

3-Methyl-4-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6(7*H*)-thione (7a). It was obtained as white crystals from EtOH; yield (72%); Mp 225-227 ºC; IR (KBr) ν cm^{-1} 3430, 3264 (2NH); ^{1}H-NMR (DMSO-d_6) δ 2.27 (s, 3H, CH_3), 7.01-8.49 (m, 5H, aromatic H), 10.65 (s, 1H, NH), 10.80(s, 1H, NH); MS: *m/z* (%) 244

(M^++2). Anal. Calcd for $C_{12}H_{10}N_4S$ (242): C, 59.48; H, 4.16; N, 23.12. Found: C, 59.49; H, 4.18; N, 23.13%.

Preparation of compound (7b). A mixture of dihydropyrimidinone derivative **2** (0.01 mol) and phenylhydrazine (0.01 mol) in EtOH containing catalytic amount of piperidine was heated under reflux for 12 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered off, washed with water and crystallized from the proper solvent to give **7b**.

3,4-Diphenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-6(7*H*)-thione (7b). It was obtained as brown crystals from EtOH; yield (84%); Mp 100-102 ºC; IR (KBr) ν cm^{-1} 3454 (NH), 3055 (CH-arom), 2923 (CH-aliph); ^{1}H-NMR ($CDCl_3$) δ 2.46 (s, 3H, CH_3), 7.21-7.50 (m, 10H, aromatic H), 8.10 (s, 1H, NH); MS: *m/z* (%) 320 (M^++2). Anal. Calcd for $C_{18}H_{14}N_4S$ (318): C, 67.08; H, 3.97; N, 18.41. Found: C, 67.09; H, 3.99; N, 18.42%.

Preparation of compound (8). A mixture of dihydropyrimidinone derivative **2** (0.01 mol) and cyanothioacetamide (0.01 mol) in pyridine (30 mL) was heated under reflux for 12 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **8**.

5-Methyl-4-phenyl-2,7-dithioxo-1,2,7,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (8). It was obtained as brown crystals from EtOH; yield (81%); Mp 180-182 ºC; IR (KBr) ν cm^{-1} 3327, 3177 (2NH), 2925 (CH-aliph), 2206 (CN); ^{1}H-NMR (DMSO-d_6) δ 1.91 (s, 3H, CH_3); 7.41-7.97 (m, 7H, aromatic H and 2NH); ^{13}C NMR δ 12.5, 79.4, 103.2, 120.6, 126.9, 126.9, 128.1, 128.1, 129, 134.1, 151.9, 160, 163, 163.8, 179; MS: *m/z* (%) 311 (M^++1). Anal. Calcd for $C_{15}H_{10}N_4S_2$ (310): C, 58.04; H, 3.25; N, 18.05. Found: C, 58.05; H, 3.27; N, 18.06%.

General procedure for the preparation of compound (10a-c). A mixture of dihydropyrimidinone derivative **2** (0.01 mol), appropriate aromatic aldehydes **9a-c** (0.01 mol) and 10% aqueous sodium hydroxide (10 mL) in EtOH (50 mL) was stirred at room temperature for about 3 h. The resulting solid was filtered off, washed with water, dried and crystallized from the proper solvent to give **10a-c**.

6-Phenyl-5-(3-phenylacryloyl)-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (10a). It was obtained as white crystals from EtOH; yield (79%); Mp 300-302 ºC; IR (KBr) ν cm^{-1} 3455 (NH), 1629 (CO); ^{1}H-NMR (DMSO-d_6) δ 3.43 (s, 1H, CH), 5.44 (br s, 1H, CH-olefinic), 6.86 (br s, 1H, CH-olefinic); 7.19-7.87 (m, 11H, aromatic H and NH); MS: *m/z* (%) 335 (M^++1). Anal. Calcd for $C_{19}H_{14}N_2O_2S$ (334): C, 68.24; H, 4.22; N, 8.38. Found: C, 68.25; H, 4.24; N, 8.39%.

5-(3-(4-Chlorophenyl)acryloyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (10b). It was obtained as yellow crystals from EtOH; yield (68%); Mp 210-212 ºC; IR (KBr) ν cm^{-1} 3468 (NH), 1659, 1630 (2CO); ^{1}H-NMR ($CDCl_3$) δ 3.38 (s, 1H, CH); 5.90 (br s, 1H, CH-olefinic), 6.85 (br s, 1H,

CH-olefinic), 6.87-7.55 (m, 10H, aromatic H and NH); MS: *m/z* (%) 369 (M^++1). Anal. Calcd for $C_{19}H_{13}ClN_2O_2S$ (368): C, 61.87; H, 3.55; N, 7.60. Found: C, 61.88; H, 3.57; N, 7.61%.

5-(3-(4-Methoxyphenyl)acryloyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (10c). It was obtained as yellow crystals from EtOH; yield (64%); Mp 190-192 °C; IR (KBr) ν cm^{-1} 3438 (NH), 2922 (CH-aliph), 1797, 1627 (2CO); MS: *m/z* (%) 364 (M+). Anal. Calcd for $C_{20}H_{16}N_2O_3S$ (364): C, 65.92; H, 4.43; N, 7.69. Found: C, 65.93; H, 4.45; N, 7.70%.

Preparation of compound (11). A mixture of dihydropyrimidinone derivative **2** (0.01 mol), malononitrile and sulfur (0.01 mol) in DMF (50 mL) containing catalytic amount of piperidine was heated under reflux for 12 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **11**.

2-Amino-4-(6-oxo-4-phenyl-2-thioxo-1,2,5,6-tetrahydropyrimidin-5-yl)thiophene-3-carbonitrile (11). It was obtained as brown crystals from EtOH; yield (81%); Mp 182-184 °C; IR (KBr) ν cm^{-1} 3428, 3320 (NH_2), 3212 (NH), 2923 (CH-aliph), 2204 (CN), 1629 (CO); ^{1}H-NMR (DMSO-d_6) δ 3.03 (s, 1H, CH), 6.40 (s, 2H, NH_2), 7.49-7.84 (m, 6H, aromatic H and CH-thiophene), 11.76 (s, 1H, NH); MS: *m/z* (%) 327 (M^++1). Anal. Calcd for $C_{15}H_{10}N_4OS_2$ (326): C, 55.20; H, 3.09; N, 17.17. Found: C, 55.21; H, 3.11; N, 17.18%.

Preparation of compound (13). A mixture of pyrimidinethione derivative **1** (0.01 mol) and chloroacetyl chloride **12** (0.01 mol) in dry toluene (30 mL) at 0-5 °C. The reaction mixture was stirred for 4 h at room temperature and reflux for 6 h. The solid obtained was washed with petroleum ether (40-60 °C) and kept in refrigerator. The solid obtained was recrystallized from the proper solvent to give **13**.

5-(2-Chloroacetyl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (13). It was obtained as white crystals from EtOH; yield (77%); Mp 140-142 °C; IR (KBr) ν cm^{-1} 3476 (NH), 2980 (CH-aliph), 1776, 1711 (2CO) cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.40 (s, 1H, CH), 4.07 (s, 2H, CH_2), 5.25-7.12 (m, 5H, aromatic H), 8.39 (s, 1H, NH); ^{13}C NMR δ 46.0, 53.1, 127.1, 127.1 128.1, 128.1, 129.0, 130.7, 160.9, 170.2, 179.1, 200; MS: *m/z* (%) 282 (M^++2). Anal. Calcd for $C_{12}H_9ClN_2O_2S$ (280): C, 51.34; H, 3.23; N, 9.98. Found: C, 51.35; H, 3.25; N, 9.99%.

Preparation of compound (14). Compound **13** (2.80 g) in toluene (30 mL) was fused for 8 h at 170 °C. The reaction mixture was left to stand; the solid product so formed was collected by filtration and recrystallized from the proper solvent to give **14**.

4-Phenyl-2-thioxo-1,2-dihydrofuro[2,3-*d*]pyrimidin-5(6*H*)-one (14). It was obtained as pale brown crystals from EtOH; yield (81%); Mp 160-162 °C; IR (KBr) ν cm^{-1} 3224 (NH), 2954 (CH-aliph), 1655 (CO); ^{1}H-NMR (DMSO-d_6) δ 4.33 (s, 2H, CH_2), 6.94-7.28 (m, 6H, aromatic H and NH); MS: *m/z* (%)

244 (M^+). Anal. Calcd for $C_{12}H_8N_2O_2S$ (244): C, 59.00; H, 3.30; N, 11.47. Found: C, 59.01; H, 3.31; N, 11.49%.

General procedure for the preparation of compound (16a-c). A mixture of compound **13** (0.01 mol) and thiourea derivatives **15a-c** (0.01 mol) in dry acetone (30 mL) was heated under reflux for 12 h. The reaction mixture was evaporated in vacuo. The separated solid was filtered, washed with ether and crystallized from the proper solvent to give **16a-c**.

6-Phenyl-5-(2-(phenylamino)thiazol-4-yl)-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (16a). It was obtained as pale yellow crystals from Et_2O; yield (79%); Mp 174-176 °C; IR (KBr) ν cm^{-1} 3417, 3343 (2NH), 2977 (CH-aliph), 1675 (CO); ^{1}H-NMR (DMSO-d_6) δ 3.98 (s, 1H, CH), 5.44 (s, 1H, CH-thiazole), 7.17-7.60 (m, 10H, aromatic H), 9.00-9.80 (hump, 2H, 2NH); MS: *m/z* (%) 378 (M^+). Anal. Calcd for $C_{19}H_{14}N_4OS_2$ (378): C, 60.30; H, 3.73; N, 14.80. Found: C, 60.31; H, 3.75; N, 14.81%.

5-(2-(4-Chlorophenylamino)thiazol-4-yl)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (16b). It was obtained as pale yellow crystals from EtOH; yield (74%); Mp 182-184 °C; IR (KBr) ν cm^{-1} 3473, 3415 (2NH), 2977 (CH-aliph), 1675 (CO); ^{1}H-NMR (DMSO-d_6) δ 4.29 (s, 1H, CH), 5.44 (s, 1H, CH-thiazole), 7.16-7.50 (m, 9 H, aromatic H), 8.60-10.40 (hump, 2H, 2NH); MS: *m/z* (%) 415 (M^++3). Anal. Calcd for $C_{19}H_{13}ClN_4OS_2$ (412): C, 55.27; H, 3.17; N, 13.57. Found: C, 55.28; H, 3.18; N, 13.59%.

Methyl-4-(4-(6-oxo-4-phenyl-2-thioxo-1,2,5,6-tetrahydropyrimidin-5-yl)thiazol-2-ylamino)benzoate (16c). It was obtained as pale yellow crystals from EtOH; yield (76%); Mp 198-200 °C; IR (KBr) ν cm^{-1} 3419, 3343 (2NH), 2976 (CH-aliph), 1745, 1676 (2CO); ^{1}H-NMR (DMSO-d_6) δ 2.51 (s, 3H, OCH_3), 4.14 (s, 1H, CH), 5.46 (s, 1H, CH- thiazole), 7.19-7.53 (m, 9H, aromatic H), 10.00-10.80 (s, 2H, 2NH); MS: *m/z* (%) 435 (M^+-1). Anal. Calcd for $C_{21}H_{16}N_4O_3S_2$ (436): C, 57.78; H, 3.69; N, 12.84. Found: C, 57.79; H, 3.71; N, 12.85%.

General procedure for the preparation of compound (23a-d). A mixture of compound **1** (0.01 mol) and benzylidene-cyanothioacetamide derivatives **18a-d** (0.01 mol) in EtOH with catalytic amount of piperidine was heated under reflux for 10 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **23a-d**.

7-Mercapto-4,5-diphenyl-2-thioxo-1,2,5,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (23a). It was obtained as pale yellow crystals from EtOH; yield (73%); Mp 118-120 °C; IR (KBr) ν cm^{-1} 3339, 3208 (2NH), 2931 (CH-aliph), 2198 (CN); ^{1}H-NMR (DMSO-d_6) δ 1.65 (hump, 1H, SH), 4.18 (s, 1H, 4H-pyridine), 6.94-7.93 (m, 10H, aromatic H), 8.40 (hump, 1H, NH), 10.00 (s, 1H, NH); MS: *m/z* (%) 374 (M^+). Anal. Calcd for $C_{20}H_{14}N_4S_2$ (374): C, 64.15; H, 3.77; N, 14.96. Found: C, 64.12; H, 3.73; N, 14.92%.

5-(4-Chlorophenyl)-7-mercapto-4-phenyl-2-thioxo-1,2,5,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (23b). It was obtained as pale yellow crystals from EtOH; yield (76%); Mp 110-112 ºC; IR (KBr) ν cm^{-1} 3325, 3189 (2NH), 2940 (CH-aliph), 2214 (CN); ^{1}H-NMR ($CDCl_3$) δ 1.65 (hump, 1H, SH), 4.34 (s, 1H, 4H-pyridine), 6.73-8.01 (m, 11H, aromatic H and 2NH); MS: *m/z* (%) 409 (M^++1). Anal. Calcd for $C_{20}H_{13}ClN_4S_2$ (408): C, 58.74; H, 3.20; N, 13.70. Found: C, 58.75; H, 3.22; N, 13.71%.

7-Mercapto-5-(4-methoxyphenyl)-4-phenyl-2-thioxo-1,2,5,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (23c). It was obtained as pale yellow crystals from EtOH; yield (69%); Mp 98-100 ºC; IR (KBr) ν cm^{-1} 3331, 3179 (2NH), 2935 (CH-aliph), 2213 (CN); ^{1}H-NMR ($CDCl_3$) δ 1.62 (hump, 1H, SH), 3.82 (s, 3H, OCH_3), 5.91 (s, 1H, 4H-pyridine), 6.82-7.54 (m, 11H, aromatic H + 2NH); ^{13}C NMR δ 37.2, 54.2, 76.8, 80.0, 117.1, 117.1, 120.0, 127.1, 127.1, 128.1, 128.1, 129.0, 130.0, 130.3, 130.6, 136, 138.6, 154.3, 155.3, 160.2, 179.0; MS: *m/z* (%) 404 (M^+). Anal. Calcd for $C_{21}H_{16}N_4OS_2$ (404): C, 62.35; H, 3.99; N, 13.85. Found: C, 62.36; H, 4.01; N, 13.86%.

5-(2,4-Dichlorophenyl)-7-mercapto-4-phenyl-2-thioxo-1,2,5,8-tetrahydropyrido[2,3-*d*]pyrimidine-6-carbonitrile (23d). It was obtained as pale yellow crystals from EtOH; yield (80%); Mp 116-118 ºC; IR (KBr) ν cm^{-1} 3346, 3207 (2NH), 3086 (CH-arom), 2938 (CH-aliph), 2192 (CN); ^{1}H-NMR ($CDCl_3$) δ 1.68 (hump, 1H, SH), 5.61 (s, 1H, 4H-pyridine), 7.27-8.22 (m, 8H, aromatic H), 10.18 (s,1H, NH), 10.42 (s,1H, NH); MS: *m/z* (%) 445 (M^++3). Anal. Calcd for $C_{20}H_{12}Cl_2N_4S_2$ (442): C, 54.18; H, 2.73; N, 12.64. Found: C, 54.15; H, 2.70; N, 12.62%.

General procedure for the preparation of compound (27a,b). A mixture of compound **1** (0.01 mol), cyclohexanone (or cyclopentanone) (0.0l mol) and cyanothioacetamide (0.01 mol) in EtOH containing catalytic amount of piperidine was heated under reflux for 10 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **27a,b**.

7'-Mercapto-4'-phenyl-2'-thioxo-2',8'-dihydro-1'*H*-spiro[cyclopentane-1,5'-pyrido[2,3-*d*]pyrimidine-6'-carbonitrile (27a). It was obtained as pale brown crystals from EtOH; yield (82%); Mp 270-272 ºC; IR (KBr) ν cm^{-1} 3354, 3215 (2NH), 2930 (CH-aliph), 2198 (CN); ^{1}H-NMR (DMSO-d_6) δ 0.85 (br, 1H, SH), 1.17-1.23 (m, 4H, $2CH_2$), 1.51-1.98 (m, 4H, $2CH_2$), 6.73-8.11 (m, 5H, aromatic H), 8.54 (hump, 2H, 2NH); ^{13}C NMR δ 25.6, 27.0, 27.0, 38.1, 38.1, 79.0, 100.1, 120.2, 126.9, 126.9, 128.1, 128.1, 129.1, 130.1, 137.1, 147.9, 160.1, 179.1; MS: *m/z* (%) 354 (M^++2). Anal. Calcd for $C_{18}H_{16}N_4S_2$ (352): C, 61.34; H, 4.58; N, 15.90. Found: C, 61.35; H, 4.60; N, 15.91%.

7'-Mercapto-4'-phenyl-2'-thioxo-2',8'-dihydro-1'*H*-spiro[cyclohexane-1,5'-pyrido[2,3-*d*]pyrimidine-6'-carbonitrile (27b). It was obtained as brown crystals from EtOH; yield (75%); Mp 140-142 ºC; IR (KBr) ν cm^{-1} 3336, 3185 (2NH), 2935 (CH-aliph), 2194 (CN); ^{1}H-NMR (DMSO-d_6) δ 1.32 (hump, 1H,

SH), 1.34-1.38 (m, 2H, CH_2), 1.51-1.79 (m, 4H, $2CH_2$), 2.56-2.89 (m, 4H, $2CH_2$), 6.94-7.28 (m, 5H, aromatic H), 7.95 (s, 2H, 2NH); MS: *m/z* (%) 367 (M^++1). Anal. Calcd for $C_{19}H_{18}N_4S_2$ (366): C, 62.27; H, 4.95; N, 15.29. Found: C, 62.28; H, 4.97; N, 15.30%.

General procedure for the preparation of compound (28a-d). A mixture of compound **1** (0.01 mol) and appropriate aromatic aldehydes **9a-d** (0.01 mol) in ethanolic potassium hydroxide (50 mL, 10%) was heated under reflux for 8 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The resulting solid was filtered off, washed with water, dried and crystallized from the proper solvent to give **28a-d**.

5-Benzylidene-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one (28a). It was obtained as white crystals from EtOH; yield (70%); Mp 180-182 °C; IR (KBr) ν cm^{-1} 3178 (NH), 2924 (CH-aliph), 1653 (CO); ^{1}H-NMR (DMSO-d_6) δ 5.15 (s, 1H, CH-oliffinic), 7.13-8.01 (m, 11H, aromatic H + NH); MS: *m/z* (%) 294 (M^++2). Anal. Calcd for $C_{17}H_{12}N_2OS$ (292): C, 69.84; H, 4.14; N, 9.58. Found: C, 69.85; H, 4.16; N, 9.59%.

5-(4-Chlorobenzylidene)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one (28b). It was obtained as yellow crystals from EtOH; yield (81%); Mp 218-220 °C; IR (KBr) ν cm^{-1} 3404 (NH), 2925 (CH-aliph), 1684 (CO); ^{1}H-NMR ($CDCl_3$) δ 7.27-8.05 (m, 10H, aromatic H and CH-oliffinic), 10.00 (s, 1H, NH); MS: *m/z* (%) 328 (M^++2). Anal. Calcd for $C_{17}H_{11}ClN_2OS$ (326): C, 62.48; H, 3.39; N, 8.57. Found: C, 62.45; H, 3.37; N, 8.54%.

5-(4-Methoxybenzylidene)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one (28c). It was obtained as yellow crystals from EtOH; yield (68%); Mp 100-102 °C; IR (KBr) ν cm^{-1} 3197 (NH), 2926 (CH-aliph), 1671 (CO); ^{1}H-NMR (DMSO-d_6) δ 3.90 (s, 3H, OMe), 8.73-8.95 (m, 9H, aromatic H, CH-oliffinic and NH); MS: *m/z* (%) 322 (M^+). Anal. Calcd for $C_{17}H_{12}N_2OS$ (322): C, 67.06; H, 4.38; N, 8.69. Found: C, 67.07; H, 4.39; N, 8.71%.

5-(4-Hydroxybenzylidene)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4-(5*H*)-one (28d). It was obtained as pale yellow crystals from EtOH; yield (68%); Mp 200-202 °C; IR (KBr) ν cm^{-1} 3420 (NH), 2924 (CH-aliph), 1665 (CO); ^{1}H-NMR (DMSO-d_6) δ 7.03-8.88 (m, 12H, aromatic H, CH-oliffinic, NH and OH); MS: *m/z* (%) 308 (M^+). Anal. Calcd for $C_{17}H_{12}N_2O_2S$ (308): C, 66.22; H, 3.92; N, 9.08. Found: C, 66.23; H, 3.94; N, 9.10%.

General procedure for the preparation of compound (30b,d). To boiling solution of compound **28b,d** (0.01 mol) in ethanolic potassium hydroxide (30 mL, 10%), thiourea (0.01 mol) was added. The reaction mixture was refluxed for 20 h, then allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **30b,d**.

5-(4-Chlorophenyl)-7-mercapto-4-phenyl-5,8-dihydropyrimido[4,5-*d*]pyrimidine-2(1*H*)-thione (30b). It was obtained as pale yellow crystals from EtOH; yield (64%); Mp 205-207 ºC; IR (KBr) ν cm^{-1} 3369, 3175 (2NH), 3064 (CH-arom), 2966 (CH-aliph); ^{1}H-NMR (DMSO-d_6) δ 1.17 (s, 1H, SH), 5.43 (s, 1H, 4H-pyrimidine), 6.67-7.73 (m, 10H, aromatic H and NH), 9.78 (hump, 1H, NH); ^{13}C NMR δ 49.6, 79.0, 126.9, 126.9, 127.1, 127.1, 128.1, 128.1, 129.1, 130.0, 130.0, 130.1, 133.0, 138.9, 155.0, 160.0, 160.9, 179.2; MS: *m/z* (%) 386 (M^++2). Anal. Calcd for $C_{18}H_{13}ClN_4S_2$ (384): C, 56.17; H, 3.40; N, 14.56. Found: C, 56.18; H, 3.42; N, 14.58%.

5-(4-Hydroxyphenyl)-7-mercapto-4-phenyl-5,8-dihydropyrimido[4,5-*d*]pyrimidine-2(1*H*)-thione (30d). It was obtained as white crystals from EtOH; yield (61%); Mp 310-312 ºC; IR (KBr) ν cm^{-1} 3425, 3212 (2NH), 2927 (CH-aliph); ^{1}H-NMR (DMSO-d_6) δ 1.67 (hump, 1H, SH), 6.24 (s, 1H, 4H-pyrimidine), 6.85-8.12 (m, 10H, aromatic H and NH), 9.78 (s, 1H, OH), 10.80 (s, 1H, NH); MS: *m/z* (%) 366 (M^+). Anal. Calcd for $C_{18}H_{14}N_4OS_2$ (366): C, 58.99; H, 3.85; N, 15.29. Found: C, 59.00; H, 3.87; N, 15.30%.

Preparation of compound (31). Method (A): A solution of compound **1** (0.01 mol), malononitrile and sulfur (0.01 mol) in dioxane (30 mL) containing catalytic amount of TEA was heated under reflux for 12 h. The reaction mixture was allowed to cool and poured into crushed ice then acidified with HCl. The separated solid was filtered, washed with water and crystallized from the proper solvent to give **31**. Method (B): to a solution of compound **32** (0.01 mol) in dry benzene (30 mL), hydrazine hydrate (10 mL) was added with stirring at room temperature for 1 h, the obtained product was filtered off, dried and recrystallized from dioxane to give compound **31**.

6-Amino-4-phenyl-2-thioxo-1,2-dihydrthieno[3,2-*d*]pyrimidine-7-carbonitrile (31). It was obtained as brown crystals from EtOH; yield (69%); Mp 114-116 ºC; IR (KBr) ν cm^{-1} 3336, 3200 (NH_2), 2939 (CH-aliph), 2211 (CN); ^{1}H-NMR (DMSO-d_6) δ 7.36-8.90 (m, 5H, aromatic H), 10.63 (hump, 1H, NH), 12.10 (hump, 2H, NH_2) ; MS: *m/z* (%) 284 (M^+). Anal. Calcd for $C_{13}H_8N_4S_2$ (284): C, 54.91; H, 2.84; N, 19.70. Found: C, 54.92; H, 2.85; N, 19.71%.

Preparation of compound (32). A mixture of compound **31** (2.82 g) and triethylorthoformate (3 mL) in acetic anhydride (10 mL) was heated under reflux for 6 h. The reaction mixture was evaporated in vacuo. The separated solid was filtered, washed with ether and crystallized from the proper solvent to give **32**.

Ethyl-*N*-[7-cyano-4-phenyl-2-thioxo-1,2-dihydrthieno[3,2-*d*]pyrimidin-6-yl]formimidate (32). It was obtained as brown crystals from EtOH; yield (65%); Mp 100-102 ºC; IR (KBr) ν cm^{-1} 3316 (NH), 2930 (CH-aliph), 2218 (CN), 1620 (C=N); ^{1}H-NMR ($CDCl_3$) δ 1.36 (t, 3H, CH_3), 4.39 (q, 2H, CH_2), 6.98-8.02 (m, 6H, aromatic H and CH-oleffinic), 12.75 (s, 1H, NH); ^{13}C NMR δ 15.2, 19.2, 60.8, 119.5, 121.1, 127.1, 127.1, 129, 129.2, 130.1, 132.3, 133, 158.9, 159.0, 160.0, 179.1; MS: *m/z* (%) 340 (M^+). Anal. Calcd for $C_{16}H_{12}N_4S_2$ (340): C, 56.45; H, 3.55; N, 16.46. Found: C, 56.46; H, 3.57; N, 16.47%.

General procedure for the preparation of compound (35a-c). A cold suspension of aryldiazonium salts **33a-c** (0.002 mol) (prepared from 0.002 mol of aromatic amine with the appropriate quantities of sodium nitrite and hydrochloric acid) was gradually added to a cold solution (0-5 ºC) of compound **1** (0.002 mol) in EtOH (50 mL) containing anhydrous sodium acetate (5 g) with continuous stirring for 1 h. The resulting reaction product was filtered off, washed with water and crystallized from the proper solvent to give compounds **35a-c**.

6-Phenyl-5-(phenylhydrazono)-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (35a). Formed as brown crystals from EtOH; yield (86%); Mp 100-102 ºC; IR (KBr) ν cm^{-1} 3218, 3184 (2NH), 3053 (CH-arom), 1676 (CO); ^{1}H-NMR ($CDCl_3$) δ 6.92-7.79 (m, 11H, aromatic H and NH), 12.71 (s, 1H, NH); MS: *m/z* (%) 308 (M^+). Anal. Calcd for $C_{16}H_{12}N_4OS$ (308): C, 62.32; H, 3.92; N, 18.17. Found: C, 62.33; H, 3.94; N, 18.18%.

5-(2-(4-Chlorophenyl)hydrazono)-6-phenyl-2-thioxo-2,3-dihydropyrimidin-4(5*H*)-one (35b). Formed as yellow crystals from EtOH; yield (89%); Mp 110-112 ºC; IR (KBr) ν cm^{-1} 3429, 3186 (2NH), 3082 (CH-arom), 1652 (CO); ^{1}H-NMR ($CDCl_3$) δ 6.91-7.78 (m, 10H, aromatic H and NH), 12.72 (s, 1H, NH); MS: *m/z* (%) 342 (M^+). Anal. Calcd for $C_{16}H_{11}ClN_4OS$ (342): C, 56.06; H, 3.23; N, 16.34. Found: C, 56.07; H, 3.25; N, 16.35%.

6-Phenyl-2-thioxo-5-(*p*-tolyldiazenyl)-2,3-dihydropyrimidin-4(5*H*)-one (35c). Formed as brown crystals from EtOH; yield (82%); Mp 98-100 ºC; IR (KBr) ν cm^{-1} 3181 (NH), 3059 (CH-arom), 2962 (CH-aliph), 1678 (CO); ^{1}H-NMR (DMSO-d_6) δ 3.34 (s, 3H, CH_3),7.00-7.80 (m, 10H, aromatic H and NH), 10.61 (s, 1H, NH); MS: *m/z* (%) 322 (M^+). Anal. Calcd for $C_{17}H_{14}N_4OS$ (322): C, 63.33; H, 4.38; N, 17.38. Found: C, 63.34; H, 4.40; N, 17.39%.

General procedure for the preparation of compound (38a-c). A mixture of compounds **35a-c** (0.01 mol), malononitrile (0.01 mol) and ammonium acetate (2 g) was exposed to microwave irradiation (power input 20%) for 3 min, the reaction mixture was allowed to reach room temperature, then diluted with EtOH with stirring and solid product that formed, was filtrated and crystallized from the proper solvent to give **38a-c**.

3-Imino-2,8-diphenyl-6-thioxo-2,3,5,6-tetrahydropyrimido[5,4-*c*]pyridazine-4-carbonitrile (38a). Formed as red crystals from EtOH; yield (79%); Mp 122-124 ºC; IR (KBr) ν cm^{-1} 3328, 3181 (2NH), 2195 (CN); ^{1}H-NMR ($CDCl_3$) δ 6.95-7.93 (m, 12H, aromatic H and 2NH); MS: *m/z* (%) 358 (M^++2). Anal. Calcd for $C_{19}H_{12}N_6S$ (356): C, 64.03; H, 3.39; N, 23.58. Found: C, 64.04; H, 3.40; N, 23.60%.

2-(4-Chlorophenyl)-3-imino-8-phenyl-6-thioxo-2,3,5,6-tetrahydropyrimido[5,4-*c*]pyridazine-4-carbonitrile (38b). Formed as brown crystals from EtOH; yield (74%); Mp 134-136 ºC; IR (KBr) ν cm^{-1} 3335, 3209 (2NH), 2195 (CN); ^{1}H-NMR ($CDCl_3$) δ 6.95-8.47 (m, 11H, aromatic H and 2NH); MS: *m/z*

(%) 392 (M^++2). Anal. Calcd for $C_{19}H_{11}ClN_6S$ (390): C, 58.39; H, 2.84; N, 21.50. Found: C, 58.40; H, 2.85; N, 21.52%.

3-Imino-8-phenyl-6-thioxo-2-*p*-tolyl-2,3,5,6-tetrahydropyrimido[5,4-*c*]pyridazine-4-carbonitrile (38c). Formed as brown crystals from EtOH; yield (76%); Mp 116-118 ºC; IR (KBr) ν cm^{-1} 3340, 3212 (2NH), 3030 (CH-arom), 2916 (CH-aliph), 2193 (CN); ^{1}H-NMR ($CDCl_3$) δ 1.23 (s, 3H, CH_3), 7.23-7.52 (m, 11H, aromatic H and 2NH); ^{13}C NMR δ 18.9, 80.1, 113.1, 119.2, 120.3, 127.1, 127.1, 128.6, 129.2, 129.2, 129.8, 130.1, 130.8, 133.1, 133.3, 151.2, 153.4, 160.0, 162.1, 179.1; MS: *m/z* (%) 370 (M^+). Anal. Calcd for $C_{20}H_{14}N_6S$ (370): C, 64.85; H, 3.81; N, 22.69. Found: C, 64.86; H, 3.82; N, 22.71%.

ACKNOWLEDGEMENTS

The authors are very grateful to Prof. Dr. A. E. Khodair, Department of Chemistry, Faculty of Science, Suez Canal University, Ismailia, Egypt, for valuable support and reviewing this manuscript.

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