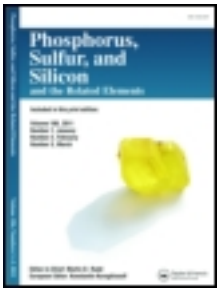

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Utility of a Pyrimidin-2-Thione Derivative in Synthesis of New Fused Thiazolo[3,2-a]pyrimidines

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Utility of a Pyrimidin-2-Thione Derivative in Synthesis of New Fused Thiazolo[3,2-a]pyrimidines

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A pyrimidin-2-thione derivative 2 was prepared and treated with 1,2-dibromoethane, chloroacetic acid and ethyl chloroacetate to give the alkylation products 3,4,9,5, respectively. Furthermore, the reaction of 2 with acrylonitrile and hydrazine hydrate yielded the pyrimidino[2,1-b]thiazine derivative 7, and [1,2,4]-triazolo[4,3-a]pyrimidine 8. Compound 9 was used as the key starting material for synthesis of thiazolo[3,2-a]pyrimidine and pyrano[2′,3′:4,5]thiazolo[3,2-a]pyrimidine derivatives 10–13, through the reaction with ethyl acetate, malononitrile, hydrazine hydrate, β-aroylacrylic acid, and chalcone, respectively. Treatment of compound 5 with 3,5-dibromo-2-aminobenzoic acid in refluxing butanol gave the 3,1-benzoxazinone derivative 6. The structure assignment of the new compounds is based on chemical and spectroscopic evidence.

Keywords Pyranothiazolopyrimidine; pyrimidines; thiazolopyrimidines; triazolopyrimidines

INTRODUCTION

Thiazolopyrimidines are of great importance in the field of medicinal chemistry for example as analgesics or due to their cerebral nervous system[1] or their antipurine activity.[2] The synthesis of thiazolopyrimidines has already been reported in the literature.[3–9] It can be achieved by two routes, firstly by initial formation of the pyrimidine ring followed by building the thiazole ring in the terminal step (azine approach),[10] or secondly by initial formation of the thiazole ring followed by building the pyrimidine ring in the terminal step (azole approach).[11] According to the first route, we used 6-(4-methylphenyl)-4-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydropyrimidin-2-thione **2**[12] as a precursor for the synthesis of thiazolopyrimidine derivatives.

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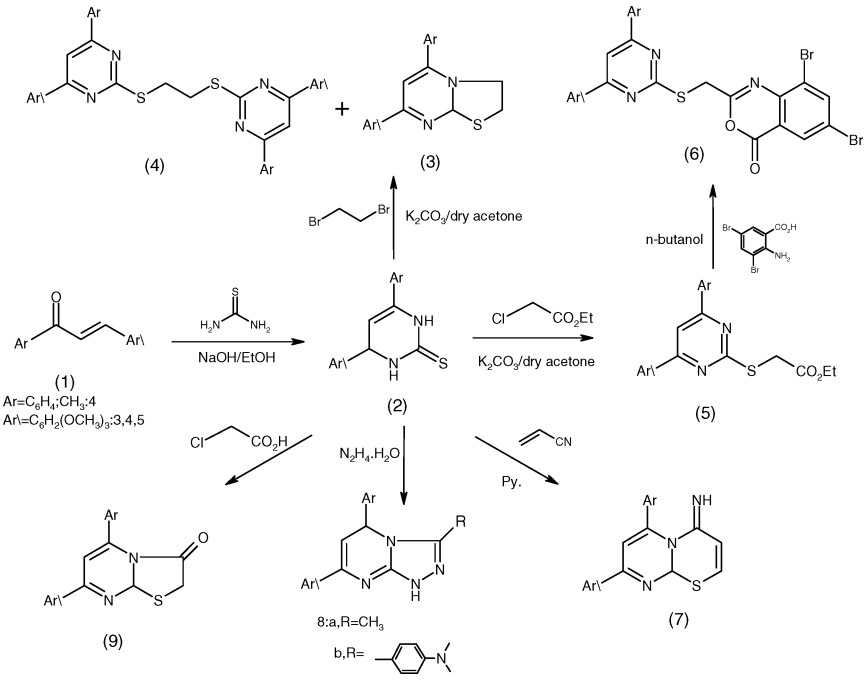
RESULTS AND DISCUSSION

The title compound **2** was prepared via the reaction of benzalacetophenone derivative **1** with thiourea in ethanolic potassium hydroxide according to a literature method.[13,14] Alkylation of **2** with 1,2-dibromoethane in the presence of anhydrous potassium carbonate in dry acetone gave a semisolid which when triturated with methanol gave two fractions, the soluble one (40%), which upon evaporation of solvent and purification, yielded 5-(4-methylphenyl)-7-(3,4,5-trimethoxyphenyl)tetrahydrothiazolo [3,2-a]pyrimidine **3** and the insoluble fraction (15%) which recrystallized to give bis-*s*-4-(4-methylphenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl]ethan-1,2-dithiol **4**. Treatment of **2** with ethyl chloroacetate in the presence of anhydrous potassium carbonate in dry acetone affords the S-alkylated product **5**. I.R spectrum of **5** displayed νC=O ester at 1728 cm^{-1} and νC=N at 1636 cm^{-1}. In order to get an additional chemical proof for structure **5**, compound **5** was allowed to react with 3,5-dibromoanthranlic acid in *n*-butanol and afforded the benzoxazinone derivative **6** (Scheme 1).



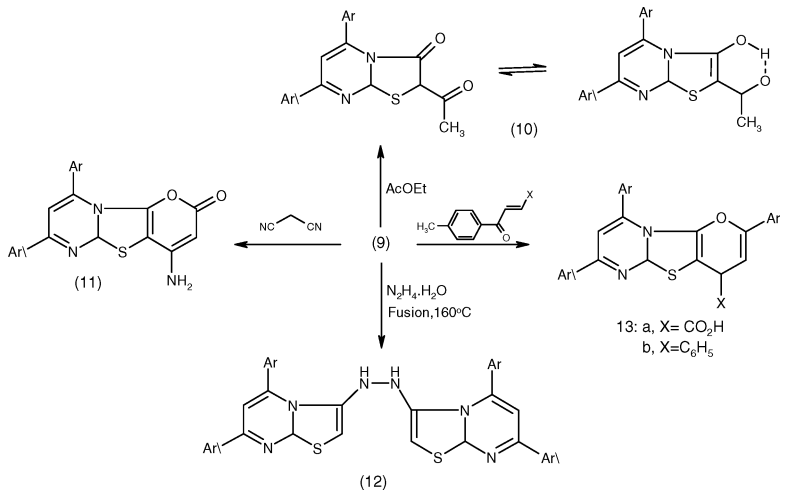
SCHEME 1

Cyanoethylation of **2** with acrylonitrile in boiling pyridine afforded pyrimidothiazine derivative **7** whose structure was confirmed by analytical and spectral data (c.f. Exp.). Moreover, on reacting **2** with hydrazine hydrate in boiling ethanol was recovered unchanged. When the reaction was repeated in boiling acetic acid yielded the triazolopyrimidine derivative **8a**. Moreover, the reaction of **2** with hydrazine hydrate in the presence of *p*-N,N-dimethylaminobenzaldehyde with drops of acetic acid afforded the triazolopyrimidine derivative **8b** (Scheme 1).

Furthermore, treatment of **2** with chloroacetic acid in the presence acetic acid/ acetic anhydride and anhydrous sodium acetate yielded thiazolopyrimidine derivative **9**, which neither dissolved nor showed evolution of CO_2 gas with aqueous sodium carbonate solution indicating the absence of carboxylic group but gave deep violet color with ethanolic ferric chloride and its I.R spectrum displayed νC=O at 1682 cm^{-1} and νC=N at 1628 cm^{-1} (c.f. Exp.).

The reactivity of methylene group in the 2-position for structure **9** has been investigated. Thus, the reaction of **9** with ethyl acetate in the presence of sodium ethoxide afforded the thiazolo[3,2-a]pyrimidine derivative **10**. I.R spectrum of **10,** displayed νC=O at 1662–1650 cm^{-1} and νOH at 3400 cm^{-1} (br.) due to intramolecular hydrogen bond system of the conjugated chelate (Scheme 2).

Furthermore, treatment of **9** with malononitrile in the presence of catalytic amount of piperidine afforded pyrano[2′,3′:4,5]thiazolo[3,2-a]pyrimidine derivative **11**, whose I.R spectrum displayed only νC=O



SCHEME 2

of unsaturated δ-lactone at 1742 $cm^{-1}$and νNH_2 at 3436, 3390, 3280 cm^{-1} and lack the $\nu C{\equiv}N$ (c.f. Exp.).

Fusion of **9** with hydrazine hydrate in an oil-bath for 2 h at 160°C yielded a compound of M.F. $C_{44}H_{44}N_6O_6S_2$ which identified as bis-[5-(4-methylphenyl)-7-(3,4,5-trimethoxyphenyl)dihydrothiazolo[3,2-a] pyrimidin-3-yl]hydrazine **12**, its I.R spectrum displayed νNH at 3314, 3238 cm^{-1} and $\nu C{=}N$ at 1630 $cm^{-1}$and lack $\nu C{=}O$.

However, the base-catalyzed addition C-2 active methylene group of **9** to β-p-tolylacrylic acid and/or benzal-*p*-methylacetophenone in the presence of sodium ethoxide and ethanol yielded the corresponding Michael adducts followed by subsequent cyclization to give **13a**,**b**, respectively (Scheme 2).

EXPERIMENTAL

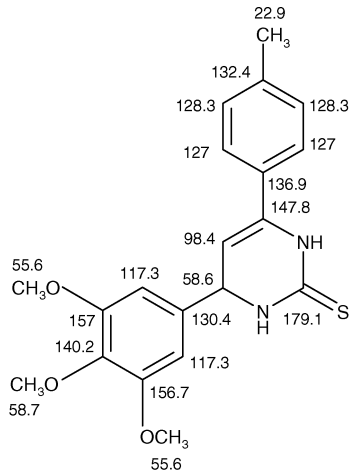
All melting points were taken on Griffin and Geory melting point apparatus and are uncorrected. IR spectra were recorded on Pye-Unicam SP1200 spectrophotometer using KBr Wafer technique. The ^{1}H-NMR spectra were determined on a Varian Gemini 200 MHz, using TMS as internal standard (chemical shifts in δ-scale). EI-MS were measured on Shimadzu-GC-MS operating at 70 eV. ^{13}C-NMR spectra were measured on JEOL 75 MHz. Elemental analyses were carried out at the Microanalytical unit, Faculty of Science, Ain Shams University by using Perkin-Elmer 2400 CHN Elemental Analyzer. The homogeneity of the synthesized compounds was controlled by TLC (aluminum sheets silica gel F_{254}Merck). All reactions have been monitored by TLC.

1-(4-Methylphenyl)-3-(3,4,5-trimethoxyphenyl)-prop-2-en-1-one 1

A mixture of *p*-methylacetophenone (1.34 g, 0.01 mol) and 3,4,5-trimethoxybenzaldehyde (1.96 g, 0.01 mol) was stirred in ethanolic potassium hydroxide for 2 h. The formed yellowish-white crystals were filtered off, washed with water, dried and recrystallized from dioxane to give **1** as yellow crystals, m.p.: 130−132°C; yield 86%. I.R(ν cm^{-1}): 1686 (CO, unsaturated ketone), 1616(C=C); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.6−6.4 (m, 6H arom.), 5.9 (d,2H, J =13.2 MHz), 3.9 (s, 9H, 3OMe), 2.1 (s, 3H, Me); MS m/z(%): 312 ($M^{+\cdot}$,100), 221 (76.4), 167 (18.6), 91 (44.6); anal. calcd. for $C_{19}H_{20}O_4$ (312): C, 73.07, H, 6.41, found: C, 73.23, H, 6.33.

6-(4-Methylphenyl)-4-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydropyrimidin-2(H)-thione 2

2 was prepared according to the described method.[13,14] Recrystallized from ethanol to give **2** as pale yellow crystals; m.p.: 186−188°C; yield 44%; I.R (ν cm^{-1}): 3385−3180 (NH), 1632 (C=N), 1230 (C=S); ^{1}H-NMR ($CDCl_3$) δ (ppm):12.3 (s, 1H, NH exchangeable with D_2O), 10.7(s, 1H, NH exchangeable with D_2O), 7.9−6.9 (m, 6H arom.), 6.5 (s,1H, C_5-H), 5.1(s,1H, C_4-H), 3.9 (s, 6H, 2OMe), 3.8 (s, 3H, OMe), 2.3 (s,3H, Ar-Me); MS m/z(%): 370($M^{+\cdot}$,100), 204 (71.3), 145 (22.8), 91 (30.4); anal. calcd. for $C_{20}H_{22}N_2O_3S$ (370): C, 64.86, H, 5.94, N,7.57, S, 8.68, found: C, 64.42, H, 6.08, N,7.33, S, 9.00.



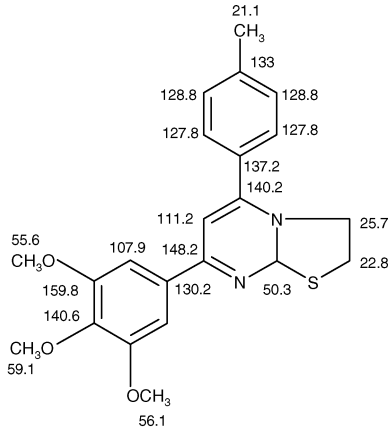
^{13}C-NMR($CDCl_3$) for compound **2**

5-(4-Methylphenyl)-7-(3,4,5-trimethoxyphenyl) tetrahydrothiazolo[3,2-a]pyrimidine 3 and Bis-s-[6-(4-methylphenyl)-4-(3,4,5-trimethoxyphenyl)dihydropyrimidin-2-yl]ethan-1,2-dithiol 4

A mixture of **2** (3.7 g, 0.01 mol), anhydrous potassium carbonate (3.5 g, 0.025 mol) and 1,2-dibromoethane (4.7 g, 0.025 mol) in 50-ml dry acetone was refluxed on water bath for 16 h. The excess solvent was evaporating till dryness, and then about 50 ml of water was added to the reaction mixture and stirred for 20 min. The solid deposited was filtered off, washed with water, dried and triturated with methanol to

give two fractions the soluble one which upon evaporation of solvent gives **3** and the insoluble fraction **4**.

3: yellow crystals; recrystallized from toluene; m.p.: 150–152°C; yield 46%; I.R (ν cm^{-1}):1632 (C=N); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.4–6.6 (m, 7Harom.+ C_6-H), 4.1 (s, 1H), 3.9 (s, 6H, 2OMe), 3.8 (s, 3H, OMe), 3.2 (t, 2H, N-$\underline{CH_2}$-CH_2, J = 4.8 MHz), 2.8 (t, 2H, S-$\underline{CH_2}$-CH_2, J = 4.8MHz), 2.3 (s, 3H, Ar-Me); MS m/z(%): 396 ($M^{+\cdot}$,33.7), 370 (22.9), 230 (100), 167 (17.6), 91 (27.9); anal. calcd. for $C_{22}H_{24}N_2O_3S$ (396): C, 66.66, H, 6.06, N,7.07, S, 8.08, found: C, 66.45, H, 5.98, N,7.33, S, 8.00.



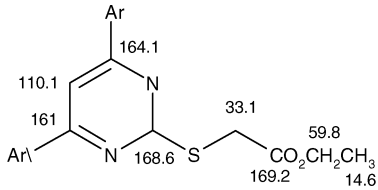
^{13}C-NMR($CDCl_3$) for compound **3**

4: light brown crystal, recrystallized from dioxane; m.p.:256–258°C; yield 15%; I.R (ν cm^{-1}): 1625 (C=N); ^{1}H-NMR (DMSO-d_6) δ (ppm): 8.1–6.7 (m, 14Harom.), 3.9–3.8 (br. s, 18H, 6OMe), 3.4 (br. s, 4H, CH_2-CH_2), 2.3(s, 6H, Ar-CH_3); anal. calcd. for $C_{42}H_{42}N_4O_6S_2$ (762): C, 66.14, H, 5.51, N,7.35, S, 8.39, found: C, 66.50, H, 5.88, N,7.07, S, 8.16.

2-Ethoxycarbonylmethylthio-6-(4-methylphenyl)-4-(3,4,5-trimethoxyphenyl)pyrimidine 5

A mixture of **2** (3.7 g, 0.01 mol), anhydrous potassium carbonate (2.7 g, 0.02 mol) and ethylchloroacetate (1.85 g, 0.015) in dry acetone (50 ml) was refluxed on a water bath for 12 h. The excess solvent was removed and the reaction mixture was poured onto ice-water and stirred for about 30 min. The solid deposited was filtered off, washed with water, dried, and recrystallized from benzene to give **5** as colorless crystals; m.p.: 136–138°C; yield 27%; I.R (ν cm^{-1}): 1728(C=O, ester), 1636(C=N); ^{1}H-NMR ($CDCl_3$)δ (ppm): 8.4–7 (m, 7H arom.), 4.2 (s, 2H, SCH_2CO),

4.1(q, 2H, $COO\underline{CH_2}CH_3$), 3.8 (s, 9H, 3OMe), 1.3 (t,3H,$COOCH_2\underline{CH_3}$); MS m/z(%): 455 ($M^{+\cdot}$+1,17.9), 410 (32.9), 382 (13.7), 288 (21.6), 181 (20.3),91 (33.4); anal. calcd. for $C_{24}H_{26}N_2O_5S$ (454): C, 63.43, H, 5.72, N,6.16, S, 7.05, found: C, 63.14, H, 5.38, N,5.76, S, 6.81.



^{13}C-NMR($CDCl_3$) for compound **5**

2-[6-(3,4,5-Trimethoxyphenyl)-4-(4-methylphenyl)pyrimidin-2-yl]thiomethyl-6,8-dibromo-3,1-benzoxazin-4(H)-one 6

A mixture of **5** (2.3 g, 0.005 mol), 3,5-dibromoanthranlic acid (1.5 g, 0.005 mol) and n-butanol (20 ml) was heated under reflux for 24 h. The excess solvent was removed under reduced pressure, and the solid deposited was triturated with diethyl ether, filtered off, dried, and recrystallized from benzene to give **6** as yellow crystals; m.p.: 120−122°C; yield 37%; I.R(ν cm^{-1}): br. 1773, 1723(C=O), 1680 (C=N); ^{1}H-NMR($CDCl_3$)δ (ppm): 8.5−6.8 (m, 9H arom.), 4.1 (s,2H, SCH_2-), 3.9 (br. s, 9H, 3OMe), 2.2 (s, 3H, Ar-Me); MS m/z (%): 685 ($M^{+\cdot}$+2,70.3), 683 ($M^{+\cdot}$100), 525 ($M^{+\cdot}$-2Br,17.9), 317 (22.8), 91 (40.2); anal. calcd. for $C_{29}H_{23}$ $Br_2N_3O_5S$ (683): C, 50.95, H, 3.36, N,6.15, S, 4.68, Br, 23.13, found: C, 51.33, H, 3.71, N,6.0, S, 4.33, Br, 23.48.

4-Imino-6-(4-methylphenyl)-8-(3,4,5-trimethoxyphenyl) dihydropyrimido[2,1-b]4H-thiazine 7

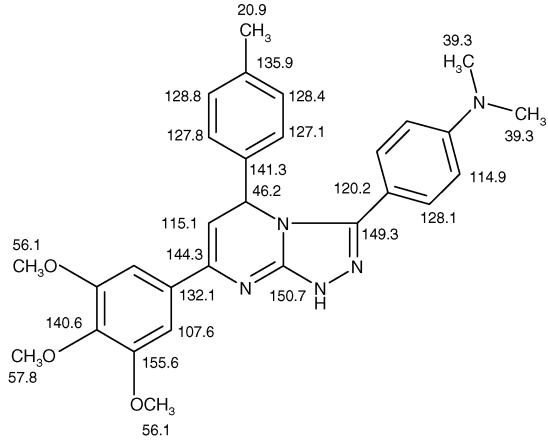
A solution of **2** (3.7 g, 0.01 mol) and acrylonitrile (0.02 mol) in pyridine (20 ml) was refluxed for 6 hrs. The reaction mixture was poured onto ice-cold water and acidified with dilute hydrochloric acid (20 ml, pH = 4), the precipitated product was filtered off, washed with water, dried and recrystallized from dioxane to give **7** as pale yellow crystals; m.p.: 166−168°C; yield 32%; I.R (ν cm^{-1}): 3330 (NH), 1642 (C=N); MS m/z(%): 421 ($M^{+\cdot}$,100), 394 ($M^{+\cdot}$−HCN,12.8), 255 (33.2), 91 (22.7); anal. calcd. for $C_{23}H_{23}N_3O_3S$ (421): C, 65.55, H, 5.46, N,9.97, S, 7.60, found: C, 65.39, H, 5.18, N,10.31, S, 7.44.

3-Methyl-5-(4-methylphenyl)-7-(3,4,5-trimethoxyphenyl) dihydro-[1,2,4]-triazolo[4,3-a] Pyrimidine 8a

A mixture of **2** (3.7 g, 0.01 mol), hydrazine hydrate (0.02 mol, 80%) in acetic acid (20 ml) was refluxed for 3 h. The H_2S was liberated during the reaction conditions. The reaction mixture was allowed to cool and the obtained solid was filtered off, washed with water, dried and recrystallized from acetic acid to give **8a** as pale yellow crystals; m.p.: 210–212^{o}C; yield 59%; I.R (ν cm^{-1}): 3210 (NH), 1628 (C=N); ^{1}H-NMR (DMSO-d_6) δ (ppm):8.1(s, 1H, exchangeable with D_2O), 7.8–6.8(m, 7H arom.+ C_6-H), 5.1(s,1H), 3.9(s, 9H, 3OMe),2.4 (s, 3H,C_3-Me), 2.2 (s, 3H, Ar-Me); MS m/z (%): 391 ($M^{+\cdot}$ –1, 100), 226 (38.8), 91 (40.7); anal. calcd. for $C_{22}H_{24}N_4O_3$ (392): C, 67.34, H, 6.12, N, 14.28, found: C, 69.86, H, 6.0, N,13.77.

3-Dimethylaminophenyl-5-(4-methylphenyl)-7-(3,4,5-trimethoxyphenyl)dihydro-[1,2,4] -triazolo[4,3-a] Pyrimidine 8b

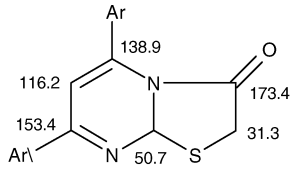
A mixture of **2** (3.7 g, 0.01 mol), hydrazine hydrate (0.02 mol, 80%), ethanol (20 ml), *p*-N,N-dimethylaminobenzaldehyde (0.01 mol) and drops of acetic acid was refluxed for 10 hrs. Evaporation of the excess solvent left a yellow solid product which recrystallized from ethanol to give **8b** as yellow crystals; m.p.: 270–272^{o}C; yield 33%; I.R (ν cm^{-1}): 3310, 3240 (NH), 1646(C=N); ^{1}H-NMR ($CDCl_3$) δ (ppm):7.9(s, 1H, exchangeable with D_2O), 8.6–6.7 (m, 11H arom.+ C_6-H), 4.5 (s,1H), 3.9 (s, 9H, 3OMe), 3.1 (s, 6H, NMe_2), 2.3 (s, 3H, Ar-Me); MS m/z(%): 377 ($M^{+\cdot}$-Ar′, 17.8), 330 (22.1), 121 (100), 91 (40.7); anal. calcd. for $C_{29}H_{31}N_5O_3$ (497): C,70.02, H, 6.23, N,14.08, found: C, 69.66, H, 5.92, N,13.98.



^{13}C-NMR($CDCl_3$) for compound **8b**

7-(3,4,5-Trimethoxyphenyl)-5-(4-methylphenyl)-3-oxo-tetrahydrothiazolo[3,2-a] Pyrimidine 9

A mixture of **2** (1.85 g, 0.005 mol), chloroacetatic acid (0.5 g, 0.005 mol) and anhydrous sodium acetate (2 g, 0.02 mol) in acetic acid (10 ml) and acetic anhydride (5 ml) was refluxed for 6 h. The reaction mixture was allowed to cool and then poured onto water, stirred for 1 h and left overnight. The deposited solid was filtered off, dried and recrystallized from light petroleum ether (b.p. 80−100°C) to give **9** as yellow crystals; m.p.: 92−94°C; yield 65%; I.R(ν cm^{-1}): 1682(C=O), 1628(C=N); ^{1}H-NMR ($CDCl_3$)δ (ppm): 8.3−6.8 (m, 6H arom.), 4.8 (s,1H), 3.9 (s, 9H, 3OMe), 3.7 (s, 2H, SCH_2CO), 2.3 (s, 3H, Ar-Me); MS m/z(%): 410 ($M^{+\cdot}$,17.8), 370 (39.4), 244 (12.6), 181(20.3), 91(100); anal. calcd. for $C_{22}H_{22}N_2O_4S$ (410): C, 64.39, H, 5.36, N,6.83, S, 7.80, found: C, 64.06, H, 4.88, N,6.71, S, 7.38.



^{13}C-NMR($CDCl_3$) for compound **9**

2-Acetyl-5-(4-methylphenyl)-3-oxo-7-(3,4,5-trimethoxyphenyl)dihydrothiazolo[3,2-a] Pyrimidine 10

A mixture of **9** (1.23 g, 0.003 mol), ethyl acetate (20 ml) in sodium ethoxide (0.5 g sodium, 20 ml absolute ethanol) was refluxed for 6 h. The cold reaction mixture poured onto ice-cold water and acidified with dilute hydrochloric acid (20 ml, pH = 4). The precipitated product was filtered off, washed with water, dried, and recrystallized from ethanol to give **10** as pale yellow crystals; m.p.: 196−198°C; yield 29%; I.R (ν cm^{-1}): br. 3400 (OH), 1662, 1650 (CO);^{1}H-NMR ($CDCl_3$)δ (ppm): 7.5−6.7 (m, 7H arom.+ C_6-H), 5.4(s,1H), 4.3 (s,1H, C_2-H), 3.8(s, 9H, 3OMe), 2.3 (s, 3H, Ar-Me), 2.1 (s, 3H, COMe); MS m/z (%): 437 ($M^{+\cdot}$-Me,30.1), 285 (22.6), 181 (19.3), 91 (100); anal. calcd. for $C_{24}H_{24}N_2O_5S$(452): C, 63.71, H, 5.31, N,6.19, S, 7.08, found: C, 63.29, H, 5.09, N,6.32, S, 6.76.

4-Amino-8-(3,4,5-trimethoxyphenyl)-10-(4-methylphenyl)-6H-pyrano[2′,3′:4,5]dihydrothiazolo[3,2-a]pyrimidin-2(H)-one 11

A mixture of **9** (4.1 g, 0.01 mol), malononitrile (1.98 g, 0.03 mol) and piperidine (1 ml) in ethanol (50 ml) was heated under reflux for 8 h. The excess solvent was removed, and the reaction mixture was poured onto ice-cold water and acidified with dilute acetic acid. The precipitated product was filtered off, washed with water, dried, and recrystallized from dioxane to give **11** as yellow crystals; m.p.: 205−207°C; yield 42%; I.R (ν cm^{-1}): 3390, 3280, 3172 (NH_2), 1742 (CO);^{1}H-NMR(DMSO-d_6)δ (ppm): 7.4−6.6 (m, 7H arom.+ C_8-H), 5.12 (br. s,2H), 4.7 (br. s,2H, NH_2exchangeable with D_2O), 3.9 (s, 9H, 3OMe), 2.34 (s, 3H, Ar-Me); MS m/z(%): 477 ($M^{+\cdot}$,100), 433 (32.7), 310 (17.9), 168 (12.3), 91(33.3); anal. calcd. for $C_{25}H_{23}N_3O_5S$(477): C, 62.89, H, 4.82, N,8.80, S, 6.70, found: C, 63.08, H, 4.82, N,9.13, S, 6.52.

Symmetrical Bis-3-[5-(4-methylphenyl)-7-(3,4,5-trimethoxyphenyl)dihydrothiazolo[3,2-a]pyrimidin-3-yl] hydrazine 12

A mixture of **9** (4.1 g, 0.01 mol) and hydrazine hydrate (0.02 mol, 80%) was fused in an oil-bath for 2 h at 160°C. The cooled reaction mixture was triturated with methanol to give light brown solid which filtered off, dried, and recrystallized from dioxane to give **12** as light brown crystals; m.p.: 218−220°C; yield 18%; I.R (ν cm^{-1}): 3238, 3314 (NH), 1630 (C=N);^{1}H-NMR (DMSO-d_6) δ (ppm): 7.4−6.8 (m, 14H arom.+ C_6-H), 6.6(br. s,2H, C_2-H), 5.1 (br. s, 2H), 3.9 (s, 9H, 3OMe), 3.8(s, 9H, 3OMe), 3.1 (br. s, 2H, 2NH exchangeable with D_2O), 2.2 (s, 6H, 2Ar-Me); anal. calcd. for $C_{44}H_{44}N_6O_6S_2$(816): C, 64.7, H, 5.39, N,10.29, S, 7.84, found: C, 65.1, H,5.0, N,10.84, S, 7.36.

2,10-di-(4-methylphenyl)-8-(3,4,5-trimethoxyphenyl)4H,6H-pyrano[2′,3′:4,5]thiazolo [3,2-a]pyrimidine-4-carboxylic Acid 13a

A mixture of **9** (4.1 g, 0.01 mol), β-p-tolylacrylic acid (1.62 g, 0.01 mol), sodium ethoxide (0.5 g sodium, 20 ml absolute ethanol) and ethanol (30 ml) was heated under reflux for 4 h. The excess solvent was removed and the residual poured onto ice-cold water and acidified with dilute hydrochloric acid (20 ml, pH = 4) to give semisolid product which was extracted with diethyl ether .The ethereal layer treated with aqueous sodium carbonate solution (10%). The aqueous layer separated and acidified with cold dilute hydrochloric acid. The deposited

solid was filtered off, washed with water, dried, and recrystallized from methanol to give **13a** as yellow crystals; m.p.: 242−244^{o}C; yield 35%; I.R (ν cm^{-1}): br. centered at 3432(OH), 1705(C=O acid), 1627(C=N);^{1}H-NMR(DMSO-d_6)δ (ppm): 11.8(br. s, 1H, COOH exchangeable with D_2O), 8.1−6.6(m, 11H arom.), 5.9 (br. s, 2H), 4.6(s,1H, C_3-H), 3.8(s, 9H, 3OMe), 2.4 (s, 3H,Me), 2.3(s, 3H, Me); anal. calcd. for $C_{33}H_{30}N_2O_6S$(582): C,68.04, H, 5.15, N,4.81 S, 5.49, found: C, 67.72, H, 5.33, N,5.10, S, 5.09.

2,10-Di-(4-methylphenyl)-4-phenyl-8-(3,4,5-trimethoxyphenyl) 4H,6H-pyrano[2′,3′:4,5] thiazolo[3,2-a]pyrimidine 13b

A mixture of **9** (4.1 g, 0.01 mol), benzal *p*-methylacetophenone (2.22 g, 0.01 mol), sodium ethoxide (0.5 g sodium, 20 ml absolute ethanol) and ethanol (30 ml) was heated under reflux for 6 h and left overnight. The reaction mixture poured onto ice-cold water and acidified with dilute hydrochloric acid (20 ml, pH = 4). The precipitated product was filtered off, washed with water, dried, and recrystallized from ethanol to give **13b** as colorless crystals; m.p.: 196−198°C; yield 52%; I.R (ν cm^{-1}): 1628(C=N);^{1}H-NMR($CDCl_3$)δ (ppm): 7.5−6.9 (m, 15H arom.), 6.7 (s, 1H, C_9-H), 4.9 (s,1H, C_3-H), 4.4 (br. s, 2H), 3.9 (s, 9H, 3OMe), 2.4−2.3 (br. s, 6H, Ar-Me); anal. calcd. for $C_{38}H_{34}N_2O_4S$ (614): C, 74.26, H, 5.53, N,4.56, S, 5.21, found: C, 74.09, H, 5.13, N,4.98, S, 5.23.

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