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Synthesis of Unusually Substituted Ureas Starting from Bis(1,3,4-thiadiazolo)-1,3,5-triazinium Halides via Oxo-imidothioate Zwitterions

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Bis(1,3,4-thiadiazolo)-1,3,5-triazinium halides **1** can be converted into various products such as guanidines or bis(azolyl)alkanes. However, they also react with hydroxide ions in aqueous solution to form novel heterocyclic-substituted ureas **2a**–**i**. The yields were increased from moderate to good or excellent in the presence of excess guanidine **3**. The assumption that hydrogen-bonded intermediate encounter complexes **EC** are formed gives a reasonable explanation for the observed reaction path. The molecular structures of some of the crystalline products **2** were determined by X-ray analysis. Furthermore, with copper(II) a dinuclear complex **8** is formed with the two metal ions in a distorted octahedral environment; a water molecule acts as a bridging ligand between the Cu^{II} ions.

Introduction

In 1998 we reported the convenient synthesis of the novel fused tricyclic ring systems bis(1,3,4-thiadiazolo)-1,3,5-triazinium halides (**SNS**).[1,2] A subsequent period of extensive research finally led to novel [1,2,4]triazolo[1,3,4]thiadiazolo[1,3,5]triazinium (**NNS**) and bis(1,2,4-triazolo)-1,3,5-triazinium halides (**NNN**) (Figure 1).[3]

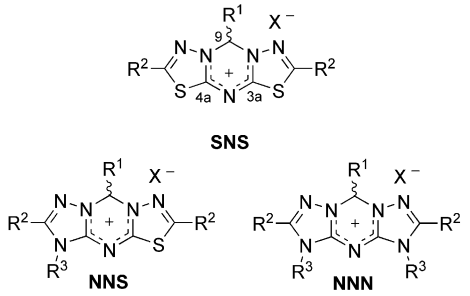

Figure 1. Structures of the 5/6/5 heterocycles **SNS**, **NNS** and **NNN** (X^- could be Cl^- or Br^-).

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By reaction with primary and secondary amines these so-called 5/6/5 cationic heterocyclic systems (**SNS**) can be converted into a wide variety of highly substituted guanidines (**G**) and bis(azolyl)alkanes (**A1** and **A2**) (Figure 2).[1,3–7]

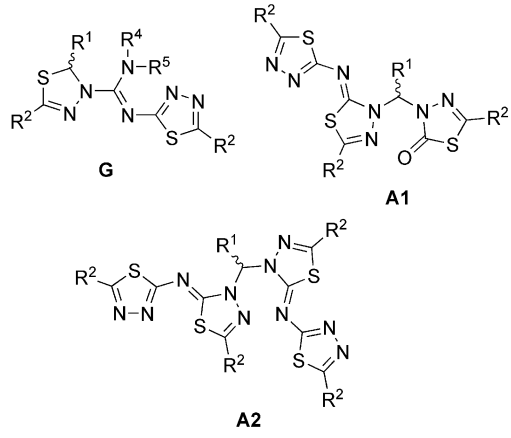


Figure 2. Heterocyclic compounds resulting from the reactions of **SNS** cations with primary and secondary amines.

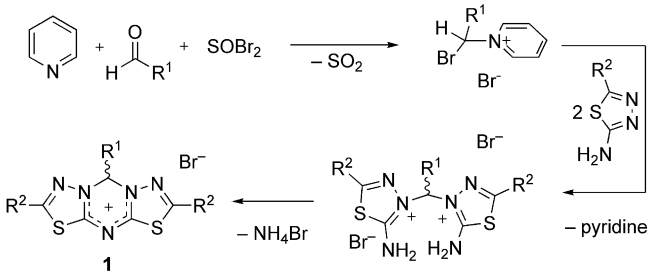
Detailed investigations of the nucleophilic reactions of primary and secondary amines with **SNS** compounds revealed that these conversions proceed on a complicated hypersurface and that the reaction paths can be reliably controlled by the reaction conditions. The pronounced electrophilicity of the C(3a) and C(4a) centers in **SNS** is responsible for the reactivity of these compounds {$q_{C(3a)} = q_{C(4a)} = +0.30e$ [NPA-B3LYP/6-311++G(d,p) results]}.[7] In the course of this fast multistep reaction cascade a highly reactive betainic triazinium imidothioate is formed, which is the key intermediate for the successive reaction.[3,7] The forma-

tion of this betainic intermediate is controlled by the influence of negative hyperconjugation [$n_{N(ex.)}/\sigma^*_{C(4a)–S(5)}$ interaction].[8]

However, not only amines could serve as nucleophiles but also water or the hydroxide ion. The previous investigations of Wermann et al.[3,7] with potassium hydroxide/potassium *tert*-butoxide prompted us to extend our investigations to the reaction between **SNS** and the hydroxide ion. This led to novel heterocyclic-substituted ureas **2**. The latter are suitable ligands for metal complexation.[9]

Results and Discussion

Bis(1,3,4-thiadiazolo)-1,3,5-triazinium halides **1a**–**i** (**SNS**) were prepared as described previously from *N*-(1-haloalkyl)pyridinium halides and aminothiadiazoles.[1,2] The *N*-(1-haloalkyl)pyridinium halides were obtained in one pot by the reaction of a 1:1:1 molar ratio of aldehyde/thionyl halide/pyridine (Scheme 1).[10–12]



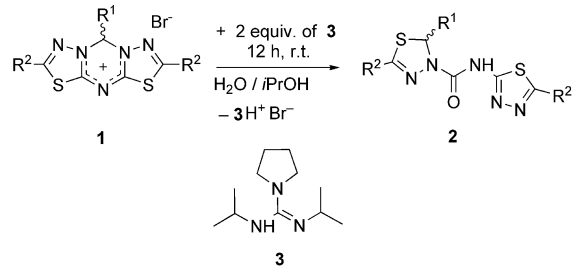
Scheme 1. Formation of **1** via bromomethylpyridinium bromide.

In our first experiments **1** was allowed to react with potassium hydroxide in water as well as with potassium hydroxide in methanol. The result was a mixture of non-isolable products as well as degradation products like tolualdehyde. Change of the reaction conditions by using triethylamine led to isolable products **2** in poor yields. Finally, by replacement of the amine base by guanidine **3** in water/2-propanol (1:1, v/v), compounds **2** were obtained in excellent yields of up to 89% (Table 1, Scheme 2). Interestingly, a double molar amount of guanidine was needed to obtain **2** in such yields. Although **1** and **3** are soluble in water, 2-propanol was necessary to dissolve the imidothioate intermediates and an excess of water was also necessary. Since the reaction can be understood as the addition of hydroxide ions to **1**, the consumption of hydroxide ions during the reaction can be observed by the decrease in the pH from 13 to 9. Experiments with equimolar amounts of water in 2-propanol or acetonitrile did not lead to the formation of **2**.

Structural assignments of **2** were made on the basis of NMR investigations, especially by HMQC, HMBC and DEPT135 experiments, as well as by mass spectrometry, IR spectroscopy, and X-ray experiments (**2a**, **2b**, **2g**, and **2h**). The purity of compounds **2** was confirmed by elemental analysis of the isolated and crystallized products. Figure 3 shows as an example the molecular structure of **2a**. For the X-ray structures of compounds **2b**, **2g**, and **2h**, see ref.[13] The bond lengths and angles of the examined molecules are

Table 1. Preparation of novel carboxamides **2a**–**i** from bis(1,3,4-thiadiazolo)-1,3,5-triazinium bromides **1a**–**i**.

1, **2**	R^1	R^2	Yield of **2** [%]
a	*p*-tolyl	methyl	74
b	*p*-tolyl	*tert*-butyl	55
c	1-naphthyl	methyl	41
d	1-naphthyl	*tert*-butyl	86
e	butyl	methyl	89
f	butyl	isopropyl	74
g	*o*-hydroxyphenyl	methyl	66
h	*o*-hydroxyphenyl	ethyl	72
i	*o*-hydroxyphenyl	*tert*-butyl	66



Scheme 2. Formation of novel carboxamides **2** from **SNS** cations **1**.

within the expected ranges.[14] All structures show a nearly planar N4–C1(O1)N3–C2–N2–N1–C3 moiety, which indicates a delocalized π system, a fact that is also indicated by the bond lengths. Furthermore, the space groups are centrosymmetric, and thus the compounds crystallize as racemates.

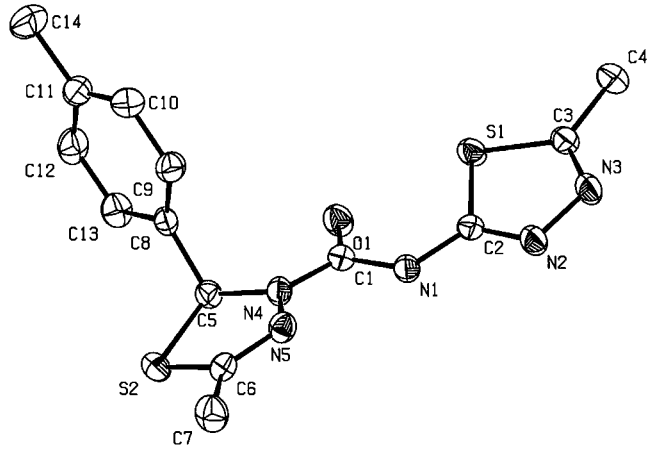


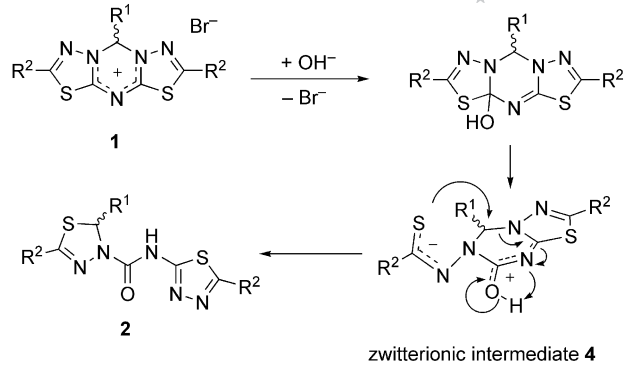
Figure 3. Molecular structure and numbering of **2a**. Thermal ellipsoids are drawn at the 40% probability level. Hydrogen atoms have been omitted for clarity. Selected bond lengths [pm] and angles [°]: N2–N3 139.5(3), N1–C2 138.0(3), C1–N1 137.9(3), C1–O1 122.6(3), C1–N4 135.9(3), N4–N5 147.5(3), C1–N1–C2 121.1(2); O1–C1–N4 121.4(2), O1–C1–N1 123.1(2), N4–C1–N1 115.5(2).

Some guanidines are known as strong bases, sometimes referred to as superbases. But they are also able to react as nucleophiles. The aforementioned reactions are promoted by guanidines in which they behave predominantly as bases

but not as nucleophiles. We carried out the reactions with the easy-to-make guanidine **3**, which was prepared according to ref.[15] by stirring isopropylcarbodiimide in pyrrolidine at reflux for 1 h followed by distillation.

In analogy to the results of the mechanistic investigations of Wermann et al.[3,7,16] and Lill et al.[8] with nitrogen nucleophiles, the hydroxide ion is the nucleophilic reagent in the described reaction. Owing to the highly basic properties of guanidine, the acid–base equilibrium is shifted to the side of the non-nucleophilic guanidinium hydrohalide. The subsequently formed hydroxide ions then attack the electrophilic centers C(3a) or C(4a), which is followed by ring-opening of the five-membered thiadiazole ring. The resulting imidothioate sulfur atom now attacks C(9) (cf. Figure 1), and the six-membered triazine ring opens to form **2** (Scheme 3).

In the course of the described ring transformation, which can be interpreted as an example of an $S_NANRORC$ mechanism (addition of the nucleophile, ring-opening, and ring closure),[17] the pro-stereogenic carbon atom C(9) (cf. Figure 1) becomes a stereocenter. The products **2** are obtained as racemates. Although ring-opening of the central triazine ring after the addition of the hydroxide at C(3a) or C(4a) is possible too (as described in ref.[3]), no such products were observed. This might be due to interactions with the guanidinium, the role of which during the reaction is not fully understood but its indispensability has been shown. We hypothesized the existence of hydrogen-bonding interactions between a guanidinium ion and the O(11)–C–N(4) moiety (formation of encounter complexes **EC**, Figure 4) stabilizing the central ring of this intermediate. Similar interactions are well known between guanidinium ions and carboxylates, amidinates, and other substrates.[18,19]



Scheme 3. Proposed mechanism for the formation of **2** by the $S_NANRORC$ mechanism.

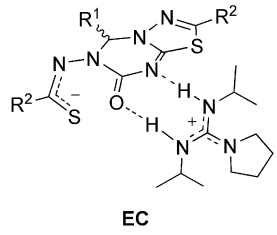


Figure 4. Proposed structure of the hydrogen-bonded stabilized encounter complex **EC** formed between the guanidinium cation and the betainic intermediate **4**.

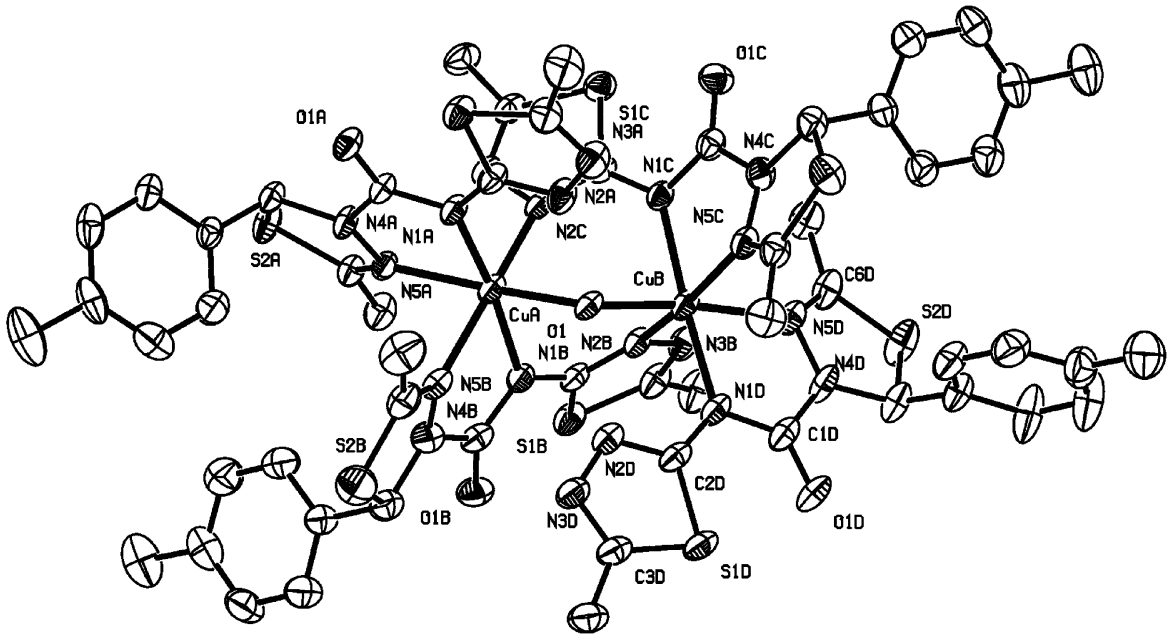
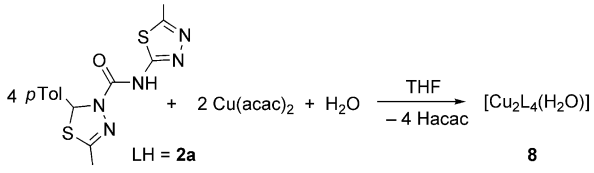


Figure 5. Molecular structure and numbering of **8**. Thermal ellipsoids are drawn at the 40% probability level. Hydrogen atoms and solvent molecules have been omitted for clarity. Selected bond lengths [pm] and angles [°]: CuA–O1 205.1(3), CuB–O1 206.3(3), CuA–N1A 207.7(4), CuB–N1D 208.0(4), CuA–N1B 205.4(4), CuB–N1C 205.5(4), CuA–N2C 212.6(4), CuB–N2B 212.3(4), CuA–N5A 212.2(4), CuA–N5B 217.7(5), CuB–N5C 217.1(4), CuB–N5D 213.7(5); CuA–O1–CuB 116.58(16).

The heterocyclic-substituted ureas obtained are suitable as ligands for metal complexation. Deprotonation of the ligand's amidic moiety can be achieved by the use of acetylacetonate compounds in anhydrous THF. Stirring of $Cu(acac)_2$ with **2a** in anhydrous THF for 24 h afforded the dinuclear complex **8**, in which the two copper centers are in a distorted octahedral environment (Scheme 4). Two ligands are arranged terminally, whereas two others act as bridging moieties between the metal ions. In addition, a bridging water molecule occupies the sixth coordination site (Figure 5). This water molecule stems from $Cu(acac)_2$, which was prepared in aqueous solution according to standard procedures. However, water-containing THF did not lead to the formation of the described copper complex. The Cu–N bond lengths and angles lie within the expected range, whereas the CuA–O1–CuB angle [116.18(16)°] is rather large. Large gaps between the complex molecules host solvent molecules, which are disordered, thus hampering the quality of the structure determination.



Scheme 4. Formation of Cu^{II} complex **8** from **2a** and $Cu(acac)_2$.

Conclusions

Bis(1,3,4-thiadiazolo)-1,3,5-triazinium halides (**SNS**) **1** are the starting compounds for a wide variety of ring transformation reactions mostly induced by reactions with aliphatic or aromatic amines. However, with hydroxide ions as the nucleophilic reactants novel heterocyclic-substituted carboxamides **2** were prepared. High yields were obtained when an excess of water and a double molar amount of guanidine **3** were used. This reaction can be explained by hydrogen-bonding interactions between the carboxamide or zwitterionic intermediate and the guanidinium cation, which in this case is the determining step that favors the formation of compounds **2**. In addition, the novel compounds **2** can be used as ligands for metal complexation, as shown by the reaction with copper(II).

Ring transformation reactions of **SNS** with amines are dependent to a significant extent on the nature of the amine (aromatic or aliphatic) and its ability to influence the reaction pathways by negative hyperconjugation. The contribution of oxygen lone-pairs to negative hyperconjugation is smaller, and thus other influences such as the hydrogen-bonding effects discussed above can become determining. In fact, the interesting reactions of these classes of compounds can be precisely controlled by small changes of the reaction conditions, thus making such reaction paths an ideal subject for high-level DFT investigations. These studies are underway.

Experimental Section

General Methods: All manipulations were performed under atmospheric conditions. Solvents other than water were purchased from commercial sources and were used as received. Anhydrous THF was prepared according to standard procedures with sodium/benzophenone. Melting points were measured with a Büchi B-549 instrument and are uncorrected. IR experiments were carried out with a Nicolet Impact 400 (ATR) spectrometer. NMR spectra were obtained with Bruker DRX 400 and Avance 250 spectrometers by using the solvent as the internal standard. ^1H and ^{13}C NMR spectra were recorded at 250/400 and 62.5/100 MHz, respectively. For ^1H and ^{13}C NMR, [D_6]DMSO (H: δ = 2.49 ppm; C: δ = 39.5 ppm) and $CDCl_3$ (H: δ = 7.24 ppm; C: δ = 77.0 ppm) were used as solvents. Mass spectrometric investigations were conducted with a Finnigan MAT SSQ 710 spectrometer, and elemental analyses (CHNS) were performed with a Leco CHNS-932 instrument. New compounds were named according to IUPAC Naming on I-Lab via ACD/ChemSketch (www.acdlabs.com).

General Procedure for the Preparation of Substituted *N*-(1,3,4-Thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamides 2a–i: Guanidine **3** (0.02 mol) was added to a solution of **1** (0.01 mol) in an equal volume of water and 2-propanol (total: 100 mL). The mixture was stirred at room temperature for 12 h before the white precipitate was collected. The remaining solution was acidified to pH = 6 by using half-concentrated hydrochloric acid, and again the precipitated compound was removed by filtration. The combined precipitates were dried in vacuo and crystallized from ethyl acetate or methanol to yield white to colorless crystals. The starting guanidine **3** was recovered from the acidic solution by adding KOH up to pH = 14 and extraction with chloroform.

5-Methyl-2-(4-methylphenyl)-*N*-(5-methyl-1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2a): Yield: 2.47 g (74%); m.p. 183 °C. ^1H NMR ($CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.63 (s, 3 H, CH_3), 6.88 (s, 1 H, CH sp^3), 7.14–7.49 (dd, 4 H, $CH_{arom.}$), 9.54 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.3, 16.4, 21.2, 70.0, 125.8, 129.7, 137.3, 150.6, 159.7, 159.8 ppm. IR (ATR): $\tilde{\nu}$ = 1531 (vs), 1673 (vs), 3121 (br., NH) cm^{-1}. MS (DCI): *m*/*z* (%) = 334 (100) $[C_{14}H_{15}N_5OS_2 + 1]^+$. $C_{14}H_{15}N_5OS_2$ (333.4): calcd. C 50.43, H 4.53, N 21.00, S 19.23; found C 50.54, H 4.79, N 20.77, S 18.73.

5-*tert*-Butyl-*N*-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl)-2-(4-methylphenyl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2b): Yield: 2.30 g (55%); m.p. 153 °C. ^1H NMR ($CDCl_3$): δ = 1.33 [s, 9 H, $(CH_3)_3$], 1.42 [s, 9 H, $(CH_3)_3$], 2.32 (s, 3 H, CH_3), 6.83 (s, 1 H, CH sp^3), 7.14–7.26 (dd, 4 H, CH_{arom}), 9.25 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2, 26.9, 30.8, 35.8, 36.3, 69.3, 125.8, 129.7, 137.6, 139.0, 149.9, 159.1, 164.3, 174.8 ppm. IR (ATR): $\tilde{\nu}$ = 1522 (vs), 1672 (vs), 3128 (br., NH) cm^{-1}. MS (DCI): *m*/*z* (%) = 418.1 (100) $[C_{20}H_{27}N_5OS_2 + 1]^+$. $C_{20}H_{27}N_5OS_2$ (417.6): calcd. C 57.53, H 6.52, N 16.77, S 15.36; found C 57.67, H 6.49, N 16.69, S 15.26.

5-Methyl-*N*-(5-methyl-1,3,4-thiadiazol-2-yl)-2-(1-naphthyl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2c): Yield: 1.51 g (41%); m.p. 232 °C. ^1H NMR ($CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 2.64 (s, 3 H, CH_3), 7.35–7.92 (m, 7 H, CH_{arom}), 7.65 (s, 1 H, CH sp^3), 9.67 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.3, 16.5, 67.5, 122.1, 122.3, 125.6, 126.1, 126.9, 128.7, 129.2, 129.6, 134.2, 134.8, 150.1, 152.4, 159.7, 160.2 ppm. IR (ATR): $\tilde{\nu}$ = 1523 (vs), 1669 (vs), 3159 (br., NH) cm^{-1}. MS (DCI): *m*/*z* (%) = 370 (100) $[C_{17}H_{15}N_5OS_2 + 1]^+$. $C_{17}H_{15}N_5OS_2$ (369.5): calcd. C 55.26, H 4.09, N 18.95, S 17.36; found C 55.02, H 4.36, N 18.90, S 16.98.

5-*tert*-Butyl-*N*-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl)-2-(1-naphthyl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2d): Yield: 3.90 g (86%); m.p.

230 °C. ^{1}H NMR ($CDCl_3$): δ = 1.23 [s, 9 H, $(CH_3)_3$], 2.43 [s, 9 H, $(CH_3)_3$], 7.32–7.92 (m, 7 H, $CH_{arom.}$), 7.62 (s, 1 H, CH sp^3), 9.41 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.2, 30.8, 35.9, 36.4, 66.9, 122.2, 122.4, 125.6, 126.0, 127.6, 128.7, 129.2, 129.5, 134.1, 135.2, 150.1, 159.2, 165.8, 175.0 ppm. IR (ATR): $\tilde{\nu}$ = 1524 (vs), 1673 (vs), 3147 (br., NH) cm^{-1}. MS (DCI): *m*/*z* (%) = 454 (100) $[C_{23}H_{27}N_5OS_2 + 1]^+$. $C_{23}H_{27}N_5OS_2$ (453.2): calcd. C 60.90, H 6.00, N 15.44, S 14.14; found C 60.98, H 5.88, N 15.68, S 14.42.

2-Butyl-5-methyl-*N*-(5-methyl-1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2e): Yield: 2.66 g (89%); m.p. 115 °C. ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, 3 H, CH_3), 1.29 (m, 4 H, CH_2), 1.81/1.97 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 2.65 (s, 3 H, CH_3), 5.96 (q, 1 H, CH), 9.41 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.9, 15.3, 16.6, 22.0, 26.6, 36.9, 69.4, 149.9, 151.7, 159.6, 159.8 ppm. IR (ATR): $\tilde{\nu}$ = 1525 (vs), 1663 (vs), 3150 (br., NH) cm^{-1}. MS (DCI): *m*/*z* (%) = 300 (100) $[C_{11}H_{17}N_5OS_2 + 1]^+$. $C_{11}H_{17}N_5OS_2$ (299.4): calcd. C 44.13, H 5.72, N 23.39, S 21.42; found C 44.11, H 5.75, N 23.41, S 21.30.

2-Butyl-5-isopropyl-*N*-(5-isopropyl-1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2f): Yield: 2.63 g (74%); m.p. 68 °C. ^{1}H NMR ($CDCl_3$): δ = 0.88 (t, 3 H, CH_3), 1.25 (d, 6 H, CH_3), 1.33 (m, 4 H, CH_2), 1.40 (d, 6 H, CH_3), 1.86/1.93 (m, 2 H, CH_2), 2.83 (m, 1 H, CH), 3.37 (m, 1 H, CH), 5.95 (q, 1 H, CH), 9.47 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 20.9, 21.0, 21.9, 23.1, 26.6, 29.7, 30.3, 36.8, 68.3, 125.5, 150.1, 162.2, 171.6 ppm. IR (ATR): $\tilde{\nu}$ = 1527 (vs), 1671 (vs), 3119 (br., NH) cm^{-1}. MS (EI): *m*/*z* (%) = 356 (100) $[C_{15}H_{25}N_5OS_2 + 1]^+$. $C_{15}H_{25}N_5OS_2$ (355.4): calcd. C 50.67, H 7.09, N 19.70, S 18.04; found C 50.51, H 6.78, N 20.16, S 18.55.

2-(2-Hydroxyphenyl)-5-methyl-*N*-(5-methyl-1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2g): Yield: 2.21 g (66%); m.p. 243 °C. ^{1}H NMR (DMSO): δ = 2.21 (s, 3 H, CH_3), 2.79 (s, 3 H, CH_3), 6.73-7.16 (m, 4 H, CH_{arom}), 7.02 (s, 1 H, CH sp^3), 10.01 (s, 1 H, OH), 11.31 (br., 1 H, NH) ppm. ^{13}C NMR (DMSO): δ = 14.8, 16.2, 65.0, 115.3, 119.2, 124.3, 126.9, 129.3, 150.6, 153.0, 158.5, 160.3 171.1 ppm. IR (ATR): $\tilde{\nu}$ = 1457 (vs), 1528 (vs), 1681 (vs), 3121 (br., NH), 3387 (s, OH) cm^{-1}. MS (DCI): *m*/*z* (%) = 336 (40) $[C_{13}H_{13}N_5O_2S_2 + 1]^+$. $C_{13}H_{13}N_5O_2S_2$ (335.4): calcd. C 46.55, H 3.91, N 20.88, S 19.12; found C 46.44, H 4.02, N 20.77, S 19.05.

5-Ethyl-*N*-(5-ethyl-1,3,4-thiadiazol-2-yl)-2-(2-hydroxyphenyl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2h): Yield: 2.62 g (72%); m.p. 209 °C. ^{1}H NMR (DMSO): δ = 1.15 (t, 3 H, CH_3), 1.23 (t, 3 H, CH_3), 2.53 (q, 2 H, CH_2), 2.91 (q, 2 H, CH_2), 6.74 (t)/6.80 (d)/6.87 (d)/7.15 (t, 4 H, CH_{arom}), 7.01 (s, 1 H, CH sp^3), 10.08 (s, 1 H, OH), 11.3 (br., 1 H, NH) ppm. ^{13}C NMR (DMSO): δ = 15.3, 16.4, 21.2, 22.1, 70.0, 116.7, 120.0, 124.4, 125.8, 129.7, 137.3, 150.6, 159.7, 159.8, 170.9 ppm. IR (ATR): $\tilde{\nu}$ = 1462 (vs), 1538 (vs), 1689 (vs), 3090 (br., NH), 3381 (s, OH) cm^{-1}. MS (DCI): *m*/*z* (%) = 364 (30) $[C_{15}H_{17}N_5O_2S_2 + 1]^+$. $C_{15}H_{17}N_5O_2S_2$ (363.5): calcd. C 49.57, H 4.71, N 19.27, S 17.64; found C 49.70, H 4.89, N 19.12, S 17.18.

5-*tert*-Butyl-*N*-(5-*tert*-butyl-1,3,4-thiadiazol-2-yl)-2-(2-hydroxyphenyl)-1,3,4-thiadiazol-3(2*H*)-carboxamide (2i): Yield: 2.77 g (66%); m.p. 254 °C. ^{1}H NMR (DMSO): δ = 1.22 [s, 9 H, $(CH_3)_3$], 1.34 [s, 9 H, $(CH_3)_3$], 6.74 (t)/6.78 (d)/6.83 (d)/7.14 (t, 4 H, CH_{arom}), 7.01 (s, 1 H, CH sp^3), 10.03 (s, 1 H, OH), 11.30 (br., 1 H, NH) ppm. ^{13}C NMR (DMSO): δ = 28.8, 30.4, 35.3, 35.7, 64.5, 115.4, 119.2, 124.3, 127.0, 129.2, 150.7, 153.0, 159.8, 162.9, 172.8 ppm. IR (ATR): $\tilde{\nu}$ = 1454 (vs), 1522 (vs), 1691 (vs), 3079 (br., NH), 3390 (OH) cm^{-1}. MS (DCI): *m*/*z* (%) = 420 (100) $[C_{19}H_{25}N_5O_2S_2 + 1]^+$. $C_{19}H_{25}N_5O_2S_2$ (419.6): calcd. C 54.39, H 6.01, N 16.69, S 15.28; found C 54.42, H 6.04, N 16.40, S 14.98.

$[Cu_2${5-methyl-2-(4-methylphenyl)-*N*-(5-methyl–1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazol-3(2*H*)-carboxamidato$}_4(H_2O)]$ (8): Copper(II) acetylacetonate (72 mg, 0.27 mmol) was dissolved in anhydrous THF (50 mL). Compound **2a** (183 mg, 0.54 mmol) was added as a solid to this blue solution, and the color changed instantaneously to green. Upon stirring for 24 h a white precipitate formed, which was then collected, washed with THF and dried in vacuo. Crystals suitable for X-ray analysis were obtained by slow solvent evaporation of a solution of **8** in chloroform/ethanol. Yield: 42 mg (21%); m.p. 260 °C. IR (ATR): $\tilde{\nu}$ = 708, 724 (s), 743, 755, 810, 873, 1122, 1179, 1186, 1337, 1368, 1399, 1459, 1599, 1622 (vs), 2905 (w), 2990 (w), 3052 (w) cm^{-1}. MS (micro-ESI in methanol/THF): *m*/*z* (%) = 1479 (2) $[C_{56}H_{56}Cu_2N_{20}O_4S_8 + 23]^+$, 1124 (2), 750 (34) $[C_{28}H_{28}CuN_{10}O_2S_4 + 23]^+$, 685(100). $C_{56}H_{58}Cu_2N_{20}O_5S_8$ (1474.8): calcd. C 45.61, H 3.96, N 18.99, S 17.39; found C 45.24, H 4.16, N 18.74, S 17.19.

X-ray Structure Determinations of 2a, 2b, 2g, 2h, and 8: The intensity data for compounds **2a**, **2b**, **2g**, **2h**, and **8** were collected with a Nonius-KappaCCD diffractometer by using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentzian and polarization effects but not for absorption effects.[20,21] The structures were solved by direct methods (SHELXS)[22] and refined by full-matrix least-squares techniques against F_o^2 (SHELXL-97).[23] For compounds **2a**, **2b**, and **2h** the amine hydrogen atoms, for compound **8** the hydrogen atoms of the water molecule, and for compound **2g** all hydrogen atoms were located by difference Fourier synthesis and refined isotropically. The other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.[23] XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations.

Supporting Information (see footnote on the first page of this article): Crystal data and refinement details.

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[13] CCDC-719782 (**2a**), -719783 (**2b**), -719784 (**2g**), -719785 (**2h**) and -719786 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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