Microwave-Assisted Synthesis of *s*-Triazino[2,1-*b*][1,3]benzoxazoles, *s*-Triazino[2,1-*b*][1,3]benzothiazoles, and *s*-Triazino[1,2-*a*]benzimidazoles[1]

Anton V. Dolzhenko,[a] Wai-Keung Chui,*[a] Anna V. Dolzhenko[b]

[a] Department of Pharmacy, Faculty of Science, National University of Singapore, 18 Science Drive 4, Singapore 117543, Singapore

[b] Perm State Pharmaceutical Academy, 48 Lenin Street, Perm 614990, Russian Federation
Fax +6567791554; E-mail: phacwk@nus.edu.sg

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Dedicated to Professor B. Ya. Syropyatov on the occasion of his 65th birthday

Abstract: 2-Amino-4-oxo-derivatives of *s*-triazino[2,1-*b*][1,3]benzoxazoles, *s*-triazino[2,1-*b*][1,3]benzothiazoles, and *s*-triazino[1,2-*a*]benzimidazoles were synthesized by carbonylation of 2-benzoxazolylguanidines, 2-benzothiazolylguanidines, and 2-benzimidazolylguanidines with phenyl isocyanate under microwave irradiation (180 °C, 15 minutes). Using phenyl isothiocyanate instead of phenyl isocyanate under the same conditions led to the successful ring closure via thiocarbonylation of 2-benzoxazolylguanidines. However, the formation of 2-imino-4-phenylimino-*s*-triazino[2,1-*b*][1,3]benzothiazoles from 2-benzothiazolylguanidines was observed instead under microwave irradiation conditions.

Key words: carbonylation, microwave irradiation, triazinobenzoxazoles, triazinobenzothiazoles, triazinobenzimidazoles

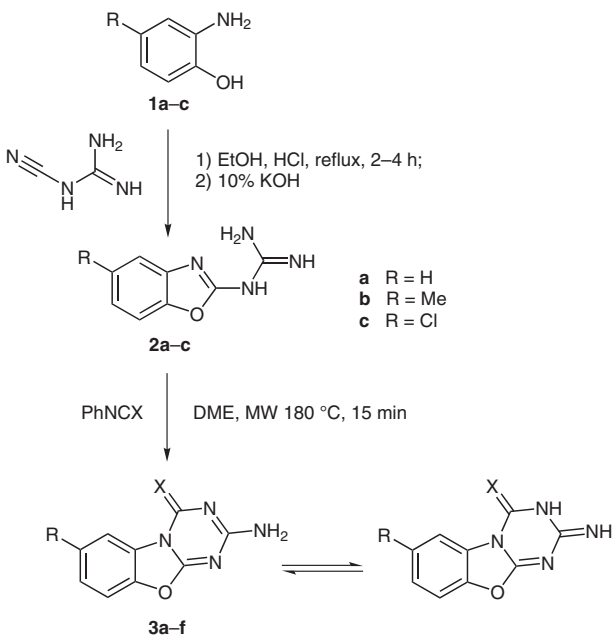
Recently the use of microwave-assisted synthesis has gained popularity in the preparation of new compounds with potential medicinal value.[2] The application of microwave irradiation in the synthesis of heterocyclic compounds, which have wide-ranging biological activities, have been reviewed recently.[3] However, there is no report on the microwave-assisted synthesis of the titled heterocyclic systems, particularly the 2-amino-4-(thi)oxo-derivatives. We are interested in such heterocyclic systems,[1,4] potential inhibitors of the enzyme dihydrofolate reductase, as they may exhibit antitumor, antibacterial, or antiparasitic properties.[5]

2-Amino(imino)-4-oxo-*s*-triazino[1,2-*a*]benzimidazoles have been prepared via two different pathways – an aza-Wittig-type reaction mechanism starting from 2-aminobenzimidazole,[6] or carbonylation and ring closure of 2-benzimidazolylguanidine.[7–12] The syntheses of similar *s*-triazino[2,1-*b*][1,3]benzoxazole and *s*-triazino[2,1-*b*][1,3]benzothiazole have been reported only via ring-closure carbonylation of 2-benzoxazolylguanidine or 2-benzothiazolylguanidine using DEAD[10,11] or aryl isocyanates[12] in refluxing solvents.

We attempted to apply microwave irradiation to the synthesis of *s*-triazino[2,1-*b*][1,3]benzoxazoles and *s*-triazino[2,1-*b*][1,3]benzothiazoles from 2-benzoxazolylguanidine or 2-benzothiazolylguanidine in reactions with tosyl isocyanate and phenyl isothiocyanate in dioxane,[12] by modifying the previously reported procedures and then extending this methodology to the synthesis of *s*-triazino[1,2-*a*]benzimidazoles.

2-Benzoxazolylguanidines **2a–c** were prepared from the corresponding 2-aminophenols **1a–c** by cyclocondensation with cyanoguanidine by the known procedure.[13]

Microwave-assisted reaction of **2a–c** with phenyl isocyanate as well as phenyl isothiocyanate led to the formation of 2-amino-4-oxo-*s*-triazino[2,1-*b*][1,3]benzoxazole **3a–c** or their 4-thioxo-analogues **3d–f**, respectively (Scheme 1). The reactions proceeded at 180 °C in 1,2-dimethoxyethane affording compounds **3a–f** in high yield and purity (Table 1).



Scheme 1 For R and X of **3a–f**, see Table 1

All new compounds **3a–f** were fully characterized (Table 3). The signals at 165.9–166.0 ppm in the ^{13}C NMR spectra confirmed the presence of the carbonyl group in **3a–c**, while the thiocarbonyl group on the triazine ring of **3d–f** appeared at 1380–1382 cm^{-1} in the IR spectra and at 176.6–176.9 ppm in the ^{13}C NMR spectra. The anisotropic effect of the oxygen (sulfur) atom led to

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Table 1 *s*-Triazino[2,1-*b*][1,3]benzoxazoles **3a–f**

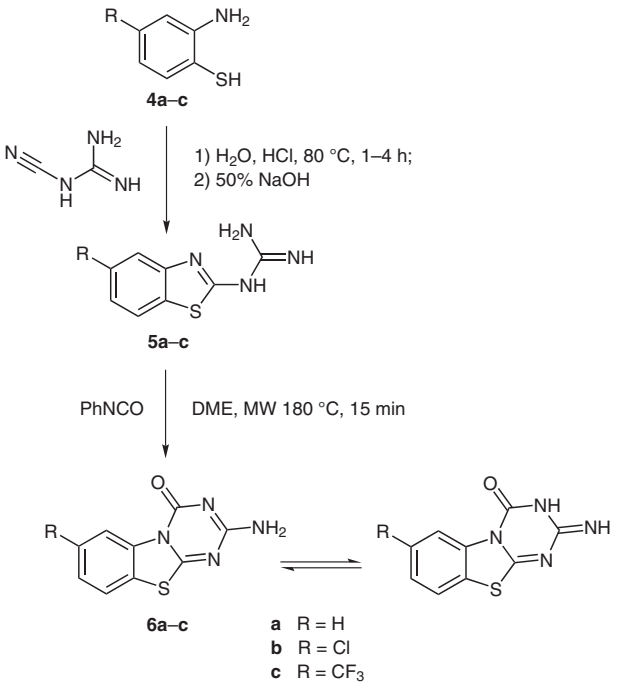
Compd	X	R	Yield (%)	Mp (°C)
3a	O	H	90	>360
3b	O	Me	92	293–295
3c	O	Cl	90	298
3d	S	H	94	289
3e	S	Me	98	305–306
3f	S	Cl	92	310

the downfield shift of H-6 to 7.90–7.98 and 8.86–9.06 ppm in the ^{1}H NMR spectra for the 4-oxo derivatives **3a–c** and 4-thioxo derivatives **3d–f**, respectively. These findings confirmed the formation of the *s*-triazine ring and are in agreement with literature data.[12]

Interestingly, the *s*-triazino[2,1-*b*][1,3]benzoxazoles **3a–f** were found as their imino tautomers in DMSO. This was supported by the evidence of two definite D_2O exchangeable singlets (7.75–8.41 ppm) in the ^{1}H NMR spectra corresponding to the N(3)H and the imino group of **3a–f**.

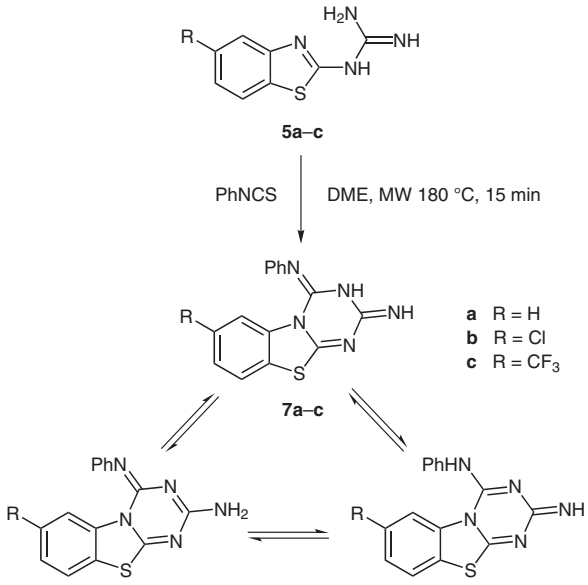
2-Benzothiazolylguanidines **5a–c** were synthesized from the corresponding 2-aminothiophenols **4a–c** by cyclocondensation with cyanoguanidine according to the reported method.[14]

The ring-closure carbonylation of 2-benzothiazolylguanidines **5a–c** was successfully achieved under microwave irradiation using phenyl isocyanate (Scheme 2). Thus 2-imino-4-oxo-2,3-dihydro-4*H*-[1,3,5]triazino[2,1-*b*][1,3]benzothiazoles **6a–c** were prepared in good yields (Table 2). Similarly to **3a** and **3c**, compounds **6a–c** were found to exist in DMSO as their imino tautomers. The analytical and spectroscopic data are in agreement with the proposed structures (Table 3).



Scheme 2

Unexpected results were obtained in the reaction of 2-benzothiazolylguanidines **5a–c** and phenyl isothiocyanate (Scheme 3). It has been reported that 2-amino-4-thioxo-*s*-triazino[2,1-*b*][1,3]benzothiazole[12] or *N*-[(1*H*-benzothiazol-2-ylamino)(imino)methyl]-*N*′-phenylthiourea[15] were obtained under conventional reaction conditions from the reaction of 2-benzothiazolylguanidine (**5a**) and phenyl isothiocyanate. In our study, under microwave irradiation, 2-imino-4-phenylimino-*s*-triazino[2,1-*b*][1,3]benzothiazole (**7a**) formed. Analogously, diimino compounds **7b** and **7c** were prepared from the appropriate benzothiazolylguanidines (**5b** and **5c**) under identical conditions. Looking at the literature, we discovered that *s*-triazino[2,1-*b*][1,3]benzothiazole **7a** had in fact been prepared before from 2-aminobenzothiazole or 2-benzothiazolylguanidine,[16] however the reactions were reported to require several days and afford very low yields (7.5% and 4.3%, respectively).



Scheme 3

Table 2 *s*-Triazino[2,1-*b*][1,3]benzothiazoles **6a–c** and **7a–c**

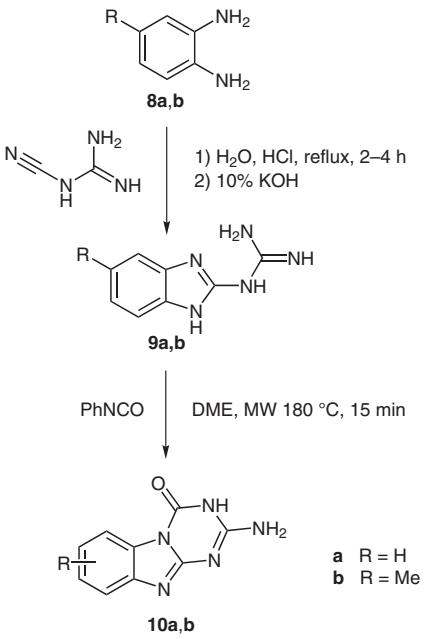
Compd	R	Yield (%)	Mp (°C)
6a	H	96	343–344
6b	Cl	90	>360
6c	CF_3	95	324
7a	H	28	300
7b	Cl	30	288–290
7c	CF_3	14	265

Several tautomeric forms are possible for compounds **7a–c** because of the amino-imino tautomerism of two potential amino groups. The 2-amino-tautomeric form may be eliminated based on the two definite D_2O exchangeable singlets for NH protons in the ^1H NMR spectra of *s*-triazino[2,1-*b*][1,3]benzothiazoles **7a–c** (Table 3). In a NOESY experiment conducted on compounds **7a–c**, cross-peaks were observed between the *ortho*-protons of the phenyl ring and H-6 but not the NH protons. The absence of the cross-peaks between NH and H-6 indicated the predominance of the diimino tautomeric form in DMSO. The cross-peaks observed between the *ortho*-protons of the phenyl ring and H-6 of the heterocyclic system strongly support a 4*Z*-configuration for **7a–c**. This configuration would result in an anisotropic effect from the coplanarity of the phenyl ring and the downfield shift of H-6 signal in ^1H NMR spectra of **7a–c** (Table 3).

Reaction of 2-benzimidazolylguanidines **9a** and **9b** with phenyl isocyanate under microwave irradiation proceeded in a similar way as described for fused *s*-triazines **3a–c** and **6a–c**. The reaction led to the formation of 2-amino-4-oxo-3*H*-[1,3,5]triazino[1,2-*a*]benzimidazoles **10a** and **10b** (Scheme 2). There have been many methods reported for the synthesis of **10a**.[7–10] However, the reaction of **9a** with phenyl isocyanate in pyridine under reflux has been reported to afford *N*-[(1*H*-benzimidazol-2-ylamino)(imino)methyl]-*N*′-phenylurea.[8] Therefore it seems likely that microwave irradiation can facilitate elimination of aniline from the addition product to furnish **10a** and **10b**.

Microwave irradiation has been shown to improve the selectivity of several reactions;[17] however, we found that the reaction of asymmetric 5-methylbenzimidazolyl-2-guanidine (**9b**) with phenyl isocyanate gave a mixture of regioisomeric 7- and 8-methyl substituted products (**10b**) in equal measure. The same ratio of isomeric forms was also observed in the reaction of **9b** with DEAD in refluxing ethanol.[18]

The microwave-assisted method we report herein is limited to phenyl isocyanates, the thioxo analogues of **10a** and **10b** did not result from the reaction of **8a** and **8b** with phenyl isothiocyanate – instead, a complex mixture of several compounds was formed. However, ring-closure thiocarbonylation of **8a** has been reported to be possible using carbon disulfite in basic conditions,[8,9,19] therefore, further optimization of the microwave-assisted reaction is warranted.



Scheme 4

Mps (uncorrected) were determined on a Gallenkamp melting point apparatus. IR spectra were collected on a Jasco FT-IR-430 spectrophotometer as KBr pellets. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer, using DMSO-d_6 as a solvent and TMS as an internal reference. Microwave-assisted syntheses were carried out using a microwave synthesizer Initiator™ (Biotage AB, Sweden).

2-Benzoxazolylguanidines 2a–c; General Procedure

A mixture of *o*-aminophenol **1a–c** (0.1 mol), cyanoguanidine (8.4 g, 0.1 mol), and concd HCl (10 mL, 0.1 mol) in EtOH (40 mL) was heated under reflux for 2–6 h. The reaction mixture was cooled and the precipitate was filtered, mixed with H_2O (100 °C, 100 mL), and KOH (10%; 25 mL) was added. After cooling, the precipitated 2-guanidinobenzoxazole **2a–c** was removed by filtration, washed with cold H_2O, dried, and recrystallized (EtOH, 20%).

2-Benzoxazolylguanidine (2a)

Yield: 68%; mp 186 °C (Lit.[13] 182–184 °C).

5-Methylbenzoxazolyl-2-guanidine (2b)

Yield: 72%; mp 236–237 °C.

^1H NMR (300 MHz): δ = 2.34 (s, 3 H, Me), 6.83 (dd, 1 H, *J* = 7.9, 1.1 Hz, H-6), 7.10 (s, 1 H, H-4), 7.18 (br s, 4 H, NH), 7.19 (d, 1 H, *J* = 7.9 Hz, H-7).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.0 (Me), 107.9 (C-7), 115.6 (C-4), 121.4 (C-6), 131.9.0 (C-5), 142.6 (C-3a), 144.6 (C-7a), 159.7 (C=NH), 166.5 (C-2).

Anal. Calcd for $C_9H_{10}N_4O$: C, 56.83; H, 5.30; N, 29.46. Found: C, 56.80; H, 5.35; N, 29.38.

5-Chlorobenzoxazolyl-2-guanidine (2c)

Yield: 63%; mp 205–207 °C.

^1H NMR (300 MHz): δ = 7.03 (dd, 1 H, *J* = 8.3, 2.3 Hz, H-6), 7.24 (br s, 4 H, NH), 7.31 (d, 1 H, *J* = 2.3 Hz, H-4), 7.33 (d, 1 H, *J* = 8.3 Hz, H-7).

^{13}C NMR (75 MHz): δ = 109.5 (C-7), 114.8 (C-4), 120.3 (C-6), 127.0 (C-5), 144.1 (C-3a), 145.3 (C-7a), 159.9 (C=NH), 167.3 (C-2).

Anal. Calcd for $C_8H_7ClN_4O$: C, 45.62; H, 3.35; N, 26.60. Found: C, 45.33; H, 3.50; N, 26.51.

2-Benzothiazolylguanidines 5a–c; General Procedure

A mixture of *o*-aminothiophenol (**4a–c**; 0.05 mol), cyanoguanidine (4.2 g, 0.05 mol), and concd HCl (10 mL, 0.1 mol) in H_2O (20 mL) was heated at 80 °C. After 1–4 h, NaOH (50%; 8 mL, 0.1 mol) was added and the mixture was stirred for 10 min at 80 °C. After cooling, the precipitated 2-guanidinobenzothiazole **5a–c** was removed by filtration, washed with cold H_2O, dried, and recrystallized (aq EtOH).

Benzothiazolyl-2-guanidine (5a)
Yield: 95%; mp 172–173 °C (Lit.[14] 173–176 °C).

^{1}H NMR (300 MHz): δ = 7.07 (td, 1 H, *J* = 7.5, 1.1 Hz, H-6), 7.2 (br s, 4 H, NH), 7.25 (td, 1 H, *J* = 7.7, 1.1 Hz, H-5), 7.45 (d, 1 H, *J* = 7.9 Hz, H-4), 7.66 (d, 1 H, *J* = 7.5 Hz, H-7).

^{13}C NMR (75 MHz): δ = 118.2 (C-4), 120.6 (C-7), 121.5 (C-6), 125.1 (C-5), 130.2 (C-7a), 152.0 (C-3a), 158.1 (C=NH), 173.9 (C-2).

Anal. Calcd for $C_8H_8N_4S$: C, 49.98; H, 4.19; N, 29.14. Found: C, 49.78; H, 4.45; N, 29.01.

5-Chlorobenzothiazolyl-2-guanidine (5b)
Yield: 92%; mp 228–229 °C.

^{1}H NMR (300 MHz): δ = 7.09 (dd, 1 H, *J* = 8.3, 1.9 Hz, H-6), 7.23 (br s, 4 H, NH), 7.46 (d, 1 H, *J* = 1.9 Hz, H-4), 7.68 (d, 1 H, *J* = 8.3 Hz, H-7).

^{13}C NMR (75 MHz): δ = 117.5 (C-4), 121.2 (C-6), 121.9 (C-7), 128.9 (C-5), 129.8 (C-7a), 153.2 (C-3a), 158.2 (C=NH), 175.5 (C-2).

Anal. Calcd for $C_8H_7ClN_4S$: C, 42.39; H, 3.11; N, 15.64. Found: C, 42.54; H, 3.56; N, 15.31.

5-Trifluoromethylbenzothiazolyl-2-guanidine (5c)
Yield: 90%; mp 225–226 °C.

^{1}H NMR (300 MHz): δ = 7.28 (br s, 4 H, NH), 7.37 (d, 1 H, *J* = 8.3 Hz, H-6), 7.71 (s, 1 H, H-4), 7.90 (d, 1 H, *J* = 8.3 Hz, H-7).

^{13}C NMR (75 MHz): δ = 114.2 (q, *J* = 3.9 Hz, C-4), 117.5 (q, *J* = 3.9 Hz, C-6), 121.6 (C-7), 124.6 (q, *J* = 272.1 Hz, CF_3), 126.1 (q, *J* = 31.6 Hz, C-5), 134.8 (C-7a), 152.1 (C-3a), 158.4 (C=NH), 175.5 (C-2).

Anal. Calcd for $C_8H_7ClN_4S$: C, 41.54; H, 2.71; N, 21.90. Found: C, 41.23; H, 2.98; N, 21.62.

2-Benzimidazolylguanidines 9a and 9b; General Procedure
A mixture of *o*-phenylenediamine **8a** or **8b** (0.1 mol), cyanoguanidine (8.4 g, 0.1 mol) and concd HCl (20 mL, 0.2 mol) in H_2O (200 mL) was heated under reflux for 1 h, cooled to 0 °C, and KOH (10%; 50 mL) was added slowly. Precipitated 2-guanidinobenzimidazole was removed by filtration, washed with H_2O, dried, and use in further reactions without further purification.

2-Benzimidazolylguanidine (9a)
Yield: 78%; mp 243–244 °C (Lit.[20] 245 °C).

5-Methylbenzimidazolyl-2-guanidine (9b)
Yield: 82%; mp 220–221 °C.

^{1}H NMR (300 MHz): δ = 2.32 (s, 3 H, Me), 6.72 (dd, 1 H, *J* = 7.9, 0.8 Hz, H-6), 6.7 (br s, 4 H, NH), 6.96 (s, 1 H, H-4), 7.03 (d, 1 H, *J* = 7.9 Hz, H-7), 10.84 [br s, 1 H, N1-H].

Anal. Calcd for $C_9H_{11}N_5$: C, 57.13; H, 5.86; N, 37.01. Found: C, 56.88; H, 6.02; N, 36.82.

2-Imino-4-(thi)oxo-2,3-dihydro-4*H*-[1,3,5]triazino-[2,1-*b*][1,3]benzoxazoles 3a–f, 2-Imino-4-oxo-2,3-dihydro-4*H*-[1,3,5]triazino[2,1-*b*][1,3]benzothiazoles 6a–c, 2-Imino-4-phenylimino-2,3-dihydro-4*H*-[1,3,5]triazino[2,1-*b*][1,3]benzothiazoles 7a and 7b, and 2-Amino-4-oxo-3*H*-[1,3,5]triazino[1,2-*a*]benzimidazoles 10a and 10b; General Procedure
A mixture of heterylguanidine (**2a–c**, **5a–c**, **9a**, or **9b**; 5 mmol) and phenyl iso(thio)cyanate (5 mmol) in DME (5 mL) were heated at 180 °C under microwave irradiation for 15 min. After cooling, the precipitated target compound was removed by filtration, washed with DME, and dried. Compounds **3a–f**, **6a–c**, **10a**, and **10b** prepared in this manner were sufficiently pure, however they could be recrystallized from DMF (**3a–f**, **6a–c**) or DMSO (**10a** and **10b**). Compounds **7a** and **7b** required recrystallization from DMF.

Table 3 Spectroscopic Data of *s*-Triazino[2,1-*b*][1,3]benzoxazoles **3a–f** and *s*-Triazino[2,1-*b*][1,3]benzothiazoles **6a–c** and **7a–c**

Compd	Molecular formula[a]	IR (KBr) (cm^{-1})	^{1}H NMR (300 MHz)	^{13}C NMR (75 MHz)
3a	$C_9H_6N_4O_2$ (202.2)	3359 (NH), 3075 (NH), 1703 (C=O), 1691, 1666, 1472, 1440, 1077, 760	7.44 (td, 1 H, *J* = 7.2, 1.5 Hz, H-8), 7.46 (td, 1 H, *J* = 7.2, 1.9 Hz, H-7), 7.71 (dd, 1 H, *J* = 7.2, 1.9 Hz, H-9), 7.78 (s, 1 H, NH), 7.80 (s, 1 H, NH), 7.98 (dd, 1 H, *J* = 7.2, 1.5 Hz, H-6)	111.0 (C-6), 114.0 (C-9), 125.3 (C-7),[b] 125.5 (C-8),[b] 126.0 (C-5a), 143.4 (C-9a), 151.1 (C-2), 161.3 (C-10a), 166.0 (C=O)
3b	$C_{10}H_8N_4O_2$ (216.2)	3372 (NH), 3318 (NH), 3191 (NH), 3034, 1705 (C=O), 1668, 1651, 1486, 1439, 1074, 782	2.43 (s, 3 H, Me), 7.22 (dd, 1 H, *J* = 8.3, 1.1 Hz, H-8), 7.56 (d, 1 H, *J* = 8.3 Hz, H-9), 7.75 (s, 1 H, NH), 7.76 (s, 1 H, NH), 7.78 (s, 1 H, H-6)	20.9 (Me), 110.5 (C-6), 114.2 (C-9), 125.8 (C-8), 125.9 (C-5a), 135.0 (C-7), 141.5 (C-9a), 151.0 (C-2), 161.4 (C-10a), 165.9 (C=O)
3c	$C_9H_5ClN_4O_2$ (236.6)	3266 (NH), 3081 (NH), 1741, 1728, 1473, 1436, 1085, 776, 667	7.49 (dd, 1 H, *J* = 8.7, 2.3 Hz, H-8), 7.75 (d, 1 H, *J* = 8.7 Hz, H-9), 7.86 (s, 1 H, NH), 7.87 (s, 1 H, NH), 7.90 (d, 1 H, *J* = 2.3 Hz, H-6)	112.5 (C-6), 113.6 (C-9), 125.2 (C-8), 127.3 (C-5a), 129.2 (C-7), 142.4 (C-9a), 150.7 (C-2), 161.6 (C-10a), 165.9 (C=O)
3d	$C_9H_6N_4OS$ (218.2)	3299 (NH), 3163 (NH), 1670, 1617, 1470, 1435, 1380 (C=S), 1325, 1057, 966, 774, 750	7.47 (td, 1 H, *J* = 7.5, 1.1 Hz, H-8), 7.52 (td, 1 H, *J* = 7.5, 1.5 Hz, H-7), 7.75 (dd, 1 H, *J* = 7.5, 1.5 Hz, H-9), 8.15 (s, 1 H, NH), 8.29 (s, 1 H, NH), 9.03 (dd, 1 H, *J* = 7.5, 1.1 Hz, H-6)	110.9 (C-6), 116.5 (C-9), 124.5 (C-7), 126.5 (C-8), 127.2 (C-5a), 143.7 (C-9a), 159.7 (C-2), 161.2 (C-10a), 176.9 (C=S)

Table 3 Spectroscopic Data of *s*-Triazino[2,1-*b*][1,3]benzoxazoles **3a–f** and *s*-Triazino[2,1-*b*][1,3]benzothiazoles **6a–c** and **7a–c** (continued)

Compd	Molecular formula[a]	IR (KBr) (cm^{-1})	^1H NMR (300 MHz)	^{13}C NMR (75 MHz)
3e	$C_{10}H_8N_4OS$ (232.3)	3363 (NH), 3279 (NH), 3134 (NH), 1649, 1611, 1489, 1433, 1382 (C=S), 1366 (Me), 1321, 1052, 969, 802, 773	2.46 (s, 3 H, Me), 7.31 (dd, 1 H, *J* = 8.3, 1.1 Hz, H-8), 7.61 (d, 1 H, *J* = 8.3 Hz, H-9), 8.13 (s, 1 H, NH), 8.28 (s, 1 H, NH), 8.86 (s, 1 H, H-6)	21.2 (Me), 110.4 (C-6), 116.7 (C-9), 126.9 (C-8), 127.2 (C-5a), 134.1 (C-7), 141.8 (C-9a), 159.8 (C-2), 161.2 (C-10a), 176.9 (C=S)
3f	$C_9H_5ClN_4OS$ (252.7)	3303 (NH), 3157 (NH), 1685, 1616, 1472, 1454, 1430, 1381 (C=S), 1170, 1051, 957, 808, 768, 657	7.59 (dd, 1 H, *J* = 8.7, 2.3 Hz, H-8), 7.80 (d, 1 H, *J* = 8.7 Hz, H-9), 8.25 (s, 1 H, NH), 8.41 (s, 1 H, NH), 9.06 (d, 1 H, *J* = 2.3 Hz, H-6)	112.3 (C-6), 115.9 (C-9), 126.2 (C-8), 128.2 (C-5a),[b] 128.4 (C-7),[b] 142.7 (C-9a), 160.0 (C-2), 161.2 (C-10a), 176.6 (C=S)
6a	$C_9H_6N_4OS$ (218.2)	3332 (NH), 3107 (NH), 1722, 1702, 1648, 1554, 1507, 1455, 1428, 1112, 779, 758, 636	7.46 (td, 1 H, *J* = 7.5, 1.1 Hz, H-8), 7.54 (td, 1 H, *J* = 7.7, 1.1 Hz, H-7), 7.63 (s, 1 H, NH), 7.70 (s, 1 H, NH), 7.98 (dd, 1 H, *J* = 7.7, 1.1 Hz, H-9), 8.63 (dd, 1 H, *J* = 7.9, 1.1 Hz, H-6)	117.7 (C-6), 121.6 (C-5a), 122.9 (C-9), 125.9 (C-8), 127.0 (C-7), 135.7 (C-9a), 151.6 (C-2), 163.5 (C=O), 170.2 (C-10a)
6b	$C_9H_5ClN_4OS$ (252.7)	3306 (NH), 3108 (NH), 1721, 1699, 1674, 1578, 1565, 1510, 1469, 1455, 1438, 1226, 1120, 799, 768, 636	7.54 (dd, 1 H, *J* = 8.3, 2.2 Hz, H-8), 7.70 (s, 1 H, NH), 7.76 (s, 1 H, NH), 8.01 (d, 1 H, *J* = 8.3 Hz, H-9), 8.62 (d, 1 H, *J* = 2.2 Hz, H-6)	117.2 (C-6), 120.7 (C-5a), 124.4 (C-9), 125.8 (C-8), 131.5 (C-7), 136.6 (C-9a), 151.3 (C-2), 163.5 (C=O), 170.5 (C-10a)
6c	$C_{10}H_5F_3N_4OS$ (286.2)	3283 (NH), 3123 (NH), 1713 (C=O), 1652, 1609, 1561, 1513, 1442, 1334, 1249, 1126, 776, 734, 663	7.71 (s, 1 H, NH), 7.78 (s, 1 H, NH), 7.82 (dd, 1 H, *J* = 8.3, 1.1 Hz, H-8), 8.23 (d, 1 H, *J* = 8.3 Hz, H-9), 8.91 (d, 1 H, *J* = 1.1 Hz, H-6)	113.9 (q, *J* = 4.5 Hz, C-6), 122.4 (q, *J* = 3.7 Hz, C-8), 123.9 (q, *J* = 272.6 Hz, CF_3), 124.2 (C-9), 126.9 (q, *J* = 1.2 Hz, C-5a), 127.3 (q, *J* = 32.1 Hz, C-7), 136.1 (C-9a), 151.5 (C-2), 163.5 (C=O), 170.4 (C-10a)
7a	$C_{15}H_{11}N_5S$ (293.4)	3437 (NH), 3145 (NH), 1662, 1633, 1578, 1564, 1509, 1488, 1451, 1430, 1227, 1001, 782, 762, 690	6.93 (t, 1 H, *J* = 7.2 Hz, H-4′), 7.12 (d, 2 H, *J* = 7.5 Hz, H-2′, H-6′), 7.25 (t, 2 H, *J* = 7.7 Hz, H-3′, H-5′), 7.25 (s, 1 H, NH), 7.37 (s, 1 H, NH), 7.44 (td, 1 H, *J* = 7.5, 1.1 Hz, H-8), 7.52 (td, 1 H, *J* = 7.5, 1.1 Hz, H-7), 7.96 (d, 1 H, *J* = 7.5 Hz, H-9), 9.21 (d, 1 H, *J* = 8.3 Hz, H-6)	119.2 (C-6), 121.3 (C-4′), 121.4 (C-5a), 122.5 (C-9), 123.2 (C-2′, C-6′), 125.5 (C-8), 126.6 (C-7), 128.2 (C-3′, C-5′), 136.1 (C-9a), 146.8 (C-1′), 148.8 (C-2), 159.4 (C-4), 169.5 (C-10a)
7b	$C_{15}H_{10}ClN_5S$ (327.8)	3434 (NH), 3113 (NH), 1660, 1640, 1581, 1566, 1510, 1487, 1454, 1425, 1234, 1021, 757, 707, 549	6.95 (t, 1 H, *J* = 7.2 Hz, H-4′), 7.11 (d, 2 H, *J* = 7.5 Hz, H-2′, H-6′), 7.27 (t, 2 H, *J* = 7.7 Hz, H-3′, H-5′), 7.33 (s, 1 H, NH), 7.46 (s, 1 H, NH), 7.51 (dd, 1 H, *J* = 8.5, 2.0 Hz, H-8), 7.98 (d, 1 H, *J* = 8.5 Hz, H-9), 9.27 (d, 1 H, *J* = 2.0 Hz, H-6)	118.7 (C-6), 120.6 (C-5a), 121.5 (C-4′), 123.1 (C-2′, C-6′), 123.9 (C-9), 125.3 (C-8), 128.3 (C-3′, C-5′), 131.0 (C-7), 137.0 (C-9a), 146.7 (C-1′), 148.6 (C-2), 159.3 (C-4), 169.8 (C-10a)
7c	$C_{16}H_{10}F_3N_5S$ (361.4)	3444 (NH), 3183 (NH), 1663, 1630, 1582, 1515, 1489, 1430, 1334, 1231, 1144, 1126, 1000, 781, 761, 732	6.96 (t, 1 H, *J* = 7.2 Hz, H-4′), 7.16 (d, 2 H, *J* = 7.5 Hz, H-2′, H-6′), 7.27 (t, 2 H, *J* = 7.7 Hz, H-3′, H-5′), 7.37 (s, 1 H, NH), 7.49 (s, 1 H, NH), 7.81 (dd, 1 H, *J* = 8.3, 1.1 Hz, H-8), 8.21 (d, 1 H, *J* = 8.3 Hz, H-9), 9.61 (d, 1 H, *J* = 1.1 Hz, H-6)	115.4 (q, *J* = 4.3 Hz, C-6), 121.6 (C-4′), 121.9 (q, *J* = 2.9 Hz, C-8), 123.2 (C-2′, C-6′), 123.6 (C-9), 124.0 (q, *J* = 272.2 Hz, CF_3), 126.8 (q, *J* = 1.2 Hz, C-5a), 126.9 (q, *J* = 32.1 Hz, C-7), 128.3 (C-3′, C-5′), 136.5 (C-9a), 146.7 (C-1′), 148.4 (C-2), 159.3 (C-4), 169.7 (C-10a)

[a] Satisfactory elemental analyses were obtained (C ± 0.27, H ± 0.28, N ± 0.34).
[b] Assignments may be reversed.

2-Imino-4-phenylimino-7-trifluoromethyl-2,3-dihydro-4*H*-[1,3,5]triazino[2,1-*b*][1,3]benzothiazoles (7c)

A mixture of 5-trifluoromethylbenzothiazolyl-2-guanidine (**5c**; 1.30 g, 5 mmol) and phenyl isothiocyanate (0.68 g, 5 mmol) in DME (5 mL) was heated at 180 °C under microwave irradiation for 15 min. The solvent was evaporated, the residue was washed with hot EtOH, and recrystallized (DMF).

2-Amino-4-oxo-3*H*-[1,3,5]triazino[1,2-*a*]benzimidazole (10a)

Yield: 95%; mp >360 °C.

IR (KBr): 3415 (NH), 3219 (NH), 3123 (NH), 2997, 2886, 2800, 1717 (C=O), 1616, 1601, 1526, 1457, 1405, 774, 736 cm^{-1}.

^1H NMR (300 MHz): δ = 7.19 (br s, 1 H, NH_2), 7.25 (td, 1 H, *J* = 7.7, 1.1 Hz, H-8), 7.34 (td, 1 H, *J* = 7.7, 1.5 Hz, H-7), 7.42 (d, 1 H, *J* = 7.2 Hz, H-9), 8.09 (d, 1 H, *J* = 7.5 Hz, H-6), 12.20 (br s, 1 H, NH).

^{13}C NMR (75 MHz): δ = 112.6 (C-6), 113.9 (C-9), 121.8 (C-7), 124.7 (C-8), 126.6 (C-5a), 133.1 (C-9a), 150.3 (C-2), 153.7 (C=O), 162.9 (C-10a).

Anal. Calcd for $C_9H_7N_5O$: C, 53.73; H, 3.51; N, 34.81. Found: C, 53.54; H, 3.64; N, 34.50.

2-Amino-7(8)-methyl-4-oxo-3*H*-[1,3,5]triazino[1,2-*a*]benzimidazoles (10b)

Yield: 92%; mp >360 °C.

^1H NMR (300 MHz): δ = 2.41 (s, 3 H, C8-Me), 2.42 (s, 3 H, C7-Me), 7.07 (d, 1 H, *J* = 8.3 Hz, H-7), 7.08 (br s, 4 H, NH_2), 7.15 (d, 1 H, *J* = 8.3 Hz, H-8), 7.20 (s, 1 H, H-9), 7.28 (d, 1 H, *J* = 8.3 Hz, H-9), 7.92 (s, 1 H, H-6), 7.93 (d, 1 H, *J* = 8.3 Hz, H-6).

Anal. Calcd for $C_{10}H_9N_5O$: C, 55.81; H, 4.22; N, 32.54. Found: C, 55.78; H, 4.53; N, 32.15.

^1H NMR spectra of **10b** (mixture of regioisomers, 1:1) is in agreement with that prepared earlier in our group from the reaction of **9b** with DEAD.[18]

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