

Article

Synthesis and Crystal Structures of Azolo[b]1,3,4-Thiadiazinium Bromides

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Abstract: Three azolo[b]1,3,4-thiadiazinium bromides were prepared from the respective *N*-amino-*N'*-methylazolethiones and phenacyl bromide, and their crystal structures were determined. 6-Phenyl-1-methylimidazo[2,1-*b*]1,3,4-thiadiazinium bromide (**1**) crystallized as methanol solvate ($P2_1/n$), 6-phenyl-1-methyl-1,2,4-triazolo[3,4-*b*]1,3,4-thiadiazinium bromide (**2**) as hemi-ethanol solvate ($P2_1/n$), and 6-phenyl-1-methyl-1,2,4-triazolo[3,2-*b*]1,3,4-thiadiazinium bromide (**3**) solvent-free ($P2_1/c$). Interionic contacts were identified.

Keywords: imidazole; thiadiazine; triazole

1. Introduction

N-Amino-*N'*-alkylazolethiones are readily converted to the bicyclic annelated title compounds by condensation with α -bromoketones. Several examples (alkyl = substituted benzyl) of this reaction involving 4-amino- and 1-amino-1,2,4-triazolinethiones have been reported [1,2]. The synthesis of an analogous benzimidazole derivative starting from 1-amino-3-methylbenzimidazoline-2-thione has been described [3]. Since the portfolio of heterocyclic aminothiones has only recently been extended [4,5], we decided to compare the crystal structures of the closely related azolo[b]1,3,4-thiadiazinium bromides derived from the simplest representatives (alkyl = methyl) of 1-aminoimidazolinethione, 4-amino-1,2,4-triazolinethione and 1-amino-1,2,4-triazolinethione. Few reactions of the title compounds

are known, such as the ring contraction to pyrazolo[5,1-c]1,2,4-triazoles or pyrazolo[1,5-a]benzimidazoles which are aromatic systems of the 3a-azapentalene type [6,7]. Thus far, no crystal structures of azolo[b]1,3,4-thiadiazinium salts have been reported.

2. Results and Discussion

The title compounds **1–3** were prepared from 1-amino-3-methylimidazoline-2-thione [4], from 4-amino-1-methyl-1,2,4-triazoline-5-thione [8,9], and from 1-amino-4-methyl-1,2,4-triazoline-5-thione [5], respectively, with phenacyl bromide in EtOH solution (Figure 1). The crystallographic data and refinement details are summarized in Table 1.

Table 1. Crystal data and refinement details.

Compound	1	2	3
CCDC No.	1014167	1014168	1014169
Chemical formula	C ₁₂ H ₁₂ N ₃ S·Br·CH ₄ O	C ₁₂ H ₁₄ N ₄ S·Br·CH ₃ O _{0.5}	C ₁₁ H ₁₁ N ₄ S·Br
<i>M_r</i>	342.26	334.24	311.21
Crystal size/mm ³	0.12 × 0.10 × 0.08	0.18 × 0.05 × 0.04	0.14 × 0.11 × 0.08
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> /Å	10.0119(2)	10.0118(2)	6.8466(3)
<i>b</i> /Å	7.4539(1)	7.0742(1)	6.8350(3)
<i>c</i> /Å	20.1285(4)	19.6760(4)	27.0085(9)
β/°	102.829(1)	99.284(1)	95.417(2)
<i>V</i> /Å ³	1464.65(5)	1375.31(4)	1258.26(9)
<i>Z</i>	4	4	4
<i>D_x</i> /g cm ^{−3}	1.55	1.61	1.64
μ/mm ^{−1}	2.95	3.13	3.42
<i>F</i> (000)/e	696	676	624
θ _{max} /°	25.0	25.0	25.0
<i>h, k, l</i> range	−11 ≤ <i>h</i> ≤ 11 −8 ≤ <i>k</i> ≤ 8 −23 ≤ <i>l</i> ≤ 23	−11 ≤ <i>h</i> ≤ 11 −8 ≤ <i>k</i> ≤ 8 −23 ≤ <i>l</i> ≤ 23	−8 ≤ <i>h</i> ≤ 7 −7 ≤ <i>k</i> ≤ 8 −30 ≤ <i>l</i> ≤ 32
Measured reflections	8091	8591	6273
Independent reflections (<i>R</i> _{int})	2565 (0.036)	2422 (0.036)	2182 (0.039)
Observed reflections [<i>I</i> ≥ 2σ(<i>I</i>)]	2235	2030	1821
Restraints, parameters	0, 187	6, 180	0, 155
<i>R</i> ₁ , w <i>R</i> ₂ [<i>I</i> ≥ 2σ(<i>I</i>)]	0.029, 0.079	0.030, 0.069	0.043, 0.080
<i>R</i> ₁ , w <i>R</i> ₂ (all data)	0.034, 0.082	0.040, 0.072	0.056, 0.083
Goodness of fit	1.04	1.04	1.14
Δρ _{max} , Δρ _{min} /e Å ^{−3}	0.28, −0.25	0.42, −0.31	0.46, −0.30

6-Phenyl-1-methylimidazo[2,1-b]1,3,4-thiadiazinium bromide crystallized from methanol and was obtained as methanol solvate **1**. The imidazole rings are arranged parallel to (2 5 $\bar{2}$) and ($\bar{2}$ 5 2) planes. There are numerous C—H···Br and O—H···Br contacts forming a network (Figure 2). The oxygen position of the methanol molecule is disordered in the ratio 65:35. For hydrogen calculation, the carbon atoms of

the solvent molecule were split into two positions with same coordinates and displacement parameters. The hydrogen bond parameters are summarized in Table 2.

Figure 1. Synthesis of 1,3,4-thiadiazinium bromides **1–3**.

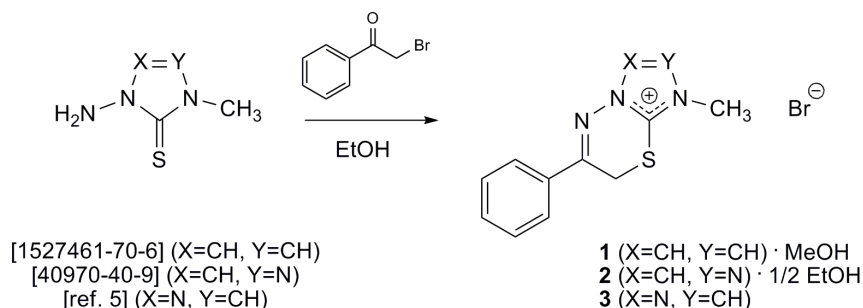


Figure 2. (a) ORTEP plot and atom numbering scheme of the cation; the displacement ellipsoids are drawn at the 50% probability level; (b) Packing and hydrogen bonding of **1**.

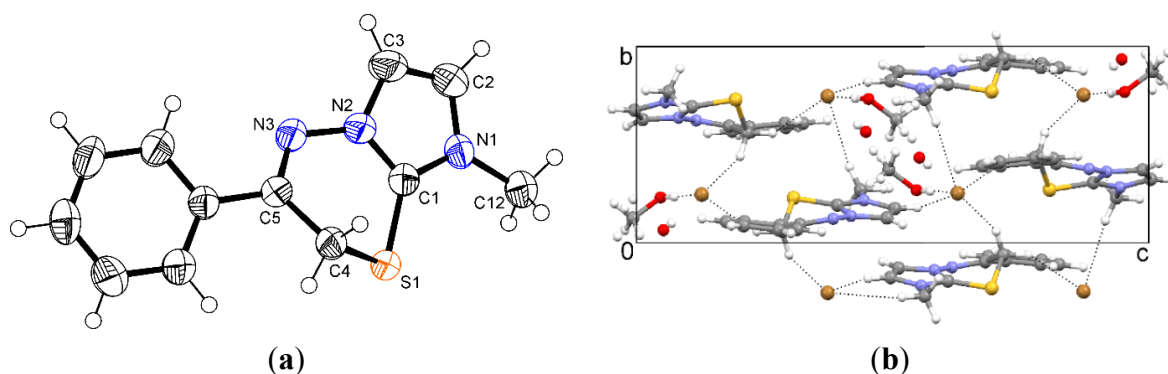


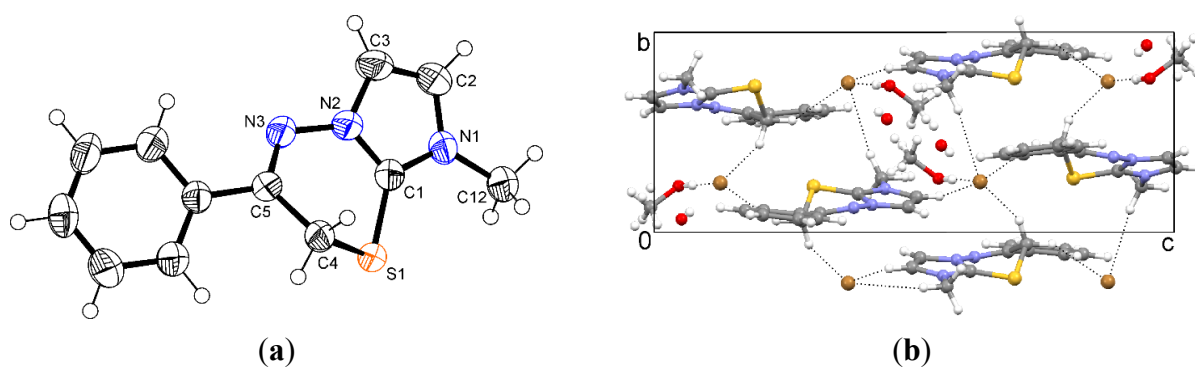
Table 2. Hydrogen bond parameters and short contacts (Å, °).

Compound	Interaction	H···A	D···A	D–H···A	Symmetry A
1	O1–H···Br	2.52	3.331(4)	167	x, y, z
	C4–H _A ···Br	2.86	3.590(2)	132	$1/2 - x, 1/2 + y, 1/2 - z$
	C12–H _B ···Br	2.87	3.796(3)	161	$1 - x, -y, 1 - z$
	C4–H _B ···Br	2.90	3.749(2)	146	x, y, z
	C2–H···Br	2.93	3.738(2)	145	$1 - x, -y, 1 - z$
	C12–H _C ···Br	2.96	3.871(2)	157	$x, 1 + y, z$
2	O1···Br	—	2.49(1)	—	x, y, z
	C2–H···Br	2.66	3.555(3)	160	$1 - x, -y, -z$
	C3–H _A ···Br	2.78	3.518(3)	132	$3/2 - x, -1/2 + y, 1/2 - z$
	C3–H _B ···Br	2.87	3.704(3)	144	x, y, z
	C11–H _C ···Br	2.95	3.767(4)	142	$x, -1 + y, z$
3	C2–H···Br	2.70	3.548(4)	151	$-x, 1 - y, 1 - z$
	C3–H _B ···Br	2.81	3.628(4)	141	$x, -1 + y, z$
	C11–H _C ···Br	2.93	3.802(4)	150	$-x, 1 - y, 1 - z$

6-Phenyl-1-methyl-1,2,4-triazolo[3,4-b]1,3,4-thiadiazinium bromide was recrystallized from methanol, but retained the reaction solvent and thus was obtained as hemi-ethanol solvate **2**. The triazole rings are parallel to (4 8 3) and (4 $\bar{8}$ 3) planes. As in the structure of **1**, numerous C–H···Br contacts

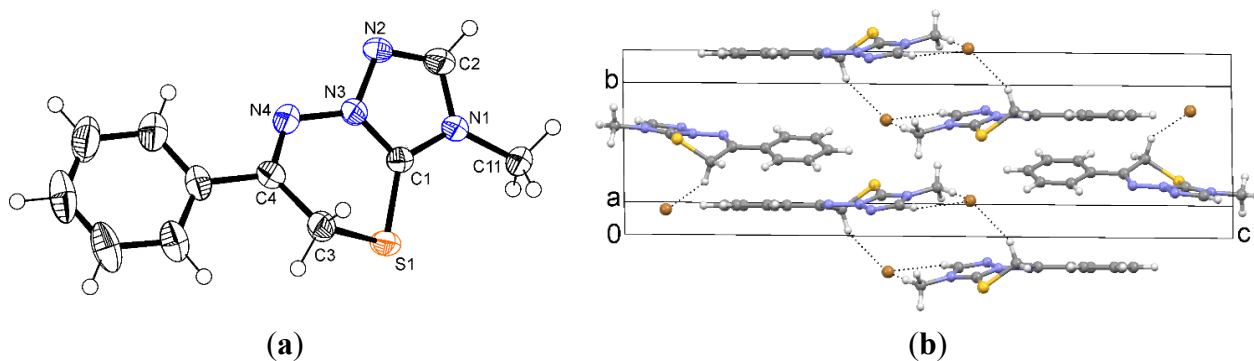
form a three-dimensional network (Figure 3). The ethanol molecule is located close to an inversion center (occupancy of 0.5 for each atom) and is additionally disordered in the ratio 1:1 for the positions of the hydroxyl and methyl group. These disordered positions were refined with isotropic displacement parameters, and bond restraints were used for the pertinent C–C and C–O bonds. Hydrogen atoms of the solvent molecule were omitted. An exceptionally short O1⋯Br1 distance is observed in the structure of compound **2**. There are precedents of similar or even shorter O⋯Br contacts in the literature. For example, distances of 2.48 and 2.31 Å (reference code YIDFAU) and 2.38, 2.41 and 2.46 Å (reference code YIDFEY) between the oxygen atoms of hydroxyethyl groups and bromide ions were found in multidentate ligands [10]. The structure of an anion binding tripodal host molecule (reference code UMIDEZ), notably a methanol solvate, showed a short contact of 2.53 Å between the oxygen atom of the methanol molecule and a bromide ion [11]. Since a host-guest relationship cannot be seriously considered here, the short O⋯Br distance may rather be due to crystal packing.

Figure 3. (a) ORTEP plot and atom numbering scheme of the cation; (b) packing and hydrogen bonding of **2**.



In contrast, 6-phenyl-1-methyl-1,2,4-triazolo[3,2-b]1,3,4-thiadiazinium bromide (**3**) precipitated from the hot reaction solution, but did not crystallize as a solvate. The triazole rings are arranged parallel to (1 13 7) and (1 $\bar{1}$ 3 7) planes. The bromide ions receive three hydrogen bonds from C2–H, C3–H and C11–H, linking the cations into cyclic dimers (Figure 4).

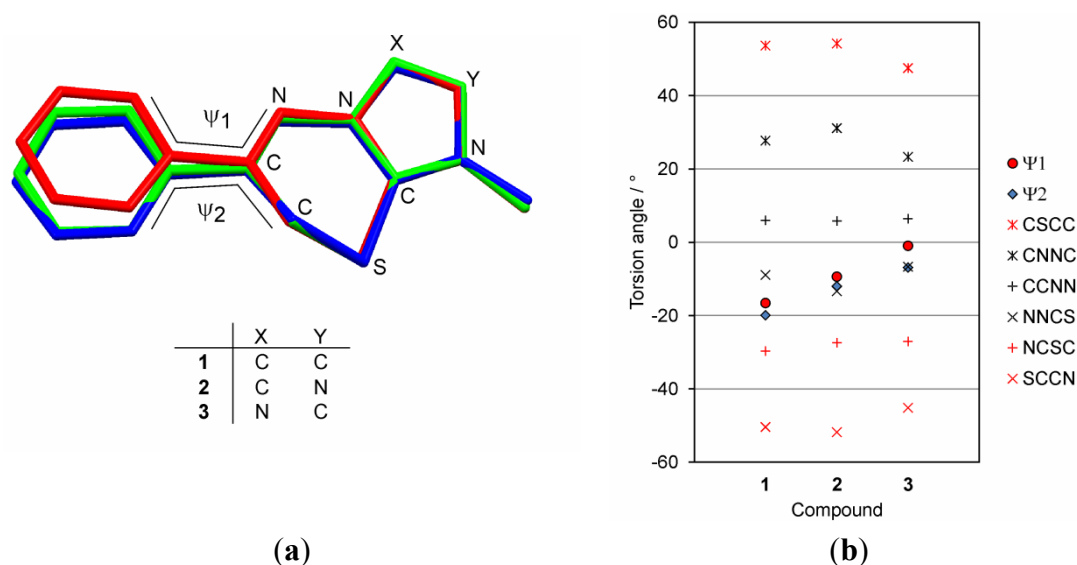
Figure 4. (a) ORTEP plot and atom numbering scheme of the cation; (b) packing and hydrogen bonding of **3**.



The thiadiazine rings themselves are quite similar in the three compounds. The C–S–C angles are between 91.5(1)° and 93.4(2)°. The S–C–C angles range from 111.1(1)° to 112.6(3)°, and the N–C–C

angles are between $122.0(2)^\circ$ and $123.9(4)^\circ$. Figure 5a illustrates the different geometries adopted by the phenylthiadiazinium cations. Differences in the conformation of the phenylthiadiazinium cations are best described by the torsion angles ψ_1 and ψ_2 . Thus, angles ψ_1 are $-16.6(3)^\circ$ for **1**, $-9.4(4)^\circ$ for **2**, and $-1.0(6)^\circ$ for **3**, whereas ψ_2 values are $-19.9(3)^\circ$ for **1**, $-12.0(4)^\circ$ for **2**, and $-6.9(6)^\circ$ for **3**, respectively. The differences between the other corresponding torsion angles within the thiadiazine rings are smaller among the three compounds. A graphical summary of these angles is depicted in Figure 5b.

Figure 5. (a) Overlay of the 1,3,4-thiadiazinium cations of **1** (green), **2** (blue), and **3** (red); (b) Torsion angles describing the conformation of the thiadiazine rings in the cations **1–3**.



3. Experimental Section

Reagents and solvents were purchased from Sigma-Aldrich (Steinheim, Germany). X-Ray diffraction data were recorded by ω and ϕ scans with a Nonius KappaCCD (Bruker, Billerica, MA, USA) diffractometer using MoK α radiation at 233 K. The structures were solved by direct methods and refined by full-matrix least-squares methods on F^2 [12]. CCDC reference numbers: 1014167–1014169. Illustrations were generated using ORTEP-3 [13] and Mercury [14] programs. NMR spectra were measured with Bruker Avance DPX 300 and Bruker Avance II+ 600 spectrometers. IR spectra were obtained with a Bruker Alpha FT-IR instrument.

3.1. 6-Phenyl-1-Methylimidazo[2,1-b]1,3,4-Thiadiazinium Bromide Methanol Solvate (**1**)

A solution of 1-amino-3-methylimidazoline-2-thione (50 mg, 0.39 mmol) and phenacyl bromide (77 mg, 0.39 mmol) in EtOH (3 mL) was stirred at 80 °C for 4 h. The solvent was removed under reduced pressure, and the residue was crystallized by slow evaporation of a solution in MeOH (1 mL). Yield: 48 mg (40%). M.p. 219–229 °C (decomposition). ^1H NMR (DMSO- d_6 , 600 MHz): δ 3.82 (s, 3H), 4.64 (s, 2H), 7.63 (t, $J = 7.6$ Hz, 2H), 7.69 (t, $J = 7.3$ Hz, 1H), 7.91 (d, $J = 2.1$ Hz, 1H), 8.06 (d, $J = 7.4$ Hz, 2H), 8.29 (d, $J = 2.1$ Hz, 1H) ppm. ^{13}C NMR (DMSO- d_6 , 151 MHz): δ 24.8, 36.6, 123.0, 124.0, 129.3 (2C), 130.6 (2C), 133.5, 134.2, 138.2, 158.6 ppm. IR (neat): $\tilde{\nu}$ 3078 w, 2986 w, 2885 w, 1591 m, 1497 m, 1449 m, 1405 m, 1319 m, 1289 m, 837 m, 768 s, 730 m, 688 s, 651 s, 585 m cm^{-1} .

3.2. 6-Phenyl-1-Methyl-1,2,4-Triazolo[3,4-b]1,3,4-Thiadiazinium Bromide Hemi-Ethanol Solvate (2)

A solution of 4-amino-1-methyl-1,2,4-triazoline-5-thione (50 mg, 0.38 mmol) and phenacyl bromide (76 mg, 0.38 mmol) in EtOH (3 mL) was stirred at 80 °C for 4 h. On cooling to 20 °C, the product precipitated. It was filtered off and washed with Et₂O. Yield: 60 mg (50%). Single crystals were obtained by slow evaporation of a solution in MeOH, m.p. 213–219 °C (decomposition). ¹H NMR (DMSO-d₆, 300 MHz): δ 1.05 and 3.43 (EtOH), 4.02 (s, 3H), 4.76 (s, 2H), 7.63–7.73 (m, 3H), 8.07–8.09 (m, 2H), 9.84 (s, 1H) ppm. ¹³C NMR (DMSO-d₆, 75 MHz): δ 18.6 and 56.0 (EtOH), 24.6, 38.0, 128.1 (2C), 129.4 (2C), 131.8, 133.4, 142.3, 145.2, 159.4 ppm. IR (neat): $\tilde{\nu}$ 3028 w, 2961 w, 2896 w, 1533 m, 1508 m, 1446 m, 1361 m, 1291 m, 1161 m, 1088 m, 839 m, 789 m, 766 s, 681 s, 657 m, 589 m, 512 m cm^{−1}.

3.3. 6-Phenyl-1-Methyl-1,2,4-Triazolo[3,2-b]1,3,4-Thiadiazinium Bromide (3)

A solution of 1-amino-4-methyl-1,2,4-triazoline-5-thione (50 mg, 0.38 mmol) and phenacyl bromide (76 mg, 0.38 mmol) in EtOH (3 mL) was stirred at 80 °C for 8 h. The product crystallized from the hot solution. It was collected by filtration, washed with EtOH, and dried. Yield: 90 mg (75%). Single crystals from hot EtOH, m.p. 207–211 °C (decomposition). ¹H NMR (DMSO-d₆, 300 MHz): δ 3.87 (s, 3H), 4.78 (s, 2H), 7.62–7.72 (m, 3H), 8.09–8.12 (m, 2H), 9.34 (s, 1H) ppm. ¹³C NMR (DMSO-d₆, 75 MHz): δ 24.1, 33.8, 128.4 (2C), 129.4 (2C), 131.7, 133.4, 143.2, 145.5, 156.8 ppm. IR (neat): $\tilde{\nu}$ 3004 w, 2880 w, 1550 m, 1474 m, 1440 m, 1341 m, 1327 m, 1403 s, 1225 s, 1073 m, 911 m, 833 m, 767 s, 685 s, 675 s, 646 m, 635 s, 507 m cm^{−1}.

4. Conclusions

The annelated heterocycles are derived from bifunctional aminothiones. These are the first crystal structures of azolo[b]1,3,4-thiadiazinium salts. We intend to continue research in this field.

Author Contributions

Gerhard Laus conceived and designed this study, carried out experimental work (synthesis, crystallization and characterization) and wrote the manuscript. Klaus Wurst determined the crystal structures. Herwig Schottenberger facilitated and supported this study.

Conflicts of Interest

The authors declare no conflict of interest.

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