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Intramolecular 4+2 cycloaddition of thieno[2,3-*e*][1,2,4]triazines: routes towards condensed thieno[2,3-*b*]pyridines

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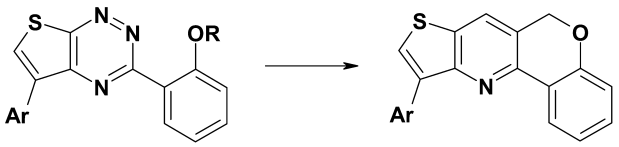
Abstract—Synthetic approaches towards new condensed thienopyridine ring systems including furo[2,3-*b*]thieno[3,2-*e*]pyridines, bisthieno[2,3-*b*:3′,2′-*e*]pyridines, 5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridines, 5*H*-benzo(*f*)chromeno[2,3-*b*]thieno[3,2-*e*]pyridines have been achieved by application of intramolecular 4+2 cycloaddition reactions of suitably designed thieno[2,3-*e*][1,2,4]triazines tethered with alkene or alkyne terminals.

1. Introduction

1,2,4-Triazines have been extensively used as electron deficient dienes for the preparation of pyridine derivatives through their reaction with electron rich dienophiles by the application of Diels–Alder cycloaddition reactions with inverse electron demand.[1,2] Recently, interesting routes towards pyridines and polypyridyl derivatives of potential diverse applications have been reported.[2,3] Some thienopyridines have been prepared from 1,2,4-triazines via intramolecular Diels–Alder cycloaddition reactions of suitably tethered 1,2,4-triazines.[1,2] Although not readily found in nature, thienopyridines have found uses as herbicides, components of antibiotics and as dyestuffs.[1] Other interesting applications of thienopyridines are their uses for the preparation of doped polymers, useful for electrodes, displays and electromagnetic shields.[4] In addition, some derivatives showed interesting therapeutic applications as antiglaucoma agents,[5] anticonvulsants,[6] calcium channel modulators,[7] and others have been tested for use in the therapy of arterial thrombotic disorders.[8]

Recently, the synthesis of the isomeric thieno[3,2-*e*]-[1,2,4]triazines and thieno[2,3-*e*][1,2,4]triazines has been described.[9–11] We have also reported the first application of thieno[3,2-*e*][1,2,4]triazines **A** as potential electron deficient azadienes in inverse electron demand Diels–Alder reactions. Results from this work gave an interesting route towards [1]benzopyrano[4,3-*b*]thieno[2,3-*e*]pyridines **B** (Scheme 1).[1a]



A, R = $CH_2CH{=}CH_2$, CH_2CCH B

Scheme 1.

In the present work, the behavior of the isomeric thieno[2,3-*e*][1,2,4]triazines towards intramolecular Diels–Alder reactions was studied. Scheme 1 illustrates the first attempts to design suitable starting thieno[2,3-*e*][1,2,4]triazine derivatives for use in the present objectives. The starting 3-methanesulfinyl-6-arylthieno[2,3-*e*][1,2,4]-triazines **5a**,**c** and 3-methanesulfonyl-6-arylthieno[2,3-*e*][1,2,4]triazines **6a-d** were synthesized as outlined in Scheme 2. Thus, condensation of the appropriate arylmethylketones **1a-e** with diethyl oxalate in methanolic sodium methoxide gave the corresponding ethyl 4-aryl-2,4-dioxobutyrates **2a-e**, respectively. Condensation of the latter with *S*-methylisothiosemicarbazide hydroiodide in pyridine gave the corresponding 3-methylsulfanyl-6-(2-oxo-2-arylethyl)-1,2,4-triazin-5(2*H*)-ones **3a-e**, respectively (following reported procedures).[12,13] Compounds **3a-e** were found to exist in equilibrium with ca. 10% of the 6-methine tautomer as shown by ^{1}H NMR measured in DMSO-d_6. Thiation and cyclization of **3a-e** took place simultaneously by the action of phosphorus pentasulfide in pyridine to give the corresponding 3-methylsulfanyl-6-arylthieno[2,3-*e*]-[1,2,4]triazines **4a-e**, respectively (following reported[11] procedure for **4a**,**b**).

Keywords: 1,2,4-triazines; thieno[2,3-*e*][1,2,4]triazines; 2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*]pyridines; bisthieno[2,3-*b*:3′,2′-*e*]pyridines; 5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridines; 5*H*-benzo(*f*)chromeno[2,3-*b*]-thieno[3,2-*e*]pyridines.
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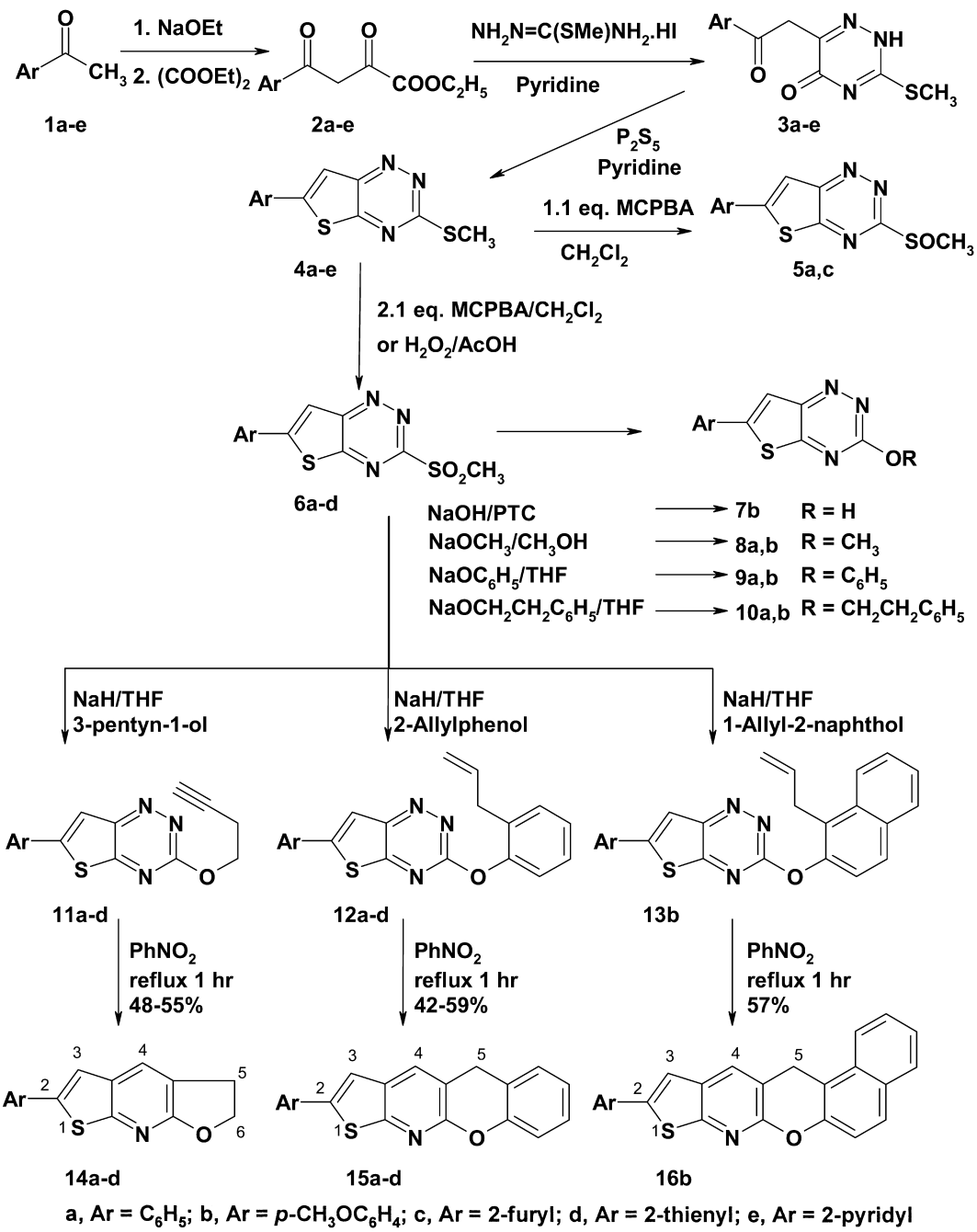


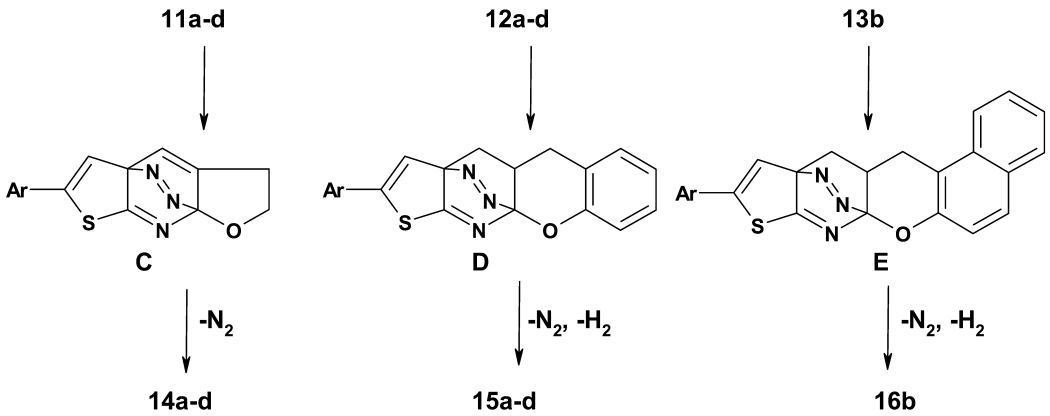
Scheme 2.

Oxidation of **4a**,**c** with *m*-chloroperoxybenzoic acid (MCPBA, 1.1 equiv.) in dichloromethane gave the corresponding sulfoxides **5a**,**c**. On the other hand, the sulfones **6a-d** were prepared by two different methods involving either oxidation with *m*-chloroperoxybenzoic acid (MCPBA, 2.1 equiv.) in dichloromethane at room temperature or oxidation with hydrogen peroxide in acetic acid.

Compounds **6a-d** were used as starting materials to prepare new functionalized thieno[2,3-*e*][1,2,4]triazines via nucleophilic substitution reactions. Scheme 2 illustrates their reactions with different nucleophiles in order to investigate the synthesis of the target starting materials suitable for intramolecular cycloaddition reactions.

Thus, hydrolysis of 3-methanesulfonyl-6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4] triazine **6b** with NaOH (in DCM/H_2O) under phase transfer catalytic conditions using benzyltriethylammonium chloride gave 6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4]triazin-3-ol **7b**. The reaction of **6a**,**b** with sodium methoxide in methanol gave the corresponding 6-aryl-3-methoxythieno[2,3-*e*][1,2,4]triazines **8a**,**b**. On the other hand, the 3-phenoxy derivatives **9a**,**b** were prepared by the reaction of **6a**,**b** with sodium phenoxide (prepared in situ from phenol and NaH in THF). Similarly, the reaction of **6a**,**b** with β-phenethyl alcohol in THF and NaH gave the corresponding 6-aryl-3-β-phenethyloxythieno[2,3-*e*][1,2,4]triazines **10a**,**b**, respectively.

Extension of these nucleophilic reactions to ω-alkenyl and



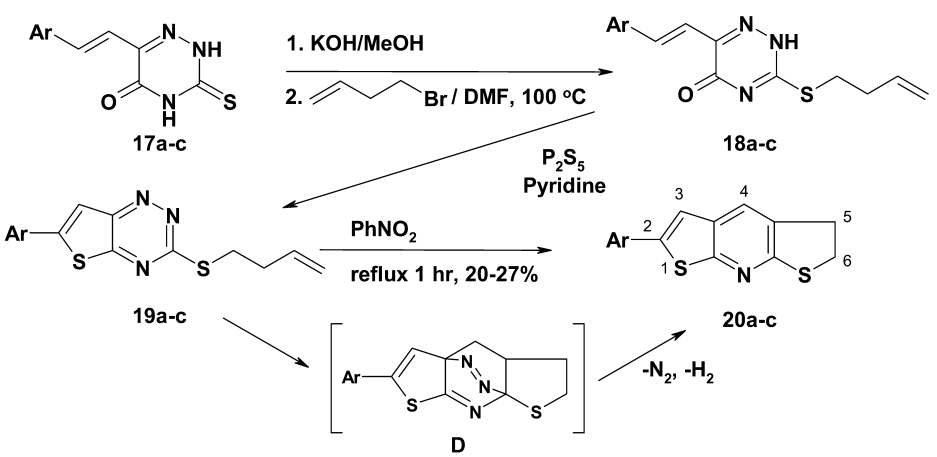
Scheme 3.

ω-alkynyl hydroxy compounds was investigated (Scheme 2). Thus, treatment of **6a-d** with sodium 3-butyn-1-oxide (prepared in situ from 3-butyn-1-ol and NaH in THF) gave the corresponding 6-aryl-3-(3-butyn-1-yloxy)thieno[2,3-*e*]-[1,2,4]triazines **11a-d** in good to excellent yields. Similarly, the 3-(2-allyphenoxy)-6-arylthieno[2,3-*e*][1,2,4]triazines **12a-d** were obtained upon treatment of the sulfones **6a-d** with sodium 2-allylphenoxide (prepared in situ from 2-allyl-phenol and NaH in THF). Also, 3-(1-allylnaphthalen-2-yloxy)-6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4]triazine **13b** was readily synthesized by the reaction of 1-allyl-2-naphthol and the sulfone **6b**.

Intramolecular cycloaddition reactions of **11a-d** were successful either by heating in an oil bath at 200°C for 1 h or in refluxing nitrobenzene for 1 h to give the corresponding expected 6-aryl-2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*] pyridines **14a-d**, respectively, in 48–55% yield. Similarly, heating each of **12a-d** in nitrobenzene at reflux for 1 h afforded the corresponding 5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]-pyridines **15a-d** in 42–59% yields. The benzochromeno derivative **16b** was similarly synthesized from **13b** in 57% yield. All these products **14**–**16** were formed by initial [4+2] intramolecular cycloaddition reactions through the 3,6-position of the triazine ring and the terminal ene or yne moiety to give the corresponding cycloadducts **C**, **D** and **E** intermediates followed by extrusion of nitrogen and loss of H_2 (from **D** and **E** only) to form finally the corresponding condensed pyridine systems **14a-d**, **15a-d**, **16b** (Scheme 3).

Alternatively, the synthesis of the bisthieno[2,3-*b*:3′,2′-*e*]-pyridines **20a-c** were accomplished as shown in Scheme 4. This starts by reacting the potassium salt of 6-β-arylvinyl-2,3-dihydro-3-thioxo-1,2,4-triazin-5(4*H*)-ones **17a-c** with 4-bromo-1-butene in DMF to give the corresponding 6-arylvinyl-3-(3-buten-1-ylsulfanyl)-1,2,4-triazin-5(2*H*)-ones **18a-c**. Compounds **18a-c** were readily converted into their corresponding 6-aryl-3-(3-buten-1-ylsulfanyl)-thieno[2,3-*e*][1,2,4]triazines **19a-e** upon heating in pyridine with phosphorus pentasulfide following our reported procedures for the preparation of this ring system.[10–12] Heating compounds **19a-e** under different conditions were investigated in order to find the optimum conditions to achieve their intramolecular cycloaddition. Thus, the best condition was achieved by heating each of compounds **19a-c** in nitrobenzene under reflux for 1 h which led to the formation of the corresponding expected 2-aryl-5,6-dihydrobisthieno[2,3-*b*:3′,2′-*e*]pyridines **20a-c** in 20–27%. The latter were formed via the intermediate 4+2 cyclo-adducts **D** which subsequently lose N_2 and H_2 to give the final products **20a-c**.

The structures of all new compounds were established by spectral and analytical data. Table 1 shows the proton NMR



Scheme 4.

Table 1. ^{1}H NMR of the thienopyridine derivatives **14a-d**, **15a-d**, **16b**, **20a-c**

Product	^{1}H NMR[a] δ=/J (Hz)				
	H^3	H^4	H^5	H^6	ArHs and other Hs
14a	7.36	7.84	3.36/8.4	4.74/8.4	7.33 (t, 1H, J=7.6 Hz), 7.43 (t, 2H, J=7.6 Hz), 7.68 (d, 2H, J=7.6 Hz)
14b	7.24	7.77	3.35/8.4	4.75/8.4	6.96 (d, 2H, J=8.4 Hz), 7.61 (d, 2H, J=8.4 Hz), 3.87 (s, 3H, OCH_3)
14c	7.28	7.78	3.36/8.4	4.74/8.4	6.50 (dd, 1H, J=1.5, 3.6 Hz), 6.59 (d, 1H, J=3.6 Hz), 7.47 (d, 1H, J=1.5 Hz)
14d	7.21	7.75	3.35/8.4	4.74/8.4	7.07 (t, 1H, J=4.2 Hz), 7.26 (d, 1H, J=4 Hz), 7.29 (d, 1H, J=4.4 Hz)
15a	7.39	7.89	4.26		7.12 (t, 1H, J=7.2 Hz), 7.21–7.28 (m, 3H), 7.38 (t, 1H, J=7.2 Hz), 7.45 (t, 2H, J=7.2 Hz), 7.71 (d, 2H, J=7.2 Hz)
15b	7.28	7.84	4.25		6.99 (d, 2H, J=8.4 Hz), 7.11 (t, 1H, J=7.2 Hz), 7.23 (m, 3H), 7.64 (d, 2H, J=8.4 Hz), 3.88 (s, 3H, OCH_3)
15c	7.59	8.15	4.25		6.67 (dd, 1H, J=1.6, 3.2 Hz), 6.97 (d, 1H, J=3.2 Hz), 7.16 (m, 2H), 7.31 (m, 2H), 7.83 (d, 1H, J=1.6 Hz)
15d	7.22	7.82	4.24		7.10 (t, 2H, J=4.0 Hz), 7.27 (m, 5H)
16b	7.32	7.99	4.59		6.99 (d, 2H, J=8.4 Hz), 7.42 (d, 1H, J=9.2 Hz), 7.50 (t, 1H, J=7.6 Hz), 7.64 (m, 3H), 7.80 (d, 1H, J=8.8 Hz), 7.90 (t, 2H, J=8.8 Hz), 3.89 (s, 3H, OCH_3)
20a	7.36	7.68	3.41/7.6	3.50/7.6	7.37 (t, 1H, J=7.5 Hz), 7.44 (t, 2H, J=7.5 Hz), 7.69 (d, 2H, J=7.5 Hz)
20b	7.22	7.68	3.40/7.6	3.50/7.6	6.96 (d, 2H, J=8.4 Hz), 7.69 (d, 2H, J=7.5 Hz), 3.87 (s, 3H, OCH_3)
20c	7.20	7.67	3.40/7.6	3.50/7.6	7.07 (dd, 1H, J=4, 4.8 Hz), 7.30 (d, 1H, J=4 Hz), 7.31 (d, 1H, J=4.8 Hz)

[a] All NMR were measured in $CDCl_3$ except **15c** in DMSO-d_6. Compounds **14a-d**, **20a-c**: H^3 (s, 1H), H^4 (s, 1H), H^5 (t, 2H), H^6 (t, 2H), for **15a-d**, **16b**: H^3 (s, 1H), H^4 (s, 1H), H^5 (s, 2H).

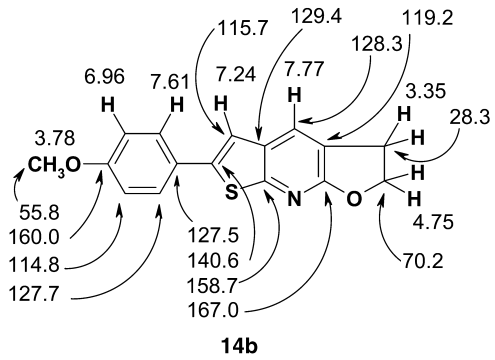


Figure 1. NMR signals assignment of **14b**.

of the new thienopyridines **14a-d**, **15a-d**, **16b**, **20a-d**. The pyridine H^4 proton of these new derivatives were found downfield in the range of δ=7.66–7.89 in $CDCl_3$. This was confirmed for compound **15a** by NOE-difference spectra upon irradiation at δ=4.26 (H^5) which enhanced H^4 and H^6. On the other hand all new thienopyridines shows their thiophene H^3 more upfield at δ=7.21–7.39 in $CDCl_3$. Full proton and carbon signal assignments of **14b** (Fig. 1) were made using ^{1}H NMR, H,H-COSY, HMQC and HMBC NMR techniques. Compound **15c** measured in DMSO-d_6 showed downfield shifts of these H^3, H^4 protons.

2. Conclusions

The present investigation offers an interesting synthetic approaches towards new condensed thienopyridine ring systems with other oxygen and sulfur heterocycles including furo[2,3-*b*]thieno[3,2-*e*]pyridines, bisthieno[2,3-*b*:3′,2′-*e*]-pyridines, 5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridines, 5*H*-benzo(*f*)chromeno[2,3-*b*]thieno[3,2-*e*]pyridines which have been achieved by application of intramolecular [4+2] cycloaddition reactions of suitably designed thieno[2,3-*e*]-[1,2,4]triazines tethered with terminal alkenes or alkynes. These new aryl and heteroaryl condensed pyridine systems contain heteroatoms suitably located for potential applications in complexation and supramolecular chemistry.

3. Experimental

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Perkin–Elmer System 2000 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, 400 MHz super-conducting NMR spectrometer. Mass spectra were measured on a VG Auto-spec-Q (high resolution, high performance, tri-sector GC/MS/MS). Microanalyses were performed on a LECO CHNS-932 Elemental Analyzer. *S*-Methylisothiosemi-carbazide hydroiodide,[14] compounds **2a**,[15] **2b**,[16] **2c**,[17] **2d**,[11] **2e**,[17] **3a**,[12] **3b**,[13] **4a**,**b**,[11] **17a**,[18] **17b**[19] were prepared following reported procedures.

3.1. 3-Methylsulfanyl-6-(2-oxo-2-arylethyl)-1,2,4-triazin-5(2*H*)-ones 3c-e. General procedure

A solution of *S*-methylisothiosemicarbazide hydroiodide (11.65 g, 50 mmol) and the appropriate ethyl 2,4-dioxo-4-arylbutyrates **2c-e** (50 mmol) in pyridine (50 ml) was heated under reflux for 1 h. After cooling, water (300 ml) was added and the solution was left at room temperature overnight. The solid precipitated was collected, washed with water and crystallized from ethanol.

3.1.1. 6-[2-(2-Furyl)-2-oxoethyl]-3-methylsulfanyl-1,2,4-triazin-5(2*H*)-one (3c). From **2c**. Yellow crystals, mp 223–224°C, yield=9.86 g (78%). MS: m/z=251 (M^+). IR: 3144, 1665, 1591, 1564, 1449, 1423, 1272, 1034. ^{1}H NMR (DMSO-d_6) δ=2.46 (s, 3H, SMe), 4.09 (s, 2H), 6.76 (dd, 1H, J=1.5, 4 Hz), 7.57 (d, 1H, J=4.0 Hz), 8.03 (d, 1H, J=1.5 Hz), 13.95 (brs, 1H, NH). ^{1}H NMR (DMSO-d_6) (methine tautomer) δ=2.45 (s, 3H, SMe), 6.25 (s, 1H), 6.67 (dd, 1H, J=1.6, 3.5 Hz), 7.22 (d, 1H, J=3.5 Hz), 7.89 (d, 1H, J=1.5 Hz), 13.54 (brs, 1H, NH), 13.95 (brs, 1H, NH). Anal. for $C_{10}H_9N_3O_3S$ (251.3) calcd: C, 47.80; H, 3.61; N,

16.72; S, 12.70. Found: C, 47.86; H, 3.75; N, 16.67; S, 12.64.

3.1.2. 3-Methylsulfanyl-6-[2-oxo-2-(2-thienyl)ethyl]-1,2,4-triazin-5(2*H*)-one (3d). From **2d**. Yellow crystals, mp 216–218°C, yield=10.36 g (78%). IR: 3188, 3054, 2929, 1691, 1602, 1417, 1341, 1022. ^{1}H NMR (DMSO-d_6) δ=2.45 (s, 3H, SMe), 4.25 (s, 2H), 7.29 (t, 1H, *J*=4.0 Hz), 7.84 (d, 1H, *J*=4.8 Hz), 8.09 (d, 1H, *J*=3.6 Hz), 13.95 (brs, 1H, NH). ^{1}H NMR (DMSO-d_6) (methine tautomer) δ=2.45 (s, 3H, SMe), 6.29 (s, 1H), 7.18 (t, 1H, *J*=4.0 Hz), 7.80 (d, 1H, *J*=3.6 Hz), 8.06 (d, 1H, *J*=4.8 Hz), 13.54 (brs, 1H, NH), 13.95 (brs, 1H, NH). Anal. for $C_{10}H_9N_3O_2S_2$ (267.3) calcd: C, 44.93; H, 3.39; N, 15.72; S, 23.99. Found: C, 44.82; H, 3.60; N, 15.79; S, 23.82.

3.1.3. 3-Methylsulfanyl-6-[2-oxo-2-(2-pyridyl)ethyl]-1,2,4-triazin-5(2*H*)-one (3e). From **2e**. Brown crystals, mp 239–241°C, yield=1.17 g (9%). MS: *m*/*z*=262 (M^+). IR: 3033, 1712, 1606, 1565, 1374, 1203, 750. ^{1}H NMR (DMSO-d_6) δ=2.43 (s, 3H, SMe), 4.32 (s, 2H), 7.64 (m, 1H), 7.95 (m, 2H), 8.69 (d, 1H, *J*=4.4 Hz), 13.87 (s, 1H, NH). ^{1}H NMR (DMSO-d_6) (methine tautomer) δ=2.41 (s, 3H, SMe), 6.99 (s, 1H), 7.64 (m, 1H), 7.95 (m, 2H), 8.61 (d, 1H, *J*=4.4 Hz), 12.60 (s, 1H, NH), 13.80 (s, 1H, NH). Anal. for $C_{11}H_{10}N_4O_2S$ (262.3) calcd: C, 50.37; H, 3.84; N, 21.36; S, 12.22. Found: C, 50.60; H, 3.99; N, 21.22; S, 12.09.

3.2. 3-Methylsulfanyl-6-arylthieno[2,3-*e*][1,2,4]triazines 4c-e. General procedure

To a cold solution (5°C) of each of **3c-e** (23 mmol) in pyridine (15 ml), phosphorus pentasulfide (10.21 g, 46 mmol) was added portionwise with stirring. The mixture was then heated under reflux for 6 h. After cooling, the solid precipitated was collected, washed with cold water and ethanol and then recrystallized from DMF.

3.2.1. 6-(2-Furyl)-3-methylsulfanylthieno[2,3-*e*][1,2,4]-triazine (4c). From **3c**. Reddish brown crystals, mp 182–183°C, yield=4.58 g (79%). MS: *m*/*z*=249 (M^+). IR: 3436, 3095, 1594, 1514, 1362, 1199, 1018. ^{1}H NMR ($CDCl_3$) δ=2.75 (s, 3H, SMe), 6.60 (dd, 1H, *J*=1.6, 3.6 Hz), 6.90 (d, 1H, *J*=3.6 Hz), 7.62 (d, 1H, *J*=1.6 Hz), 7.70 (s, 1H). Anal. for $C_{10}H_7N_3OS_2$ (249.3) calcd: C, 48.18; H, 2.83; N, 16.85; S, 25.72. Found: C, 47.98; H, 2.92; N, 16.76; S, 25.67.

3.2.2. 3-Methylsulfanyl-6-(2-thienyl)thieno[2,3-*e*]-[1,2,4]triazine (4d). From **3d**. Yellow crystals, mp 160–162°C, yield=4.82 g (79%). MS: *m*/*z*=265 (M^+). IR: 3435, 1623, 1550, 1496, 1373, 1240, 1067. ^{1}H NMR ($CDCl_3$) δ=2.76 (s, 3H, SMe), 7.16 (dd, 1H, *J*=3.6, 4.8 Hz), 7.47 (dd, 1H, *J*=1.2, 3.6 Hz), 7.51 (dd, 1H, *J*=1.2, 4.8 Hz), 7.64 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=14.6, 115.2, 128.0, 128.9, 129.1, 135.9, 141.4, 154.1, 162.1, 168.1. Anal. for $C_{10}H_7N_3S_3$ (265.4) calcd: C, 45.26; H, 2.66; N, 15.83. Found: C, 45.33; H, 2.82; N, 15.85.

3.2.3. 3-Methylsulfanyl-6-(2-pyridyl)thieno[2,3-*e*]-[1,2,4]triazine (4e). From **3e**. Green crystals, mp 230–232°C, yield=2.99 g (50%). MS: *m*/*z*=260 (M^+). IR: 1583, 1511, 1457, 1433, 1371, 1244, 1116, 1070, 991, 887, 88, 772, 709. ^{1}H NMR (DMSO-d_6) δ=2.69 (s, 3H, SMe), 7.52 (t, 1H, *J*=6.0 Hz), 8.03 (t, 1H, *J*=8.0 Hz), 8.40 (d, 1H, *J*=8.0 Hz), 8.64 (s, 1H), 8.68, (d, 1H, *J*=4.0 Hz). Anal. for $C_{11}H_8N_4S_2$ (260.3) calcd: C, 50.75; H, 3.10; N, 21.52; S, 24.63. Found: C, 50.57; H, 3.24; N, 21.41; S, 24.93.

3.3. 6-Aryl-3-methanesulfinylthieno[2,3-*e*][1,2,4]-triazines 5a,c. General procedure

To a stirred solution of each of **4a**,**c** (7.7 mmol) in anhydrous dichloromethane (50 ml) at 0°C, 3-chloroperoxybenzoic acid (77%, 1.9 g, 8.47 mmol, 1.1 equiv.) was added portionwise. The solution was left stirring at room temperature overnight. After removal of the solvent on rotavap and trituration with ether, the product was recrystallized from dichloromethane and ethanol.

3.3.1. 3-Methanesulfinyl-6-phenylthieno[2,3-*e*][1,2,4]-triazine (5a). From **4a**. Yellow crystals, mp 179–180°C, yield=1.59 g (75%). IR: 2992, 2910, 1532, 1492, 1373, 1068, 756, 684. ^{1}H NMR ($CDCl_3$) δ=3.17 (s, 3H), 7.58 (m, 3H), 7.84 (dd, 2H, *J*=2.4, 7.2 Hz), 8.03 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=41.5, 115.5, 127.6, 130.1, 131.9, 132.0, 154.3, 157.8, 163.1, 168.0. Anal. for $C_{12}H_9N_3OS_2$ (275.4) calcd: C, 52.35; H, 3.29; N, 15.26; S, 23.29. Found: C, 52.39; H, 3.32; N, 15.11; S, 23.68.

3.3.2. 6-(2-Furyl)-3-methanesulfinylthieno[2,3-*e*][1,2,4]-triazine (5c). From **4c**. Yellow crystals, mp 188–190°C, yield=1.43 g (70%). IR: 3117, 3098, 3007, 2909, 1583, 1517, 1480, 1412, 1384, 1366, 1236, 1209, 1117, 1070, 1033, 958, 881, 853, 841, 784. MS: *m*/*z*=265 (M^+). ^{1}H NMR (DMSO-d_6) δ=3.06 (s, 3H, SOMe), 6.85 (dd, 1H, *J*=1.6, 3.6 Hz), 7.53 (d, 1H, *J*=3.6 Hz), 8.07 (d, 1H, *J*=1.6 Hz), 8.24 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=41.5, 113.3, 113.4, 113.6, 142.0, 146.3, 147.3, 157.5, 163.2, 167.7. Anal. for $C_{10}H_7N_3OS_2$ (265.4) calcd: C, 45.27; H, 2.66; N, 15.84; S, 24.17. Found: C, 45.45; H, 2.75; N, 16.03; S, 23.95.

3.4. 3-Methanesulfonyl-6-arylthieno[2,3-*e*][1,2,4]-triazines 6a-d. General procedures

(a) To a stirred ice cooled solution of each of the appropriate derivative **4** (7.7 mmol) in dichloromethane (50 ml) and acetic acid (50 ml) was added hydrogen peroxide (30%, 8.7 ml) and the mixture was left stirring over night at room temperature. Dichloromethane was distilled off under reduced pressure at 50°C. After cooling and dilution with water the precipitate was collected and recrystallized from dichloromethane and ethanol.

(b) To a stirred solution of each of the appropriate derivative **4** (7.7 mmol) in anhydrous dichloromethane (50 ml) at 0°C, 3-chloroperoxybenzoic acid (77%, 3.44 g, 15.4 mmol, 2 equiv.) was added portionwise. The solution was left stirring at room temperature overnight. After triturating with ether, the product was collected and recrystallized from DCM/EtOH.

3.4.1. 3-Methanesulfonyl-6-phenylthieno[2,3-*e*][1,2,4]-triazine (6a). From **4a** using procedures a and b. Yellow crystals, mp 263–264°C, yield=1.7 g (76%).

IR: 3082, 3051, 2920, 1652, 1534, 1491, 1476, 1118, 1069, 841, 754, 684. ^{1}H NMR (DMSO-d_6) δ=3.59 (s, 3H, SO_2Me), 7.59 (m, 3H), 8.05 (m, 2H), 8.63 (s, 1H). Anal. for $C_{12}H_9N_3O_2S_2$ (291.4) calcd: C, 49.47; H, 3.11; N, 14.42; S, 22.01. Found: C, 49.08; H, 3.28; N, 14.42; S, 21.86.

3.4.2. 3-Methanesulfonyl-6-(4-methoxyphenyl)thieno-[2,3-*e*][1,2,4]triazine (6b). From **4b** using procedures a and b. Orange crystals, mp 256–257°C, yield 1.63 g (73%). MS: *m*/*z*=321 (M^+). IR: 3086, 2927, 1603, 1502, 1379, 1247, 1183, 1128, 1083, 1026, 838, 577, 535, 495. ^{1}H NMR (DMSO-d_6) δ=3.57 (s, 3H, SO_2Me), 3.87 (s, 3H, OCH_3), 7.14 (m, 2H), 8.02 (m, 2H), 8.48 (s, 1H). ^{13}C NMR (DMSO-d_6) δ=41.3, 56.5, 115.0, 116.0, 124.6, 130.0, 155.3, 159.3, 160.3, 162.3, 163.0. Anal. for $C_{13}H_{11}N_3O_3S_2$ (321.4) calcd: C, 48.59; H, 3.45; N, 13.07; S, 19.95. Found: C, 48.40; H, 3.51; N, 13.02; S, 20.17.

3.4.3. 6-(2-Furyl)-3-methanesulfonylthieno[2,3-*e*][1,2,4]-triazine (6c). From **4c** using procedure a. Yield 1.67 g (74%) mp 253–255°C. IR: 3148, 3110, 3041, 3017, 2936, 1589, 1510, 1445, 1389, 1365, 1310, 1140, 1117, 1072, 1026, 973, 955, 883, 823, 787. MS: *m*/*z*=281 (M^+). ^{1}H NMR (DMSO-d_6) δ=3.57 (s, 3H, SO_2Me), 6.87 (dd, *J*=2.4, 3.6 Hz, 1H), 7.59 (d, 1H, *J*=3.6 Hz), 8.10 (d, 1H, *J*=1.6 Hz), 8.32 (s, 1H). Anal. for $C_{10}H_7N_3O_3S_2$ (281.3) calcd: C, 42.70; H, 2.51; N, 14.94; S, 22.80. Found: C, 43.01; H, 2.65; N, 15.08; S, 22.82.

3.4.4. 3-Methanesulfonyl-6-(2-thienyl)-thieno[2,3-*e*]-[1,2,4]triazine (6d). From **4d** using procedure a. Yield 1.76 g (80%), mp 262–264°C. MS: *m*/*z*=297 (M^+). ^{1}H NMR (DMSO-d_6) δ=3.57 (s, 3H, SO_2Me), 7.32 (t, 1H, *J*=3.6 Hz), 7.98 (m, 2H), 8.35 (s, 1H). Anal. for $C_{10}H_7N_3O_2S_3$ (297.4) calcd: C, 40.39; H, 2.37; N, 14.13; S, 32.35. Found: C, 40.64; H, 2.49; N, 14.31; S, 32.37.

3.4.5. 6-(4-Methoxyphenyl)thieno[2,3-*e*][1,2,4]triazin-3-ol (7b). To a stirred solution of **6b** (0.1 g, 0.31 mmol) in DCM (10 ml) and benzyltriethylammonium chloride (0.1 g) was added a solution of NaOH (1.35 g in 2 ml of water). The mixture was kept stirring overnight at room temperature and DCM was removed by heating on water bath at 50°C. The mixture was then acidified with dilute HCl and the precipitate was collected, washed with water and crystallized from ethanol into yellow crystals of **7b**, mp 303°C, yield=0.05 g (62%). MS: *m*/*z*=259 (M^+). IR: 3433, 1638, 1601, 1502, 1256, 1179, 1079. ^{1}H NMR (DMSO-d_6) δ=3.84 (s, 3H, OMe), 7.09 (d, 2H, *J*=8.8 Hz), 7.64 (s, 1H), 7.79 (d, 2H, *J*=8.8 Hz), 13.60 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=56.3, 113.1, 115.6, 125.0, 128.9, 144.9, 147.0, 152.5, 162.0, 173.7. Anal. for $C_{12}H_9N_3O_2S$ (259.3) calcd: C, 55.59; H, 3.50; N, 16.21; S, 12.37. Found: C, 55.32; H, 3.70; N, 15.90; S, 12.63.

3.5. 3-Methoxy-6-arylthieno[2,3-*e*][1,2,4]triazines 8a,b. General procedure

To a solution of sodium methoxide (prepared from 0.19 g Na in 10 ml of distilled methanol) was added each of **6a**,**b** (1.7 mmol) with stirring. Stirring was then continued overnight at room temperature under nitrogen. After dilution with water the precipitate was collected, dried and crystallized from ethanol.

3.5.1. 3-Methoxy-6-phenylthieno[2,3-*e*][1,2,4]triazine (8a). From **6a**. Yellow crystals, mp 169–170°C, yield=0.25 g (60%). MS: *m*/*z*=243 (M^+). IR: 1625, 1529, 1475, 1384, 1305, 1128, 1095, 1055. ^{1}H NMR ($CDCl_3$) δ=4.28 (s, 3H, OMe), 7.52 (m, 3H), 7.76 (m, 2H), 7.83 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=56.7, 115.8, 127.3, 130.0, 130.9, 133.0, 148.0, 154.3, 162.6, 164.3. Anal. for $C_{12}H_9N_3OS$ (243.3) calcd: C, 59.24; H, 3.73; N, 17.27; S, 13.18. Found: C, 59.24; H, 3.79; N, 17.27; S, 13.37.

3.5.2. 3-Methoxy-6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4]triazine (8b). From **27**. Yellow crystals, mp 210–212°C, yield=0.31 g (67%). MS: *m*/*z*=273 (M^+). IR: 1604, 1536, 1507, 1473, 1387, 1312, 1256, 1180, 1051, 837. ^{1}H NMR (DMSO-d_6) δ=3.83 (s, 3H, ArOMe), 4.11 (s, 3H, OMe), 7.05 (d, 2H, *J*=7.5 Hz), 7.80 (d, 2H, *J*=7.5 Hz), 8.07 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=56.1, 56.7, 114.0, 115.3, 125.5, 128.7, 148.0, 154.6, 161.9, 162.4, 164.4. Anal. for $C_{13}H_{11}N_3O_2S$ (273.3) calcd: C, 57.13; H, 4.06; N, 15.37; S, 11.73. Found: C, 57.32; H, 4.03; N, 15.48; S, 11.78.

3.6. Preparation of 9–13. General procedure

A mixture of NaH (0.1 g NaH 60% in mineral oil washed with hexane) in dry THF (5 ml) and each of phenol, 2-phenylethanol, 3-butyn-1-ol, 2-allylphenol or 1-allyl-2-naphthol (2 mmol) was warmed till hydrogen gas cease to evolve. To this mixture was added each of **6a**,**b** (1.7 mmol) with stirring. After stirring overnight at room temperature under nitrogen, water was added to the mixture and precipitate was collected, dried and crystallized from ethanol.

3.6.1. 3-Phenoxy-6-phenylthieno[2,3-*e*][1,2,4]triazine (9a). From phenol and **6a**. Yellow crystals, mp 165–167°C, yield=0.46 g (88%). MS: *m*/*z*=305 (M^+). IR: 1631, 1600, 1564, 1498, 1456, 1433, 1361, 1349, 1275, 752. ^{1}H NMR ($CDCl_3$) δ=7.33 (m, 3H), 7.52 (m, 5H), 7.74 (m, 2H), 7.86 (s, 1H). Anal. for $C_{17}H_{11}N_3OS$ (305.4) calcd: C, 66.87; H, 3.63; N, 13.76; S, 10.50. Found: C, 66.67; H, 3.72; N, 13.79; S, 10.56.

3.6.2. 6-(4-Methoxyphenyl)-3-phenoxythieno[2,3-*e*][1,2,4]triazine (9b). From phenol and **6b**. Yellow crystals, mp 216–218°C, yield=0.4 g (70%). IR: 3093, 3056, 2971, 1603, 1532, 1507, 1489, 1422, 1397, 1357, 1306, 1259, 1195, 1182, 1132, 1094, 1026, 845, 808, 783, 765, 689. ^{1}H NMR (DMSO-d_6) δ=3.84 (s, 3H, OMe), 7.10 (d, 2H, *J*=8.3 Hz), 7.33 (m, 3H), 7.50 (t, 2H, *J*=7.5 Hz), 7.87 (d, 2H, *J*=8.4 Hz), 8.20 (s, 1H). Anal. for $C_{18}H_{13}N_3O_2S$ (335.4) calcd: C, 64.46; H, 3.91; N, 12.53; S, 9.56. Found: C, 64.37; H, 3.86; N, 12.58; S, 9.48.

3.6.3. 6-Phenyl-3-(2-phenylethoxy)thieno[2,3-*e*][1,2,4]-triazine (10a). From 2-phenylethanol and **6a**. Yellow crystals, mp 131–132°C, yield=0.42 g (74%). MS: *m*/*z*=333 (M^+). IR: 1531, 1483, 1467, 1448, 1428, 1374, 1300, 1088, 1055, 754. ^{1}H NMR ($CDCl_3$) δ=3.26 (t, 2H, *J*=7.2 Hz), 4.85 (t, 2H, *J*=7.2 Hz), 7.27 (t, 1H, *J*=6.0 Hz), 7.36 (m, 4H), 7.51 (m, 3H), 7.75 (d, 2H, *J*=7.5 Hz), 7.82 (s,

1H). Anal. for $C_{19}H_{15}N_3OS$ (333.4) calcd: C, 68.45; H, 4.53; N, 12.60; S, 9.62. Found: C, 68.17; H, 4.55; N, 12.61; S, 9.44.

3.6.4. 6-(4-Methoxyphenyl)-3-(2-phenylethoxy)-thieno[2,3-*e*][1,2,4]triazine (10b). From 2-phenylethanol and **6b**. Yellow crystals, mp 157–158°C, yield=0.45 g (73%). MS: *m*/*z*=363 (M^+). IR: 3419, 1604, 1503, 1428, 1347, 1310, 1259, 1177. ^{1}H NMR (Acetone-d_6) δ=3.23 (t, 2H, *J*=6.8 Hz), 3.90 (s, 3H, OMe), 4.80 (t, 2H, *J*=6.8 Hz), 7.11 (d, 2H, *J*=7.1 Hz), 7.25 (t, 1H, *J*=7.3 Hz), 7.34 (t, 2H, *J*=6.9 Hz), 7.41 (d, 2H, *J*=7.3 Hz), 7.86 (d, 2H, *J*=7.1 Hz), 7.91 (s, 1H). Anal. for $C_{20}H_{17}N_3O_2S$ (363.41) calcd: C, 66.16; H, 4.71; N, 11.56; S, 8.82. Found: C, 65.77; H, 4.78; N, 11.67; S, 8.68.

3.6.5. 3-(But-3-ynyloxy)-6-phenylthieno[2,3-*e*][1,2,4]-triazine (11a). From 3-butyn-1-ol and **6a**. Yellow crystals, mp 177–178°C, yield=0.35 g (73%). MS: *m*/*z*=281 (M^+). IR: 1521, 1486, 1449, 1371, 1303, 1281, 1094, 1015, 756, 786. ^{1}H NMR ($CDCl_3$) δ=2.08 (t, 1H, *J*=2.4 Hz), 2.87 (dt, 2H, *J*=2.4, 7.1 Hz), 4.76 (t, 2H, *J*=7.1 Hz), 7.53 (m, 3H), 7.76 (dd, 2H, *J*=1.6, 7.6 Hz), 7.84 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=19.6, 66.9, 70.8, 80.2, 115.5, 127.1, 129.8, 130.8, 132.7, 148.2, 154.4, 161.6, 164.1. Anal. for $C_{15}H_{11}N_3OS$ (281.3) calcd: C, 64.04; H, 3.94; N, 14.94; S, 11.40. Found: C, 63.91; H, 4.02; N, 15.05; S, 11.81.

3.6.6. 3-(But-3-ynyloxy)-6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4]triazine (11b). From 3-butyn-1-ol and **6b**.Yellow crystals, mp 170–171°C, yield=0.38 g (72%). IR: 1605, 1535, 1505, 1492, 1428, 1314, 1256, 1184, 1047, 824. ^{1}H NMR ($CDCl_3$) δ=2.08 (t, 1H, *J*=2.4 Hz), 2.86 (dt, 2H, *J*=2.4, 7.2 Hz), 3.91 (s, 3H), 4.75 (t, 2H, *J*=7.2 Hz), 7.03 (dd, 2H, *J*=2, 6.8 Hz), 7.69 (dd, 2H, *J*=2, 6.8 Hz), 7.70 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=19.6, 56.0, 66.8, 70.7, 80.2, 113.8, 115.2, 125.3, 128.6, 148.1, 154.6, 161.5, 161.8, 164.2. Anal. for $C_{16}H_{13}N_3O_2S$ (311.4) calcd: C, 61.72; H, 4.21; N, 13.50; S, 10.30. Found: C, 61.66; H, 4.26; N, 13.51; S, 10.08.

3.6.7. 3-(But-3-ynyloxy)-6-(2-furyl)thieno[2,3-*e*][1,2,4]-triazine (11c). From 3-butyn-1-ol and **6c**. Orange crystals, mp 174–175°C, yield=0.40 g (87%). MS: *m*/*z*=271 (M^+). IR: 1599, 1520, 1427, 1359, 1304, 1091, 1024, 972, 824. ^{1}H NMR ($CDCl_3$) δ=2.08 (t, 1H, *J*=2.4 Hz), 2.85 (dt, 2H, *J*=2.4, 6.8 Hz), 4.74 (t, 2H, *J*=6.8 Hz), 6.59 (dd, 1H, *J*=1.5, 3.5 Hz), 6.87 (d, 1H, *J*=3.5 Hz), 7.61 (d, 1H, *J*=1.5 Hz), 7.70 (s, 1H). Anal. for $C_{13}H_9N_3O_2S$ (271.3) calcd: C, 57.55; H, 3.34; N, 15.49; S, 11.82. Found: C, 57.73; H, 3.51; N, 15.56; S, 12.12.

3.6.8. 3-(But-3-ynyloxy)-6-(2-thienyl)thieno[2,3-*e*]-[1,2,4]triazine (11d). From 3-butyn-1-ol and **6d**. Green crystals, mp 153–154°C, yield=0.42 g (87%). MS: *m*/*z*=287 (M^+). IR: 3266, 3087, 3059, 1543, 1523, 1485, 1434, 1373, 1304, 1283, 1098, 1022, 847, 784. ^{1}H NMR ($CDCl_3$) δ=2.08 (t, 1H, *J*=2 Hz), 2.85 (dt, 2H, *J*=2, 7 Hz), 4.74 (t, 2H, *J*=7 Hz), 7.15 (dd, 1H, *J*=4.0, 8.4 Hz), 7.48 (m, 2H), 7.64 (s, 1H). Anal. for $C_{13}H_9N_3OS_2$ (287.4) calcd: C, 54.34; H, 3.16; N, 14.62; S, 22.32. Found: C, 53.99; H, 3.30; N, 14.61; S, 22.62.

3.6.9. 3-(2-Allylphenoxy)-6-phenylthieno[2,3-*e*][1,2,4]-triazine (12a). From 2-allylphenol and **6a**. Yellow crystals, mp 124–126°C, yield=0.41 g (69%). MS: *m*/*z*=345 (M^+). IR: 3056, 2976, 2907, 2841, 1639, 1520, 1487, 1403, 1297, 1077. ^{1}H NMR ($CDCl_3$) δ=3.42 (d, 2H, *J*=6.4 Hz), 5.00 (m, 2H), 5.92 (m, 1H), 7.23 (dd, 1H, *J*=1.6, 7.6 Hz), 7.34 (m, 3H), 7.52 (m, 3H), 7.76 (dd, 2H, *J*=1.6, 7.6 Hz), 7.87 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=34.9, 115.6, 116.8, 122.4, 126.7, 127.2, 128.2, 129.8, 130.9, 131.2, 132.7, 132.8, 136.2, 148.8, 151.3, 154.8, 162.4, 163.9. Anal. for $C_{20}H_{15}N_3OS$ (345.4) calcd: C, 69.54; H, 4.38; N, 12.16; S, 9.28. Found: C, 69.72; H, 4.47; N, 12.44; S, 9.14.

3.6.10. 3-(2-Allylphenoxy)-6-(4-methoxyphenyl)-thieno[2,3-*e*][1,2,4]triazine (12b). From 2-allylphenol and **6b**. Yellow crystals from chloroform and ethanol, mp 143–144°C, yield=0.33 g (57%). MS: *m*/*z*=375 (M^+). IR: 3064, 3000, 2930, 2840, 1603, 1485, 1400, 1292, 1263, 1219, 1082, 1016, 920. ^{1}H NMR (DMSO-d_6) δ=3.34 (br, 2H), 3.85 (s, 3H, OMe), 4.96 (2d, 2H, *J*=9.3, 18.4 Hz), 5.86 (m, 1H), 7.10 (d, 2H, *J*=8.8 Hz), 7.30 (t, 2H, *J*=6.8 Hz), 7.37 (t, 2H, *J*=9.2 Hz), 7.87 (d, 2H, *J*=8.8 Hz), 8.23 (s, 1H). Anal. for $C_{21}H_{17}N_3O_2S$ (375.45) calcd: C, 67.18; H, 4.56; N, 11.19; S, 8.54. Found: C, 67.24; H, 4.53; N, 11.20; S, 8.25.

3.6.11. 3-(2-Allylphenoxy)-6-(2-furyl)thieno[2,3-*e*]-[1,2,4]triazine (12c). From 2-allylphenol and **6c**. Orange crystals, mp 130–132°C, yield=0.41 g (68%). MS: *m*/*z*=335 (M^+). IR: 3132, 3102, 3077, 3054, 3004, 2977, 2906, 1586, 1526, 1488, 1400, 1302, 1216, 1171, 1075, 816. ^{1}H NMR ($CDCl_3$) δ=3.42 (d, 2H, *J*=6.4 Hz), 5.00 (m, 2H), 5.90 (m, 1H), 6.60 (dd, 1H, *J*=1.6, 3.6 Hz), 6.88 (d, 1H, *J*=3.6 Hz), 7.22 (dd, 1H, *J*=1.2, 7.6 Hz), 7.31 (m, 3H), 7.62 (d, 1H, *J*=1.6 Hz), 7.74 (s, 1H). Anal. for $C_{18}H_{13}N_3O_2S$ (335.4) calcd: C, 64.46; H, 3.91; N, 12.53; S, 9.56. Found: C, 64.57; H, 3.98; N, 12.52; S, 9.50.

3.6.12. 3-(2-Allylphenoxy)-6-(2-thienyl)thieno[2,3-*e*]-[1,2,4]triazine (12d). From 2-allylphenol and **6d**. Yellow crystals, mp 105–106°C, yield=0.38 g (64%). MS: *m*/*z*=350 (M^+). IR: 3060, 2976, 2922, 2906, 1640, 1485, 1402, 1303, 1218, 1091, 706. ^{1}H NMR ($CDCl_3$) δ=3.41 (d, 2H, *J*=6.5 Hz), 5.00 (2d, 2H, *J*=9.2, 15.2 Hz), 5.93 (m, 1H), 7.15 (t, 1H, *J*=4.4 Hz), 7.22 (d, 1H, *J*=7.6 Hz), 7.33 (m, 3H), 7.45 (d, 1H, *J*=3.6 Hz), 7.50 (d, 1H, *J*=5.2 Hz), 7.68 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=34.9, 114.9, 116.8, 122.4, 126.7, 127.9, 128.2, 128.9, 129.0, 131.2, 132.7, 135.9, 136.1, 141.8, 151.3, 154.6, 162.4, 164.0. Anal. for $C_{18}H_{13}N_3OS_2$ (351.5) calcd: C, 61.52; H, 3.73; N, 11.96; S, 18.25. Found: C, 61.80; H, 3.89; N, 11.92, S, 18.43.

3.6.13. 3-(1-Allyl-2-naphthalenyloxy)-6-(4-methoxyphenyl)thieno[2,3-*e*][1,2,4]triazine (13b). From **6b** and 1-allyl-2-naphthol. Yield 69%, green crystals, mp 176–178°C. IR: 3085, 3000, 2959, 1635, 1604, 1576, 1504, 1489, 1421, 1398, 1304, 1256, 1214, 1180, 1092, 1026, 984, 918, 841, 818. ^{1}H NMR ($CDCl_3$) δ=3.91 (s, 3H, OMe), 3.92 (d, 2H, *J*=8.8 Hz) 4.96 (2d, 2H, *J*=8.4, 16.8 Hz), 5.98 (m, 1H), 7.03 (d, 2H, *J*=8.3 Hz), 7.37 (d, 1H, *J*=8.8 Hz), 7.55 (m, 2H), 7.69 (d, 2H, *J*=8.4 Hz), 7.76 (s, 1H), 7.86 (d, 1H, *J*=8.8 Hz), 7.92 (d, 1H, *J*=8 Hz), 8.09 (d, 1H, *J*=8.4 Hz).

Anal. for $C_{25}H_{19}N_3O_2S$ (425.5) calcd: C, 70.57; H, 4.50; N, 9.88; S, 7.54. Found: C, 70.31; H, 4.54; N, 9.98; S, 7.21.

3.6.14. 3-Mercapto-6-[2-(2-thienyl)vinyl]-1,2,4-triazin-5(2*H*)-one 17c. A mixture of 4-(2-thinyl)-2-oxo-3-butenoic acid (20 mmol) and thiosemicarbazide (20 mmol) in water (50 ml) was heated under reflux for 15 min. The mixture was left overnight at room temperature. The precipitate formed was collected, washed with cold water, dried to give 2-oxo-4-(2-thienyl)but-3-enoic acid thiosemicarbazone (4.72 g, 93%) which was dissolved in aqueous potassium hydroxide solution (1 M, 25 ml). The mixture was then heated under reflux for 20 min. After cooling, the solution was acidified with hydrochloric acid and the precipitate was collected, washed with water and recrystallized from DMF to give yellow crystals of **17c**, mp 288–290°C, yield 4.88 g (91%). IR: 3196, 3093, 2899, 2200–3200 (br), 1699, 1611, 1548, 1518, 1500, 1437, 1326, 1274, 1214, 1198, 1139, 1100, 1009, 960, 814, 775, 701, 676. ^{1}H NMR (DMSO-d_6) δ=6.74 (d, 1H, J=16.4 Hz), 7.11 (t, 1H, J=4.0 Hz), 7.40 (d, 1H, J=3.2 Hz), 7.61 (d, 1H, J=5.2 Hz), 7.96 (d, 1H, J=16.4 Hz), 13.20 (br, 1H), 13.58 (br, 1H). ^{13}C NMR (DMSO-d_6) δ=119.1, 129.0, 129.6, 129.8, 130.9, 142.2, 145.1, 154.0, 173.4. Anal. for $C_9H_7N_3OS_2.H_2O$ (225.3) calcd: C, 42.34; H, 3.55; N, 16.46; S, 25.12. Found: C, 42.30; H, 3.53; N, 16.28; S, 25.00.

3.7. 3-(3-Buten-1-ylsulfanyl)-6-(2-Arylvinyl)-1,2,4-triazin-5(2*H*)-ones 18a-c. General procedure

Each of **17a-c** (7.66 mmol) was dissolved in methanolic potassium hydroxide solution (0.47 g, 1.1 equiv. in 20 ml of distilled methanol). After evaporating the methanol, 4-bromo-1-butene (1.14 g, 1.1 equiv.) was added followed by DMF (10 ml). The mixture was then heated on a boiling water bath for 1 h then cooled and poured over 100 ml of cold water. The precipitate formed was collected, washed with water, dried and recrystallized from ethanol.

3.7.1. 3-(3-Buten-1-ylsulfanyl)-6-styryl-1,2,4-triazin-5(2*H*)-one (18a). From **17a**. Pale yellow crystals, mp 198–200°C, yield 1.5 g (69%). IR: 3180, 3060, 3025, 2978, 1603 (br), 1555, 1510, 1442, 1381, 1325, 1304, 1281, 1222, 1206, 1002, 973, 917, 745, 690. ^{1}H NMR (DMSO-d_6) δ=2.45 (m, 2H), 3.24 (t, 2H, J=7.2 Hz), 5.11 (m, 2H), 5.83 (m, 1H), 7.14 (d, 2H, J=16.4 Hz), 7.39 (m, 3H), 7.65 (d, 2H, J=7.2 Hz), 7.96 (d, 1H, J=16.4 Hz), 14.0 (br, 1H). Anal. for $C_{15}H_{15}N_3OS$ (285.4) calcd: C, 63.13; H, 5.30; N, 14.72; S, 11.24. Found: C, 63.12; H, 5.31; N, 14.71; S, 11.16.

3.7.2. 3-(3-Buten-1-ylsulfanyl)-6-(2-*p*-methoxyphenyl-vinyl)-1,2,4-triazin-5(2*H*)-one (18b). From **17b**. Yellow crystals, mp 212–213°C, yield 19.6 g (81%). IR: 3179, 3070, 2978, 2905, 1685 (w), 1604 (br), 1571, 1511, 1450, 1421, 1381, 1329, 1290, 1252, 1222, 1175, 1031, 1001, 977, 915, 825, 792. ^{1}H NMR ($CDCl_3$) δ=2.52 (t, 2H, J=7.2 Hz), 3.37 (q, 2H, J=7.6 Hz), 3.83 (s, 3H, OMe), 5.15 (2d, 2H, J=9.2, 16 Hz), 5.82 (m, 1H), 6.92 (d, 2H, J=8.4 Hz), 7.10 (d, 1H, J=16.4 Hz), 7.56 (d, 2H, J=8.4 Hz), 8.00 (d, 1H, J=16.4 Hz), 10.26 (br, 1H, NH). Anal. for $C_{16}H_{17}N_3O_2S$ (305.4) calcd: C, 60.93; H, 5.43; N, 13.32; S, 10.17. Found: C, 60.78; H, 5.39; N, 13.59; S, 10.05.

3.7.3. 3-(3-Buten-1-ylsulfanyl)-6-[2-(2-thienyl)vinyl]-1,2,4-triazin-5(2*H*)-one (18c). From **17c**. Yellow crystals, mp 200–202°C, yield 2.0 g (89%). IR: 3195, 3075, 3004, 2964, 2900, 1700 (m), 1593 (br), 1504, 1448, 1373, 1357, 1282, 1201, 1042, 1008, 963, 916, 853, 790, 701. ^{1}H NMR ($CDCl_3$) δ=2.52 (q, 2H, J=7.2 Hz), 3.35 (t, 2H, J=7.2 Hz), 5.12 (2d, 2H, J=8.6, 16.5 Hz), 5.80 (m, 1H), 6.99 (d, 1H, J=16.0 Hz), 7.07 (m, 1H), 7.25 (d, 1H, J=3.6 Hz), 7.28 (s, 1H), 7.34 (d, 1H, J=5 Hz) 8.28 (d, 1H, J=16.0 Hz), 10.50 (brs, 1H, NH). Anal. for $C_{13}H_{13}N_3OS_2$ (291.4) calcd: C, 53.59; H, 4.50; N, 14.42; S, 22.01. Found: C, 53.90; H, 4.56; N, 14.42; S, 22.22.

3.8. 3-(3-Buten-1-ylsulfanyl)-6-arylthieno[2,3-*e*][1,2,4]-triazines 19a-c. General procedure

Phosphorus pentasulfide (0.7 g, 3.2 mmol, 2 equiv.) was added portionwise with shaking to a solution of each of **18a-c** (1.6 mmol) in pyridine (5 ml). The reaction mixture was heated under reflux for 6 h. After cooling, the mixture was added to ice cold potassium hydroxide solution, left overnight and the precipitate formed was collected, washed with water and crystallized from ethanol.

3.8.1. 3-(3-Buten-1-ylsulfanyl)-6–phenylthieno[2,3-*e*]-[1,2,4]triazine (19a). From **18a**. Pale yellow crystals, mp 190–191°C, yield 0.17 g (35%). IR: 3091, 3053, 2975, 2901, 1636, 1538, 1512, 1490, 1442, 1369, 1237, 1173, 1116, 1064, 997, 914, 887, 839, 756, 690. ^{1}H NMR ($CDCl_3$) δ=2.61 (q, 2H. J=6.8 Hz), 3.42 (t, 2H. J=7.2 Hz), 5.15 (2d, 2H, J=10.4, 16.8 Hz), 5.94 (m, 1H), 7.52 (m, 3H), 7.77 (d, 2H, J=6.4 Hz), 7.82 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=30.7, 33.6, 115.9, 117.1, 127.2, 129.8, 130.9, 132.7, 136.5, 148.5, 154.4, 162.0, 167.8. Anal. for $C_{15}H_{13}N_3S_2$ (299.4) calcd: C, 60.17; H, 4.38; N, 14.03; S, 21.42. Found: C, 60.18; H, 4.37; N, 14.36; S, 21.67.

3.8.2. 3-(3-Buten-1-ylsulfanyl)-6-(4-methoxyphenyl)-thieno[2,3-*e*][1,2,4]triazine (19b). From **18b**. Brown crystals, mp 126–127°C, yield 0.15 g (28%). ^{1}H NMR ($CDCl_3$) δ=2.61 (q, 2H, J=7.2 Hz), 3.42 (t, 2H, J=7.2 Hz), 3.91 (s, 3H), 5.16 (2d, 2H, J=10.4, 16.8 Hz), 5.93 (m, 1H), 7.04 (d, 2H, J=8.8 Hz), 7.70 (s, 1H), 7.71 (d, 2H, J=8.8 Hz). Anal. for $C_{16}H_{15}N_3OS_2$ (329.5) calcd: C, 58.33; H, 4.59; N, 12.75; S, 19.47. Found: C, 58.22; H, 4.35; N, 12.85; S, 19.25.

3.8.3. 3-(3-Buten-1-ylsulfanyl)-6-(2-thienyl)thieno[2,3-*e*]-[1,2,4]triazine (19c). From **18c**. Yellow crystals, mp 104–105°C, yield=0.18 g (36%). ^{1}H NMR ($CDCl_3$) δ=2.60 (q, 2H, J=7.2 Hz), 3.42 (t, 2H, J=7.2 Hz), 5.15 (2d, 2H, J=10.4, 16.8 Hz), 5.95 (m, 1H), 7.16 (t, 1H, J=4.4 Hz), 7.47 (d, 1H, J=3.6 Hz), 7.51 (d, 1H, J=4.8 Hz), 7.64 (s, 1H). Anal. for $C_{13}H_{11}N_3S_3$ (305.4) calcd: C, 51.12; H, 3.63; N, 13.76; S, 31.49. Found: C, 51.26; H, 3.69; N, 13.80; S, 31.08.

3.9. Thienopyridines 14–16, 20. General procedures

(a) A solution of each of **11**–**13**, **19** (0.2 mmol) in nitrobenzene (2 ml) was heated under reflux for 1 h. After cooling the precipitated crystals were collected, washed with petroleum ether (40–60) and recrystallized from choroform/ethanol to give the corresponding thieno-pyridines **14**–**16** and **20**.

(b) Compound **11a** (0.17 mmol) was heated neat at 200°C on an oil bath for 1 h. After cooling, the solid was recrysallized from chloroform and ethanol.

3.9.1. 6-Phenyl-2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*]pyridine (14a). From **11a** using procedures a (yield 48%) and b (yield 54%). Pale brown crystals, mp 257–258°C. IR: 3064, 2972, 2917, 1558, 1570, 1518, 1487, 1473, 1437, 1403, 1358, 1249, 1224, 1195, 1048, 995, 954, 938, 911, 757, 742, 703, 687. MS: *m*/*z*=253 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.36 (t, 2H, *J*=8.4 Hz), 4.74 (t, 2H, *J*=8.4 Hz), 7.33 (t, 1H, *J*=7.6 Hz), 7.36 (s, 1H), 7.43 (t, 2H, *J*=7.6 Hz), 7.68 (d, 2H, *J*=7.6 Hz), 7.84 (s, 1H). Anal. for $C_{15}H_{11}NOS$ (253.3) calcd: C, 71.12; H, 4.38; N, 5.53; S, 12.66. Found: C, 70.79; H, 4.39; N, 5.86; S, 12.57.

3.9.2. 6-(4-Methoxyphenyl)-2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*]pyridine (14b). From **11b**. Orange crystals, mp 260–261°C, yield=25 mg (52%). IR: 2909, 2836, 1607, 1567, 1524, 1494, 1450, 1405, 1248, 1181, 1046, 1028, 995, 907, 832, 807, 745, 698. MS: *m*/*z*=283 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.35 (t, 2H, *J*=8.4 Hz), 3.87 (s, 3H), 4.75 (t, 2H, *J*=8.4 Hz), 6.96 (d, 2H, *J*=8.4 Hz), 7.24 (s, 1H), 7.61 (d, 2H, *J*=8.4 Hz), 7.77 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=28.3, 55.8, 70.2, 114.8, 115.7, 119.2, 127.5, 127.7, 128.3, 129.4, 140.6, 158.7, 160.0, 167.0. Anal. for $C_{16}H_{13}NO_2S$ (283.4) calcd: C, 67.82; H, 4.62; N, 4.94; S, 11.32. Found: C, 67.52; H, 4.60; N, 5.18; S, 10.98.

3.9.3. 6-(2-Furyl)-2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*]pyridine (14c). From **11c**. Green crystals, mp 254–255°C, yield=20 mg (49%). IR: 3075, 2973, 2920, 1561, 1513, 1475, 1437, 1402, 1357, 1250, 1211, 1185, 1152, 1043, 1017, 994, 970, 954, 922, 850, 793, 743, 727, 670. ^{1}H NMR ($CDCl_3$) δ=3.36 (t, 2H, *J*=8.4 Hz), 4.74 (t, 2H, *J*=8.4 Hz), 6.50 (dd, 1H, *J*=1.5, 3.6 Hz), 6.59 (d, 1H, *J*=3.6 Hz), 7.28 (s, 1H), 7.47 (d, 1H, *J*=1.5 Hz), 7.78 (s, 1H). Anal. for $C_{13}H_9NO_2S$ (243.3) calcd: C, 64.24; H, 3.57; N, 5.76; S, 13.18. Found: C, 63.92; H, 3.67; N, 5.83; S, 13.36.

3.9.4. 6-(2-Thienyl)-2,3-dihydrofuro[2,3-*b*]thieno[3,2-*e*]pyridine (14d). From **11d**. Orange crystals, mp 237–238°C, yield=24 mg (55%). IR: 3116, 3064, 2969, 2925, 1606, 1567, 1534, 1492, 1470, 1420, 1399, 1358, 1247, 1180, 1042, 993, 953, 917, 836, 814, 742, 692. ^{1}H NMR ($CDCl_3$) δ=3.35 (t, 2H, *J*=8.4 Hz), 4.74 (t, 2H, *J*=8.4 Hz), 7.07 (t, 1H, *J*=4.2 Hz), 7.21 (s, 1H), 7.26 (d, 1H, *J*=4 Hz), 7.29 (d, 1H, *J*=4.4 Hz), 7.75 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=28.2, 70.4, 117.2, 118.4, 125.0, 125.5, 128.36, 128.38, 128.9, 133.9, 137.9, 158.8, 167.3. Anal. for $C_{13}H_9NOS_2$ (259.4) calcd: C, 60.21; H, 3.50; N, 5.40; S, 24.73. Found: C, 60.10; H, 3.56; N, 5.84; S, 24.84.

3.9.5. 2-Phenyl-5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridine (15a). From **12a**. Buff crystals, mp 287–288°C, yield=23 mg (42%). IR: 3055, 3027, 1589, 1555, 1518, 1488, 1388, 1302, 1284, 1265, 1228, 1188, 1062, 895, 910, 750, 687. MS: *m*/*z*=314 (M^+). ^{1}H NMR ($CDCl_3$) δ=4.26 (s, 2H), 7.12 (t, 1H, *J*=7.2 Hz), 7.21–7.28 (m, 3H), 7.38 (t, 1H, *J*=7.2 Hz), 7.39 (s, 1H), 7.45 (t, 2H, *J*=7.2 Hz), 7.71 (d, 2H, *J*=7.2 Hz), 7.89 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=28.9, 113.4, 116.3, 117.6, 118.7, 120.0, 124.2, 126.7, 128.5, 128.9, 129.0, 129.5, 132.0, 132.8, 134.4, 143.2, 152.1, 156.5. Anal. for $C_{20}H_{13}NOS$ (315.4) calcd: C, 76.17; H, 4.15; N, 4.44; S, 10.17. Found: C, 75.81; H, 4.25; N, 4.72; S, 9.97.

3.9.6. 2-(4-Methoxyphenyl)-5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridine (15b). From **12b**. White crystals, mp 280–281°C, yield=29 mg (50%). IR: 3033, 2952, 2910, 2835, 1607, 1589, 1555, 1525, 1499, 1458, 1389, 1307, 1291, 1253, 1231, 1182, 1031, 896, 831, 817, 810, 749, 730. MS: *m*/*z*=345 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.88 (s, 3H), 4.25 (s, 2H), 6.99 (d, 2H, *J*=8.4 Hz), 7.11 (t, 1H, *J*=7.2 Hz), 7.23 (m, 3H), 7.28 (s, 1H), 7.64 (d, 2H, *J*=8.4 Hz), 7.84 (s, 1H). Anal. for $C_{21}H_{15}NO_2S$ (345.4) calcd: C, 73.02; H, 4.38; N, 4.05; S, 9.28. Found: C, 73.09; H, 4.37; N, 4.29; S, 9.12.

3.9.7. 2-(2-Furyl)-5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridine (15c). From **12c**. Brown crystals, mp 223–224°C, yield=26 mg (50%). IR: 3109, 3060, 1589, 1549, 1490, 1459, 1429, 1389, 1305, 1271, 1231, 1058, 1015, 970, 913, 896, 754, 728. MS: *m*/*z*=305 (M^+). ^{1}H NMR (DMSO-d_6) δ=4.25 (s, 2H), 6.67 (dd, 1H, *J*=1.6, 3.2 Hz), 6.97 (d, 1H, *J*=3.2 Hz), 7.16 (m, 2H), 7.31 (m, 2H), 7.59 (s, 1H), 7.83 (d, 1H, *J*=1.6 Hz), 8.15 (s, 1H). Anal. for $C_{18}H_{11}NO_2S$ (305.4) calcd: C, 70.80; H, 3.63; N, 4.59; S, 10.50. Found: C, 70.76; H, 3.66; N, 4.80; S, 10.26.

3.9.8. 2-(2-Thienyl)-5*H*-chromeno[2,3-*b*]thieno[3,2-*e*]pyridine (15d). From **12d**. Green crystals, mp 253–254°C, yield=32 mg (59%). IR: 3063, 3035, 1589, 1555, 1532, 1489, 1458, 1421, 1386, 1305, 1269, 1229, 1188, 1058, 962, 895, 836, 812, 758, 693. MS: *m*/*z*=320 (M^+). ^{1}H NMR ($CDCl_3$) δ=4.24 (s, 2H), 7.10 (m, 2H), 7.22 (s, 1H), 7.27 (m, 5H), 7.82 (s, 1H). ^{13}C NMR ($CDCl_3$) δ=28.9, 113.7, 116.6, 117.7, 120.1, 124.4, 125.9, 126.3, 128.6, 128.7, 129.1, 131.9, 132.7, 136.5, 137.7, 152.2, 156.7, 158.3. Anal. for $C_{18}H_{11}NOS_2$ (321.4) calcd: C, 67.26; H, 3.45; N, 4.36; S, 19.95. Found: C, 67.35; H, 3.51; N, 4.59; S, 20.12.

3.9.9. 2-(4-Methoxyphenyl)-5*H*-benzo(*f*)chromeno[2,3-*b*]thieno[3,2-*e*]pyridine (16b). From **13b**. Buff crystals, mp=270–272°C, yield=38 mg (57%). IR: 3060, 2936, 2835, 1626, 1607, 1526, 1498, 1443, 1388, 1292, 1253, 1175, 1079, 1033, 813, 743. MS: *m*/*z*=394 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.89 (s, 3H), 4.59 (s, 2H), 6.99 (d, 2H, *J*=8.4 Hz), 7.32 (s, 1H), 7.42 (d, 1H, *J*=9.2 Hz), 7.50 (t, 1H, *J*=7.6 Hz), 7.64 (m, 3H), 7.80 (d, 1H, *J*=8.8 Hz), 7.90 (t, 2H, *J*=8.8 Hz), 7.99 (s, 1H). Anal. for $C_{25}H_{17}NO_2S$ (395.5) calcd: C, 75.93; H, 4.33; N, 3.54; S, 8.11. Found: C, 75.63; H, 4.33; N, 3.79; S, 7.88.

3.9.10. 2-Phenyl-5,6-dihydrobisthieno[2,3-*b*:3′,2′-*e*]pyridine (20a). From **19a**. Pale brown crystals, mp 220–221°C, yield=10 mg (25%). IR: 3045, 2969, 2920, 2845, 1585, 1505, 1477, 1423, 1355, 1260, 1203, 1123, 1071, 1019, 933, 896, 825, 758, 742, 722, 686. MS: *m*/*z*=269 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.41 (t, 2H, *J*=7.6 Hz), 3.51 (t, 2H, *J*=7.6 Hz), 7.36 (s, 1H), 7.37 (t, 1H, *J*=7.5 Hz), 7.44 (t, 2H, *J*=7.5 Hz), 7.68 (s, 1H), 7.69 (d, 2H, *J*=7.5 Hz). ^{13}C NMR ($CDCl_3$) δ=32.2, 33.7, 116.8, 125.9, 126.6, 128.8, 129.4, 131.0, 131.5, 134.5, 142.5, 160.8, 166.7. Anal. for $C_{15}H_{11}NS_2$ (269.4) calcd: C, 66.88; H, 4.12; N, 5.20; S, 23.80. Found: C, 66.51; H, 4.22; N, 5.41; S, 23.70.

3.9.11. 2-(4-Methoxyphenyl)-5,6-dihydrobisthieno[2,3-*b*:3′,2′-*e*]pyridine (20b). From **19b**. Pale brown crystals, mp 235–236°C, yield=9 mg (20%). IR: 3005, 2935, 2834, 1604, 1576, 1514, 1483, 1439, 1356, 1297, 1250, 1179, 1110, 1030, 898, 819. MS: *m*/*z*=299 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.40 (t, 2H, *J*=7.6 Hz), 3.50 (t, 2H, *J*=7.6 Hz), 3.87 (s, 3H), 6.96 (d, 2H, *J*=8.4 Hz), 7.22 (s, 1H), 7.68 (s, 1H), 7.69 (d, 2H, *J*=7.5 Hz). Anal. for $C_{16}H_{13}NOS_2$ (299.4) calcd: C, 64.18; H, 4.38; N, 4.68; S, 21.42. Found: C, 64.24; H, 4.50; N, 4.99; S, 21.49.

3.9.12. 2-(2-Thienyl)-5,6-dihydrobisthieno[2,3-*b*:3′,2′-*e*]-pyridine (20c). From **19c**. Green crystals, mp 198–199°C, yield=11 mg (27%). IR: 3100, 3057, 2934, 1584, 1520, 1478, 1411, 1357, 1338, 1263, 1185, 1122, 1016, 897, 836, 815, 743, 697. MS: *m*/*z*=275 (M^+). ^{1}H NMR ($CDCl_3$) δ=3.40 (t, 2H, *J*=7.6 Hz), 3.50 (t, 2H, *J*=7.6 Hz), 7.07 (dd, 1H, *J*=4, 4.8 Hz), 7.20 (s, 1H), 7.30 (d, 1H, *J*=4 Hz), 7.31 (d, 1H, *J*=4.8 Hz), 7.67 (s, 1H). Anal. for $C_{13}H_9NS_3$ (275.4) calcd: C, 56.69; H, 3.29; N, 5.09; S, 34.93. Found: C, 56.87; H, 3.49; N, 5.37; S, 34.66.

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