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THE CLEAVAGE OF HETEROCYCLIC COMPOUNDS IV.[1] STUDY OF THE REACTIVITY OF THE [1]BENZOTHIENO[2,3-*E*]-1,2,4-TRIAZINE SYSTEM TOWARDS NUCLEOPHILIC REAGENTS

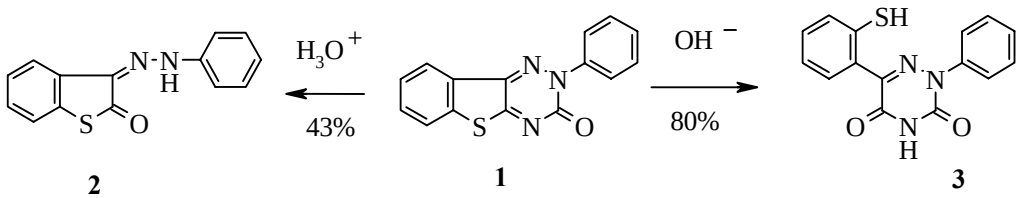
Jiří Filipčík, Jakub Stýskala,* and Jan Slouka

Department of Organic Chemistry, Faculty of Science, Palacky University, Tr. Svobody 8, 771 46 Olomouc, Czech Republic. E-mail: styskala@prfnw.upol.cz

Abstract - A series of 5-substituted 1,2,4-triazines were prepared by nucleophilic cleavage of the thiophene ring of [1]benzothieno[2,3-*e*]-1,2,4-triazine **1** with some nitrogen, oxygen, sulfur and carbon containing nucleophilic agents. The thiophene ring of compound **1** was transformed by oxidative cleavage to the corresponding sulfonic acid **10**.

INTRODUCTION

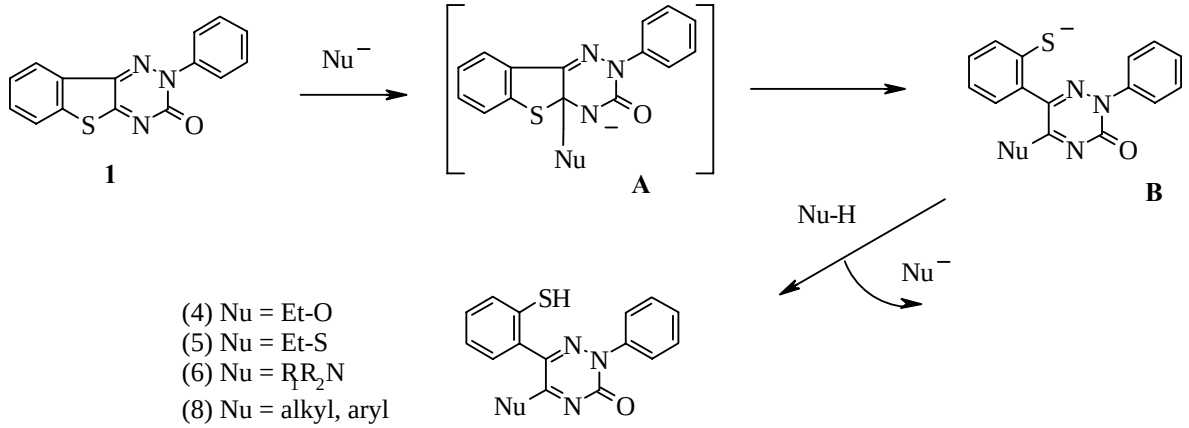
As part of a systematic study of cleavage reactions in heterocycles we have focused on the reactivity of the [1]benzothieno[2,3-*e*]-1,2,4-triazine ring. We selected 2-phenyl-2,3-dihydro[1]benzothieno[2,3-*e*]-1,2,4-triazine-3-one **1**[2] as our model compound. The compound reacted differently depending on the pH of the reaction medium. Cleavage of the triazine ring occurred to give phenylhydrazone[2] **2** under acidic hydrolysis, whereas ring opening of thiophen nucleus proceeded under basic conditions to form a 6-azauracil derivative[2] **3**. (Scheme 1). We paid especial attention to the behavior of the compound **1** in the presence of O, S, N and C-nucleophiles.



Scheme 1. Acid and basic hydrolysis of 1,2,4-triazine **1**

RESULTS AND DISCUSSION

We have shown that, with few exceptions, for strong ionic nucleophiles there was predominantly cleavage of the thiophene ring. This provides evidence of nucleophilic attack on the double bond between the atoms 4 and 5.

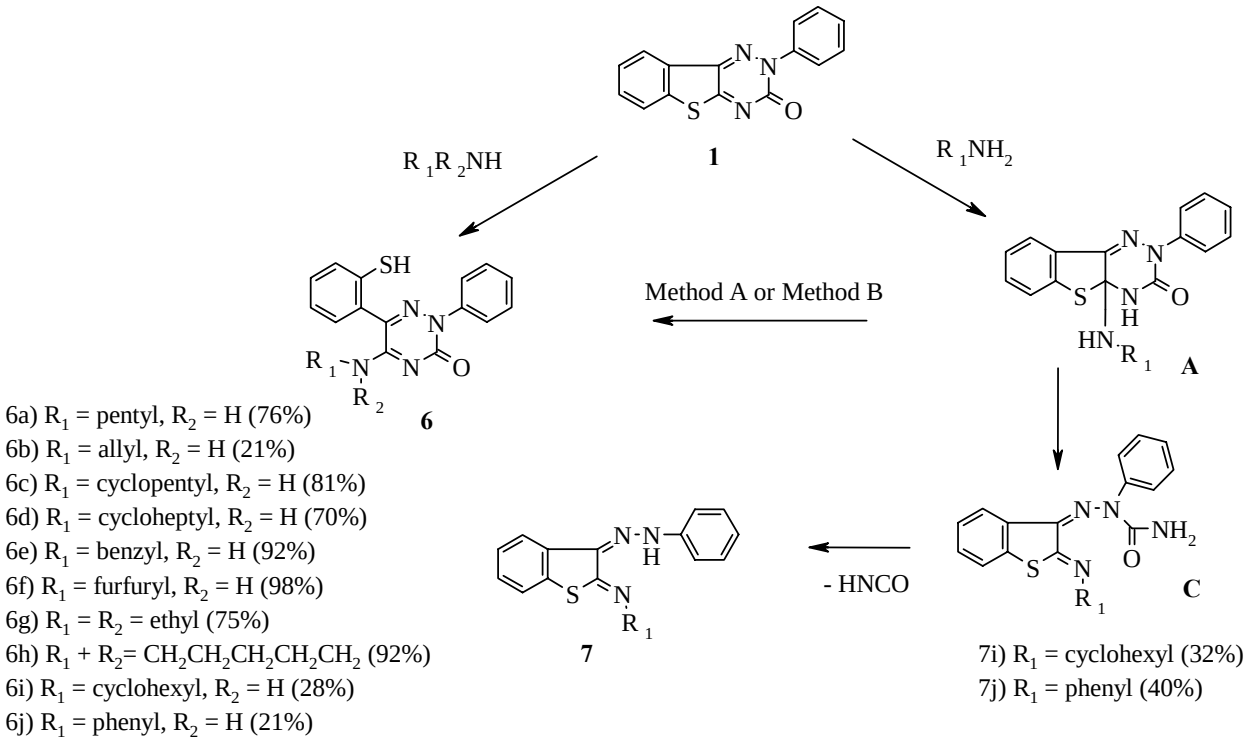


Scheme 2. Cleavage of 1,2,4-triazine **1** by nitrogen, oxygen, sulfur and carbon nucleophilic agents

Ethoxy derivative **4** was prepared by a reaction of compound **1** with sodium ethoxide. Analogously, a representative of the thio derivative of 1,2,4-triazine **5**, was prepared using sodium ethanethiolate. During heating in methanol, a novel reaction of 5-ethylsulfanyl-1,2,4-triazine **5** proceeded to give starting material **1**.

For the purpose of preparing a series of derivatives of 6-azacytosines, the reactivity of compound **1** towards primary and secondary amines was studied. The reaction with secondary amines followed an unambiguous course according to scheme 2. The same reaction did not proceed when the nucleophiles were the primary amines. In case of primary amines, elimination can proceed in two directions from the intermediate (**A**). All reactions were carried out at 90-130 °C to afford the corresponding derivatives of 6-azacytosines **6a-6h** according to Scheme 3 (Method A). On the other hand, the reactions with aniline or cyclohexylamine proceeded at 160-180 °C to afford the corresponding iminohydrazones **7i-7j**. This type of reaction was previously unknown in the analogous benzofuran series.[1,3] The abnormal cleavage of the initial [1]benzothieno[2,3-*e*]-1,2,4-triazine **1** using cyclohexylamine and aniline, forming iminohydrazones **7i-7j**, can be most readily explained on the basis of their specific steric properties: these play a role in the cleavage of transition state (**A**) after the addition of amine. In the case of amines **a-h**, scission of the double bond between the carbon and sulfur atom takes place, the thiophene ring is opened and corresponding derivatives of 6-azacytosine **6a-6h** are formed. This is impossible in the case of aniline and cyclohexylamine. The cleavage of the 1,2,4-triazine ring occurs at higher temperature (160-180 °C)

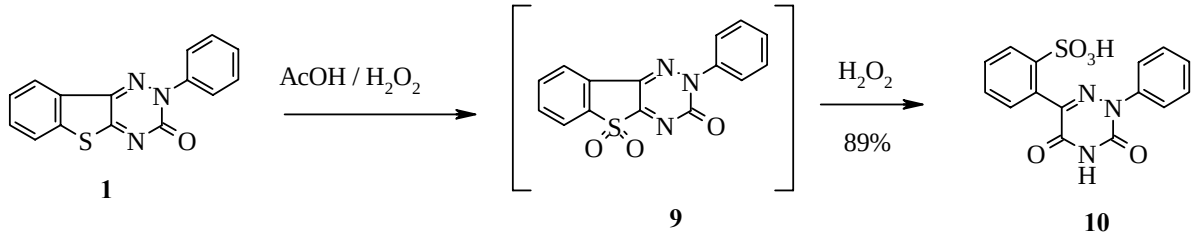
in which case HNCO is eliminated directly, or via the semicarbazide (**C**). This speculative step involving the elimination of isocyanic acid suggests the participation of phenylurea as an intermediate; in fact, it was isolated from the reaction mixture and confirmed by MS and ^{1}H NMR spectroscopy.



Scheme 3. Reaction mechanism for cleavage of 1,2,4-triazine **1** by N-nucleophiles

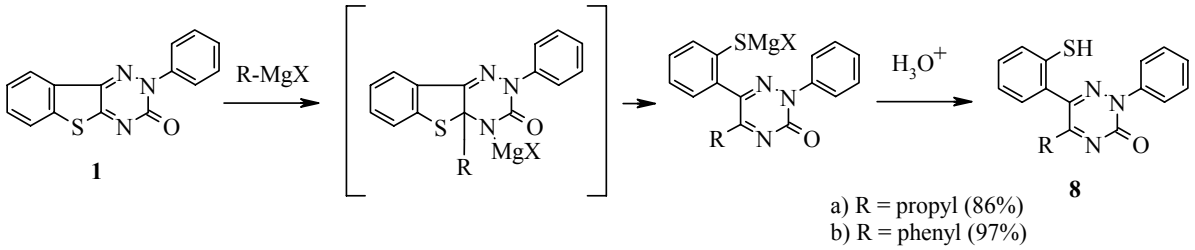
It was interesting to investigate which way compound **1** would be cleaved by aniline, cyclohexylamine and, for comparison, pentylamine in the presence of butyllithium (Method B). It was found that this method affords predominantly the corresponding 6-azacytosines **6a, 6i** and **6j** by cleavage of the thiophene ring at elevated temperature.

Likewise, the thiophene ring of compound **1** was opened by oxidative cleavage in the presence of hydrogen peroxide and AcOH resulting in 2-(2-phenyl-4*H*-3,5-dioxo-1,2,4-triazin-6-yl)benzensulfonic acid **10.** This was presumably formed by hydrolysis, following the oxidation of sulfone **9,** which was not isolated.



Scheme 4. Oxidative cleavage of 1,2,4-triazine **1** by peracetic acid

We also studied the course of the reaction of compound **1** with C-nucleophiles of Grignard type. We found that these reactions proceed very easily under mild conditions according to Scheme 2. These reactions are of great significance since they open a route to the synthesis of 2,3-dihydro-1,2,4-triazin-3-ones (**8**) substituted in position 5 with alkyl or aryl groups. Methods developed so far,[4-7] based on condensation of α-dicarbonyl compounds with semicarbazide do not afford these compounds With the exception of the symmetrical α-dicarbonyl compound a mixture of products variously substituted in positions 5 and 6 are the most frequently formed.



Scheme 5. Cleavage of 1,2,4-triazine **1** by C-nucleophiles (Grignard reagents)

EXPERIMENTAL

Melting points were determined on a Boetius stage and are uncorrected. The IR spectra were recorded in KBr wafers on an ATI Unicam Genesis FTIR instrument. The NMR spectra were registered on a Bruker Avance 300 MHz DRX spectrometer; chemical shifts are reported in ppm, the coupling constants *J* in Hz. Elemental analyses were performed with an EA 1108 Elemental Analyser (Fison Instruments). Mass spectra were taken using an LCQ ion trap mass spectrometer (Finnigan MAT, San Jose, CA, USA).

2-Phenyl-6-(2-sulfanylphenyl)-5-ethoxy-1,2,4-triazin-3(2*H*)-one (4). The starting 1,2,4-triazine **1** (148.9 mg; 0.53 mmol) was dissolved in solution of sodium ethoxide, prepared from sodium (212 mg) and anhydrous EtOH (20 mL). The resulting solution was stirred at rt for 5 min. Water (20 mL) and 50% aqueous AcOH (10 mL) were added. The precipitated product was collected by vacuum filtration, washed with water, dried and recrystallized from a mixture of acetone/water. Yield: 110.0 mg (63.4%), mp 129-130 °C. IR (cm^{-1}): 1657, 1461, 1268, 1196, 593. ^{1}H-NMR, (DMSO-d_6): δ 1.35 (t, 3H, C**H$_3$**CH$_2$, *J* = 6.9 Hz), 4.30 (q, 2H, CH$_3$C**H$_2$**, *J* = 6.9 Hz), 7.35 (t, 1H, H$_{arom.}$, *J* = 8.4 Hz), 7.42 – 7.49 (m, 2H, H$_{arom.}$), 7.53 (t, 2H, H$_{arom.}$, *J* = 7,5 Hz), 7.90 (d, 1H, H$_{arom.}$, *J* = 7.8 Hz), 8.09 (d, 2H, H$_{arom.}$, *J* = 7.5 Hz), 8.61 (d, 1H, H$_{arom.}$, *J* = 8.1 Hz), 11.81 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 14.2, 62.4, 121.9, 122.3, 122.6, 124.7, 126.2, 129.0, 129.5, 129.7, 130.6, 132.3, 149.1, 152.0, 153.8. MS (APCI, *m/z*): 326.1 $[M+H]^+$. Anal. Calcd for $C_{17}H_{15}N_3O_2S$ (325.4): C, 62.75; H, 4.65; N, 12.91; S, 9.85. Found: C, 62.90; H, 4.67; N, 12.62; S, 9.57.

2-Phenyl-6-(2-sulfanylphenyl)-5-ethylsulfanyl-1,2,4-triazin-3(2*H*)-one (5). The starting 1,2,4-triazine **1** (370.2 mg; 1.33 mmol) was dissolved in solution of sodium thioethanolate, prepared by dissolution of sodium (506 mg) in ethanethiol (40 mL). The resulting solution was stirred at rt for 18 h. The precipitated product was collected by vacuum filtration, washed with water and 50% AcOH and dried on a filter. Due to the presence of unreacted triazine, further purification on silica gel column using $CHCl_3$ was carried out. A sample for analysis was prepared by recrystallization from a mixture of acetone/water. Yield: 114.2 mg (25.2%), mp 167-169 °C. IR (cm^{-1}): 1534, 1409, 1263, 1137, 753. ^{1}H-NMR, (DMSO-d_6): δ 1.32 (t, 3H, J = 6.0 Hz, CH_3), 3.03 (q, 2H, J = 6.0 Hz, CH_2), 7.36 – 7.58 (m, 5H, $H_{arom.}$), 7.87 (d, 1H, J = 6.9 Hz, H_{arom}), 7.97 (d, 2H, J = 8.4 Hz, $H_{arom.}$), 8.51 (d, 1H, J = 9.0 Hz, $H_{arom.}$), 12.86 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 14.9, 24.2, 120.8, 122.4, 122.5, 125.6, 125.8, 126.5, 129.0, 129.2, 131.3, 132.9, 149.9, 150.4, 169.9. MS (APCI, *m/*z): 342.2 $[M+H]^+$. Anal. Calcd for $C_{17}H_{15}N_3OS_2$ (341.5): C, 59.80; H, 4.43; N, 12.31; S, 18.78. Found: C, 59.66; H, 4.25; N, 12.11; S, 18.47.

General procedure for 5-N-substituted derivatives of 2-phenyl-6-(2-sulfanylphenyl)-1,2,4-triazin-3(2*H*)-one (6a-6j).

Method A for derivatives 6a-6h: Compound **1** (0.5 mmol) was heated with the corresponding amine (2 mL) in a sealed vial. After cooling to rt, water (10 mL) followed by 50% AcOH (10 mL) was added. The precipitate was collected by vacuum filtration, washed with water and dried on a filter. A sample for analysis was prepared by recrystallization from a mixture of acetone/water. The reaction conditions are shown below.

2-Phenyl-6-(2-sulfanylphenyl)-5-pentylamino-1,2,4-triazin-3(2*H*)-one (6a). Reaction conditions: 120 °C/3 h. Yield: 76.2%, mp 105-108 °C. IR (cm^{-1}): 2964, 1648, 1535, 1450, 706. ^{1}H-NMR, (DMSO-d_6): δ 0.90 (t, 3H, J = 7.2 Hz, C**H$_3$**$(CH_2)_4$NH-), 1.19 – 1.36 (m, 4H, CH_3C**H$_2$**C**H$_2$**$(CH_2)_2$NH-), 1.55 (p, 2H, J = 6.9 Hz, $CH_3(CH_2)_2$C**H$_2$**CH_2NH-), 3.24 (q, J = 6.9 Hz, $CH_3(CH_2)_3$C**H$_2$**NH-), 7.25 – 7.53 (m, 6H, $H_{arom.}$), 7.66 – 7.72 (m, 1H, $H_{arom.}$), 7.85 (d, 1H, J = 7.8 Hz, $H_{arom.}$), 8.12 (d, 1H, J = 6.9 Hz, $H_{arom.}$), 8.34 (t, 1H, J = 6.9 Hz, $CH_3(CH_2)_4$N**H**-), 12.93 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 19.1, 19.2, 20.1, 30.6, 51.0, 118.1, 119.8, 122.9, 126.0, 126.9, 127.1, 130.4, 131.5, 132.0, 137.3, 149.2, 157.9, 160.1. MS (APCI, *m/z*): 367.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{22}N_4OS$ (366.5): C, 65.55; H, 6.05; N, 15.29; S, 8.75. Found: C, 65.46; H, 6.12; N, 15.41; S, 8.50.

2-Phenyl-6-(2-sulfanylphenyl)-5-allylamino-1,2,4-triazin-3(2*H*)-one (6b). Reaction conditions: 105 °C/24 h. Yield: 21.6%, mp 170-173 °C. IR (cm^{-1}): 2987, 1659, 1549, 1442, 662. ^{1}H-NMR, (DMSO-d_6): δ 3.91 (t, 2H, J = 6.0 Hz, C**H$_2$**=CH-CH_2-), 5.14 – 5.31 (m, 2H, CH_2=CH-C**H$_2$**-), 5.88 – 6.02 (m, 1H, CH_2=C**H**-CH_2-), 7.25 – 7.42 (m, 3H, $H_{arom.}$), 7.50 (t, 2H, J = 6.0 Hz, $H_{arom.}$), 7.67 – 7.70 (m, 1H, $H_{arom.}$), 7.86 (d, 2H, J = 7.8 Hz, $H_{arom.}$), 8.07 (d, 1H, J = 6.5 Hz, $H_{arom.}$), 8.53 (t, 1H, J = 6.0 Hz, NH),

13.03 (s, 1H, SH). MS (APCI, *m/z*): 337.1 $[M+H]^+$. Anal. Calcd for $C_{18}H_{16}N_4OS$ (336.4): C, 64.27; H, 4.79; N, 16.65; S, 9.53. Found: C, 64.27; H, 4.64; N, 16.59; S, 9.63.

2-Phenyl-6-(2-sulfanylphenyl)-5-cyclopentylamino-1,2,4-triazin-3(2*H*)-one (6c). Reaction conditions: 125 °C/2.5 h. Yield: 81.6%, mp 205-207 °C. IR (cm^{-1}): 1710, 1565, 1513, 662. ^{1}H-NMR, (DMSO-d_6): δ 1.46 – 1.78 (m, 6H, cyclopentyl), 1.90 – 1.97 (m, 2H, cyclopentyl), 4.05 – 4.14 (m, 1H, cyclopentyl), 7.26 – 7.41 (m, 3H, $H_{arom.}$), 7.51 (t, 2H, *J* = 8.1 Hz, $H_{arom.}$), 7.69 (d, 1H, *J* = 6.9 Hz, $H_{arom.}$), 7.85 (d, 2H, *J* = 7.8 Hz, $H_{arom.}$), 8.13 (d, 1H, *J* = 7.5 Hz, $H_{arom.}$), 8.22 (d, 1H, *J* = 6.6 Hz, NH), 12.71 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 23.4, 32.3, 51.7, 118.2, 120.6, 122.5, 125.9, 126.3, 126.2, 129.2, 130.2, 130.8, 134.6, 146.8, 157.1, 157.8. MS (APCI, *m/z*): 365.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{20}N_4OS$ (364.5): C, 65.91; H, 5.53; N, 15.37; S, 8.80. Found: C, 65.92; H, 5.65; N, 15.23; S, 8.67.

2-Phenyl-6-(2-sulfanylphenyl)-5-cycloheptylamino-1,2,4-triazin-3(2*H*)-one (6d). Reaction conditions: 130 °C/4 h. Yield: 70.8%, mp 198-200 °C. ^{1}H-NMR, (DMSO-d_6): δ 1.42 – 1.70 (m, 10H, cycloheptyl), 1.91 – 1.98 (m, 2H, cycloheptyl), 3.73 – 3.84 (m, 1H, cycloheptyl), 7.26 – 7.40 (m, 3H, $H_{arom.}$), 7.51 (t, 2H, *J* = 8.1 Hz, $H_{arom.}$), 7.68 (d, 1H, *J* = 6.9 Hz, $H_{arom.}$), 7.85 (d, 2H, *J* = 7.8 Hz, $H_{arom.}$), 8.14 – 8.18 (m, 2H, $H_{arom.}$ + NH), 12.60 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 23.6, 27.6, 34.4, 51.2, 118.4, 120.6, 122.5, 125.9, 126.2, 126.4, 129.2, 130.2, 130.7, 134.5, 147.0, 156.3, 157.5. IR (cm^{-1}): 1712, 1562, 1514, 735, 662. MS (APCI, *m/z*): 393.1 $[M+H]^+$. Anal. Calcd for $C_{22}H_{24}N_4OS$ (392.5): C, 67.32; H, 6.16; N, 14.27; S, 8.17. Found: C, 67.49; H, 6.30; N, 14.12; S, 8.04.

2-Phenyl-6-(2-sulfanylphenyl)-5-benzylamino-1,2,4-triazin-3(2*H*)-one (6e). Reaction conditions: 130 °C/2 h. Yield: 92.5%, mp 186-188 °C. IR (cm^{-1}): 3314, 3028, 1638, 1550, 1251, 1054, 751. ^{1}H-NMR, (DMSO-d_6): δ 4.48 (d, 2H, *J* = 5.7 Hz, CH_2), 7.23 – 7.31 (m, 2H, $H_{arom.}$), 7.33 – 7.41 (m, 6H, $H_{arom.}$), 7.48 (t, 2H, *J* = 8.1 Hz, $H_{arom.}$), 7.68 (d, 1H, *J* = 7.2 Hz, $H_{arom.}$), 7.84 (d, 2H, *J* = 7.8 Hz, $H_{arom.}$), 8.10 (d, 1H, *J* = 7.5 Hz, $H_{arom.}$), 8.85 (t, 1H, *J* = 5.7 Hz, NH), 13.08 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 43.5, 117.9, 120.5, 122.6, 125.9, 126.2, 126.5, 127.1, 127.5, 128.4, 129.3, 130.4, 131.0, 134.7, 139.0, 146.3, 158.2, 158.9. MS (APCI, *m/z*): 387.1 $[M+H]^+$. Anal. Calcd for $C_{22}H_{18}N_4OS$ (386.5): C, 68.37; H, 4.69; N, 14.50; S, 8.30. Found: C, 68.14; H, 4.98; N, 14.12; S, 8.55.

2-Phenyl-6-(2-sulfanylphenyl)-5-furfurylamino-1,2,4-triazin-3(2*H*)-one (6f). Reaction conditions: 125 °C/2.5 h. Yield: 98.7%, mp 183-184 °C. IR (cm^{-1}): 3295, 1641, 1549, 1261, 1052, 749. ^{1}H-NMR, (DMSO-d_6): δ 4.47 (d, 2H, *J* = 4.8 Hz, CH_2), 6.38 - 6.44 (m, 2H, $H_{arom.}$), 7.24 – 7.31 (m, 1H, $H_{arom.}$), 7.33 – 7.41 (m, 2H, $H_{arom.}$), 7.49 (t, 2H, *J* = 9.0 Hz, $H_{arom.}$), 7.63 – 7.70 (m, 2H, $H_{arom.}$), 7.85 (d, 2H, *J* = 7.8 Hz, $H_{arom.}$), 8.11 (d, 1H, *J* = 7.8 Hz, $H_{arom.}$), 8.80 (t, 1H, *J* = 4.8 Hz, NH), 12.96 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 36.7, 107.4, 110.5, 118.0, 120.6, 122.6, 126.0, 126.3, 126.4, 129.2, 130.3, 131.0, 134.6, 142.4, 146.4, 151.8, 157.8, 158.7. MS (APCI, *m/z*): 377.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{16}N_4O_2S$ (376.4): C, 63.81; H, 4.28; N, 14.88; S, 8.52. Found: C, 63.68; H, 4.12; N, 14.62; S, 8.74.

2-Phenyl-6-(2-sulfanylphenyl)-5-diethylamino-1,2,4-triazin-3(2*H*)-one (6g). Reaction conditions: 90 °C/5.5 h. Yield: 75.2%, mp 154-156 °C. IR (cm^{-1}): 2967, 1626, 1542, 1411, 1245, 1058, 751. ^{1}H-NMR, (DMSO-d_6): δ 1.21 (bs, 6H, CH_3), 3.60 (bs, 4H, CH_2), 7.19 – 7.24 (m, 1H, $H_{arom.}$), 7.34 – 7.42 (m, 2H, $H_{arom.}$), 7.46 – 7.53 (m, 4H, $H_{arom.}$), 7.58 – 7.63 (m, 1H, $H_{arom.}$), 7.87 – 7.90 (m, 1H, $H_{arom.}$), 14.11 (s, 1H, SH). MS (APCI, *m/z*): 353.1 $[M+H]^+$. Anal. Calcd for $C_{19}H_{20}N_4OS$ (352.5): C, 64.75; H, 5.72; N, 15.90; S, 9.10. Found: C, 64.93; H, 5.50; N, 15.64; S, 9.21.

2-Phenyl-6-(2-sulfanylphenyl)-5-piperidino-1,2,4-triazin-3(2*H*)-one (6h). Reaction conditions: 125 °C/2.5 h. Yield: 91.9%, mp 205-206 °C. IR (cm^{-1}): 2940, 1638, 1544, 1413, 1252, 1081, 754. 1H-NMR, ($CDCl_3$): δ 1.76 (bs, 6H, piperidine), 3.80 (bs, 4H, piperidine), 7.13 – 7.21 (m, 1H, $H_{arom.}$), 7.31 – 7.35 (m, 2H, $H_{arom.}$), 7.39 – 7.43 (m, 5H, $H_{arom.}$), 7.88 – 7.92 (m, 1H, $H_{arom.}$), 13.50 (bs, 1H, SH). ^{13}C-NMR, ($CDCl_3$): 25.2, 26.7, 46.3, 116.1, 120.8, 123.3, 125.3, 126.4, 128.2, 130.3, 132.1, 134.5, 137.1, 143.8, 160.8, 167.4. MS (APCI, *m/z*): 365.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{20}N_4OS$ (364.5): C, 65.91; H, 5.53; N, 15.37; S, 8.80. Found: C, 65.75; H, 5.46; N, 15.61; S, 8.51.

Method B for derivatives 6a, 6i and 6j: A 2M solution of BuLi in pentane (2.2 mL; 4.44 mmol) was added to a solution of the corresponding amine (4.44 mmol) in anhydrous THF (2 mL) at -50°C. Complete dissolution was achieved after heating to rt. The resulting solution was slowly dripped into a suspension of 1,2,4-triazine **1** (200 mg; 0.72 mmol) in anhydrous THF (4.5 mL). The reaction mixture was stirred under the conditions stated below. After cooling to rt, EtOH (10 mL) was added and the mixture was evaporated to dryness under reduced pressure. A solution of 1M HCl (4 mL) and H_2O (25 mL) was added to the residue and the product obtained was filtered off, washed with water and dried on a filter. The product was purified by column chromatography using $CHCl_3$. A sample for analysis was prepared by recrystallization from a mixture of acetone/water.

2-Phenyl-6-(2-sulfanylphenyl)-5-pentylamino-1,2,4-triazin-3(2*H*)-one (6a). Reaction conditions: 25 °C/5 h. Yield: 142.6 mg (54.3%). Physical and spectral data are identical to compound **6a** prepared by method A.

2-Phenyl-6-(2-sulfanylphenyl)-5-cyclohexylamino-1,2,4-triazin-3(2*H*)-one (6i). Reaction conditions: 60 °C/3 h. Yield: 76.8 mg (28.3%), mp 203-204 °C. IR (cm^{-1}): 3320, 3103, 2935, 2359, 1698, 1547, 1434, 1252, 1060, 844, 702. ^{1}H-NMR, (DMSO-d_6): δ 1.18 – 1.41 (m, 6H, cyclohexyl), 1.71 – 1.92 (m, 4H, cyclohexyl), 3.58 – 3.68 (m, 1H, cyclohexyl), 7.25 – 7.39 (m, 3H, H_{arom} + $NH_.$), 7.49 (t, 2H, J = 7.8 Hz, $H_{arom.}$), 7.66 (d, 1H, J = 7.2 Hz, $H_{arom.}$), 7.84 (d, 2H, J = 7.2 Hz, $H_{arom.}$), 8.14 (m, 2H, $H_{arom.}$), 12.67 (bs, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 24.5, 25.1, 32.5, 49.0, 118.3, 120.6, 122.5, 125.9, 126.2, 126.4, 129.2, 130.2, 130.8, 134.5, 146.9, 156.6, 157.7. MS (APCI, *m/z*): 379.2 $[M+H]^+$. Anal. Calcd for $C_{21}H_{22}N_4OS$ (378.5): C, 66.64; H, 5.86; N, 14.80; S, 8.47. Found: C, 66.39; H, 5.98; N, 14.46; S, 8.80.

2-Phenyl-6-(2-sulfanylphenyl)-5-anilino-1,2,4-triazine-3(2*H*)-on (6j). Reaction conditions: 60 °C/15 h. Yield: 57.1 mg (21.4%), mp 207-209 °C. IR (cm^{-1}): 3395, 2925, 2381, 1649, 1542, 1432, 1315, 1262, 1062, 747, 661. ^{1}H-NMR, (DMSO-d_6): δ 7.12 (t, 1H, J = 7.2 Hz, $H_{arom.}$), 7.28 (t, 1H, J = 7.2 Hz, $H_{arom.}$), 7.36 – 7.42 (m, 4H, $H_{arom.}$), 7.52 (t, 1H, J = 7.8 Hz, $H_{arom.}$), 7.68 – 7.71 (m, 3H, $H_{arom.}$), 7.87 (d, 2H, J = 7.8 Hz, $H_{arom.}$), 8.07 (d, 1H, J = 6.6 Hz, $H_{arom.}$), 10.49 (s, 1H, NH), 13.29 (bs, 1H, SH). ^{13}C-NMR, ((DMSO-d_6): 117.7, 119.0, 120.4, 122.7, 123.4, 126.1, 126.9, 128.9, 129.3, 130.2, 131.6, 134.8, 138.6, 145.3, 156.5, 160.4. MS (APCI, *m/z*): 373.2 $[M+H]^+$. $C_{21}H_{16}N_4OS$ (372.5): C, 67.72; H, 4.33; N, 15.04; S, 8.61. Found: C, 67.50; H, 4.54; N, 14.88; S, 8.76.

General procedure for 2-substitued imino derivatives of 3-phenylhydrazono-2,3-dihydro-benzo[*b*]thiophene 7i and 7j: Compound **1** (140 mg; 0.5 mmol) was heated with corresponding amine (2 mL) in a sealed vial. After cooling to rt, water (10 mL) and 50% AcOH (10 mL) were added to the resulting solution. The precipitated product was collected by vacuum filtration, washed with water, dried on a filter and crystallized from a mixture of acetone/water. The reaction conditions are shown below.

2-Cyclohexylimino-3-phenylhydrazono-2,3-dihydrobenzo[*b*]thiophene (7i). Reaction conditions: 160 °C/7 h. Yield: 53.5 mg (31.9%), mp 210-212 °C. IR (cm^{-1}): 3326, 2928, 2851, 1627, 1258, 1052. ^{1}H-NMR, (DMSO-d_6): δ 1.02 – 2.09 (m, 10 H, cyclohexyl), 5.56 (s, 1H, cyclohexyl), 7.01 – 7.08 (m, 1H, $H_{arom.}$), 7.29 – 7.44 (m, 7H, $H_{arom.}$), 7.74 – 7.80 (m, 1H, $H_{arom.}$), 14.26 (s, 1H, NH). ^{13}C-NMR, (DMSO-d_6): 25.7, 26.3, 34.4, 50.7, 116.9, 121.2, 123.1, 124.5, 124.9, 126.6, 131.0, 131.4, 136.5, 143.1, 156.2, 160.8, 168.9. MS (APCI, *m/z*): 336.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{21}N_3S$ (335.5): C, 71.61; H, 6.31; N, 12.53; S, 9.56. Found: C, 71.45; H, 6.75; N, 12.24; S, 9.71.

2-Phenylimino-3-phenylhydrazono-2,3-dihydrobenzo[*b*]thiophene (7j). Reaction conditions: 180 °C/6 h. Yield: 65.3 mg (39.5%), mp 161-162 °C. IR (cm^{-1}): 1587, 1485, 1263, 1051, 751. ^{1}H-NMR, (DMSO-d_6): 7.09 (t, 1H, J = 7.4 Hz, $H_{arom.}$), 7.28 – 7.43 (m, 7H, $H_{arom.}$), 7.49 – 7.55 (m, 5H, $H_{arom.}$), 7.81 – 7.87 (m, 1H, $H_{arom.}$), 14.12 (s, 1H, NH). ^{13}C-NMR, (DMSO-d_6): 167.2, 159.3, 149.3, 142.5, 133.1, 132.5, 132.0, 131.9, 129.5, 128.4, 126.1, 123.4, 123.3, 120.8, 120.4, 114.6. MS (APCI, *m/z*): 330.1 $[M+H]^+$. Anal. Calcd for $C_{20}H_{15}N_3S$ (329.4): C, 72.94; H, 4.59; N, 12.76; S, 9.73. Found: C, 72.73; H, 4.44; N, 12.34; S, 9.49.

General procedure for 5-C-substituted derivatives of 2-phenyl-6-(2-sulfanylphenyl)-1,2,4-triazin-3(2*H*)-one (8a and 8b). The starting 1,2,4-triazine **1** (140 mg, 0.50 mmol) was suspended in anhydrous toluene (6 mL) and 2M solution of propyl(or phenyl)magnesium chloride in Et_2O (1 mL; 2.0 mmol) was slowly dripped at -50 °C. The reaction mixture was heated to –10 °C. The resulting solution was further stirred for 25 min at rt EtOH (1 mL) was added and the stirring continued for 10 min. The solution was

evaporated under reduced pressure and 1M HCl (1 mL) and H_2O (5 mL) were added to the residue. The precipitated product was filtered off, washed with water and dried. A sample for analysis was recrystallized from a mixture of EtOH/water.

2-Phenyl-6-(2-sulfanylphenyl)-5-propyl-1,2,4-triazin-3(2*H*)-one (8a). Yield: 140 mg (86.4%), mp 168-170°C. IR (cm^{-1}): 3430, 3203, 2960, 1848, 1680, 1494, 1112, 757. ^{1}H-NMR, (DMSO-d_6): δ 0.90 (t, 3H, J = 7.2 Hz, C**H$_3$**CH$_2$CH$_2$-), 1.37 – 1.60 (m, 2H, CH$_3$C**H$_2$**CH$_2$-), 1.84 – 2.02 (m, 2H, CH$_3$CH$_2$C**H$_2$**-), 7.26 – 7.33 (m, 2H, $H_{arom.}$), 7.42 – 7.49 (m, 4H, $H_{arom.}$), 7.51 – 7.56 (m, 2H, $H_{arom.}$), 7.72 (d, 1H, J = 7.8 Hz, $H_{arom.}$), 9.07 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 13.5, 17.1, 42.9, 71.0, 123.3, 123.5, 124.5, 125.7, 125.8, 128.2, 129.1, 132.0, 141.2, 141.9, 148.2, 151.3. MS (APCI, *m/z*): 322.7 $[M-H]^-$. Anal. Calcd for $C_{18}H_{17}N_3OS$ (323.4): C, 66.85; H, 5.30; N, 12.99; S, 9.91. Found: C, 66.43; H, 5.64; N, 12.93; S, 9.72.

2-Phenyl-6-(2-sulfanylphenyl)-5-phenyl-1,2,4-triazin-3(2*H*)-one (8b). Yield: 174 mg (97.2%), mp 226-228°C. IR (cm^{-1}): 3111, 2985, 2348, 1710, 1513, 1480, 1301, 1168, 1004, 893, 759. ^{1}H-NMR, (DMSO-d_6): δ 7.24 - 7.31 (m, 1H, $H_{arom.}$), 7.32 – 7.54 (m, 12H, $H_{arom.}$), 7.86 (d, 2H, J = 7.5 Hz, $H_{arom.}$), 9.78 (s, 1H, SH). ^{13}C-NMR, (DMSO-d_6): 69.6, 123.3, 123.6, 123.7, 124.2, 125.9, 126.0, 128.3, 128.7, 128.8, 129.0, 132.4, 140.9, 141.5, 142.3, 148.6, 151.2. MS (APCI, *m/z*): 356.7 $[M-H]^-$. Anal. Calcd for $C_{21}H_{15}N_3OS$ (357.4): C, 70.57; H, 4.23; N, 11.76; S, 8.97. Found: C, 70.73; H, 4.38; N, 11.59; S, 8.64.

2-(2-Phenyl-4*H*-3,5-dioxo-1,2,4-triazin-6-yl)benzensulfonic acid (10). A mixture of triazine **1** (698.0 mg; 2.50 mmol), AcOH (19.0 mL) and hydrogen peroxide (30%, 6.3 mL) was heated at 90 °C for 3 h. After cooling, the yellowish solution was evaporated in vacuum. The residue was treated with EtOH and evaporated again. The resulting syrup was dried in vacuum over P_4O_{10}. A sample for analysis was recrystallized from a mixture of EtOH/Et_2O. Yield: 770.3 mg (89.3%), mp 210-218 °C. IR (cm^{-1}): 1700, 1492, 1224, 576. ^{1}H-NMR, (DMSO-d_6): δ 7.30 – 7.35 (m, 2H, $H_{arom.}$), 7.38 – 7.48 (m, 4H, $H_{arom.}$), 7.62 (d, 2H, J = 8.7 Hz, $H_{arom.}$), 7.79 (d, 1H, J = 8.7 Hz, $H_{arom.}$), 12.13 (s, 1H, NH). ^{13}C-NMR, (DMSO-d_6): 125.2, 127.1, 127.2, 128.2, 128.3, 128.7, 129.2, 129.6, 140.2, 146.3, 147.5, 148.4, 156.5. MS (APCI, *m/z*): 346.0 $[M+H]^+$. Anal. Calcd for $C_{15}H_{11}N_3O_5S$ (345.3): C, 52.17; H, 3.21; N, 12.17; S, 9.28. Found: C, 52.25; H, 3.57; N, 12.33; S, 9.48.

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