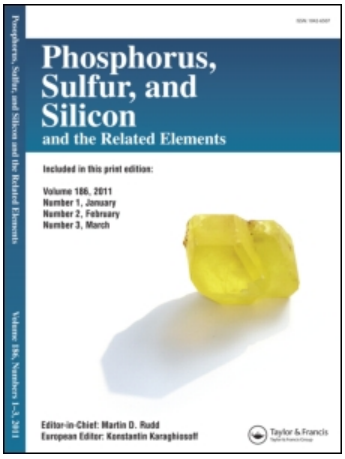

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Regioselective Synthesis and Reactions of a Polynuclear Heterocyclic Derived From Pyrido[2,3-*d*]pyrimidines With a New Ring System

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Regioselective Synthesis and Reactions of a Polynuclear Heterocyclic Derived From Pyrido[2,3-*d*]pyrimidines With a New Ring System

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*2-thioxopyrido[2,3-*d*]pyrimidin-4-(1*H*)-ones **3** were synthesized by a reaction of α,β-unsaturated ketones with aminouracil. A series of pyrido[2,3-d]pyrimidine derivatives have been synthesized by a reaction of **3** with arylaldehydes, hydroxylamine hydrochloride, alkyl halides, arylazoketones, hydrazine hydrate, and thioureas to give a series of a new polynuclear heterocyclic ring added to parent compound **3** with a new ring system. 2-methylthio derivatives were converted to corresponding 2-methylsulphone derivatives **16** on treatment with hydrogen peroxide.*

Keywords 6-Amino-thiouracil; pyrido[2,3-*d*]pyrimidine; isoxazolothiazolopyridopyrimidine; thiazolopyridopyrimidine; ^{13}C NMR

INTRODUCTION

Pyrido[2,3-*d*]pyrimidin-(1*H*)4-ones have attracted pharmaceutical companies due to a wide range of biological activities associated with this scaffold. Thus, a search carried out with *SciFinder Scolar* 2004 revealed that over 3,000 structures of type pyridopyrimidines have been described, with biological activities ranging from kinase inhibitors platelet-derived growth factor (PDGFr), fibroblast growth factor (FGFr), and epidermal growth factor (EGFr) inhibitors.[1,2] Also, these are used for antiinflammatory activity,[3] as anti-tumor agents,[4] as anti-thyroid substance for iodine fixation,[5,6] and as an antihistamnic reagent.[7]

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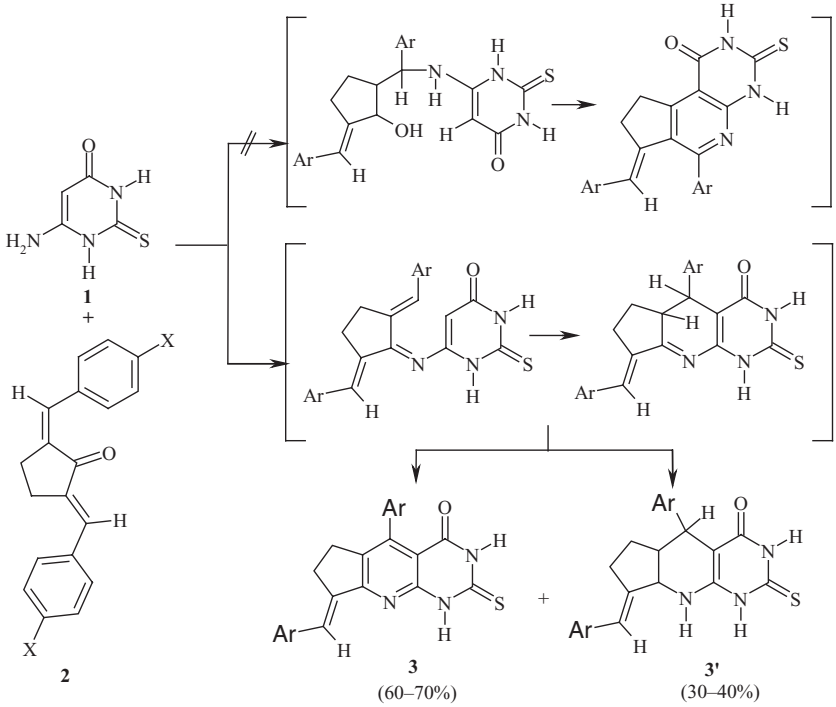


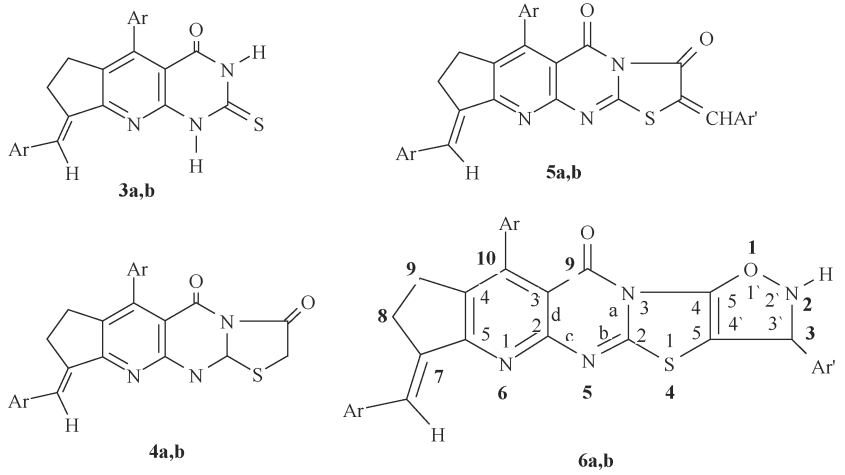
a, Ar = 4-chlorophenyl; **b**, Ar = 4-methoxyphenyl

SCHEME 1

Our group has actively been working on the development of synthetic strategies for the preparation of 2-thioxopyrido[2,3-*d*]pyrimidin-4(1*H*)-ones (**3**) from α,β-unsaturated ketones[8,9] **2** (Scheme 1). Thus, in a so-called cyclic strategy, 8-arylidine-5-aryl-2,3,6,7-tetrahydro-cyclopenteno-2-thioxopyrido[2,3-*d*]pyrimidin-4(1*H*)-ones (**3**) were obtained by the reaction of an α,β-unsaturated ketones (**2**) and 6-aminothiouracil (**1**) in refluxing dimethylformamide solution with stirring for a long time (30–50 h). TLC revealed yields of 60–70%. The non-oxidized form 8-arylidine-5-aryl-2,3,6,5,7,9-hexahydro-cyclopenteno-2-thioxo-pyrido[2,3-*d*]pyrimidin-4(1*H*)-ones (**3′**) had modest yields of 25–40% after 15 h of reflux in dimethylformamide. The structures of **3** and **3′** were established by analytical and spectral data. The ^{1}H NMR spectrum (DMSO-d_6) of **3a**, as an example, showed signals at δ 2.47–2.56 (t, 2H, CH_2), 2.72–2.88 (t, 2H, CH_2), 6.95–7.05 (d, 2H, phenyl), 7.10–7.18 (d, 2H, phenyl), 7.20–7.32 (d, 2H, phenyl), 7.47–7.60 (d, 2H, phenyl), 7.87 (s, 1H, methylenic proton), 11.30 brs, NH), and 11.30 (brs, NH). The mass spectrum for **3a** showed a molecular

ion [M^+] peak at m/z 452 (100%). Also, the ^{13}C NMR (DMSO-d_6) spectrum of **3b** as an example showed 4 signals for sp^3carbon atoms and 15 signals for sp^2, and carbon atoms at 162.23 (CO) and 174.96 (CS) ppm. Moreover, the mass spectrum for this compound showed a molecular ion [M^+] peak at m/z 444 (31%) and the fragmentation pattern [M^+-H] with m/z 443 (91%), and [M^+-2H] with m/z 442 (100%).

In addition, we report here simple and convenient methods for the syntheses of thiazolo-pyridopyrimidines, isoxazolothiazolopyridopyrimidines, and pyridotriazolo-pyrimidines. Thus, when a ternary mixture of 8-arylidine-5-aryl-2,3,6,7-tetra-hydrocyclo-penteno-2-thioxopyrido[2,3-*d*]pyrimidin-4(1*H*)-one (**3a,b**), chloroacetic acid, and a proper aldehyde were heated under reflux in a mixture of acetic acid, acetic anhydride, and anhydrous sodium acetate, 6-aryl-2, 9-diarylmethylene-2,3,4,5,7,8-hexahydrothiazolo[4,5-*a*]cyclopenteno-pyrido[2,3-*d*]pyrimidine-3,5-diones (**5a–e**) were obtained in high yields (Scheme 2).



3, 4a, Ar = 4-chlorophenyl
3, 4b, Ar = 4-methoxyphenyl
5c, Ar = 4-chlorophenyl, Ar' = 2-thienyl
5e, Ar = 4-methoxyphenyl, Ar' = 4-chlorophenyl
6a, Ar = 4-chlorophenyl; A' = 2-Thienyl

5a, Ar = 4-chlorophenyl, Ar' = phenyl
5b, Ar = 4-methoxyphenyl, Ar' = phenyl
5d, Ar = Ar' = 4-chlorophenyl

6b, Ar = 4-methoxyphenyl; Ar' = phenyl

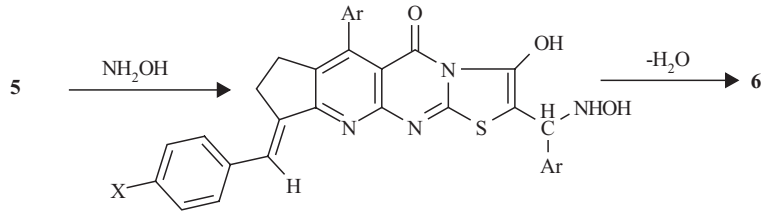
SCHEME 2

Structure assignments were based on an independent preparation of **5a** by condensation of **4a** with benzaldehyde in acetic acid in the presence of anhydrous sodium acetate; the correct values in elemental analysis, and compatible spectral data (Experimental). The ^{13}C NMR (DMSO-d_6) spectrum for compound **5c** showed signals at 27.01 and

27.95 ppm for two sp^3 carbons, 54.98 and 55.17 ppm for two sp^3 ($2OCH_3$), 108.47–159.23 ppm for 22 sp^2 carbons with 6 symmetric carbons, and 162.08 and 163.93 (2CO) ppm. Moreover, the condensation of thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*]pyrimidine-2,5-diones (**4a**) with benzaldehyde in acetic acid in the presence of anhydrous sodium acetate afforded 2-benzylidene derivatives **5a**, with identical data.

Moreover, the structure of**4** was established by elemental analysis and on an infrared spectrum of **4**, which, for **4a**, displayed absorption bands around 1689 and 1675 cm^{-1} for 2 carbonyl groups.

Compounds **5b,c** underwent cycloaddition with hydroxylamine hydrochloride by heating in boiling acetic acid in the presence of anhydrous sodium acetate to give 3-aryl-2,3,8,9-tetrahydroisoxazolo-[5',4':4,5]thiazolo[3,2-*a*]cyclopentenopyrido[2,3-*d*]pyrimidin-9(9*H*)one (**6a,b**), with a new ring system. The ^1H NMR (DMSO-d_6) spectrum of **6a**, as an example, showed a singlet signal at δ 6.56 for the oxazole proton. IR spectra of **6a,b** displayed absorption bands around 3390 cm^{-1} (NH) and 1688 cm^{-1} (CO). The formation of **6** from **5** proceeded by first a 1,4-addition of hydroxylamine on the ethylenic double bond, followed by a loss of water as shown in Scheme 3.

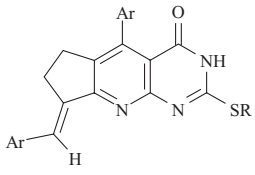


Ar = 4-chlorophenyl

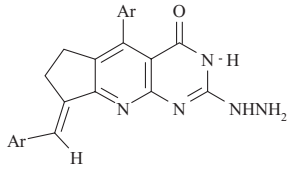
SCHEME 3

Alkylation of an ethanolic potassium hydroxide solution of **3** with methyl iodide yielded 2-alkylthio derivatives **7a–g**. Assignment of structures **7** is based on the fact that both **7a,b** gave the same 2-hydrazino derivatives (**8a,b**) with the evolution of methyl or ethyl mercaptan on treatment with hydrazine hydrate. The ^{13}C NMR (DMSO-d_6) spectrum for **7e** as an example showed signals at 14.00, 27.06, and 28.04 ppm for 3 sp^3 carbons; 61.18 and 66.41 ppm 2 sp^3 carbon (OCH_2, SCH_3); 16C sp^2 carbon atoms; and 164. 43 and 168.17 (2CO) ppm. Moreover, the mass spectrum for **7e** showed a molecular ion [M^+] peak at m/z 529 (100%).

On the other hand, trials to add hydrazine hydrate to **5** failed and yielded instead 8-arylidine-5-aryl-2-hydrazino-,3,6,7-trihydro-cyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-ones (**8a**,**b**), which were



7a,d



8a–g

a, Ar = 4-methoxyphenyl; R = CH_3 **e** , Ar = 4-chlorophenyl; R = $CH_2COOC_2H_5$

b, Ar = 4-methoxyphenyl; R = C_2H_5 **f**, Ar = 4-methoxyphenyl; R = $CH(COCH_3)_2$

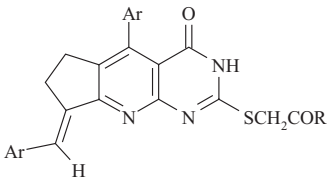
c, Ar = 4-methoxyphenyl; R = $CH_2CONHC_6H_4$-Cl-(*p*)

d, Ar = 4-chlorophenyl; R = CH_3 **g**, Ar = 4-methoxyphenyl; R = $CH_2COOC_2H_5$

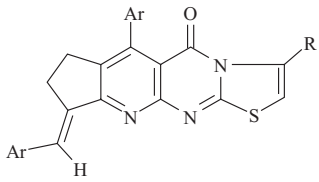
SCHEME 4

reported according to Shishoo and Jain[10] upon heating 2-methylthio derivative with hydrazine hydrate (Scheme 4). Assignments of structures **8** are based on correct elemental analyses and IR and NMR spectroscopy. The ^{1}H NMR (DMSO-d_6) spectrum for **8a** showed the absorption peak at δ 2.10 (brs, d, NH_2), 2.73–2.76 (t, 2H, CH_2), 2.80–2.98 (t, 2H, CH_2), 3.80 (brs, 1H, NH), 6.98–7.05 (d, 2H, phenyl), 7.10–7.19 (d, 2H, phenyl), 7.43–7.50 (d, 2H, phenyl), 7.54–7.60 (d, 2H, phenyl), 8.02 (s, 1H, methylenic protons), 12.00 (brs, NH). Moreover, the ^{13}C NMR (DMSO-d_6) spectrum for **8b** showed absorption peaks at 27.01, 27.95 ppm (2C, $2CH_2$), 54.98, 55.17 ppm (2C, $2OCH_3$), 16 sp^2 carbon atoms with four symmetric carbons and absorption at 163.93 (CO) ppm.

The reaction of **3b** in an ethanolic potassium hydroxide solution with α-haloketones, such as chloroacetone and/or phenacylbromide, yielded 2-(S-acetone or/ S-phenacyl)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclo-pentenopyrido[2,3-*d*]-pyrimidin-4 (4H)-ones (**9a,b**). Assignments of structures **9a,b** were based on correct elemental analyses. The IR spectra were in agreement with the structure and revealed the presence of a free keto-group around



9



10

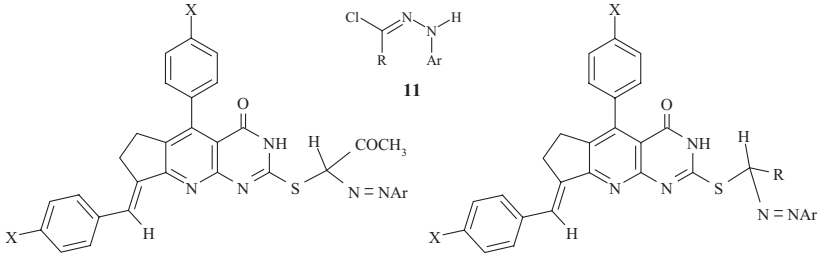
a, Ar = 4-methoxyphenyl; R = CH_3; **b**, Ar = 4-methoxyphenyl; R = C_6H_5

SCHEME 5

1720 cm^{-1}. The ^1H NMR (DMSO-d_6) spectrum for compound **9a** showed an absorption peak at δ 1.85 (s, 3H, CH_3), 2.73–2.85 (t, 3H, CH_2), 3.00–3.12 (t, 2H, CH_2), 3.55 (brs, NH, H_2O overlaped, D_2O exchangeable), 3.80, 3.83 (two singlets for 6H, $2OCH_3$), 4.33 (s, 2H, CH_2), 6.95–7.05 (m, two doublets for 4H, p-sub-phenyl), 7.15–7.25 (d, 2H, p-sub-phenyl), and 7.55–7.63 (m, douplet for 2H p-sub-phenyl + singlet for 1H, methylenic proton).

The latter compound **9a,b** was cyclized under reflux in a mixture of glacial acetic acid and sulphoric acid (2 mL) to give 3-(methyl/or phenyl)-9-(4-methoxyphenyl-methylene)-6-(4-methoxyphenyl)-1,2-dihydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido-[2,3-*d*]pyrimidin-5-ones (**10a,b**). Structures **10a,b** were preferred on the basis of ^1H and ^{13}C NMR spectral data. Thus, the ^1H NMR (DMSO-d_6) spectrum for compound **10b** showed absorption peaks at δ 2.73–2.85 (t, 3H, CH_2), 3.00–3.15 (t, 2H, CH_2), 3.80, 3.84 (two singlets for 6H, $2OCH_3$), 6.95–7.05 (m, two doublets for 4H, p-sub-phenyl), 7.17–7.26 (d, 2H, p-sub phenyl), 7.46–7.80 (m, 5H phenyl + singlet for 1H, thiazole proton), 7.88 (s, 1H, methylenic proton), and 8.05–8.10 (d, 2H, p-sub-phenyl). The ^{13}C NMR (DMSO-d_6) spectrum for compound **10a** showed an absorption peak at 23.09 (1C, CH_3) ppm, 27.29, 30.03 (2C, $2CH_2$) ppm, 55.13, 55.29 (2C, $2OCH_3$) ppm, 18 sp^2 carbon atoms with 4 symmetric carbon, and absorption at 164.8 (CO) ppm.

Stirring compound **3** under reflux with 1-arylazo-1-chloroacetone **11** in dry chloroform for 5 h afforded 2-[S-(acetonyl-1-*p*-chlorophenyl-azo)]-8-(4-arylmethylene)-5-(4-aryl)-3,6,7-trihydro-cyclopentenopyrido-[2,3-*d*]-pyrimidin-4(4*H*)-4-ones (**12a,b**) and 2-[S-(ethylcarboxy-late-1-phenylazo)]-8-(4-arylmethyl-ene)-5-(4-aryl)-3,6,7-trihydro-cyclopentenopyrido[2,3-*d*]-pyrimidin-4(4*H*)-4-ones (**13a,b**), respectively (Scheme 6).



a, X = Cl, Ar = chlorophenyl-(p)

b, X = OCH_3, Ar = chlorophenyl-(p)

a, X = Cl, Ar = phenyl, R = $COOC_2H_5$

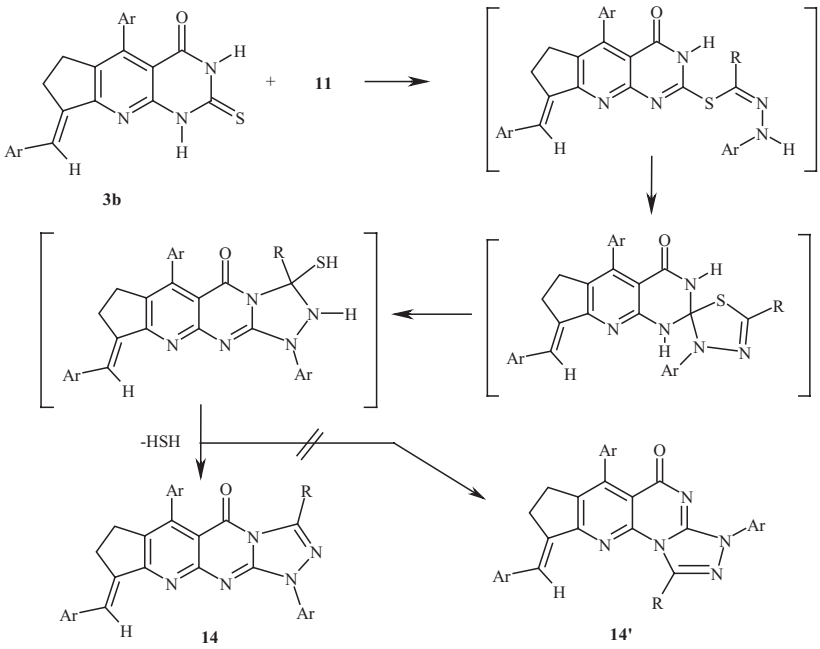
b, X = OCH_3, Ar = phenyl, R = $COOC_2H_5$

SCHEME 6

IR, ^{1}H NMR, and ^{13}C NMR spectra were in agreement with the assigned structures. The ^{1}H NMR (DMSO-d_6) spectrum for compound **12a** showed absorption peaks at δ 2.71–2.74 (t, 2H, CH_2), 3.02–3.07 (t, 2H, CH_2), 3.56 (s, 3H, $COCH_3$), 7.76–7.29 (m, 3H, (d, 2H, p-sub-phenyl + s, 1H methylene protons), 7.30–7.48 (2 doublets, 4H, p-sub-phenyl), 7.50–7.53 (two doublets, 4H, p-sub-phenyl), 7.55 (s, 1H, methylenic proton) and 11.87 (brs, NH). The ^{13}C NMR (DMSO-d_6) spectrum for **12a** showed signals at 26.97, 28.06 (2C, $2CH_2$) ppm, 29.04 (1C, CH_3) ppm, 66.46 (1C, CH) ppm, 20C sp^2 carbon atoms with 6 symmetric carbons, and absorption at 163.89, 175.20 (2 carbonyl groups). Moreover, the ^{1}H NMR (DMSO-d_6) spectrum for 2-[S-(ethylcarboxylate-1-phenylazo)]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (**13b**) showed peaks at δ 1.28–1.31 (t, 3H, CH_3), 2.78–2.81 (t, 2H, CH_2), 3.03–3.04 (t, 2H, CH_2), 3.80, 3.83 (2 singlets, 6H, $2OCH_3$), 4.38–4.43 (q, 2H, CH_2), 6.97–6.99 [m, 3H (singlet for CH, doublet for 2H, p-subphenyl)], 7.21–7.23 (d, 2H, p-subphenyl), 7.44–7.46 (m, 3H, phenyl), 7.54–7.57 (d, 2H, p-sub-phenyl), 7.60–7.66 (m, 4H, phenyl), 8.20 (s, 1H, methylenic proton). The ^{13}C NMR (DMSO-d_6) spectrum for compound **13b** showed the signals at 13.61 (1C, CH_3) ppm, 27.15, 28.11 (2C, $2CH_2$) ppm, 55.25, 55.37 (2C, $2OCH_3$) ppm, 63.30 (1C, OCH_2) ppm, 66.48 (1C, CH) ppm, 20 sp^2 carbon atoms, and absorption at 160.49 and 166.45 (2CO) ppm.

Stirring compond **3b** under reflux with **11** in dry chloroform with a few drops of triethylamine added as a catalyst (for 20–30 h) afforded, after removing hydrogen sulfide, the rearranged and cyclized product 9-(4-methoxy-phenylmethylene)-(1-aryl and 3-aryl or 3-acetyl or 3-ethylcarboxylate)-6-(4-methoxy-phenyl)-3,7,8-trihydro-5*H*-cyclopenteno-pyrido[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidin-5-ones (**14a–c**), respectively (Scheme 7).

Structures **14** were prefered on the basis of ^{1}H and ^{13}C NMR spectral data. Thus, the ^{1}H NMR (DMSO-d_6) spectrum for compound **14a,** as an example, showed absorption peaks at δ 2.77–2.79 (t, 2H, CH_2), 3.04–3.05 (t, 2H, CH_2), 3.80, 3.81 (two singlets for 6H, $2OCH_3$), 6.93–6.95 (d, 2H, phenyl), 6.99–7.01 (d, 2H, phenyl), 7.20–7.22 (d, 2H, phenyl), 7.40–7.48 (m, 5H, phenyl), 7.56–7.68 (m, 3H, phenyl), 7.70–7.72 (m, 3H, 2H phenyl + 1H methylenic proton), 8.29–8.31 (d, 2H, phenyl). The ^{13}C NMR (DMSO-d_6) spectrum showed absorption at 27.23, 28.18 (2C, $2CH_2$) ppm, 55,45, 55.51 (2C, $2OCH_3$) ppm, 25 sp^2 carbon atoms, and absorption at 166.20 (CO) ppm. The mass spectrum for **14c** showed a molecular ion [M^+] at m/z 613 (72%) and fragmention patterns for [M^++1] at m/z 614 (10%), [M^+-H] at m/z 612 (100%), and



a, Ar' = 4-methoxyphenyl; R = Ar = C_6H_5

b, Ar' = 4-methoxyphenyl; R = $COCH_3$; Ar = *p*-C_6H_4-Cl

c, Ar' = 4-methoxyphenyl; R = $COOC_2H_5$; Ar = *p*-C_6H_4-CH_3

SCHEME 7

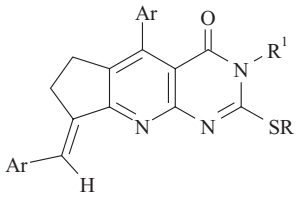
$[M^+\text{-}COOC_2H_5]$ at m/z 540 (50%). The reaction mechanism may have occurred through the intermediates (Scheme 7).

2-alkylthio derivatives **8a,b** underwent further alkylation at the N-3 nitrogen atom on treatment with alkyl iodides, in aqueous ethanolic sodium ethoxide solution, to afford 2-methylthio-3-alkyl-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-6,7-dihydro-cyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-ones (**15a,b)**.

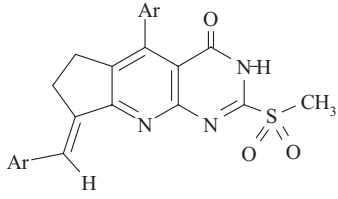
Assignment of structures **15** was based on spectral data. The ^{1}H NMR (DMSO-d_6) spectrum of **15a**, as an example, showed absorption peaks at δ 2.71 (s, 2H, SCH_3), 2.75–2.78 (t, 2H, CH_2), 2.97–3.18 (t, 2H, CH_2), 3.80, 3.83 (two singlets, 6H, $2OCH_3$), 4.27 (s, 3H, N-CH_3), 6.94–6.99 (d, 2H, phenyl), 7.00–7.15 (d, 2H, phenyl), 7.20–7.22 (d, 2H, phenyl), 7.50–7.53 (d, 2H, phenyl), and 7.68 (s, 1H, methylenic proton). The ^{13}C NMR (DMSO-d_6) spectrum of **15a** showed peaks at 14.73 (1C, SCH_3) ppm, 27.45, 27.94 (2C, $2CH_2$) ppm, 30.04 (1C, N-CH_3) ppm, 55.23, 55.27 (2C,

$2OCH_3$) ppm, 16 sp^2 carbon atoms and absorption at 163.25 (CO) ppm. Moreover, its mass spectrum for **15a** showed the molecular ion [M^+] at m/z 471 (100%).

Oxidation of **8d** with hydrogen peroxide in acetic acid yielded 2-methyl sulphone-8-(4-chlorophenylmethylene)-5-(4-chlorophenyl)-3,6,7-trihydro-cyclopentenopyrido[2,3-d]-pyrimidin-4(4*H*)-one derivatives **16** (Scheme 8). Structures **16** were preferred from analytical data and spectroscopic analysis. The ^1H NMR (DMSO-d_6) spectrum of **16** showed signals at δ 2.67–2.75 (t, 2H, CH_2), 2.97–3.03 (t, 2H, CH_2), 3.30 (s, 3H, SCH_3), 7.21–7.30 (d, 2H, phenyl), 7.41–7.47 (m, 2 doublets, 4H, phenyl), 7.55–7.60 (d, 2H, phenyl), 8.60 (s, 1H, methylenic proton), and 11.40 (brs, NH, D_2O exchangeable).



15



16

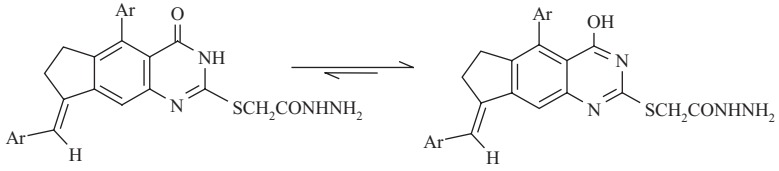
a, Ar = 4-methoxyphenyl; R = CH_3, R^1 = CH_3 Ar = 4-chlorophenyl

b, Ar = 4-methoxyphenyl; R = CH_3, R^1 = C_2H_5

SCHEME 8

Compounds **8e,g** gave 2-[8-(4-arylmethylene)-5-(4-aryl)-3,6,7-trihydrocyclopenteno-pyrido[2,3-*d*]pyrimidin-4(4*H*)-one-2-yl]-thioacethydrazide **17a,b** (Scheme 9) on treatment with equi-molecular amounts of hydrazine hydrate in ethanol. The IR spectrum of **17a,b** displayed a band around 3310 cm^{-1} (br s, OH and NH). The ^1H NMR (DMSO-d_6) spectrum for **17b**, as an example, showed signals at δ 2.66–2.68 (t, 2H, CH_2), 2.70–2.72 (t, 2H, CH_2), 2.89 (s, 2H, CH_2), 3.79, 3.81 (two singlets, 6H, $2OCH_3$), 7.20–7.22 (d, 2H, phenyl), 7.39–7.42 (d, 2H, phenyl), 7.43–7.46 (d, 2H, phenyl), 7.51–7.56 (d, 2H, phenyl), 8.12 (s, 1H, methylenic proton), and 11.68 (brs, NH). The ^{13}C NMR (DMSO-d_6) spectrum for **17a** showed signals at 26.86, 28.10, and 35.68 (3C, $3CH_2$) ppm; 16 sp^2 carbon atoms, and absorption at 162.25 and 175.27 (2CO) ppm.

On the other hand, compound **8f**, as typical 1,3-diketones, reacted with hydrazine hydrate, 2,4,6-trichlorophenylhydrazine, and thiourea



17a,b

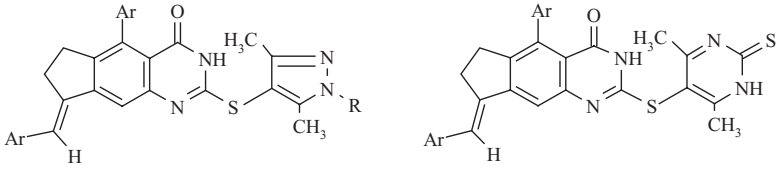
a, Ar = 4-chlorophenyl; b, Ar = 4-methoxyphenyl

SCHEME 9

to afford the corresponding 2-(3,5-dimethyl-1*H*-pyrazol-4-yl-thio)-, 2-(3,5-dimethyl-1-phenylpyrazol-4-yl-thio)-, and 2-(4,6-dimethyl-2-thioxo-1,2-dihydropyrimidin-5-yl-thio)-cyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one derivatives **18** and **19**, respectively.

IR spectra of **18a,b** and **19** displayed absorption bands around 3400 cm^{-1} (NH), and 1685 cm^{-1} for the carbonyl group. The ^{13}C NMR (DMSO-d_6) spectrum for **18b**, as an example, showed absorption peaks at 27.43, 28.08 (2C, $2CH_2$) ppm, 30.23, 30.50 (2C, $2CH_3$) ppm, 55.20, 55.35 (2C, $2OCH_3$) ppm, 23 sp^2 carbon atoms, and absorption at 164.99 (CO) ppm. The the mass spectrum for **18a** showed the absorption molecular ion [M^+] at m/z 537 (31%), [M^+-2H] at m/z 535 (20%), and [M^+-$C_5H_7N_2$] at m/z 443 (100%).

Heating **8f** under reflux on acetic anhydride/pyridine mixture led to the cyclization and formation of 2-acetyl-3-methyl-9-(4-methoxyphenylmethylene)-6-(4-methoxy-phenyl)-1,2,10,-11-tetrahydro-5*H*-thiazolo[4,5-a]cyclopentenopyrido[2,3-*d*]pyrimidin-5-one (**20**) in good yield. Assignments of structures **20** were based on spectral data in addition to our previous report on a related compound.[12] Thus, the N-3 nitrogen atom and not the N-1 nitrogen atom was involved in



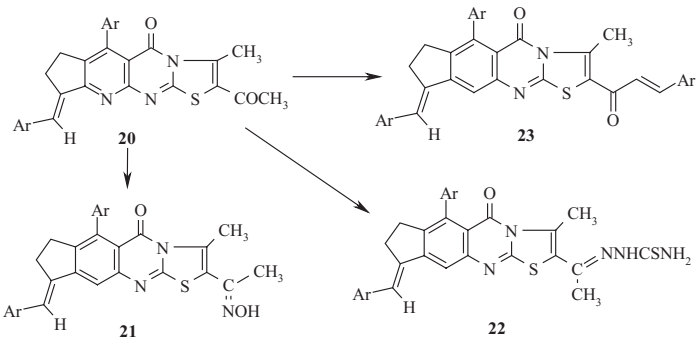
18 **19**

a, Ar = 4-methoxyphenyl; R = hydrogen

b, Ar = 4-methoxyphenyl; R = 2,4,6-trichlorophenyl

SCHEME 10

the cyclization.[8,12] IR spectrum of **20** displayed 2 carbonyl absorption bands at 1718 and 1690 cm^{-1}. ^1H NMR (DMSO-d_6) spectrum showed signals at δ 2.46–2.48 (t, 2H, CH_2), 2.53 (s, 3H, CH_3), 2.79–2.82 (t, 2H, CH_2), 2.84 (s, 3H, CH_3), 3.80, 3.83 (two singlets, 6H, $2OCH_3$), 6.97–6.99 (two doublets overlaped, 4H, phenyl), 7.01–7.21 (d, 2H, phenyl), 7.23–7.53 (d, 2H, phenyl), and 7.57 (s, 1H, methylenic proton). Furtheremore, the ^{13}C NMR (DMSO-d_6) spectrum showed signals at 16.23 (1C, CH_3) ppm, 27.43, 28.08 (2C, $2CH_2$) ppm, 30.50 (1C, CH_3) ppm, 55.46 (2C, $2OCH_3$) ppm, 18 sp^2 carbon atoms, and absorption at 165.99, and 190.87 (2CO). The mass spectrum showed molecular ion [M^+] at m/z 523 (47%) and fragmentation patterns for [M^+-H] at m/z 522 (100%), [M^+- CH_3] at m/z 508 (5%), and [M^+-$COCH_3$] at m/z 480 (15%) (Scheme 11).



SCHEME 11

In support of structure **20**, characteristic reactions for 2-acetyl group were observed. Thus, its reaction with each of hydroxylamine hydrochloride and thiosemi-carbazide gave the corresponding oxime and thiosemicarbazone derivatives **21** and **22**, respectively (Scheme 11). Compounds **21** and **22** gave correct values in elemental analyses and compatible data in IR and ^1H NMR spectra. The ^1H NMR (DMSO-d_6) spectrum for **21**, as an example, showed signals at δ 2.73, 2.76 (t, 2H, CH_2), 3.02–3.05 (t, 2H, CH_2), 3.05 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 3.80, 3.82 (2 singlets, 6H, $2OCH_3$), 6.94–6.97 (d, 2H, p-sub-phenyl), 6.99–7.01 (d, 2H, p-sub-phenyl), 7.17–7.19 (d, 2H, p-sub-phenyl), 7.34–7.48 (d, 2H, p-sub-phenyl), 7.50 (s, 1H, methylenic proton) and 11.84 (brs, NH). Furtheremore, the ^1H NMR (DMSO-d_6) spectrum for **22** showed the absorption peak at δ 2.75–2.79 (t, 2H, CH_2), 3.01–3.05 (t, 2H, CH_2), 3.10 (s, 3H, CH_3), 3.59 (s, 3H, CH_3), 7.16–7.19 (d, 2H, p-sub-phenyl),

7.24–7.26 (d, 2H, p-sub-phenyl), 7.35–7.39 (d, 2H, p-sub-phenyl), 7.40–7.46 (d, 2H, p-sub-phenyl), 8.29 (s, 1H, methylenic proton), 10.82 (brs, NH), and 11.30 (brs, NH). The mass spectrum showed an absorption ion peak at m/z 596 for [M^+] (100%).

Moreover, compound **20** yielded the 2-cinnamoyl-3-methyl-9-(4-methoxyphenyl-methylene)-6-(4-methoxyphenyl)-1,2,10,11-tetrahydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido-[2,3-*d*]pyrimidin-5-one derivatives **23** on heating with the proper aldehyde at 180°C in the presence of a catalytic amount of piperidine. IR spectra of **23** displayed 2 carbonyl absorption bands around 1700–1685 cm^{-1} for 2 carbonyl groups. The ^1H NMR (DMSO-d_6) spectrum for **23** showed signals at δ 2.55 (s, 3H, CH_3), 2.83–2.8 (t, 2H, CH_2), 3.00–3.03 (t, 2H, CH_2), 3.76, 3.78, 3.80 (three singlets, 9H, $3OCH_3$), 5.28, 5.50 (two doublets, 2H, CH=CH), 6.93–6.96 (d, 2H, p-sub-phenyl), 7.18–7.23 (d, 2H, p-sub-phenyl), 7.25–7.31 (d, 2H, p-sub-phenyl), 7.43–7.46 (d, 2H, p-sub-phenyl), and 8.34 (s, 1H, methylenic proton).

EXPERIMENTAL

All melting points were uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on JEOL JNM-LA-400 FT NMR spectrometer (Universitat Konstanz, Konstanz, Germany), and chemical shifts were expressed as δ values aganist $SiMe_4$ as the internal standard. IR spectra were recorded as KBr pellets on a Perkin-Elmer 1430 spectrometer, (National Research Center, Giza, Egypt). Mass spectra were recorded on GCMS-QP 1000 EX Shimadzu Japan (gas chromato-graphy-mass spectrometer). Microanalytical data were performed by the Microanalytical Center at Cairo University (Giza, Egypt). The starting materials were prepared according to Quiroga et al.[11] and El-gazzar et al.[12]

8-arylidine-5-aryl-2,3,6,7-tetrahydrocyclopenteno-2-thioxopyrido[2,3-*d*]pyrimidin-4(1*H*)-ones (3a,b)

General Procedure

A mixture of compound **2** (10 mmol) and 6-aminothiouracil (**1**) (1.43 g, 10 mmol) was refluxed in dimethylformamide (50 mL) for 20–30 h (under TLC control). The reaction mixture was cooled, and the deposited precipitate was filtered off, washed with ethanol, dried, and crystallized from an appropriate solvent to produce **3a,b** in good yields. The filtrate was concentrated and left overneight at 0°C. The precipitate formed was filtered off and crystallized from an appropriate solvent to afford **3′a,b** in low yields.

*8-(4-Chlorobenzylidene)-5-(4-chlorophenyl)-2,3,6,7-tetrahydrocyclopenteno-2-thioxopyrido-[2,3-*d*]pyrimidin-4(1*H*)-ones (*3a*)*

The compound was obtained from **2a** (3.29 g, 10 mmol), as yellow powder and crystallized from dimethylformamide (81%), m.p. 369–372°C (melted); IR (KBr) cm^{-1}: 3342 (brs, NH), 3059 (CH aryl), 2918 (CH alkyl), 1693 (CO), 1651 (C=N). ^{1}H NMR (DMSO-d_6): δ 2.47–2.56 (t, 2H, CH_2), 2.72–2.88 (t, 2H, CH_2), 6.95–7.05 (d, 2H p-sub-phenyl), 7.10–7.18 (d, 2H, p-sub-phenyl), 7.20–7.32 (d, 2H, p-sub-phenyl), 7.47–7.60 (d, 2H, phenyl) 7.87 (s, 1H, methylenic proton), 11.30 (brs, NH), 12.10 (brs, NH). The MS: [M^+], m/z 452 (100%). Analysis: $C_{23}H_{15}Cl_2N_3OS$ (452.3); requires C, 61.06; H, 3.34; N, 9.28; found: C, 61.11; H, 3.33; N, 9.31.

*8-(4-Methoxybenzylidene)-5-(4-methoxyphenyl)-2,3,6,7-tetrahydro-cyclopenteno-2-thioxo-pyrido[2,3-*d*]pyrimidin-4(1*H*)-ones (*3b*)*

The compound was obtained from **2b** (3.20 g, 10 mmol), as a yellow powder and crystallized from dimethylformamide (86%), m.p. 315–316°C (melted); IR (KBr) cm^{-1}: 3365 (brs, NH), 3043 (CH aryl), 2908 (CH alkyl), 1691 (CO), 1642 (C=N). ^{1}H NMR (DMSO-d_6): δ 2.49–2.56 (t, 2H, CH_2), 2.72–2.88 (t, 2H, CH_2), 3.76 (s, 3H, 3), 3.91 (s, 3H, OCH_3), 6.81–6.98 (d, 2H p-sub-phenyl), 7.00–7.18 (d, 2H, p-sub-phenyl), 7.20–7.31 (d, 2H, p-sub-phenyl), 7.47–7.60 (d, 2H, phenyl) 7.95 (s, 1H, methylenic proton), 11.85 (brs, NH), 12.53 (brs, NH); ^{13}C NMR (DMSO-d_6): δ 27.18, 28.00 (2C, $2CH_2$), 55.17, 55.32 (2C, $2OCH_3$), 107.97, 113.30, 114.47, 126.11, 129.12, 129.15, 129.18, 130.81, 135.47, 138.21, 148.84, 152.85, 158.72, 159.00, 159.37 (15C, sp^2) 162.23 (CO), 174.96 (CS) . The MS: [M^+], m/z 444 (31%), [M^+-H], m/z 443 (91%), [M^+-2H], m/z 442 (100%) Analysis: $C_{25}H_{21}N_3O_3S$ (443.5); requires C, 67.69; H, 4.77; N, 9.47; found: C, 67.70; H, 4.67; N, 9.46.

9-(4-Chlorophenylmethylene)-6-(4-chlorophenyl)-2,7,8-trihydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*] pyrimidine-3,5-dione (4a)

A mixture of compound **3a** (4.52 g, 10 mmol), chloroacetic acid (0.95 g, 10 mmol) and (1.64 g, 20 mmol), anhydrous sodium acetate was heated gently with stirring on a water bath (60°C) for 2 h. The reaction mixture was allowed to cool to r.t. and poured into water (100 mL). The deposited precipitate was filtered off and crystallized from dioxane. The compound was produced as a yellow powder (63%), m.p. 311–313°C (melted); IR

(KBr) cm^{-1}: 3063 (CH aryl), 2913 (CH alkyl), 1689, 1675 (2CO), 1619 (C=N), 1516 (C=C); ^1H NMR (DMSO-d_6): δ 2.44 (s, 2H, CH_2), 2.75–2.78 (t, 2H, CH_2), 3.07–3.13 (t, 2H, CH_2), 7.14–7.16 (d, 2H, p-sub-phenyl), 7.17–7.19 (d, 2H, p-sub-phenyl), 7.35–7.37 (d, 2H, p-sub-phenyl), 7.41–7.43 (d, 2H, p-sub-phenyl) and 8.30 (s, 1H, methylenic proton). Analysis: $C_{25}H_{15}Cl_2N_3O_2S$ (492.4); requires C, 60.98; H, 3.07; N, 8.53; found: C, 61.01; H, 3.11; N, 8.50.

9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-1,2-dihydro-5*H*-thiazolo[4,5-*a*]-cyclopentenopyrido[2,3-*d*]pyrimidine-3,5-dione (4b)

A mixture of compound **3b** (4.44 g, 10 mmol), chloroacetic acid (0.95 g, 10 mmol), and (1.64 g, 20 mmol) anhydrous sodium acetate was heated gently with stirring on a water bath (60°C) for 2 h. The reaction mixture was allowed to cool to r.t. and poured into water (100 mL). The deposited precipitate was filtered off and crystallized from dioxane. The compound was produced as a yellow powder (56%), m.p. 301–303°C (melted); IR (KBr) cm^{-1}: 3043 (CH aryl), 2931 (CH alkyl), 1686, 1672 (2CO), 1623 (C=N), 1535 (C=C); ^1H NMR (DMSO-d_6): δ 2.53 (s, 2H, CH_2), 2.80–2.83 (t, 2H, CH_2), 3.05–3.07 (t, 2H, CH_2), 3.81, 3.83 (2s, 6H, $2OCH_3$), 6.98–7.02 (2d, 4H, p-sub-phenyl), 7.22–7.24 (d, 2H, p-sub-phenyl), 7.54–7.56 (d, 2H, p-sub-phenyl) and 7.63 (s, 1H, methylenic proton). Analysis: $C_{27}H_{21}N_3O_4S$ (483.5); requires C, 67.06; H, 4.37; N, 8.69; found: C, 67.01; H, 4.39; N, 8.73.

6-Aryl-2,9-diarylmethylene-2,3,4,5,7,8-hexahydrothiazolo[4,5-*a*]cyclopentenopyrido-[2,3-*d*]pyrimidine-3,5-diones (5a–e)

Method (A)

A mixture from compound **3** (10 mmol), chloroacetic acid (0.95 g, 10 mmol), the appropriate aromatic aldehyde (10 mmol), and (1.64 g, 20 mmol) of anhydrous sodium acetate was stirred under reflux in 30 mL glacial acetic acid and 15 mL acetic anhydride for 15 h. The reaction mixture was cooled and poured into cold water (100 mL). The deposited precipitate was filtered off and crysttallized from an appropriate solvent to produce (**5a–e**).

Method (B)

A mixture of compound **4** (10 mmol), the appropriate aromatic aldehyde (10 mmol), and (1.64 g, 20 mmol) anhydrous sodium acetate was

stirred under reflux in 30 mL glacial acetic acid and 15 mL acetic anhydride for 5 h. The reaction mixture was allowed to cool to r.t. and, poured into cold water (100 mL). The deposited precipitate was filtered off and crystallized from an appropriate solvent to produced (**5a,c**).

9-(4-Chlorophenylmethylene)-2-phenylmethylene-6-(4-chlorophenyl)-2,3,4,5,7,8-hexahydrothiazolo[4,5-a]cyclopentenopyrido[2,3-d]-pyrimidine-3,5-dione (5a)

The compound was obtained from **3a** (4.52 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) as a yellow powder and crystallized from dimethylformamide (61%), m.p. 319–321°C (melted); IR (KBr) cm^{-1}: 3055 (CH aryl), 2931 (CH alkyl), 1687 1675 (2CO), 1626 (C=N), 1537 (C=C); ^1H NMR (DMSO-d_6): δ 2.77–2.85 (t, 2H, CH_2), 3.02–3.15 (t, 2H, CH_2), 7.12–7.17 (2d, 4H, p-sub-phenyl), 7.20–7.28 (d, 2H, p-sub phenyl), 7.36–7.65 [m, 6H, (5H, phenyl + 1H, thiazole proton)],7.88 (s, 1H, methylenic proton), 8.04–8.12 (d, 2H, p-sub-phenyl). Analysis: $C_{32}H_{19}Cl_2N_3O_2S$ (580.4); requires C, 66.21; H, 3.30; N, 7.24; found: C, 66.19; H, 3.29; N, 7.35.

9-(4-Methoxyphenylmethylene)-6-(4-methoxyphenyl)-2-phenylmethylene-2,3,4,5,7,8-hexahydrothiazolo[4,5-a]cyclopentenopyrido[2,3-d]pyrimidine-3,5-dione (5b)

The compound was obtained from **3b** (4.44 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) as yellow powder and crystallized from dimethylformamide (67%), m.p. 297–300°C (melted); IR (KBr) cm^{-1}: 3051 (CH aryl), 2927 (CH alkyl), 1690 1676 (2CO), 1632 (C=N), 1545 (C=C); ^1H NMR (DMSO-d_6): δ 2.76–2.84 (t, 2H, CH_2), 3.02–3.14 (t, 2H, CH_2), 3.83, 3.86 (2s, 6H, $2OCH_3$), 6.96–7.05 (2d, 4H, p-sub-phenyl), 7.18–7.26 (d, 2H, p-sub-phenyl), 7.45–7.80 [m, 6H, (5H, phenyl + 1H, methylenic proton)], 8.15–8.21 (d, 2H, p-sub-phenyl). ^{13}C NMR (DMSO-d_6): δ 27.01, 27.95 (2C, $2CH_2$), 54.98, 55.17 (2C, $2OCH_3$) 108.47, 112.99, 113.08, 114.22, 118.34, 124.38, 128.91, 129.56, 129.75, 129.86, 130.62, 130.73, 130.83, 132.96, 134.85, 138.90, 148.11, 148.23, 154.77, 158.33, 158.84, 159.23 (22C, sp^2 with 6 symmetric carbons), 162.08 (CO) and 163.93 (CO). Analysis: $C_{34}H_{25}N_3O_4S$ (571.6); requires: C, 71.43; H, 4.41; N, 7.35; found: C, 71.37; H, 4.36; N, 7.29.

9-(4-Chlorophenylmethylene)-6-(4-chlorophenyl)-2-thienylmethylene-2,3,4,5,7,8-hexahydrothiazolo[4,5-a]cyclopentenopyrido[2,3-d]pyrimidine-3,5-dione (5c)

The compound was obtained from **3a** (4.52 g, 10 mmol), and 2-thiophene carboxaldehyde (1.22 g, 10 mmol) as brown crystals and

crystallized from dioxane (61%), m.p. 340–342°C (melted); IR (KBr) cm^{-1}: 3023 (CH aryl), 2902 (CH alkyl), 1687, 1672 (2CO), 1651 (C=N), 1543 (C=C); ^1H NMR (DMSO-d_6): δ 2.70–2.75 (t, 2H, CH_2), 2.81–2.87 (t, 2H, CH_2), 7.23–7.25 (d, 2H, p-sub-phenyl), 7.32–2.37 (t, 1H, thienyl proton), 7.41–7.43 (d, 2H, p-sub-phenyl), 7.45–7.48 (d, 2H, p-sub-phenyl), 7.52–7.58 (d, 2H, p-sub-phenyl), 7.85–7.90 (d, 1H, thienyl proton), 8.14, 8.23 (2s, 2H, methylenic proton), 8.30–8.32 (d, 1H, thienyl proton). Analysis: $C_{30}H_{17}Cl_2N_3O_2S_2$ (587.4); requires C, 61.43; H, 2.92; N, 7.16; found: C, 61.38; H, 2.87; N, 7.12.

*6-(4-Chlorophenyl)-2,9-di(4-chlorophenylmethylene)-2,3,4,5,7,8-hexahydro-thiazolo[4,5-a]-cyclopentenopyrido[2,3-*d*]pyrimidine-3,5-dione (*5d*)*

The compound was obtained from **3a** (4.52 g, 10 mmol) and 4-chlorobenzaldehyde (1.40 g, 10 mmol) as yellow crystals and crystallized from dimethylformamide (64%), m.p. 321–323°C (melted); IR (KBr) cm^{-1}: 3067 (CH aryl), 2915 (CH alkyl), 1693, 1682 (2CO), 1640 (C=N), 1523 (C=C); ^1H NMR (DMSO-d_6): δ 2.73–2.83 (t, 2H, CH_2), 2.84–2.89 (t, 2H, CH_2), 7.21–7.26 (d, 2H, p-sub-penyl), 7.28–7.30 (d, 2H, p-sub-phenyl), 7.40–7.42 (d, 2H, p-sub-phenyl), 7.44–7.46 (d, 2H, p-sub-phenyl), 7.50–7.54 (d, 2H, p-sub-phenyl), 8.31–8.33 (d, 2H, p-sub-phenyl) and 8.85, 9.41 (2s, 2H, methylenic protons). Analysis: $C_{32}H_{18}Cl_3N_3O_2S$ (614.9); requires C, 62.50; H, 2.95; N, 6.83; found: C, 62.46; H, 2.88; N, 6.80.

*2-(4-Chlorophenylmethylene)-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-2,3,4,-5,7,8-hexahydrothiazolo[4,5-a]cyclopentenopyrido [2,3-*d*]pyrimidine-3,5-dione (*5e*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and 4-chlorobenzaldehyde (1.40 g, 10 mmol) as a brown powder and crystallized from dimethylformamide (63%), m.p. 306–308°C (melted); IR (KBr) cm^{-1}: 3049 (CH aryl), 2908 (CH alkyl), 1688, 1681 (2CO), 1632 (C=N), 1545 (C=C); ^1H NMR (DMSO-d_6): δ 2.77–2.79 (t, 2H, CH_2), 3.04–3.05 (t, 2H, CH_2), 3.80–3.84 (2s, 6H, $2OCH_3$), 6.93–6.95 (d, 2H, p-sub-phenyl), 6.99–7.01 (d, 2H, p-sub-phenyl), 7.20–7.22 (d, 2H, p-sub-phenyl), 7.40–7.45 (d, 2H, p-sub-phenyl), 7.48–7.56 (d, 2H, p-sub-phenyl), 7.68–7.72 (d, 2H, p-sub-phenyl) and 8.29, 8.31 (2s, 2H methylenic protons). Analysis: $C_{34}H_{24}ClN_3O_4S$ (606.1); requires C, 67.37; H, 3.99; N, 6.93; found: C, 67.34; H, 4.01; N, 6.85.

3,7,10-Triaryl-2,3,8,9-tetrahydroisoxazolo[5′,4′:4,5]thiazolo-[3,2-*a*]cyclopentenopyrido-[2,3-*d*]pyrimidin-9(9*H*)-ones (6a,b)

General Procedure

A mixture of compound **5b,c** (10 mmol), hydroxylamine hydrochloride (0.70 g, 10 mmol), and (1.64 g, 10 mmol) anhydrous sodium acetate was stirred under reflux in 30 mL glacial acetic acid for 5 h. The reaction mixture was allowed to cool to r.t. and poured into cold water (100 mL). The deposited precipitate was filtered off, dried, and crystallized from an appropriate solvent to produce **6a,b**.

*7-(4-Chlorophenyl)-10-(4-chlorophenylmethylene)-3-(2-thienyl)-2,3,8,9-tetrahydroisoxazolo-[5′,4′:4,5]thiazolo[3,2-a]cyclopentenopyrido[2,3-*d*]pyrimidin-9(9*H*)-one (*6a*)*

The compound was obtained from **5c** (5.87 g, 10 mmol) as green crystals and crystallized from benzene in a 50% yield, m.p. 340–341°C (melted); IR (KBr) cm^{-1}: 3390 (brs, NH), 3056 (CH aryl), 2928 (CH alkyl), 1689, (CO), 1640 (C=N), 1524 (C=C); ^1H NMR (DMSO-d_6): δ 2.73–2.78 (t, 2H, CH_2), 2.80–2.88 (t, 2H, CH_2), 6.56 (br, 1H, isooxazole proton), 7.22–7.24 (d, 2H, p-sub-phenyl), 7.28–2.38 (t, 1H, thienyl proton), 7.40–7.42 (d, 2H, p-sub-phenyl), 7.43–7.45 (d, 2H, p-sub-phenyl), 7.46–7.48 (d, 2H, p-sub-phenyl), 7.88–7.95 (d, 1H, thienyl proton), 8.15 (s, 1H, methylenic proton), 8.32–8.41 (d, 1H, thienyl proton) and 10.46 (brs, NH). Analysis: $C_{30}H_{18}Cl_2N_4O_2S_2$ (601.5); requires C, 59.90; H, 3.02; N, 9.31; found: C, 59.87; H, 3.05; N, 9.33.

*3-Phenyl-10-(4-methoxyphenylmethylene)-7-(4-methoxyphenyl)-2,3,8,9-tetrahydroisoxazolo-[5′,4′:4,5]thiazolo[3,2-a]cyclopentenopyrido[2,3-*d*]pyrimidin-9(9*H*)-one (*6b*)*

The compound was obtained from **5b** (5.71 g, 10 mmol) as green powder and crystallized from dimethylformamide (53%), m.p. 369–371°C (melted); IR (KBr) cm^{-1}: 3385 (brs, NH), 3053 (CH aryl), 2919 (CH alkyl), 1687, (CO), 1636 (C=N), 1522 (C=C). ^1H NMR (DMSO-d_6): δ 2.73–2.84 (t, 2H, CH_2), 3.01–3.05 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 6.63 (br, 1H, isooxazole proton) 7.19–7.21 (d, 2H, p-sub-phenyl), 7.27–2.31 (m, 5H, phenyl protons), 7.40–7.42 (2d, 4H, p-sub-phenyl), 7.46–7.48 (d, 2H, p-sub-phenyl), 7.46–7.48 (d, 2H, p-sub-phenyl), 7.94 (s, 1H, methylenic proton) and 10.80 (brs, NH). Analysis: $C_{34}H_{26}N_4O_4S$ (586.6); requires C, 69.60; H, 4.46; N, 9.55; found: C, 69.54; H, 4.50; N, 9.49.

8-arylidine-5-aryl-2-hydrazino-,3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-ones (7a,d)

General Procedure

A suspention of dry compound **3a,b** (10 mmol) in hydrazine hydrate (99–100%) (25 mL) was stirred under gentle reflux. The insoluble solid went into solution within 10 min with copious evolution of methylmercaptan to form a clear solution. After 30 min when the solid product started separating out, heating was continued for 8 h, and the reaction mixture was allowed to cool to r.t. The solid, which separated, was filtered, washed with ethanol, and dried to produced **7a,d** in good yields.

*8-(4-Chlorophenylmethylene)-5-(4-chlorophenyl)-2-hydrazino-,3,6,7-trihydro-cyclopenteno-pyrido[2,3-*d*]pyrimidin-4(4*H*)-one (7a)*

The compound was obtained from **3a** (4.52 g, 10 mmol) as yellow powder crystals and crystallized from dimethylformamide (89%), m.p. 233–236°C (melted); IR (KBr) cm^{-1}: 3410 (brs, NH), 3042 (CH aryl), 2916 (CH alkyl), 1686, (CO), 1640 (C=N), 1533 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.10 (brs, d, NH_2), 2.73–2.76 (t, 2H, CH_2), 2.80–2.98 (t, 2H, CH_2), 3.80 (brs, 1H, NH), 6.98–7.05 (d, 2H, p-sub-phenyl), 7.10–7.19 (d, 2H, p-sub-phenyl), 7.43–7.50 (d, 2H, p-sub-phenyl), 7.54–7.60 (d, 2H, p-sub-phenyl), 8.02 (s, 1H, methylenic protons), 12.00 (brs, NH). Analysis: $C_{23}H_{17}Cl_2N_5O$ (450.3); requires C, 61.34; H, 3.80; N, 15.55; found: C, 61.29; H, 3.75; N, 15.57.

*2-Hydrazino-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydro-cyclopent-enopyrido [2,3-*d*]pyrimidin-4(4*H*)-one (7d)*

The compound was obtained from **3b** (4.44 g, 10 mmol) as pale-yellow powder crystals and crystallized from dimethylformamide (87%), m.p. 292–295°C (melted); IR (Potassium bromide) cm^{-1}: 3395 (brs, NH), 3039 (CH aryl), 2918 (CH alkyl), 1689, (CO), 1646 (C=N), 1527 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.00 (brs, d, NH_2), 2.70–2.72 (t, 2H, CH_2), 2.80–2.98 (t, 2H, CH_2), 3.80 (brs, 1H, NH). 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 6.92–6.96 (d, 2H, p-sub-phenyl), 7.00–7.19 (d, 2H, p-sub-phenyl), 7.50–7.53 (d, 2H, p-sub-phenyl), 7.56–7.61 (d, 2H, p-sub-phenyl), 8.16 (s, 1H, methylenic protons), 11.50 (brs, NH). ^{13}C NMR (DMSO-d_6): δ 27.01, 27.95 (2C, $2CH_2$), 54.98, 55.17 (2C, $2OCH_3$) 108.47, 112.99, 113.08, 114.22, 124.38, 128.91, 129.56, 130.62, 130.73, 130.83, 132.96, 138.90, 148.23, 154.77, 158.33, 158.84 (16C, sp^2) and 163.93 (CO). Analysis: $C_{25}H_{23}N_5O_3$ (441.5); requires C, 68.01; H, 5.25; N, 15.86; found: C, 68.00; H, 5.23; N, 15.90.

2-Alkylthio-8-arylidine-5-aryl-,3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4 (4*H*)-ones (8a–g).

General Procedure

To a warmed ethanolic potassium hydroxide solution (prepared by dissolving 0.56 g, 10 mmol of potassium hydroxide in 50 mL ethanol) was added each of compound **3** (10 mmol); the heating was continued for 30 min, and the mixture was allowed to cool to r.t. the proper halo-compound (12 mmol) was added. The mixture was stirred under reflux for 5 h, cooled to r.t., and poured into cold water (100 mL). The solid product so-precipitated was filtered off washed with 100 mL water; the product was dried and crystallized from an appropriate solvent to produce (**8a–g**).

2-(Methylthio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-,3,6,7-trihydrocyclopentenopyrido[2,3-d]pyrimidin-4 (4H)-one (8a)

The compound was obtained from **3b** (4.44 g, 10 mmol) and methyliodide (1.72 g, 10 mmol) as pale yellow crystals and crystallized from dioxane (82%), m.p. 209–210°C (melted); IR (KBr) cm^{-1}: 3403 (brs, NH), 3036 (CH aryl), 2925 (CH alkyl), 1687, (CO), 1652 (C=N), 1526 (C=C); ^1H NMR (DMSO-d_6): δ 2.72–2.75 (t, 2H, CH_2), 2.88 (s, 3H, CH_3), 3.00–3.01 (t, 2H, CH_2), 3.80, 3.81 (2s, 6H, $2OCH_3$), 6.81–6.96 (d, 2H, p-sub-phenyl), 6.98–7.03 (d, 2H, p-sub-phenyl), 7.15–7.17 (d, 2H, p-sub-phenyl), 7.47–7.60 (d, 2H, p-sub-phenyl), 7.95 (s, 1H, methylenic proton) and 11.85 (brs, NH). Analysis: $C_{26}H_{23}N_3O_3S$ (457.5); requires C, 68.24; H, 5.06; N, 9.18; found: C, 68.21; H, 5.03; N, 9.20.

2-(Ethylthio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-,3,6,7-trihydrocyclopentenopyrido[2,3-d]pyrimidin-4(4H)-one (8b)

The compound was obtained from **3b** (4.44 g, 10 mmol) and ethyl iodide (1.86 g, 12 mmol) as orange crystals and crystallized from dioxane (90%), m.p. 241–244°C (melted); IR (KBr) cm^{-1}: 3385 (brs, NH), 3061 (CH aryl), 2908 (CH alkyl), 1679, (CO), 1635 (C=N), 1512 (C=C); ^1H NMR (DMSO-d_6): δ 1.35–1.38 (t, 3H, CH_3), 2.86–2.89 (t, 2H, CH_2), 2.93–3.08 (t, 2H, CH_2), 3.81, 3.87 (2s, 6H, $2OCH_3$), 4.43–4.49 (q, 2H, CH_2), 6.92–6.96 (d, 2H, p-sub-phenyl), 6.97–6.99 (d, 2H, p-sub-phenyl), 7.21–7.23 (d, 2H, p-sub-phenyl), 7.84–7.97 (d, 2H, p-sub-phenyl), 7.90 (s, 1H, methylenic proton) and 8.51 (brs, NH). Analysis: $C_{27}H_{25}N_3O_3S$ (471.5); requires C, 68.76; H, 5.34; N, 8.92; found: C, 68.67; H, 5.36; N, 8.76.

*2-[S-(N-p-Chlorophenylacetamido)]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydro-cyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*8c*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and 2-chloroacetanilide (1.69 g, 10 mmol) as yellow crystals and crystallized from dioxane (80%), m.p. 361–363°C (melted); IR (KBr) cm^{-1}: 3417 (brs, NH) 2999 (CH aryl), 2920 (CH alkyl), 1678 (CO), 1644 (CO), 1609 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.70–2.75 (t, 2H, CH_2), 2.95–3.05 (t, 2H, CH_2), 3.35 (s, 2H, CH_2), 3.75 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.95–7.05 (2d, 4H, p-sub-phenyl), 7.15–7.25 (d, 2H, p-sub-phenyl), 7.35–7.45 (d, 2H, p-sub-phenyl), 7.55–7.65 [m, 3H, (d, 2H, p-sub-phenyl + s, 1H, methylenic proton)], 7.75–7.85 (d, 2H, p-sub-phenyl), 11.25, 12.10 (2brs, 2NH, D_2O exchangeable). The MS: [M^+], m/z 611, (5%), [M^{+1}-Cl], m/z 577 (11%), [M^{+2}-$CONHC_6H_4Cl$], m/z 488 (22%), [M^{+1}-$CH_2CONHC_6H_4Cl$], m/z 473 (33%); Analysis: $C_{33}H_{27}ClN_4O_4S$ (611.1); requires C, 64.85; H, 4.45; N, 9.16; found: C, 64.83; H, 4.42; N, 9.18.

*8-(4-Chlorophenylmethylene)-5-(4-chlorophenyl)-2-(methylthio)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4 (4*H*)-one (*8d*)*

The compound was obtained from **3a** (4.52 g, 10 mmol) and methyliodide (1.72 g, 10 mmol) as yellow crystals and crystallized from dioxane (77%), m.p. 325–327°C (melted); IR (KBr) cm^{-1}: 3367 (brs, NH), 3059 (CH aryl), 2929 (CH alkyl), 1678, (CO), 1631 (C=N), 1541 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.42 (s, 3H, SCH_3), 2.65–2.75 (t, 2H, CH_2), 2.95–3.05 (t, 2H, CH_2), 7.25–7.35 (d, 2H, p-sub-phenyl), 7.43–7.48 (m, two doublets, 4H, p-sub-phenyl), 7.57–7.65 (d, 2H, p-sub-phenyl), 7.95 (s, 1H, methylenic proton), 11.50 (brs, NH, D_2O exchangeable). Analysis: $C_{24}H_{17}Cl_2N_3OS$ (466.4); requires C, 61.80; H, 3.67; N, 9.00; found: C, 61.76; H, 3.59; N, 9.02.

*8-(4-Chlorophenylmethylene)-5-(4-chlorophenyl)-2-(Ethylacetatethio)-3,6,7-trihydrocyclo-pentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*8e*)*

The compound was obtained from **3a** (4.52 g, 10 mmol) and ethylbromoacetate (2.00 g, 12 mmol) as yellow crystals and crystallized from dioxane (76%), m.p. 293–296°C (melted); IR (KBr) cm^{-1}: 3400 (brs, NH), 3067 (CH aryl), 2923 (CH alkyl), 1715, 1683, (2CO), 1661 (C=N), 1550 (C=C); ^{1}H NMR (DMSO-d_6): δ 1.26–1.30 (t, 3H, CH_3), 2.74–2.78 (t, 2H, CH_2), 3.05–3.06 (t, 2H, CH_2), 3.56 (s, 2H, CH_2), 4.13–4.22 (q, 2H, CH_2), 7.26–7.27 (d, 2H, p-sub-phenyl), 7.28–7.30 (d, 2H, p-sub-phenyl), 7.42–7.46 (d, 2H, p-sub-phenyl), 7.59–7.60 (d, 2H, p-sub-phenyl), 7.61 (s, 1H,

methylenic proton) and 12.39 (brs, NH); ^{13}C NMR (DMSO-d_6): δ 14.00 (1C, CH_3), 27.06, 28.04 (2C, $2CH_2$), 61.18 (1C, OCH_2), 66.41 (1C, SCH_2), 111.61, 124.45, 127.72, 128.66, 129.45, 130.83, 132.15, 132.40, 135.47, 136.55, 136.89, 141.88, 147.24, 158.56, 159.20, 159.27 (16C, SP^2) 164. 43, 168.17 (2C, 2CO). Analysis: $C_{27}H_{21}Cl_2N_3O_3S$ (538.4); requires C, 60.22; H, 3.93; N, 7.80; found: C, 60.19; H, 3.90; N, 7.74.

*2-(Acetylacetonethio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*8f*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and chloroacetylacetone (1.61 g, 12 mmol) as yellow crystals and crystallized from dioxane (90%), m.p. 217–218°C (melted); IR (KBr) cm^{-1}: 3410 (brs, NH), 3056 (CH aryl), 2918 (CH alkyl), 1716, 1710, 1671, (3CO), 1658 (C=N), 1541 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.76–2.79 (t, 2H, CH_2), 2.80–2.88 (t, 2H, CH_2), 3.03–3.06 (2s, 6H, 2 $COCH_3$), 3.87, 3.90 (2s, 6H, $2OCH_3$), 3.93 (s, 1H, CH), 6.92–6.95 (d, 2H, p-sub-phenyl), 7.00–7.15 (d, 2H, p-sub-phenyl), 7.26–7.30 (d, 2H, p-sub-phenyl), 7.51–7.53 (d, 2H, p-sub-phenyl), 7.90 (s, 1H, methylenic proton) and 12.26 (brs, NH); ^{13}C NMR (DMSO-d_6): δ 24.79, 25.18 (2C, $2CH_3$), 27.79, 28.50 (2C, $2CH_2$), 39.18 (1C, CH), 55.18, 55.37 (2C, $2OCH_3$), 110.77, 113.81, 128.14, 128.55, 128.78, 128.91, 130.10, 130.39, 131.30, 131.37, 137.32, 137.60, 148.71, 159.31, 159.71, 160.08 (16C, SP^2) 166.97, 199.00, 199.09 (3CO); the MS: [M^+], m/z 541, (100%), [M^+-$COCH_3$], m/z 498 (44%), [M^{+1}-$CH(COCH_3)$], m/z 443 (85%), [M^{+1}-$SCH(COCH_3)$], m/z 411 (19%). Analysis: $C_{30}H_{27}N_3O_5S$ (541.6); requires C, 66.52; H, 5.02; N, 7.75; found: C, 66.49; H, 5.07; N, 7.77.

*2-(Ethylacetatethio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*8g*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and ethylbromoacetate (2.00 g, 12 mmol) as pale yellow crystals and crystallized from dioxane (88%), m.p. 257–259°C (melted); IR (KBr) cm^{-1}: 3387 (brs, NH), 3054 (CH aryl), 2927 (CH alkyl), 1713, 1687, (2CO), 1656 (C=N), 1543 (C=C); ^{1}H NMR (DMSO-d_6): δ 1.27–1.30 (t, 3H, CH_3), 2.76–2.79 (t, 2H, CH_2), 3.03–3.06 (t, 2H, CH_2), 3.56 (s, 2H, CH_2), 3.80, 3.81 (2s, 6H, $2OCH_3$), 4.18–4.22 (q, 2H, CH_2), 6.92–6.95 (d, 2H, p-sub-phenyl), 7.00–7.15 (d, 2H, p-sub-phenyl), 7.16–7.18 (d, 2H, p-sub-phenyl), 7.52–7.55 (d, 2H, p-sub-phenyl), 7.57 (s, 1H, methylenic proton) and 12.26 (brs, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.00 (1C, CH_3), 27.29, 27.99 (2C, $2CH_2$), 55.13, 55.29 (2C, $2OCH_3$), 61.16 (1C, OCH_2), 66.42 (1C, SCH_2),

111.34, 111.36, 113.26, 114.39, 125.48, 129.02, 129.5, 130.24, 130.78, 136.42, 138.59, 148.23, 158.70, 159.20, 159.24, 159.27 (16C, SP^2) and 164.84, 168.23 (2CO). Analysis: $C_{29}H_{27}N_3O_5S$ (529.6); requires C, 65.76; H, 5.14; N, 7.93; found: C, 65.69; H, 5.10; N, 7.88.

2-(S-Acetone or/S-phenacyl)-8-(4-methoxyphenyl-methylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4 (4*H*)-ones (9a,b)

General Procedure

To a warmed ethanolic potassium hydroxide solution (prepared by dissolving 0.56 g, 10 mmol of potassium hydroxide in 50 mL ethanol) was added each of compound **3** (10 mmol). The heating was continued for 30 min, the mixture was allowed to cool to r.t., the propered haloketone (12 mmol) was added. The mixture was stirred under reflux for 5 h, cooled to r.t., and poured into cold water (100 mL). The solid product so-precipitated was filtered off and washed with 100 mL water. The product was dried and crystallized from an appropriate solvent to produce (**9a,b**).

*2-(S-Acetone)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido [2,3-*d*]pyrimidin-4(4*H*)-one (*9a*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and chloroacetone (1.12 g, 12 mmol) as yellow crystals and crystallized from ethanol (75%), m.p. 243–244°C (melted); IR (KBr) cm^{-1}: 3430 (brs, NH), 3059 (CH aryl), 2909 (CH alkyl), 1718, 1683, (2CO), 1651 (C=N), 1527 (C=C); ^1H NMR (DMSO-d_6): δ 1.85 (s, 3H, CH_3), 2.73–2.85 (t, 2H, CH_2), 3.00–3.12 (t, 2H, CH_2), 3.55 (brs, NH, H_2O overlaped, D_2O exchangeable), 3.80, 3.83 (2s, 6H, $2OCH_3$), 4.33 (s, 2H, CH_2), 6.95–7.05 (2d, 4H, p-sub-phenyl), 7.15–7.25 (d, 2H, p-sub phenyl), 7.55–7.63 [m, 3H (d, 2H, p-sub-phenyl + s, 1H, methylenic proton)]; the MS: [M^+], m/z 499, (22%), [M^+-H], m/z 498 (37%), [M^{+2}-OCH_3], m/z 466 (100%), [M^+-CH_2COCH_3], m/z 422 (66%), [M^+-SCH_2CO-CH_3], m/z 410 (28%). Analysis: $C_{28}H_{25}N_3O_4S$ (499.5); requires C, 67.31, H, 5.04; N, 8.41; found; C, 67.28; H, 5.02; N, 8.50.

*2-(S-Phenacyl)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*9b*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and phenacylbromide (1.99 g, 10 mmol) as pale yellow crystals and crystallized from

ethanol/dioxae (1:1) (78%), m.p. 227–228°C (melted); IR (KBr) cm^{-1}: 3437 (brs, NH), 3078 (CH aryl), 2923 (CH alkyl), 1721, 1689, (2CO), 1647 (C=N), 1514 (C=C); ^1H NMR (DMSO-d_6): δ 2.75–2.85 (t, 2H, CH_2), 3.00–3.15 (t, 2H, CH_2), 3.80, 3.90 (2s, 6H, $2OCH_3$), 5.00 (s, 2H, CH_2), 6.95–7.05 (2d, 4H, p-sub-phenyl), 7.15–7.25 (d, 2H, p-sub phenyl), 7.45–7.75 (m, 5H [4H, phenyl + s, 1H, methylenic proton]), 8.10–8.15 (d, 2H, p-sub-phenyl), 12.51 (brs, NH, D_2O exchangeable); the MS: [M^+], m/z 561, (31%), [M^{+1}-OCH_3], m/z 529 (100%), [M^+-COC_6H_5], m/z 456 (15%), [M^+-$CH_2COC_6H_5$], m/z 442 (19%), [M^+-SCH_2CO-C_6H_5], m/z 410 (20%). Analysis: $C_{33}H_{27}N_3O_4S$ (561.6); requires C, 70.56; H, 4.84; N, 7.48; found: C, 70.47; H, 4.83; N, 7.50.

3-(Methyl/or phenyl)-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-1,2-dihydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*]pyrimidin-5-ones (10a,b)

General Procedure

A solution of compound **9a,b** (10 mmol) in glacial acetic acid (40 mL) and a catalytic amount of sulphuric acid (1 mL) was stirred under reflux for 8 h. The reaction mixture was allowed to cool, poured into cold water (100 mL), and neutralized by ammonia solution. The solid so-precipitated was filtered off, washed with water, dried, and crystallized from an appropriate solvent to produce (**10a,b**).

*3-Methyl-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-1,2-dihydrl-5*H*-thiazolo-[4,5-a]cyclopentenopyrido[2,3-*d*]pyrimidine-5-diones (*10a*)*

The compound was obtained from **9a** (4.99 g, 10 mmol) as yellow crystals and crystallized from dimethylformamide (78%), m.p. 287–289°C (melted); IR (KBr) cm^{-1}: 3066 (CH aryl), 2907 (CH alkyl), 1691 (CO), 1650 (C=N), 1533 (C=C); ^1H NMR (DMSO-d_6) ppm: δ ^1H NMR (DMSO-d_6): δ 2.21 (s, 3H, CH_3), 2.75–2.84 (t, 2H, CH_2), 3.05–3.15 (t, 2H, CH_2), 3.80, 3.82 (2s, 6H, $2OCH_3$), 6.95–7.05 (2d, 4H, p-sub-phenyl), 7.10–7.20 (d, 2H, p-sub phenyl), 7.55–7.65 [m,3H (d, 2H, p-sub-phenyl + s, 1H, methylenic proton)], 7.87 (s, 1H, thiazole proton). ^{13}C NMR (DMSO-d_6): δ 23.09 (1C, CH_3), 27.29, 30.03 (2C, $2CH_2$), 55.13, 55.29 (2C, $2OCH_3$), 111.21, 112.36, 113.96, 114.79, 125.48, 127.86, 129.02, 129.5, 130.24, 130.78, 132.43, 136.42, 138.99, 148.53, 158.70, 159.20, 159.24, 159.27 (18C, SP^2 with four symmetric carbon) and 164.84 (1C, CO). The MS: [M^+], m/z 481, (100%), [M^+-CH_3], m/z 466 (85%). Analysis: $C_{28}H_{23}N_3O_3S$ (481.5); requires C, 69.83; H, 4.81; N, 8.72; found: C, 69.84; H, 4.76; N, 8.75.

*9-(4-Methoxyphenylmethylene)-6-(4-methoxyphenyl)-3-phenyl-1,2-dihydro-5*H*-thiazolo-[4,5-a]cyclopentenopyrido[2,3-*d*]pyrimidine-5-diones (*10b*)*

The compound was obtained from 9b (5.61 g, 10 mmol) as yellow crystals and crystallized from dimethylformamide (78%), m.p. 301–303°C (melted); IR (KBr) cm^{-1}: 3054 (CH aryl), 2918 (CH alkyl), 1693, (CO), 1647 (C=N), 1524 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.73–2.85 (t, 2H, CH_2), 3.00–3.15 (t, 2H, CH_2), 3.80, 3.84 (2s, 6H, $2OCH_3$), 6.95–7.05 (2d, 4H, p-sub-phenyl), 7.17–7.26 (d, 2H, p-sub phenyl), 7.46–7.80 [m, 6H (5H, phenyl + s, 1H, thiazole proton)], 7.88 (s, 1H, methylenic proton), 8.05–8.10 (d, 2H, p-sub-phenyl); the MS: [M^+], m/z 543, (100%), [M^+-C_6H_5], m/z 466 (100%). Analysis: $C_{33}H_{25}N_3O_3S$ (543.6); requires C, 72.90; H, 4.63; N, 7.72; found: C, 72.78; H, 4.60; N, 7.80.

2-[S-(Acetonyl-1-(4-chlorophenylazo)]-8-(4-arylmethylene)-5-(4-aryl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-4-ones (12a,b)

General Procedure

A suspention of compound **3** (10 mmol) and 1-*p*-chlorophenylazo-1-chloroacetone (2.31 g, 10 mmol) in (30 mL) dry chloroform was stirred under reflux for 5 h. The deposited so-precipitated was filtered off, washed with 30 mL chloroform, dried, and crystallized from an appropriate solvent to produce (**12a,b**) in high yields.

*2-[S-(Acetonyl-1-p-chlorophenylazo)]-8-(4-chlorophenylmethylene)-5-(4-chlorophenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*12a*)*

The compound was obtained from **3a** (4.52 g, 10 mmol) and 1-p-chlorophenylazo-1-chloroacetone (1.96 g, 10 mmol) as pale brown crystals and crystallized from dioxane (65%), m.p. 351–353°C (melted); IR (KBr) cm^{-1}: 3450 (brs, NH), 3039 (CH aryl), 2916 (CH alkyl), 1734, 1683, (2CO), 1659 (C=N), 1523 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.71–2.74 (t, 2H, CH_2), 3.02–3.07 (t, 2H, CH_2), 3.56 (s, 3H, $COCH_3$), 7.26–7.29 [m, 3H, (d, 2H, p-sub-phenyl + s, 1H, methylene proton)], 7.30–7.40 (2d, 4H, p-sub-phenyl), 7.39–7.44 (d, 2H, p-sub-phenyl), 7.50–7.53 (2d, 4H, p-sub-phenyl), 7.55 (s, 1H, methlyenic proton), 11.87 (brs, NH); ^{13}C NMR (DMSO-d_6): δ 26.97, 28.06 (2C, $2CH_2$), 29.04 (1C, CH_3), 66.46 (1C, CH), 108.48, 125.05, 127.80, 128.56, 128.64, 128.77, 129.32, 129.51, 129.65, 130.79, 132.61, 132.68, 135.27, 135.64, 135.89, 141.59, 147.93, 148.32, 152.77, 158.68 (20C, SP^2) and 163.89, 175.20 (2CO). Analysis:

$C_{32}H_{22}Cl_3N_5O_2S$ (646.9); requires C, 59.40; H, 3.42; N, 10.82; found: C, 59.41; H, 3.39; N, 10.78.

*2-[S-(Acetonyl-1-p-chlorophenylazo)]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (12b)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and 1-p-chlorophenylazo-1-chloroacetone (1.96 g, 10 mmol) as pale yellow crystals and crystallized from dimethylformamide (55%), m.p. 160–162°C (melted); IR (KBr) cm^{-1}: 3430 (brs, NH), 3039 (CH aryl), 2909 (CH alkyl), 1731, 1679, (2CO), 1653 (C=N), 1539 (C=C); ^1H NMR (DMSO-d_6): δ 2.61–2.74 (S, 3H, CH_3), 2.76–2.80 (t, 2H, CH_2), 2.81–2.88 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 6.97–7.01 [m, 3H, (d, 2H, p-sub-phenyl + s, 1H, CH)], 7.20–7.22 (d, 2H, p-sub-phenyl), 7.40–7.43 (d, 2H, p-sub-phenyl), 7.54–7.56 (d, 2H, p-sub-phenyl), 7.67 (s, 1H, methylenic proton), 7.68–7.70 (d, 2H, p-sub-phenyl), 8.25–8.27 (d, 2H, p-sub-phenyl), 11.56 (brs, NH). Analysis: $C_{34}H_{28}ClN_5O_4S$ (638.1); requires C, 63.99; H, 4.42; N, 10.97; found: C, 63.89; H, 4.39; N, 11.04.

2-[S-(Ethylcarboxylate-1-phenylazo)]-8-(4-arylmethylene)-5-(4-aryl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)ones (13a,b)

General Procedure

Suspension of compound **3** (10 mmol) and 1-phenylazo-1-chloroethylacetate (2.27 g, 10 mmol) in (30 mL) dry chloroform was stirred under reflux for 5 h. The deposited so-precipitated was filtered off, washed with 30 mL chloroform, dried, and crystallized from an appropriate solvent to produce (**13a,b**) in high yields.

*2-[S-(Ethylcarboxylate-1-phenylazo)]-8-(4-chlorophenylmethylene)-5-(4-chlorophenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (13a)*

The compound was obtained fom **3a** (4.52 g, 10 mmol) and 1-phenylazo-1-chloroethylacetate (2.27 g, 10 mmol) as pale brown crystals and crystallized from dioxane (58%), m.p. 328–330°C (melted); IR (KBr) cm^{-1}: 3412 (brs, NH), 3047 (CH aryl), 2930 (CH alkyl), 1730, 1674, (2CO), 1638 (C=N), 1561 (C=C); ^1H NMR (DMSO-d_6): δ 1.27–1.30 (t, 3H, CH_3), 2.76–2.79 (t, 2H, CH_2), 3.02–3.06 (t, 2H, CH_2), 4.18–4.20 (q, 2H, CH_2), 4.22 (s, 1H, CH), 6.93–6.95 (d, 2H, p-sub-phenyl), 6.98–7.00 (d, 2H, p-sub-phenyl), 7.15–7.17 (d, 2H, p-sub-phenyl), 7.52–7.55 (d, 2H, p-sub-phenyl), 7.57 (s, 1H, methylenic proton) and 12.26 (brs, NH).

Analysis: $C_{33}H_{25}Cl_2N_5O_3S$ (642.5); requires C, 61.68; H, 3.92; N, 10.90; found: C, 61.53; H, 3.88; N, 10.83.

*2-[S-(Ethylcarboxylate-1-phenylazo)]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (*13b*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and 1-phenylazo-1-chloroethylacetate (2.27 g, 10 mmol) as yellow crystals and crystallized from ethanol/dimethylformamide (20/10 mL) (61%), m.p. 231–233°C (melted); IR (KBr) cm^{-1}: 3425 (brs, NH), 3053 (CH aryl), 2931 (CH alkyl), 1724, 1681, (2CO), 1658 (C=N), 1527 (C=C); ^{1}H NMR (DMSO-d_6): δ 1.28–1.31 (t, 3H, CH_3), 2.78–2.81 (t, 2H, CH_2), 3.03–3.04 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 4.38–4.43 (q, 2H, CH_2), 6.97–6.99 [m, 3H, (s, CH + d, 2H, p-sub-phenyl)], 7.21–7.23 (d, 2H, p-subphenyl), 7.44–7.46 (m, 3H, phenyl), 7.54–7.57 (d, 2H, p-subphenyl), 7.60–7.66 (m, 4H, phenyl), 8.20 (s, 1H, methylenic proton), 10.55 (brs, NH, D_2O exchangeable). ^{13}C NMR (DMSO-d_6): δ 13.61 (1C, CH_3), 27.15, 28.11 (2C, $2CH_2$), 55.25, 55.37 (2C, $2OCH_3$), 63.30 (1C, OCH_2), 66.48 (1C, CH), 107.19, 113.61, 114.49, 120.99, 126.59, 127.29, 129.04, 129.29, 129.55, 130.26, 131.00, 134.76, 135.55, 136.67, 138.59, 148.93, 154.91, 156.30, 159.00, 159.44 (20C, SP^2) and 160.49, 166.45 (2C, 2CO). Analysis: $C_{35}H_{31}N_5O_5S$ (633.7); requires C, 66.33; H, 4.93; N, 11.05; found: C, 66.28; H, 4.86; N, 11.02.

9-(4-Arylmethylene)-1,6-diaryl-3-substituted-7,8-trihydro-5*H*-cyclopentenopyrido-[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidin-5-ones (14a–c)

General Procedure

A mixture from compound **3** (10 mmol) and the appropriate hydrazonoyl chlorides **11** (10 mmol) was stirred under reflux in dry chloroform (30 mL) and 4 drops of triethylamine for 5 h. The solvent was evaporated under reduced pressure. The solid produced was washed by 30 mL methanol and crystallized to produce (**14a–c**) in a high yield.

*N1,3-Diphenyl-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-3,7,8-trihydro-5*H*-cyclopentenopyrido[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidin-5-one (*14a*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and N-phenylbenzene-carbo-hydrazonoyl chloride **11a** (2.31 g, 10 mmol) as yellow crystals and crystallized from dioxane (78%), m.p. 310–313°C (melted); IR (KBr) cm^{-1}: 3056 (CH aryl), 2921 (CH alkyl), 1702 (CO), 1626 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.77–2.79 (t, 2H, CH_2),

3.04–3.05 (t, 2H, CH_2), 3.80, 3.81 (2s, 6H, $2OCH_3$), 6.93–6.95 (d, 2H, p-sub-phenyl), 6.99–7.01 (d, 2H, p-sub-phenyl), 7.20–7.22 (d, 2H, p-sub-phenyl), 7.40–7.48 (m, 5H, phenyl), 7.56–7.68 (m, 3H, phenyl), 7.70–7.72 [m, 3H, (2H, phenyl + 1H methylenic proton)], 8.29-8.31 (d, 2H, p-sub-phenyl). ^{13}C NMR (DMSO-d_6): δ 27.23, 28.18 (2C, $2CH_2$), 55.45, 55.51 (2C, $2OCH_3$), 107.42, 113.68, 114.59, 120.79, 126.31, 126.68, 126.73, 127.62, 128.93, 129.19, 129.77, 130.07, 130.27, 130.88, 130.94, 134.35, 137.26, 138.86, 144.41, 147.02, 149.18, 156.24, 158.90, 159.49, 160.45 (25C, SP^2) 166.20 (CO). Analysis: $C_{38}H_{29}N_5O_3$ (603.6); requires C, 75.60; H, 4.84; N, 11.60; found: C, 75.56; H, 4.73; N, 11.57.

*3-Acetyl-N1-(4-chlorophenyl)-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-3,7,8-trihydro-5*H*-cyclopenteno-pyrido[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidin-5-one (*14b*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and 2-oxo-N-(4-chlorophenyl)-propane hydrazonoyl chloride **11b** (1.96 g, 10 mmol) as yellow powder and crystallized from ethanol/dimethylformamide (20/10 mL) (72%), m.p. 224–226°C (melted); IR (KBr) cm^{-1}: 2998 (CH aryl), 2924 (CH alkyl), 1749 (CO), 1696 (CO), 1668 (C=N); ^{1}H NMR (DMSO-d_6): δ 2.60–2.73 (S, 3H, CH_3), 2.77–2.79 (t, 2H, CH_2), 2.80–2.88 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 6.97–7.01 (2d, 4H, p-sub-phenyl), 7.21–7.23 (d, 2H, p-sub-phenyl), 7.55–7.57 (d, 2H, p-sub-phenyl),7.67 (s, 1H methylenic proton), 7.68–7.70 (d, 2H, p-sub-phenyl), 8.25–8.28 (d, 2H, p-sub-phenyl). ^{13}C NMR (DMSO-d_6): δ 27.11, 28.06 (2C, $2CH_2$), 29.40 (1C, CH_3), 55.14, 55.30 (2C, $2OCH_3$), 107.37, 113.50, 114.41, 122.08, 126.48, 128.94, 129.33, 129.38, 130.14, 130.99, 131.39, 134.93, 135.49, 138.47, 141.47, 146.21, 148.93, 155.06, 158.85, 159.34, 160.15 (21C, SP^2) and 166.32, 187.02 (2CO). The MS: [M^+], m/z 604 (66%), [M^++1], m/z 605 (31%), [M^+-H], m/z 603 (47%), [M^+-2H], m/z 602 (100%), [M^+-$COCH_3$], m/z 561 (20%). Analysis: $C_{34}H_{26}ClN_5O_4$ (604.0); requires C, 67.60; H, 4.34; N, 11.59; found: C, 67.52; H, 4.36; N, 11.61.

*3-Ethylacetate-N1-(4-tolyl)-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-3,7,8-trihydro-5*H*-cyclopentenopyrido[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidin-5-one (*14c*)*

The compound was obtained from **3b** (4.44 g, 10 mmol) and chloro(4-tolylhydrazono) ethylacetate **11f** (2.41 g, 10 mmol) as white crystals and crystallized from dimethylformamide (83%), m.p. 272–274°C (melted); IR (KBr) cm^{-1}: 3036 (CH aryl), 2920 (CH alkyl), 1747 (CO), 1700 (CO), 1619 (C=N); ^{1}H NMR ($CDCl_3$): δ 1.35–1.38 (t, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.86–2.93 (t, 2H, CH_2), 3.08–3.09 (t, 2H, CH_2), 3.83, 3.87 (2s, 6H, $2OCH_3$), 4.43–4.49 (q, 2H, OCH_2), 6.92–6.94 (d, 2H, p-sub-phenyl), 6.97–6.99 (d, 2H, p-sub-phenyl), 7.23–7.25 (d, 2H, p-sub-phenyl),

7.32–7.34 (d, 2H, p-sub-phenyl), 7.53–7.55 (d, 2H, p-sub-phenyl), 7.89 (s, 1H, methylenic proton), 8.12–8.14 (d, 2H, p-sub-phenyl); ^{13}C NMR ($CDCl_3$): δ 13.88, 21.13 (2C, $2CH_3$), 27.64, 28.59 (2C, $2CH_2$), 55.23, 55.34 (2C, $2OCH_3$), 63.65 (1C, OCH_2), 107.15, 113.77, 114.23, 121.20, 128.50, 128.91, 129.90, 129.96, 130.27, 131.36, 134.24, 135.51, 135.61, 137.45, 137.85, 145.80, 149.57, 155.17, 156.48, 159.30, 159.61 (21C, SP^2) and 160.97, 167.77 (2CO). The MS: [M^+], m/z 613 (72%), [M^++1], m/z 614 (10%), [M^+-H], m/z 612 (100%), [M^+-$COOC_2H_5$], m/z 540 (50%). Analysis: $C_{36}H_{31}N_5O_5$ (613.6); requires C, 70.45; H, 5.09; N, 11.41; found: C, 70.47; H, 5.11; N, 11.50.

3-Alkyl-2-methylthio-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-6,7-dihydro-cyclopentenopyrido[2,3-d]pyrimidin-4 (4*H*)-ones (15a,b)

General Procedure

To a warmed ethanolic sodium ethoxide solution (prepared by dissolving [0.23 g, 10 mmol] sodium metal in 30 mL absolute ethanol) was added each of compound **8a** (10 mmol). Heating was continued for 30 min, the mixture was allowed to cool to r.t., and the proper alkyliodide (12 mmol) was added. The mixture was stirred under reflux for 3 h, cooled to r.t., and poured into cold water (100 mL). The solid so-precipitated was filtered off, washed with water, and dried to produces **15a,b** in high yields.

2-Methylthio-3-methyl-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-6,7-dihydro-cyclopentenopyrido[2,3-d]pyrimidin-4(4H)-one (15a)

The compound was obtained from **8a** (4.57 g, 10 mmol) and methyliodode (1.72 g, 12 mmol) as red crystals and crystallized from benzene (85%), m.p. 295–296°C (melted); IR (KBr) cm^{-1}: 3066 (CH aryl), 2931 (CH alkyl), 1653 (C=N), 1545 (C=C); ^{1}H NMR ($CDCl_3$): δ 2.71 (s, 3H, SCH_3), 2.75–2.78 (t, 2H, CH_2), 2.97–3.18 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 4.27 (s, 3H, N-CH_3), 6.94–6.99 (d, 2H, p-sub-phenyl), 7.00–7.15 (d, 2H, p-sub-phenyl), 7.20–7.22 (d, 2H, p-sub-phenyl), 7.50–7.53 (d, 2H, p-sub-phenyl) and 7.68 (s, 1H, methylenic proton); ^{13}C NMR ($CDCl_3$): δ 14.73 (1C, SCH_3), 27.45, 27.94 (2C, $2CH_2$), 30.04 (1C, N-CH_3), 55.23, 55.27 (2C, $2OCH_3$), 113.17, 113.23, 114.30, 114.33, 125.23, 128.86, 128.96, 129.12, 129.73, 130.67, 131.08, 138.29, 149.12, 151.88, 158.22, 158.80 (16C, SP^2 carbon atoms) and 163.25 (CO). The MS: [M^+], m/z 471, (56%), [M^{+1}-H], m/z 470 (100%), [M^+-CH_3], m/z 456 (12%), [M^+-SCH_3], m/z 424 (5%). Analysis: $C_{27}H_{25}N_3O_3S$ (471.5); requires C, 68.76; H, 5.34; N, 8.91; found: C, 68.71; H, 5.32; N, 8.76.

3-Ethyl-2-methylthio-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-6,7-dihydrocyclo-pentenopyrido[2,3-d]pyrimidin-4 (4H)-one (15b)

The compound was obtained from **8a** (4.57 g, 10 mmol) and ethyliodode (1.86 g, 12 mmol) as yellow powder and crystallized from dioxane (73%), m.p. 302–305°C (melted); IR (KBr) cm^{-1}: 3043 (CH aryl), 2921 (CH alkyl), 1650 (C=N), 1527 (C=C); ^1H NMR ($CDCl_3$): δ 1.28–1.31 (t, 3H, CH_3), 2.78–2.80 (t, 2H, CH_2), 2.96 (s, 3H, SCH_3), 3.00–3.04 (t, 2H, CH_2), 3.80, 3.83 (2s, 6H, $2OCH_3$), 4.38–4.43 (q, 2H, N-CH_2), 6.97–7.00 (d, 2H, p-sub-phenyl), 7.21–7.23 (d, 2H, p-sub-phenyl), 7.44–7.46 (d, 2H, p-sub-phenyl), 7.54–7.57 (d, 2H, p-sub-phenyl) and 8.18 (s, 1H, methylenic proton). Analysis: $C_{28}H_{27}N_3O_3S$ (485.5); requires C, 69.25; H, 5.60; N, 8.65; found: C, 69.18; H, 5.58; N, 8.70.

5-(4-Chlorophenyl)-2-methyl-sulphone-8-(4-chlorophenyl-methylene)-3,6,7-trihydro-cyclopentenopyrido[2,3-*d*]pyrimidin-4 (4*H*)-one (16)

A mixture of compound **8d** (4.66 g, 10 mmol) and an excess amount of hydrogen peroxide (5 mL) in acetic acid (30 mL) was heated gently with stirring for 10 h. The reaction mixture was allowed to cool to 0°C. The deposited precipitate was filtered off and crystallized from dioxane (67%), m.p. 327–328°C (dec.); IR (KBr) cm^1: 3405 (brs, NH), 3042 (CH aryl), 2906 (CH alkyl), 1643 (C=N), 1539 (C=C), 1167, 1342 (SO_2); ^1H NMR (DMSO-d_6): δ 2.67–2.75 (t, 2H, CH_2), 2.97–3.03 (t, 2H, CH_2), 3.30 (s, 3H, SCH_3), 7.21–7.30 (d, 2H, p-sub-phenyl), 7.41–7.47 (2d, 4H, p-sub-phenyl), 7.55–7.60 (d, 2H, p-sub-phenyl), 8.60 (s, 1H, methylenic proton), 11.40 (brs, NH, D_2O exchangeable). The MS: [M^+], m/z 498 (34%), [M^{+1}-SO], m/z 449 (100%), [M^+-CH_3SO_2], m/z 419 (29%), [M^+-C_6H_4Cl]. Analysis: $C_{24}H_{17}Cl_2N_3O_3S$ (498.4); requires C, 57.83; H, 3.44; N, 8.43; found: C, 57.77; H, 3.38; N, 8.36.

5-(4-Aryl)-2-[8-(4-arylmethylene)-3,6,7-trihydrocyclopenteno-pyrido[2,3-*d*]pyrimidin-4(4*H*)-one-2-yl]thioacethydrazides (17a,b)

General Procedure

A mixture of compound **8e,g** (10 mmol) and 6 mL hydrazine hydrate (99–100%) in ethanol (30 mL) was stirred under reflux for 5 h. The reaction mixture was allowed to cool to 0°C, and the deposited precipitate was filtered off, dried, and crystallized. The solid so-precipitated was filtered off and dried to produce **17a,b** in high yields.

*2-[8-(4-Chlorophenylmethylene)-5-(4-chlorophenyl)-3,6,7-trihydrocyclopentenopyrido-[2,3-*d*]pyrimidin-4(4*H*)-one-2-yl]thioacethydrazide (*17a*)*

The compound was obtained from **8e** (5.39 g, 10 mmol) as yellow powder and crystallized from dimethylformamide (63%), m.p. 233–236°C (melted); IR (KBr) cm^{-1}: 3400 (brs, NH), 3035 (CH aryl), 2918 (CH alkyl), 1689, 1675 (2CO), 1632 (C=N), 1521 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.43 (brs, 2NH, D_2O exchangeable), 2.67–2.68 (t, 2H, CH_2), 2.70–2.73 (t, 2H, CH_2), 2.88 (s, 2H, CH_2), 7.21–7.23 (d, 2H, p-sub-phenyl), 7.39–7.41 (d, 2H, p-sub-phenyl), 7.43–7.45 (d, 2H, p-sub-phenyl), 7.52–7.57 (d, 2H, p-sub-phenyl), 8.15 (s, 1H, methylenic proton), 11.60 (brs, NH), 12.20 (brs, NH, D_2O exchangeable); ^{13}C NMR(DMSO-d_6): 26.86, 28.10, 35.68 (3C, $3CH_2$), 108.99, 123.50, 127.60, 127.78, 128.61, 128.76, 129.43, 129.51, 130.67, 130.78, 131.90, 132.14, 135.82, 137.61, 142.39, 155.01 (16C, SP^2) and 162.25, 175.27 (2CO). Analysis: $C_{25}H_{19}Cl_2N_5O_2S$ (524.4); requires C, 57.25; H, 3.65; N, 13.35; found: C, 57.18; H, 3.63; N, 13.57.

*2-[8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido-[2,3-*d*]pyrimidin-4(4*H*)-one-2-yl]thioacethydrazide (*17b*)*

The compound was obtained from **8g** (5.29 g, 10 mmol) as brown powder and crystallized from dimethylformamide (78%), m.p. 278–280°C (melted); IR (KBr) cm^{-1}: 3395 (brs, NH), 3056 (CH aryl), 2912 (CH alkyl), 1688, 1679 (2CO), 1629 (C=N), 1520 (C=C); ^{1}H NMR ($CDCl_3$): δ 2.39–2.41 (brs, 2NH, D_2O exchangeable) 2.66–2.68 (t, 2H, CH_2), 2.70–2.72 (t, 2H, CH_2), 2.89 (s, 2H, CH_2), 3.79, 3.81 (2s, 6H, $2OCH_3$), 7.20–7.22 (d, 2H, p-sub-phenyl), 7.39–7.42 (d, 2H, p-sub-phenyl), 7.43–7.46 (d, 2H, p-sub-phenyl), 7.51–7.56 (d, 2H, p-sub-phenyl), 8.12 (s, 1H, methylenic proton), 11.68 (brs, NH, D_2O exchangeable), 12.15 (brs, NH, D_2O exchangeable). Analysis: $C_{27}H_{25}N_5O_4S$ (515.5); requires C, 62.89; H, 4.88; N, 13.58; found: C, 62.86; H, 4.79; N, 13.60.

2-(3,5-Dimethyl-1*H* or sub-phenyl-pyrazol-4-ylthio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (18a,b)

General Procedure

A mixture of compound **8f** (5.41 g, 10 mmol) and hydrazine hydrate (99–100%) or 2,4,6-trichlorophenyl hydrazine (10 mmol) in dioxane

(20 mL) and ethanol (10 mL) was stirred under reflux for 12 h. The reaction mixture was allowed to cool to r.t. and poured into cold water (100 mL). The deposited precipitate was filtered off, dried, and cyrstallized from an appropriate solvent to produce (**18a,b**) in high yields.

*2-[3,5-Dimethyl-1,2-dihydro-1*H*-pyrazol-4-ylthio]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (LXVIIIa)*

The compound was obtained from **8f** (5.41 g, 10 mmol) and hydrazine hydrate (99–100%) (6 mL) as pale yellow powder and crystallized from ethanol/dioxane (1:1) (82%), m.p. 282–285°C (melted); IR (KBr) cm^{-1}: 3400 (brs, NH), 3023 (CH aryl), 2929 (CH alkyl), 1687 (CO), 1653 (C=N), 1531 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.43 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.74–2.84 (t, 2H, CH_2), 3.01–3.05 (t, 2H, CH_2), 3.80, 3.81 (2s, 6H, $2OCH_3$), 6.93–6.98 (2d, 4H, p-sub-phenyl), 7.01–7.18 (d, 2H, p-sub-phenyl), 7.31–7.48 (d, 2H, p-sub-phenyl), 7.60 (s, 1H, methylenic proton), 11.34 (brs, NH), 12.10 (brs, NH). The MS: [M^+], m/z 537 (31%), [M^+-2H], m/z 535 (20%), [M^+-$C_5H_7N_2$], m/z 443 (100%). Analysis: $C_{30}H_{27}N_5O_3S$ (537.6); requires C, 67.01; H, 5.06; N, 13.03; found: C, 66.97; H, 5.03; N, 13.05.

*2-[3,5-Dimethyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazol-4-ylthio]-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4-(4*H*)-one (*18b*)*

The compound was obtained from **8f** (5.41 g, 10 mmol) and 2,4,6-trichlorophenyl-hydrazine (2.11 g, 10 mmol) as yellow crystals and crystallized from benzene (65%), m.p. 299–300°C (melted); IR (KBr) cm^{-1}: 3387 (brs, NH), 3029 (CH aryl), 2921 (CH alkyl), 1679 (CO), 1648 (C=N), 1524 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.45 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 2.79–2.82 (t, 2H, CH_2), 3.01–3.04 (t, 2H, CH_2), 3.80, 3.81 (2s, 6H, $2OCH_3$), 6.94–6.99 (2d, 4H, p-sub-phenyl), 7.01–7.19 (d, 2H, p-sub-phenyl), 7.34–7.50 [m, 4H, (2H, p-sub-phenyl + singlet 2H tri-sub-phenyl)], 7.62 (s, 1H, methylenic proton), 11.84 (brs, NH); ^{13}C NMR (DMSO-d_6): 27.43, 28.08 (2C, $2CH_2$), 30.23, 30.50 (2C, $2CH_3$), 55.20, 55.35 (2C, $2OCH_3$), 107.99, 113.34, 114.52, 120.46, 126.14, 128.46, 128.83, 129.14, 129.22, 130.21, 130.54, 130.80, 135.24, 138.24, 138.55, 142.04, 148.88, 152.34, 152.83, 158.07, 159.02, 159.41, 159.57 (23C, SP^2), 164.99 (1C, CO). Analysis: $C_{36}H_{28}Cl_3N_5O_3S$ (717.1); requires C, 60.29; H, 3.93; N, 9.76; found: C, 60.31; H, 3.87; N, 9.80.

2-(4,6-Dimethyl-2-thioxo-1,2-dihydropyrimidin-5-ylthio)-8-(4-methoxyphenylmethylene)-5-(4-methoxyphenyl)-3,6,7-trihydrocyclopentenopyrido[2,3-*d*]pyrimidin-4(4*H*)-one (19)

A mixture of compound **8f** (5.41 g, 10 mmol) and thiourea (0.76 g, 10 mmol) was stirred under reflux in dioxane (30 mL) in the presence of a catalytic amount of piperidine for 15 h. The reaction mixture was allowed to cool to r.t. and was poured into water (100 mL); the deposited precipitate was filtered off, washed with ethanol (30 mL), dried, and crystallized from dimethylformamide as yellow powder (61%), m.p. 190–193°C (melted); IR (KBr) cm^{-1}: 3415 (brs, NH), 3063 (CH aryl), 2927 (CH alkyl), 1681, (CO), 1652 (C=N), 1543 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.40 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.74–2.77 (t, 2H, CH_2), 3.01–3.03 (t, 2H, CH_2), 3.79, 3.81 (2s, 6H, $2OCH_3$), 6.91–6.97 (2d, 4H, p-sub-phenyl), 7.00–7.18 (d, 2H, p-sub-phenyl), 7.34–7.56 [m, 3H (d, 2H p-sub-phenyl + s, 1H methylenic proton)], 11.82, 12.23 (2brs, 2NH); ^{13}C NMR (DMSO-d_6): δ 23.91, 25.23 (2C, $2CH_3$), 27.23, 28.02 (2C, $2CH_2$), 55.09, 55.27 (2C, $2OCH_3$), 107.97, 113.34, 114.40, 114.49, 124.40, 125.58, 128.84, 128.91, 128.97, 129.03, 130.78, 130.82, 138.53, 139.12, 147.88, 152.34, 158.07, 159.22, 159.75 (19C, SP^2 carbon atoms), 164.99 (1C, CO), 172.11 (1C, CS). The MS: [M^+], m/z 581 (42%), [M^+-2H], m/z 579 (19%), [M^+-$C_6H_7N_2S$], m/z 443 (100%). Analysis: $C_{31}H_{27}N_5O_3S_2$ (581.7); requires C, 64.00; H, 4.68; N, 12.04; found: C, 63.97; H, 4.62; N, 12.10.

2-Acetyl-3-methyl-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-1,2,10,11-tetra-hydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*]pyrimidin-5-one (20)

A solution of compound **8f** (5.41 g, 10 mmol) in a mixture of acetic anhydride-pyridine (20:10) mL was stirred under reflux for 4 h. The reaction mixture was allowed to cool to r.t. and then was poured into cold water (100 mL). The deposited precipitate was filtered off, dried, and crystallized from benzene. The compound was obtained as yellow crystals (68%), m.p. 295–298°C (melted); IR (KBr) cm^1: 3076 (CH aryl), 2931 (CH alkyl), 1718 1690, (2CO), 1650 (C=N), 1542 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.46–2.48 (t, 2H, CH_2), 2.53 (s, 3H, CH_3), 2.79–2.82 (t, 2H, CH_2), 2.84 (s, 3H, CH_3), 3.80, 3.83 (2s, 6H, $2OCH_3$), 6.97–6.99 (2d, 4H, p-sub-phenyl), 7.01–7.21 (d, 2H, p-sub-phenyl), 7.23–7.53 (d, 2H, p-sub-phenyl), 7.57 (s, 1H, methylenic proton); ^{13}C NMR (DMSO-d_6): δ 16.23 (1C, CH_3), 27.43, 28.08 (2C, $2CH_2$), 30.50 (1C, CH_3), 55.23, 55.46 (2C, $2OCH_3$), 109.61, 113.74, 114.62, 120.46, 126.55, 128.88, 129.59, 130.65, 130.96, 136.19, 138.55, 142.04, 148.11, 158.11, 159.01, 159.40, 159.57,

160.37 (18C, SP^2), 165.99, 190.87 (2CO). The MS: [M^+], m/z 523, (47%), [M^+-H], m/z 522 (100%), [M^+-CH_3], m/z 508 (5%), [M^+-$COCH_3$], m/z 480 (15%). Analysis: $C_{30}H_{25}N_3O_4S$ (523.6); requires C, 68.81; H, 4.81; N, 8.02; found: C, 68.83; H, 4.76; N, 7.98.

2-(Acetoxime)-3-methyl-9-(4-methoxyphenylmethylene)-6-(4-methoxyphenyl)-1,2,10,11-tetrahydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*]pyrimidin-5-one (21)

A mixture of compound **20** (5.23 g, 10 mmol) and hydroxylamine hydrochloride (0.70 g, 10 mmol) in dioxane (30 mL) and a catalytic amount of piperidine were added. The reaction mixture was stirred under reflux for 15 h, allowed to cool to r.t., and poured into water (100 mL). The deposited precipitate was filtered off, dried, and crystallized from ethanol/dioxane (1:1) (52%), m.p. 216–219°C (melted.); IR (KBr) cm^{-1}: 3560 (brs, OH), 3060 (CH aryl), 2909 (CH alkyl), 1686, (CO), 1655 (C=N), 1537 (C=C); ^{1}H NMR (DMSO-d_6): δ 2.73–2.76 (t, 2H, CH_2), 3.02–3.05 (t, 2H, CH_2), 3.05 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 3.80, 3.82 (2s, 6H, 2OCH_3), 6.94–6.97 (d, 2H, p-sub-phenyl), 6.99–7.01 (d, 2H, p-sub-phenyl), 7.17–7.19 (d, 2H, p-sub-phenyl), 7.34–7.48 (d, 2H, p-sub-phenyl), 7.50 (s, 1H, methylenic proton) and 11.84 (brs, NH). Analysis: $C_{30}H_{26}N_4O_4S$ (538.6); requires: C, 66.89; H, 4.86; N, 10.40; found: C, 66.75; H, 4.83; N, 10.29.

2-(Acetothiosemicarbazone)-3-methyl-9-(4-methoxyphenylmethylene)-6-(4-methoxy-phenyl)-1,2,10,11-tetrahydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido-[2,3-*d*]pyrimidin-5-one (22)

A mixture of compound **20** (5.23 g, 10 mmol) and thiosemicarbazide (0.91 g, 10 mmol) in dioxane (30 mL) and a catalytic amount of piperidine were added. The reaction mixture was stirred under reflux for 12 h, allowed to cool to r.t., and poured into water (100 mL). The deposited so-precipitated was filtered off, dried, and crystallized from dioxane. The compound was obtained as green powder (48%), m.p. 220–223°C (dec.); IR (KBr) cm^{-1}: 3450 (brs, NH), 3091 (CH aryl), 2931 (CH alkyl), 1688, (CO), 1645 (C=N), 1519 (C=C); ^{1}H NMR (DMSO-d_6) ppm: δ 2.75–2.79 (t, 2H, CH_2), 3.01–3.05 (t, 2H, CH_2), 3.10 (s, 3H, CH_3), 3.59 (s, 3H, CH_3), 7.16–7.19 (d, 2H, p-sub-phenyl), 7.24–7.26 (d, 2H, p-sub-phenyl), 7.35–7.39 (d, 2H, p-sub-phenyl), 7.40–7.46 (d, 2H, p-sub-phenyl), 8.29 (s, 1H, methylenic proton), 10.82 (brs, NH) and 11.30 (brs, NH). Analysis: $C_{31}H_{28}N_6O_3S_2$ (596.7); requires C, 62.39; H, 4.73; N, 14.08; Found: C, 62.41; H, 4.68; N, 14.11.

2-Cinnamoyl-3-methyl-9-(4-methoxyphenyl-methylene)-6-(4-methoxyphenyl)-1,2,10,11-tetrahydro-5*H*-thiazolo[4,5-*a*]cyclopentenopyrido[2,3-*d*]pyrimidin-5-one (23)

A mixture of compound of **20** (5.23 g, 10 mmol) and 4-methoxybenzaldehyde (1.36 g, 10 mmol) and a catalytic amount of piperidine were heated at 170–180°C in a test tube for 3 h. The product was solidified by cooling and the addition of methanol (50 mL). The precipitate so-formed was collected by filtration and crystallized from dioxane as brown powder (54%), m.p. 288–290°C (dec.); IR (KBr) cm^{-1}: 3086 (CH aryl), 2937 (CH alkyl), 1705, 1683, (2CO), 1655 (C=N), 1524 (C=C). ^1H NMR (DMSO-d_6): δ 2.55 (s, 3H, CH_3), 2.83–2.8 (t, 2H, CH_2), 3.00–3.03 (t, 2H, CH_2), 3.76, 3.78, 3.80 (3s, 9H, $3OCH_3$), 5.28, 5.50 (2d, 2H, CH=CH), 6.93–6.96 (d, 2H, p-sub-phenyl), 7.18–7.23 (d, 2H, p-sub-phenyl), 7.25–7.31 (d, 2H, p-sub-phenyl), 7.43–7.46 (d, 2H, p-sub-phenyl) and 8.34 (s, 1H, methylenic proton). Analysis: $C_{38}H_{31}N_3O_5S$ (641.7); requires C, 71.12; H, 4.87; N, 6.54; found: C, 71.08; H, 4.89; N, 6.47.

CONCLUSION

The prepared new ring systems seem to be interesting for biological activity studies. Furthermore, the present investigation offers rapid and effective new procedures for the synthesis of polycondensed, new heterocyclic ring systems.

REFERENCES

[1] D. H. Boschelli, Z. Wu, S. R. Klutchko, H. D. H. Showalter, J. M. Hamby, G. H. Lu et al., *J. Med. Chem.*, **41,** 4365 (1998).
[2] M. Mohammadi, S. Frounm, J. M. Hamby, M. C. Schroeder, R. L. Panek, G. H. Lu, A. V. Eliseenkova, D. Green, J. Schlessinger, and S. R. Hubbard, *The EMBO Journal*, **17**(20), 5896–5904 (1998).
[3] G. E. Hardtmann, B. Huegi, G. Koletar, S. Kroin, H. Ott, J. W. Perrine et al., *J. Med. Chem.*, **17,** 636 (1974).
[4] G. Singh, A. K. Sharma, A. K. Mishra, and L. Prakash, *Phosphorus, Sulfur, and Silicon*, **133,** 83 (1998).
[5] E. Genazzani, E. De Nito, and E. De Marco, *Arch. Ital. Sci. Farmacol.*, **8,** 247 (1952); C.A., **50,** 2071i (1956).
[6] T. Nakajima, *Nippon Kakin. Gakkaishi*, **31,** 412 (1994); C.A., **122,** 104732*u* (1995).
[7] J. Binet and G. Defosse (Synthelabo S.A.) *Fr. DemandeFR 2,666,582 (Cl.CO7D40-114)13 Mar* (1992), *Appl. 90/11, 100,07 Sep* (1990); *C.A.*, **118,** 6986*c* (1993).
[8] A. B. A. El-Gazzar, A. E. M. Gaafar, H. N. Hafez, and A. S. Aly, *Phousphours, Sulphur, and Silicon,* **181,** 1 (2006).
[9] A. B. A. El-Gazzar, Kh. M. Abu-Zied, and N. Khir El-Din, *Heteroatom Chemistry*, **17** accepted, (2006).

[10] C. J. Shishoo and K. S. Jain, *J. Heterocycl. Chem.,* **29,** 883 (1992).
[11] J. Quiroga, B. Insuasty, A. Sanchez, M. Nogueras, and H. Meier, *J. Heterocyclic Chem.*, **29,** 1045 (1992), and references cited therein.
[12] A. B. A. El-Gazzar, A. E. M. Gaafar, and A. S. Aly, *Phousphours, Sulphur, and Silicon*, **177,** 45 (2002).