# A facile synthesis and heteroannulation of thiazolopyrimidine and related heterocyclic systems

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Reaction of pyrimidinylacetic acid **2** with different electrophilic and nucleophilic reagents gave annulated pyrimidine derivatives **3–11**, respectively. Compound **3** ([7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-a]-pyrimidin-6-yl]acetic acid) was transformed to pyrimidinylacetyl azide **12**, which upon heterocyclisation with active methylene compounds, acidic and basic reagents furnished functionally substituted heteroaromatic compounds **13–21**, respectively. The structures of the synthesised derivatives were elucidated by elemental and spectral analyses.

**Keywords:** polycyclic pyrimidines, triazolylpyrimidines, acid azide cyclisation

Pyrimidine derivatives and heterocyclic annulated pryimidine are well known in medicinal chemistry for their pronounced therapeutic applications[1-5] such as inhibitors of HIV-1 integrase, CNS stimulants, protein kinase inhibitors and anticancer drugs. Non-medicinal applications[6-10] include use as herbicides, agricultural fungicides, growth promoters and UV absorbants. One possible reason for their activity is the presence of a pyrimidine base in thymine, cytosine and uracial which are essential building blocks of nucleic acids, DNA and RNA. Our studies[11-13] related to the synthesis of annulated pyrimidines for testing as potential biodegradable agrochemical and antimicrobial agents by the functionalisation and cyclisation reactions of [4-(dibenzothien-2-yl)-2-mercapto-6-phenyl-1,6-dihydro-pyrimidin-5-yl]acetic acid (**2**) with different reagents.

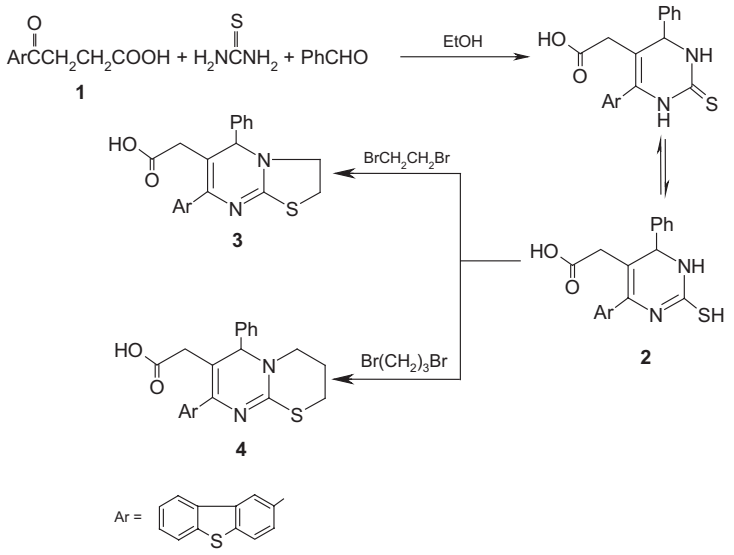
## Results and discussion

The required starting material, [4-(dibenzothien-2-yl)-2-mercapto-6-phenyl-1,6-dihydropyrimidin-5-yl]acetic acid (**2**) was prepared from readily available 3-[(dibenzothien-2-yl) carbonyl]propanoic acid (**1**), thiourea and benzaldehyde in ethanolic solution containing anhydrous potassium carbonate. The structure of compound **2** was assigned on the basis of elemental analysis and compatible spectroscopic data, thus, its IR spectrum showed characteristic absorption bands at 3410–3260 due to ν(OH,NH) and at 1695 $cm^{-1}$ for νCO. The $^1H$ NMR ($CDCl_3$) spectrum showed signals at δ 2.95 ppm for methylene protons, singlet at 4.63 for methine proton, multiplet signals (12 H) for aromatic protons at (7.11–7.95) ppm, two broad singlet at (8.40–8.60) ppm for two NH and singlet at 10.61 ppm for OH, which disappeared upon addition of $D_2O$ to the NMR sample. Also, the mass spectrum of **2** revealed a molecular ion peak at *m/z* = 430 which corresponds to the molecular formula $C_{24}H_{18}N_2O_2S_2$.

Pyrimidinylacetic acid **2** is used as a versatile intermediate for the preparation of a variety of multifunctionalised polyheterocycles, due to the presence of two adjacent reactive functional groups. Thus, the reaction of **2** with 1,2-dibromoethane gave [7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-a] pyrimidin-6-yl]acetic acid (**3**). The condensation of **2** with 1,3-dibromopropane gave the corresponding pyrimido[2,1-b][1,3]thiazine derivative **4** (Scheme 1).

The preparative use of pyrimidinylacetic acid **2** was extended to prepare new annulated pyrimidine derivatives. Thus, the alkylation of **2** with chloroacetic acid in a mixture of glacial acetic acid/acetic anhydride containing anhydrous sodium acetate gave [7-(dibenzothien-2-yl)-3-oxo-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-6-yl]acetic acid **5**, which condensed with benzaldehyde to give the corresponding benzylidene derivative **6** (Scheme 2).

Compound **6** underwent cyclisation into isoxazolothiazolo-pyrimidine derivative **7** upon treatment with hydroxylamine




**Scheme 1**

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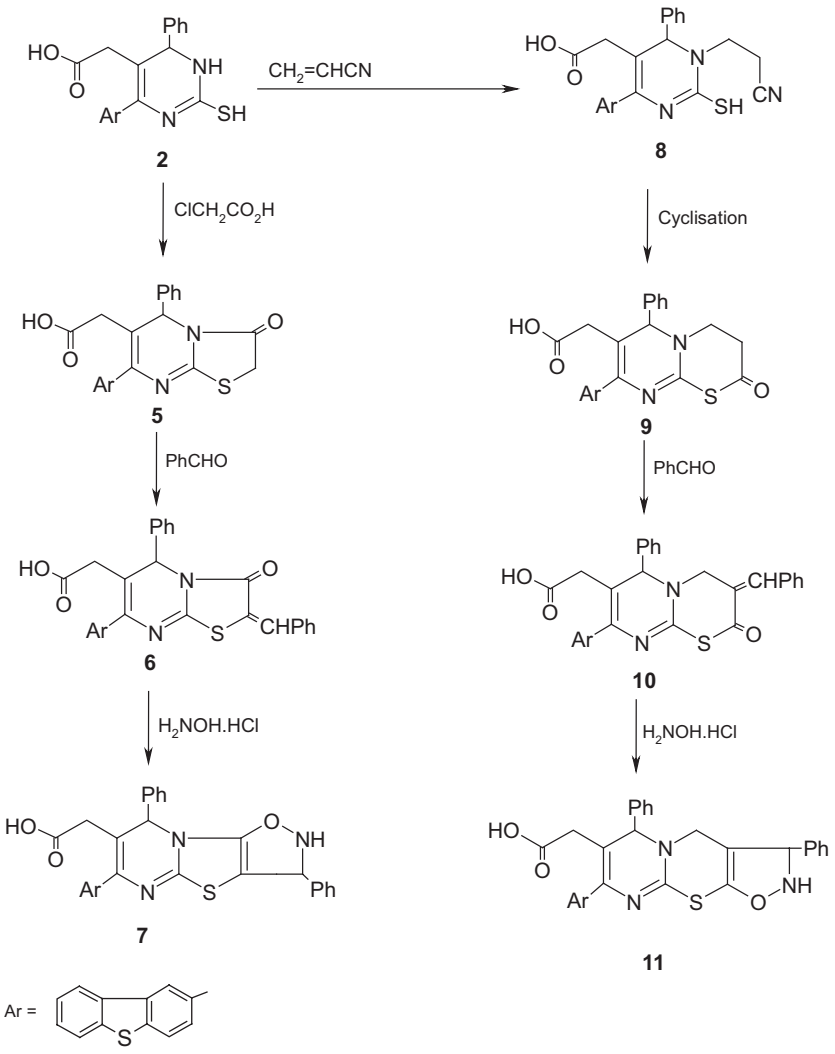



**Scheme 2**

hydrochloride in refluxing pyridine. Cyanoethylation of compound **2** with an equimolar amount of acrylonitrile in pyridine underwent a Michael-type addition to the activated double bond of the nitrile to give the propionitrile derivative **8**, which underwent cyclisation to pyrimidothiazine **9** by refluxing in a mixture of glacial acetic acid and hydrochloric acid (3 : 1). The condensation of compound **9** with benzaldehyde gave [3-benzylidene-8-(dibenzothien-2-yl)-2-oxo-6-phenyl-3,4-dihydro-2*H*,6*H*-pyrimido-[2,1-*b*][1,3]thiazin-7-yl]acetic acid (**10**), which reacted with hydroxylamine hydrochloride to give the cyclised tricyclic derivative **11** (Scheme 2).

In recent years, there has been increasing interest in the synthesis of alkyl azide, this stems from its applicability for synthesis of polyfunctionally substituted heterocycles.[14-16] Thus, thiazolopyrimidinylacetyl azide **12** was synthesised following the reported method[17] by stirring equimolar amounts of [7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*b*]pyrimidin-6-yl]acetyl chloride and aqueous sodium azide in dry acetone at 0–5°C (Scheme 3).

The azide **12** is a building blocks for the synthesis of bioactive triazole,[18] oxadiazole,[19] quinazoline[20] derivatives. Accordingly, the cycloaddition reaction of alkyl azide **12** with active methylene compounds (*viz* malononitrile, ethyl cyanoacetate, ethyl acetoacetate and diethyl malonate) gave the triazole derivatives[21] **13–16**, respectively (Scheme 3). While, the cycloaddition addition reaction of **12** with phenyl isocyanate in dry benzene gave 5-{[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-a]pyrimidin-6-yl]-methyl}-3-phenyl-1,3,4-oxadiazol-2(3*H*)-one (**17**).

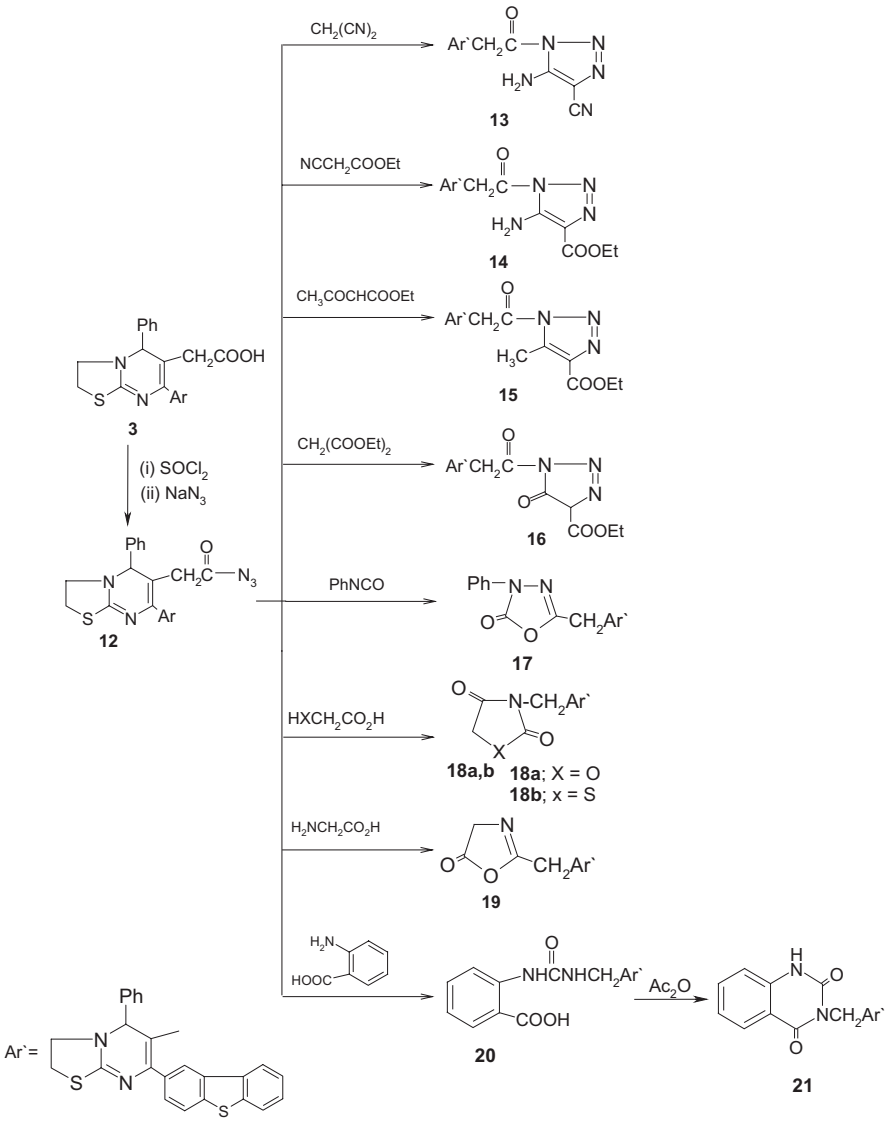
Additionally, the reaction of azide **12** with glycollic acid and/or thioglycollic acid in boiling dry benzene gave oxazolidine-2,4-dione and thiazolidine-2,4-dione **18a,b**, respectively, *via* Curtius rearrangement followed by 1,2-dipolar addition and cyclisation to give the desired product. Moreover, azide **12** decomposed through azido-displacement pathway upon treatment with glycine in dry toluene containing catalytic amount of piperidine to give 2-{[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-6-yl]-methyl}-oxazol-5(4*H*)-one (**19**).

Finally, the reaction of azide **12** with anthranilic acid gave disubstituted urea **20**, which was easily cyclised by boiling in acetic anhydride to give the quinazoline derivative **21** (Scheme 3).

The structures of the synthesised compounds were assigned on the basis of elemental analysis and spectral data (see Experimental).

## Experimental

Melting points are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 298 spectrophotometer. Elemental analyses were carried out at the Micro-analytical Centre of Cairo University, Egypt. $^1$H and $^{13}$C NMR spectra were obtained on an Varian Gemini 200 MHz and 50 MHz instrument using TMS as internal reference with chemical shifts expressed as δ ppm. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 instrument (70 eV El mode).




**Scheme 3**

$^{13}$C NMR values of phenyl and dibenzothiophene groups for compounds **3**–**21** are the same as in compound **2** with δ ± 0.1-0.5 ppm.

*[4-(Dibenzothien-2-yl)-2-mercapto-6-phenyl-1,6-dihydro-pyrimidin-5-yl]acetic acid* (**2**): A mixture of 3-[(dibenzothien-2-yl)carbonyl] propanoic acid (**1**), (5.7 g, 20 mmol), thiourea (1.6 g, 20 mmol), benzaldehyde (2.1 ml, 20 mmol) and $K_2CO_3$ (2.8 g, 20 mmol) in ethanol (60 ml) was refluxed for 10 h. The reaction mixture was cooled and the solid obtained was dissolved in hot water. The filtrate was neutralised with acetic acid to give solid product which recrystallised from ethanol to give **2**. Yield, 5.4 g (63%); m.p. 221–223°C; IR: ν = 3410–3260 (multiple bands OH, NH), 1695 (CO), 1265 cm$^{-1}$ (CS); $^1$H NMR ($CDCl_3$): δ = 2.95 (s, 2H, $CH_2$), 4.63 (s, 1H, methine), 7.11–7.95 (m, 12H, ArH), 8.40–8.60 (br s, 2H, 2NH, exchangeable), 10.61 (s, 1H, OH, exchangeable); $^{13}$C NMR: δ = 26.8($CH_2$), 59.3 (C-6), 108.3(C-5), 136.3(C-4), 160.3(CO), 167.2(CS); 115.2, 115.8, 117.3, 118.2, 121.4, 126.3(C-of phenyl ring); 120.2, 120.8, 121.6, 122.2, 124.4, 124.9, 130.2, 130.9, 136.2, 137.1, 140.2, 141.3(C-of dibenzothiophene ring); Anal. Calcd for $C_{24}H_{18}N_2O_2S_2$ (430.54): C, 66.95; H, 4.21; N, 6.51%. Found: C, 66.80; H, 4.11; N, 6.71%.

*[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidin-6-yl]acetic acid* (**3**): 1,2-Dibromoethane (1.9 ml, 10 mmol) in DMF (20 ml) was added dropwise to a stirred solution containing compound 2 (4.3 g, 10 mmol) and sodium hydroxide (0.07 g in 10 ml $H_2O$). The reaction mixture was refluxed for 2 h, then stirred at room temperature for an additional 2 h. The solid product which formed was filtered off, washed with water and triturated with ethanol to give colourless product which recrystallised from ethanol to give **3**. Yield, 3.4 g (74%); m.p. 163–165°C; IR: ν = 3390–3170 (OH), 1695 cm$^{-1}$ (CO); $^1$H NMR ($CDCl_3$): δ = 2.71–2.85 (m, 4H, 2$CH_2$ of thiazole), 3.96 (s, 2H, $CH_2$), 4.71 (s, 1H, methine), 7.51–8.21 (m, 12H, ArH), 10.80 (s, 1H, OH, exchangeable); $^{13}$C NMR: δ = 21.6(C-2), 28.1($CH_2$), 56.2(C-3), 62.7(C-5), 125.1(C-6), 138.2 (C-7), 163.4(CO), 176.2(C-8a); Anal. Calcd for $C_{26}H_{20}N_2O_2S_2$ (456.58): C, 68.39; H, 4.42; N, 6.14%. Found: C, 68.53; H, 4.51; N, 6.26%.

*[8-(Dibenzothien-2-yl)-6-phenyl-3,4-dihydro-2H,6H-pyrimido [2,1-b][1,3]thiazin-7-yl]acetic acid* (**4**): 1,3-Dibromopropane (1 ml, 5 mmol) in DMF (20 ml) was added dropwise to a stirred solution containing compound **2** (2.2 g, 5 mmol) and sodium hydroxide (0.07 g in $H_2O$, 10 ml). The reaction mixture was refluxed for 3 h, then stirred at room temperature for an additional 2 h. The solid product which formed was filtered off, washed with water and triturated with ethanol to give a colourless product which recrystallised from ethanol to give **4**. Yield 1.6 g (67%); m.p. 183–185°C. IR: ν = 3385–3180 (OH), 1690 cm$^{-1}$ (CO); $^1$H NMR ($CDCl_3$): δ = 2.65–2.93 (m, 6H, 3$CH_2$ of thiazine), 3.93 (s, 2H, $CH_2$), 4.13 (s, 1H, methine), 7.29–8.11 (m, 12H, ArH), 10.71 (s, 1H, OH, exchangeable); Anal. Calcd for $C_{27}H_{22}N_2O_2S_2$ (470.61): C, 68.91; H, 4.71; N, 5.95%. Found: C, 68.80; H, 4.91; N, 5.83%.

*[7-(Dibenzothien-2-yl)-3-oxo-5-phenyl-2,3-dihydro-5H-thiazolo [3,2-a]pyrimidin-6-yl]acetic acid* (**5**): A mixture of compound **2** (4.3 g, 10 mmol), chloroacetic acid (0.95 g, 10 mmol) and anhydrous sodium acetate (2.0 g) was refluxed in a mixture of glacial acetic acid (30 ml) and acetic anhydride (20 ml) for 4 h. The reaction mixture was cooled and poured onto crushed ice (50 g). The solid which formed was filtered off and recrystallised from benzene to give **5**. Yield, 3.5 g (75%); m.p. 201–203°C; IR: ν = 3380–3210 (OH), 1690–1685 cm$^{-1}$ (CO); $^1$H NMR ($CDCl_3$); δ = 2.85 (s, 2H, $CH_2$ of thiazole), 3.11

(s, 2H, $CH_2$), 4.12 (s, 1H, methine), 7.15–7.85 (m, 12H, ArH), 10.65 (s, 1H, OH, exchangeable); Anal. Calcd for $C_{26}H_{18}N_2O_3S_2$ (470.56): C, 66.36; H, 3.86; N, 5.95%. Found: C, 66.50; H, 3.97; N, 4.81%.

*[2-Benzylidene-7-(dibenzothien-2-yl)-3-oxo-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]acetic acid* (**6**): A mixture of compound **5** (4.7, 10 mmol) and benzaldehyde (1.1 ml, 10 mmol) in glacial acetic acid (25 ml) containing anhydrous sodium acetate (1 g) was refluxed for 6 h. The reaction mixture left to cool, then poured onto crushed ice (30 g) and the solid formed was recrystallised from dioxane to give **6**. Yield, 3.8 g (68%); m.p. 230–232°C; IR: ν = 3405–3190 (OH), 1690–1680 $cm^{-1}$ (CO); MS: *m/z* = 558 ($M^+$); Anal. Calcd for $C_{33}H_{22}N_2O_3S_2$ (558.67): C, 70.95; H, 3.97; N, 5.01%. Found: C, 70.81; H, 3.82; N, 5.15%.

*[6-(Dibenzothien-2-yl)-3,8-diphenyl-2,3-dihydro-8H-isoxazolo[5',4':4,5]thiazolo[2,3-a]pyrimidin-7-yl]acetic acid* (**7**): A mixture of compound **6** (2.2 g, 4 mmol) and hydroxylamine hydrochloride (0.28 g, 4 mmol) was refluxed in pyridine (25 ml) for 6 h. The reaction mixture was cooled, then poured onto ice–HCl (30 g, 10 ml) and the solid formed was filtered off and recrystallised from dioxane to give **7**. Yield, 1.5 g (66%); m.p. 213–215°C; IR: ν = 3395–3185 (multiple bands, OH, NH), 1685 $cm^{-1}$ (CO); $^1H$ NMR (DMSO-$d_6$): δ = 2.76 (s, 2H, $CH_2$), 4.11–4.30 (br s, 2H, 2CH, two methine), 7.35–8.12 (m, 17H, ArH), 9.12 (s, 1H, NH, exchangeable), 10.90 (s, 1H, OH, exchangeable); $^{13}C$ NMR: δ = 28.3($CH_2$), 59.6(C-4), 62.6(C-9), 78.8(C-8a), 114.2(C-5), 137.3(C-6), 160.1(C-7a), 162.2(C-2a), 165.2(CO); 119.1, 119.9, 120.2, 120.9, 123.2, 125.1(C-of phenyl ring of oxazole); Anal. Calcd for $C_{33}H_{23}N_3O_3S_2$ (573.69): C, 69.09; H, 4.04; N, 7.32%. Found: C, 69.22; H, 4.21; N, 7.16%.

*[1-(2-Cyanoethyl)-4-(dibenzothien-2-yl)-2-mercapto-6-phenyl-1,6-dihydropyrimidin-5-yl]acetic acid* (**8**): A mixture of compound **2** (4.3 g, 10 mmol) and acrylonitrile (0.74 ml, 14 mmol) in pyridine (30 ml) was refluxed for 6 h. The colourless solid which formed after concentration and cooling was recrystallised from ethanol to give **8**. Yield 3.6 g (74%); m.p. 216–218°C; IR: ν = 3375–3190 (OH), 2510 (SH), 2210 (CN), 1685 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.22 (t, 2H, $CH_2$), 2.86 (s, 2H, $CH_2$), 3.3 (t, 2H, $CH_2CN$), 4.35 (s, 1H, methine), 7.14–7.95 (13H, ArH and SH), 10.76 (s, 1H, OH, exchangeable); MS: *m/z* = 483 ($M^+$); Anal. Calcd for $C_{27}H_{21}N_3O_2S_2$ (483.61): C, 67.06; H, 4.38; N, 8.69%. Found: C, 67.18; H, 4.50; N, 8.73%.

*[8-(Dibenzothien-2-yl)-2-oxo-6-phenyl-3,4-dihydro-2H,6H-pyrimido[2,1-b][1,3]thiazin-7-yl]acetic acid* (**9**): Compound **8** (2 g) in a mixture of glacial acetic acid (30 ml) and hydrochloric acid (10 ml) was refluxed for 5 h. The reaction mixture was concentrated by evaporation under reduced pressure, the solid formed was filtered off, washed with water and recrsytallised from dioxane to give **9**. Yield 1.4 g (69%); m.p. 195–197°C; IR: ν = 3390–3200 (OH), 1695–1690 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.81 (s, 2H, $CH_2$), 2.90–3.1 (m, 4H, $2CH_2$ of thiazine), 4.13 (s, 1H, methine), 7.51–8.13 (m, 12H, ArH), 10.76 (s, 1H, OH, exchangeable); MS: *m/z* = 484 ($M^+$); Anal. Calcd for $C_{27}H_{20}N_2O_3S_2$ (484.59): C, 66.92; H, 4.16; N, 5.78%. Found: C, 66.79; H, 4.01; N, 5.57%.

*[3-Benzylidene-8-(dibenzothien-2-yl)-2-oxo-6-phenyl-3,4-dihydro-2H,6H-pyrimido[2,1-b][1,3]thiazin-7-yl]acetic acid* (**10**): A mixture of compound **9** (4.8 g, 10 mmol) and benzaldehyde (1.1 ml, 10 mmol) in glacial acetic acid (30 ml) containing anhydrous sodium acetate (1.5 g) was refluxed for 6 h. The reaction mixture was cooled, poured onto crushed ice (30 g) and the solid formed was recrystallised from ethanol to give **10**. Yield 3.8 g (66%); m.p. 230–232°C; IR: ν = 3410–3180 (OH), 1690–1680 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.90 (s, 2H, $CH_2$), 3.70 (s, 2H, $CH_2$ of thiazine), 4.20 (s, 1H, methine), 7.13–8.11 (m, 18H, ArH and benzylic proton), 10.50 (s, 1H, OH, exchangeable); MS: *m/z* = 572 ($M^+$); Anal. Calcd for $C_{34}H_{24}N_2O_3S_2$ (572.70): C, 71.31; H, 4.22; N, 4.89%. Found: C, 71.50; H, 4.32; N, 4.96%.

*[8-(Dibenzothien-2-yl)-3,6-diphenyl-2,3-dihydro-4H,6H-isoxazolo[4,5-e]pyrimido[2,1-b][1,3]thiazin-7-yl]acetic acid* (**11**): A mixture of compound **10** (2.3 g, 4 mmol) and hydroxylamine hydrochloride (0.28 g, 4 mmol) in pyridine (30 ml) was refluxed for 6 h. The reaction mixture was cooled, then poured onto crushed ice (40 g) and the solid product was filtered off and recrystallised from DMF to give **11**. Yield, 1.7 g (69%); m.p. 207–209°C; IR: ν = 3390–3180 (multiple bands, OH, NH), 1690 $cm^{-1}$ (CO); $^1H$ NMR (DMSO-$d_6$): δ = 2.91 (s, 2H, $CH_2$), 3.60 (s, 2H, $CH_2$ of thiazine), 4.15–4.30 (br s, 2H, two methine), 9.55 (br s, 1H, NH, exchangeable); 10.75 (s, 1H, OH, exchangeable); Anal. Calcd for $C_{34}H_{25}N_3O_3S_2$ (587.71): C, 69.48; H, 4.29; N, 7.15%. Found: C, 69.61; H, 4.40; N, 7.31%.

*[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]acetyl azide* (**12**): A saturated solution of sodium azide (0.78 g, 12 mmol) in $H_2O$ (2 ml) was added dropwise to a stirred solution of thiazolopyrimidinylacetyl chloride (5.79, 12 mmol) in dry acetone (30 ml) at 0–5°C, then the mixture was stirred for further 1 h at room temperature. The reaction mixture was added to crushed ice (40 g) and the precipitated product was filtered off to give the acid azide **12**.Yield, 3.8 g (65%); m.p. 117–119°C (with decomposition); IR: ν = 2215 ($CON_3$), 1680 $cm^{-1}$ (CO).

*General procedure for the preparation of triazole derivatives* (**13–16**) A cold solution of compound **12** (0.96 g, 2 mmol) in absolute ethanol (25 ml) was added to a cold solution of active methylene compounds (2 mmol) (*viz* malononitrile, ethyl cyanoacetate, ethyl acetoacetate and diethyl malonate) in ethanolic sodium ethoxide solution (prepared from sodium 1.66 g in absolute ethanol 20 ml). The reaction mixture was stirred at room temperature overnight, then the solvent was evaporated under vacuum. The concentrated ethanol solution was poured onto crushed ice (50 g) and the solid obtained was filterated off and recrystallised to give the compounds **13–16**.

*5-Amino-1-{2-[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]acetyl}-1H-1,2,3-triazole-4-carbonitrile* (**13**): Yield, 0.73 g (66%) (benzene); m.p. 195–197°C; IR: ν = 3350, 3280 ($NH_2$), 2220 (CN), 1680 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.71–2.95 (m, 4H, $2CH_2$ of thiazole), 3.95 (s, 2H, $CH_2$), 4.51 (s, 1H, methine), 5.85 (br s, 2H, $NH_2$), 7.51–8.25 (m, 12H, ArH); $^{13}C$ NMR: δ = 27.5($CH_2$), 29.4(C-2), 54.3(C-3), 56.8(C-5), 116.2(C-4 of triazole), 118.2(C-6), 124.2(C-7), 143.2(CN), 146.1 (C-5 of triazole), 170.2(C-8a), 180.2(CO); Anal. Calcd for $C_{29}H_{21}N_7OS_2$ (547.66): C, 63.60; H, 3.86; N, 17.90%. Found: C, 63.72; H, 3.95; N, 17.79%.

*Ethyl 5-amino-1-{2-[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]acetyl}-1H-1,2,3-triazole-4-carboxylate* (**14**): Yield, 0.74 g (62%) (xylene); m.p. 226–228°C; IR: ν = 3340, 3270 ($NH_2$), 1725, 1680 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 1.40 (t, 3H, $CH_3$), 2.65–2.95 (m, 4H, $2CH_2$ of thiazole), 3.75 (s, 2H, $CH_2$), 4.12 (q, 2H, $CH_2$), 4.65 (s, 1H, methine), 5.91 (br s, 2H, $NH_2$), 7.61–8.23 (m, 12H, ArH); Anal. Calcd for $C_{31}H_{26}N_6O_3S_2$ (594.71): C, 62.61; H, 4.41; N, 14.13%. Found: C, 62.49; H, 4.63; N, 14.25%.

Ethyl 1-{2-[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo *[3,2-a]pyrimidin-6-yl]acetyl}-5-methyl-1H-1,2,3-triazole-4-carboxylate* (**15**): Yield, 0.73 (61%) (xylene); m.p. 240–242°C; IR: ν = 1725, 1680 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 1.40 (t, 3H, $CH_3$), 2.50 (s, 3H, $CH_3$), 2.85–2.95 (m, 4H, $2CH_2$ of thiazole), 3.50 (s, 2H, $CH_2$), 4.20 (q, 2H, $CH_2$), 4.25 (s, 1H, methine), 7.23–8.31 (m, 12H, ArH); MS: m/z = 593 ($M^+$); Anal. Calcd for $C_{32}H_{27}N_5O_3S_2$ (593.72): C, 64.74; H, 4.58; N, 11.80%. Found: C, 64.85; H, 4.67; N, 11.96%.

*Ethyl 1-{2-[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo [3,2-a]pyrimidin-6-yl]acetyl}-5-oxo-4,5-dihydro-1H-1,2,3-triazole-4-carboxylate* (**16**): Yield, 0.68 g (57%) (toluene); m.p. 217–219°C; IR: ν = 1730 (CO of ester), 1685–1680 $cm^{-1}$ (CO of amide); $^1H$ NMR ($CDCl_3$): δ = 1.3 (t, 3H, $CH_3$), 2.71–2.90 (m, 4H, $2CH_2$ of thiazole), 3.62 (s, 2H, $CH_2$), 4.11 (q, 2H, $CH_2$), 4.35, 4.51 (2 s, 2H, two methine), 7.15–8.11 (m, 12H, ArH); $^{13}C$ NMR: δ = 12.2($CH_3$), 22.1($CH_2$), 27.3(C-2), 50.1(CH of triazole), 56.7(C-3), 63.2 (C-5), 64.2($\underline{CH_2}CH_3$), 127.2(C-6), 129.2(C-7), 165.2(CO of ester), 168.1($\underline{CO}CH_2$), 173.1(CO of triazole); Anal. Calcd for $C_{31}H_{25}N_5O_4S_2$ (595.69): C, 62.51; H, 4.23; N, 11.76%. Found: C, 62.65; H, 4.34; N, 11.85%.

*5-{[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]-methyl}-3-phenyl-1,3,4-oxadiazol-2(3H)-one* (**17**): A mixture of compound **12** (0.96 g, 2 mmol) and phenyl isocyanate (3 ml) in dry benzene (40 ml) was heated under reflux for 5 h. The solid that separated after concentration and cooling was recrystallised from benzene to give **17**. Yield, 0.76 g (69%); m.p. 201–203°C; IR: ν = 1725 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.63-2.85(m, 4H, $2CH_2$ of thiazole), 3.42 (s, 2H, $CH_2$), 4.35 (s, 1H, methine), 7.37–8.13(m, 17H, ArH); $^{13}C$ NMR: δ = 22.1($CH_2$), 26.1(C-2), 53.1(C-3), 55.2(C-5), 117.2(C-6), 123.3(C-7), 143.2 (C-5, oxadiazole), 160.1(CO), 171.2(C-8a); 117.1, 118.2, 120.3, 121.4, 124.3, 126.2(phenyl ring of oxadiazole); Anal. Calcd for $C_{33}H_{24}N_4O_2S_2$ (572.70): C, 69.21; H, 4.22; N, 9.78%. Found: C, 69.11; H, 4.10; N, 9.86%.

*3-{[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidin-6-yl]-methyl}oxazolidine-2,4(3H,5H)-dion*e (**18a**) and *3-{[7-(dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidin-6-yl]methyl}thiazolidine-2,4(3H,5H)-dione* (**18b**): A solution of **12** (0.96 g, 2 mmol) in dry benzene (30 ml), containing piperidine (1 ml), glycolic acid and/or thioglycollic acid (3 mmol) was heated under reflux temperature for 2 h. The solvent was evaporated under reduced pressure and the residue was redissolved in ether (40 ml). The solution was washed with 10% sodium carbonate

(3 × 25 ml) and water (40 ml), dried over anhydrous $Na_2SO_4$. Evaporation of the dried etheral layer under vacuum gave the compounds **18a,b**.

**18a:** Yield, 0.71 g (71%) (ethanol); m.p. 214–216°C; IR: ν = 1710 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.80–2.95 (m, 4H, $2CH_2$ of thiazole), 3.40, 3.60 (2 s, 4H, $2CH_2$), 4.31 (s, 1H, methine), 7.23–8.13 (m, 12H, ArH); Anal. Calcd for $C_{28}H_{21}N_3O_3S_2$ (511.62): C, 65.73; H, 4.14; N, 8.21%. Found: C, 65.52; H, 4.10; N, 8.09%.

**18b:** Yield, 0.84 g (76%) (ethanol); m.p. 230–232°C; IR: ν = 1705 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.75–2.90 (m, 4H, $2CH_2$ of thiazole), 3.50, 3.65 (2 s, 4H, $2CH_2$), 4.35 (s, 1H, methine), 7.35–8.41 (m, 12H, ArH); MS: *m/z* = 527 ($M^+$); Anal. Calcd for $C_{28}H_{21}N_3O_2S_3$ (527.68): C, 63.73; H, 4.01; N, 7.96%. Found: C, 63.84; H, 4.18; N, 7.83%.

*2-{[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidin-6-yl]methyl}-oxazol-5(4H)-one* (**19**): A mixture of **12** (0.96 g, 2 mmol) and glycine (0.15 g, 2 mmol) in dry toluene (30 ml) containing piperidine (1 ml) was heated under reflux for 7 h. The solid that separated after concentration and cooling was recrystallised from toluene to give **19**. Yield, 0.73 g (73%); m.p. 223–225°C; IR: ν = 1726 (CO), 1610 $cm^{-1}$ (C=N); $^1H$ NMR ($CDCl_3$): δ = 2.70–2.81 (m, 4H, $2CH_2$ of thiazole), 3.71, 3.92 (2 s, 4H, $2CH_2$), 4.57 (s, 1H, methine), 7.63–8.25 (m, 12H, ArH); $^{13}C$ NMR: δ = 24.2($CH_2$), 26.2(C-2), 49.2(C-4, oxazole), 53.2(C-3), 57.1(C-5), 118.2(C-6, oxazole), 128.3(C-7), 157.2(C-2, oxazole), 173.2(CO), 176.1(C-8a); Anal. Calcd for $C_{28}H_{21}N_3O_2S_2$ (495.62): C, 67.85; H, 4.27; N, 8.48%. Found: C, 67.76; H, 4.10; N, 8.31%.

*1-{[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a] pyrimidin-6-yl]methyl}-3-o-tolylurea* (**20**): A mixture of compound **12** (0.96 g, 2 mmol) and anthranilic acid (0.27 g, 2 mmol) in dry benzene (30 ml) was refluxed for 30 min, the reaction mixture was allowed to cool and the solid which precipitated after cooling, filtered off, dried and recrystallised from benzene to give **20**. Yield, 1.0 g (84%); m.p. 242–244°C; IR: ν = 3460–3260 (OH, NH), 1690–1680 $cm^{-1}$ (CO); $^1H$ NMR ($CDCl_3$): δ = 2.73–2.95 (m, 4H, $2CH_2$ of thiazole), 3.55 (s, 2H, $CH_2$), 4.20 (s, 1H, methine), 7.12–8.25 (m, 16H, ArH), 9.21, 9.30, 10.10 (3 s, 3H, 2NH, OH, exchangeable); MS: *m/z* = 590 ($M^+$); Anal. Calcd for $C_{33}H_{26}N_4O_3S_2$ (590.72): C, 67.10; H, 4.44; N, 9.48%. Found: C, 67.23; H, 4.53; N, 9.61%.

*3-{[7-(Dibenzothien-2-yl)-5-phenyl-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-6-yl]methyl}-quinazoline-2,4(1H, 3H)-dione* (**21**): A solution of **20** (1 g) in acetic anhydride (10 ml) was refluxed for 1 h. The reaction mixture was cooled, poured onto crushed ice (50 g) and the precipitated product was filtered off and recrystallised from *n*-butanol to give **21**. Yield, 0.61 g (63%); m.p. 196–198°C; IR: ν = 3210 (NH), 1680–1670 $cm^{-1}$ (CO); $^1H$ NMR (DMSO-$d_6$): δ = 2.72–2.93 (m, 4H, $2CH_2$ of thiazole), 3.95 (s, 2H, $CH_2$), 4.45 (s, 1H, methine), 7.61–8.13 (m, 16H, ArH), 9.22 (br s, 1H, NH, exchangeable); $^{13}C$ NMR: δ = 25.1($CH_2$), 26.8(C-2), 54.1(C-3), 58.1(C-5), 119.1(C-6), 127.2(C-7), 176.7(C-8a); 149.2, 150.2(2 CO); 118.1, 119.3, 120.5, 126.2, 132.2, 134.3(C-of quinazolinedione); Anal. Calcd for $C_{33}H_{24}N_4O_2S_2$ (572.70): C, 69.21; H, 4.22; N, 9.78%. Found: C, 69.35; H, 4.37; N, 9.86%.

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