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Article

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Switchable Synthesis of 4,5-Functionalized 1,2,3-Thiadiazoles and 1,2,3-Triazoles from 2-Cyanothioacetamides under Diazo Group Transfer Conditions

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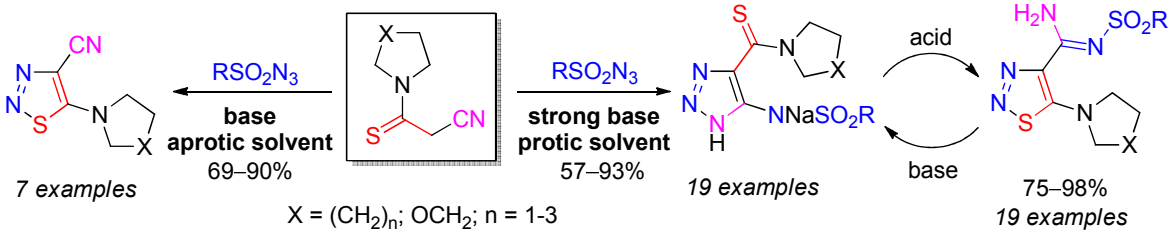
Graphical abstract



Abstract

High yield solvent-base-controlled, transition metal-free synthesis of 4,5-functionalized 1,2,3-thiadiazoles and 1,2,3-triazoles from 2-cyanothioacetamides and sulfonyl azides is described.

Under diazo transfer conditions in the presence of a base in an aprotic solvent 2-cyanothioacetamides operating as C–C–S building blocks produce 5-amino-4-cyano-1,2,3-thiadiazoles exclusively. The use of alkoxide/alcohol system completely switches the reaction course due to the change of one of the reaction centers in the 2-cyanothioacetamide (C–C–N building block) resulting in the formation of 5-sulfonamido-1,2,3-triazole-4-carbothioamide sodium salts as the only products. The latter serve as good precursors for 5-amino-1,2,3-thiadiazole-4-carboximidamides, the products of Cornforth-type rearrangement occurring in neutral protic medium or under acid conditions. According to DFT calculations (B3LYP/6-311+G(d,p)) the rearrangement proceeds via intermediate formation of a diazo compound, and can be catalyzed by acids via the protonation of oxygen atom of the sulfonamide group.

Introduction

1,2,3-Triazoles and 1,2,3-thiadiazoles have been receiving permanent interest due to their exciting chemical reactivity including ring rearrangements[1] and transformations[1a-d,2] to other heterocyclic compounds and valuable organic building blocks. 1,2,3-Thiadizole derivatives exhibit antibacterial, antiviral, anticancer, fungicidal, herbicidal growth regulating (plants) and defoliating (cotton) activity.[3] After the CuAAC (copper-catalyzed cycloaddition of azides to acetylenes) had been discovered[4] huge variety of different series of 1,2,3-triazole derivatives became easily available. 1,2,3-Triazoles have shown many important biological properties, such as antibacterial, including bioactivity against the *Mycobacterium tuberculosis*, antiviral (HIV), antifungal, high activity against leukemia L1210, anticancer and many other types of bioactivity.[5] There are four compounds bearing 1*H*-1,2,3-triazole core in clinical studies which may appear in the market of drugs in nearest future (Figure 1).[5] 1,2,3-Triazoles can act as bioconjugates,[6] chemosensors,[7] ligands,[8] or anion receptors.[9] In turn, 1,2,3-triazoles may be used in materials chemistry, medicine and in analytical chemistry. Although sulfonamide group is known as a good pharmacophore group many compounds bearing this moiety are found to

exhibit interesting biological activities[5] only a few 5-sulfonylamido-1,2,3-triazoles are published.[10]

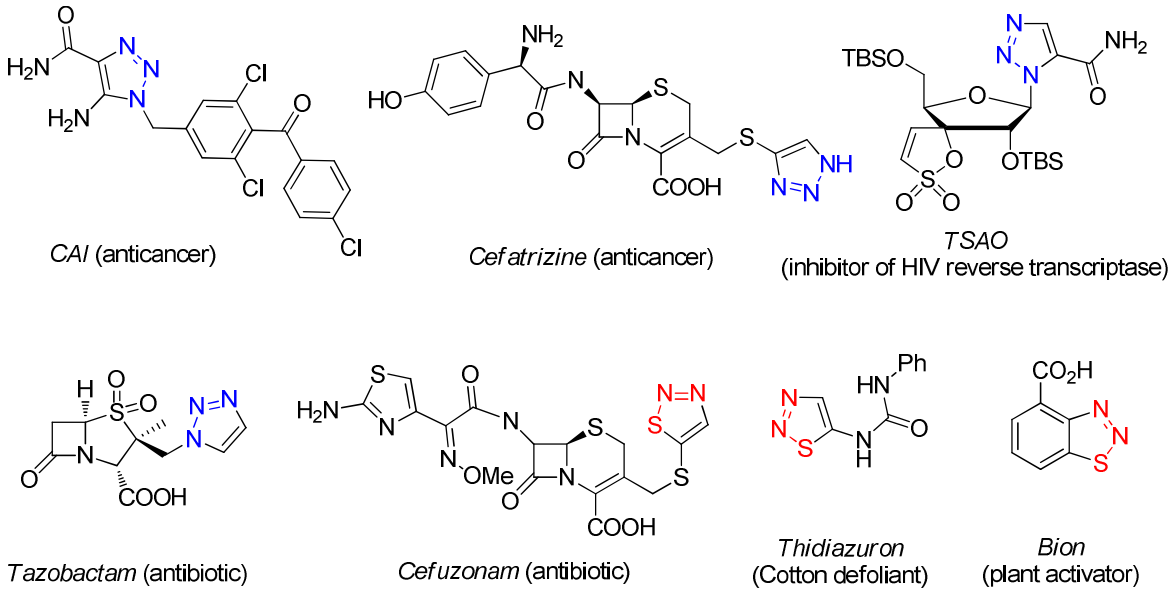
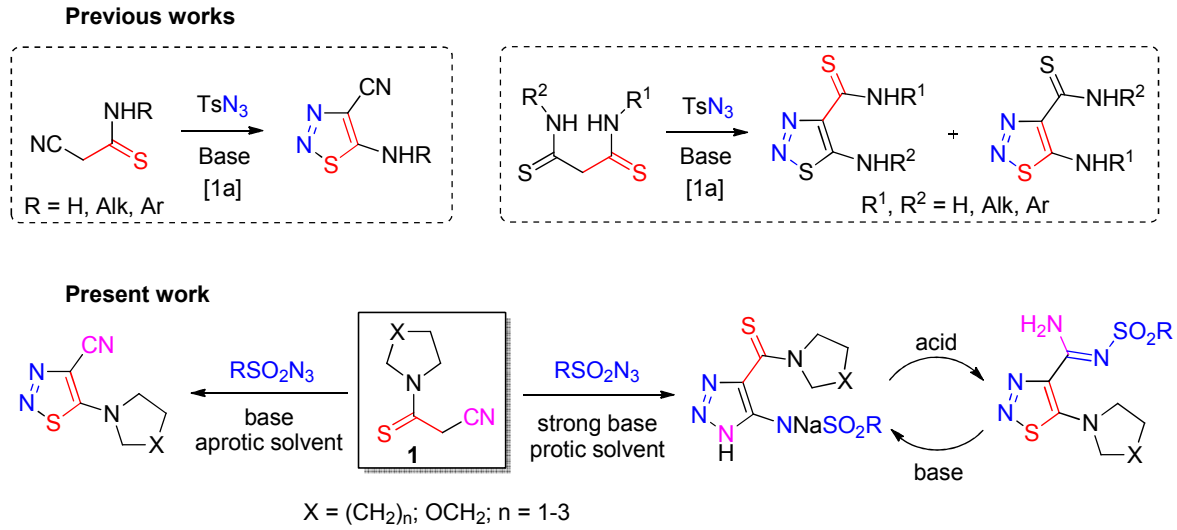


Figure 1. Medicine and agricultural preparations among 1,2,3-triazoles and 1,2,3-thiadiazoles.

There are several powerful methods for the synthesis of 1,2,3-triazoles published in the literature: thermal and metal catalyzed addition of azides to acetylenes; 1,3-dipolar cycloaddition of azides to alkynes;[1b,4] reactions of azides with methylene active carbonyl compounds;[11] reactions of NH-1,2,3-triazoles with electrophiles; intramolecular cyclizations of α-diazoimines[11] and dipolar cycloaddition reactions of diazo compounds and nitriles.[11b] CuAAC reaction is the most effective among them and widely used to the synthesis of various types of 1,2,3-triazole derivatives.[4] Despite of good yields this method is not applicable for the synthesis of 5-amino-1,2,3-triazole derivatives due to the poor availability of the starting compounds. Therefore the search of new routes to functionalized 1,2,3-triazoles remains a synthetic challenge. Since few 5-amino-1,2,3-triazole-4-carbothioamides were prepared in reactions of aryl azides with 2-cyanothioacetamides[12] we turned our attention to reaction of sulfonyl azides with cyanothioacetamides to find an approach to 1,2,3-triazoles bearing both thioamide and sulfonamide groups. At the same time, the reactions of primary and secondary methylene active

thioamides with sulfonyl azides led to 5-amino-1,2,3-thiadiazoles (Scheme 1). Actually, the generally accepted opinion on the single "thiadiazole direction" of the reactions of methylene active thioamides with sulfonyl azides has been helding for long time.[1a] The combined experimental and theoretical studies of reaction of tertiary cyanothioacetamides **1** with sulfonyl azides **2** and comparison of their reactivity with that of primary and secondary 2-cyanothioacetamides used in the present study demonstrated three directions of this reaction leading to 5-amino-4-cyano-1,2,3-thiadiazoles **3**, 5-sulfonamido-1,2,3-triazole-4-carbothioamides **4** and 5-cycloamino-1,2,3-thiadiazole-4-carbimidamides **5** (Scheme 1). Depending on nature of starting reagents, nature of a solvent and type and amount of a base used a direction of the reaction can be switched of in favor of each compound as an exclusive product. The proper conditions were found and methods were elaborated for the selective and efficient synthesis of 4-cyano-5-cycloamino-1,2,3-thiadiazoles **3**, 5-sulfonamido-1,2,3-triazole-4-carbothioamides **4** and 5-cycloamino-1,2,3-thiadiazole-4-carbamidines **5**.

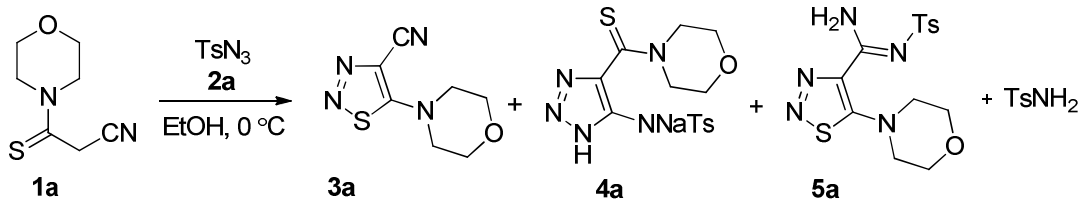


Scheme 1. Reactions of thioamides with sulfonyl azides.

Results and discussions

In order to involve sulfonyl azides as a N=N−N building blocks in the formation of 1,2,3-triazoles from 2-cyanothioacetamides, we decided to screen the reaction conditions using 3-

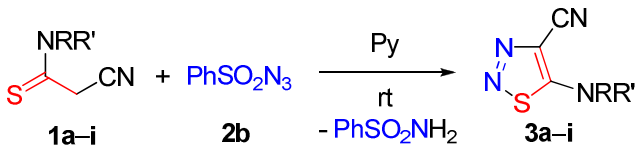
(morpholin-1-yl)-3-thioxopropanenitrile (**1a**) and tosyl azide (**2a**) as a model precursors. Using ethanol as a solvent we tested various bases including sodium ethoxide, pyridine, triethylamine and DBU (1,8-diazabicycloundec-7-ene) at 0 °C. To our delight the reaction with EtONa provided triazole **4a** in significant amounts along with thiadiazoles **3a**,**5a** and tosylamide (the ratio **3a**,**4a**,**5a,**$TsNH_2$ = 11:73:3:11) (Scheme 2).

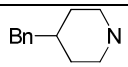


Scheme 2. Reaction of thioamide **1a** with azide **2a**.

Surprisingly, substitution of EtONa by any nitrogen base leads to the increase of selectivity of the process and the formation of thiadiazole **3a** as the only reaction product. Prior to continue the search for optimal conditions for synthesis of triazoles **4** the generality of the effect of a base nature to direct the reaction for various 2-cyanothioacetamides was estimated. Thus, the reaction of 2-cyanothioacetamides **1a**–**i** with azide **2b** (Table 1) was thoroughly studied. Exclusive formation of thiadiazole **3e** either in pyridine or ethanol in the presence of triethylamine or DBU or under action of EtONa in 1,4-dioxane was found for reaction of thioamide **1e** with benzene sulfonyl azide (**2b**). Pyridine as a base and a solvent, and room temperature (Table 1) proved to be optimal for this reaction. In this case the reaction is completed in 1–2 h. With these conditions in hand we have prepared a series of 4-cyano-5-dialkylamino-1,2,3-thiadiazoles **3a**–**i**, including novel 5-cycloamino-1,2,3-thiadiazoles **3a**–**e**, in 69–90% yields. The structures of compounds **3a**–**e** are consistent with NMR and mass spectra and confirmed by X-ray analysis data for single-crystal of compound **3a** (Figure S1 of Supporting Information).

Table 1. Synthesis of thiadiazoles 3a–i



entry	thioamide **1**	NRR′	thiadiazole **3**	time of reaction, min.[a]	yield, %
1	**1a**		**3a**	5	85
2	**1b**		**3b**	80	86
3	**1c**		**3c**	10	90
4	**1d**		**3d**	20	80
5	**1e**		**3e**	60[b]	69
6	**1f**	Me_2N	**3f**	ND[c]	74
7	**1g**	Ph_2N	**3g**	ND[c]	78
8	**1h**	H_2N	**3h**[13]	20	77
9	**1i**	4-MeC_6H_4NH	**3i**[11]	120	81

[a]Reaction times were measured for reaction of azides **2a–e** (1.0 mmol) with appropriate thioamide **1** (2.5 mmol) in 1 mL of pyridine by IR spectroscopy. The end of reaction was determined based on the disappearance of azide group stretching at 2115–2134 cm^{-1} in IR spectra of a reaction mass after fast evaporation of pyridine; [b]reaction time for the reaction of thioamide **1e** with azide **2a** (TsN_3) is 125 min, azide **2b** ($PhSO_2N_3$) - 60 min, azide **2c** (4-$MeOC_6H_4SO_2N_3$) - 135 min, azide **2d** (4-$FC_6H_4SO_2N_3$) - 30 min, with azide **2e** (MsN_3) - 5 min; [c]ND = not determined

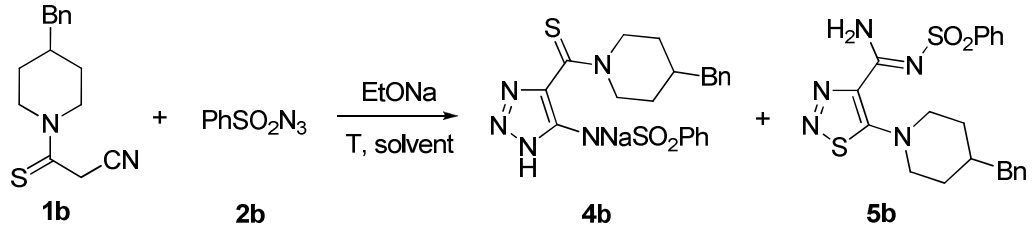
The reactions time of thioamide **1e** with arylsulfonyl azides **2a–e** increases in the following order: MsN_3 (**2e**) >> 4-$FC_6H_4SO_2N_3$ (**2d**) > $PhSO_2N_3$ (**2b**) > TsN_3 (**2a**) > 4-$MeOC_6H_4SO_2N_3$ (**2c**) that coincides with their activity as diazo transfer agents.

The tolerance of the reaction to primary, secondary, and tertiary thioacetamides **1** coupled with the availability of these compounds provides a reason to consider the suggested protocol as a versatile and convenient route to 5-amino-4-cyano-1,2,3-thiadiazoles **3**.

As it was mentioned above the use of EtONa/EtOH system instead of pyridine results in the realization of competitive reactions leading triazoles **4** and thiadiazoles **5** with the exception of thioamide **1d** which furnishes thiadiazole **3d** under all used conditions.

Our further efforts were focused on the optimal conditions for the preparation of 1,2,3-triazoles **4** using cyanothioacetamide **1b** and azide **2b** as precursors. In order to increase the ratio of **4**:**5** we varied alcohol, temperature, type and amount of a base (Table 2).

Table 2. Optimizations of the Reaction Conditions for Reaction of 1b with 2b[a]



entry	base (equiv)	solvent	T (°C)	total yield **4b**+**5b** (%)	ratio **4b**:**5b**
1	MeONa (1.0)	MeOH	−10	58	**23**:77
2	MeONa (1.0)	MeOH	+10	56	**16**:84
3	EtONa (1.0)	EtOH	−10	61	**51**:49
4	EtONa (1.0)	EtOH	+10	69	40:60
5	EtONa (1.0)	EtOH	+20	60	40:60
6	EtONa (1.0)	EtOH	+30	50	40:60
7	EtONa (2.0)	EtOH	+10	85	**92**:8

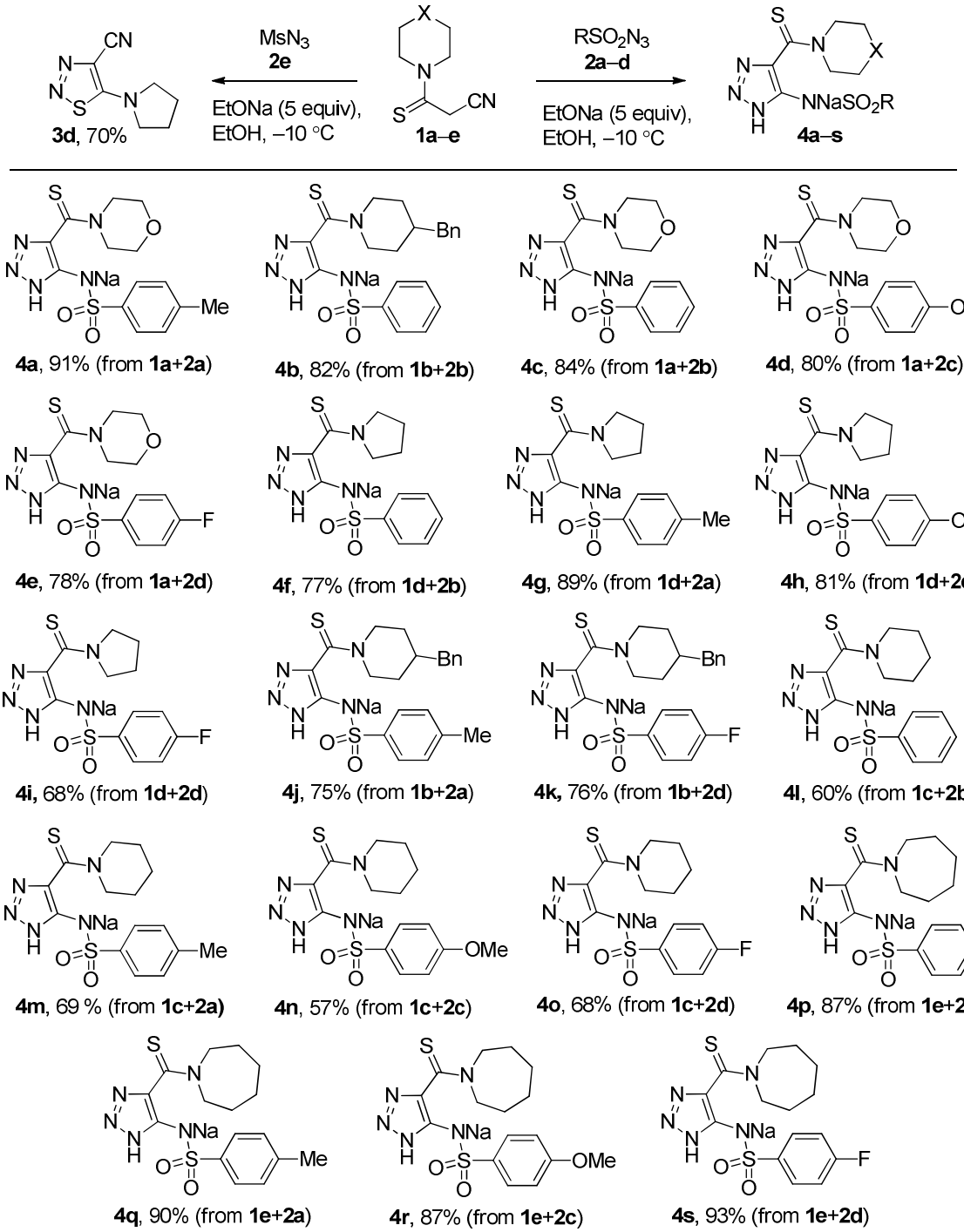
8	EtONa (5.0)	EtOH	+10	78	**100**:0
9	EtONa (5.0)	EtOH	−10	83	**100**:0
10	EtONa (5.0)	EtOH	+20	73	**100**:0
11	PrONa (1.0)	PrOH	+10	82	**95**:5

[a]Reaction conditions: **1b** (1.0 mmol, 1.0 equiv), **2b** (1.0 mmol, 1.0 equiv), base (1.0−5.0 equiv), solvent (4 mL), −10+30°C, 1 h

Though the use of less polar alcohols and lower temperature enhances the formation of triazole **4b**, more crucial is the increase of amount of sodium ethoxide. Table 2 demonstrates the exclusive formation of triazole **4b** when 5.0 equiv of sodium ethoxide are used. Thus, the optimal conditions for the synthesis of triazoles include the use of thioamide **1b** and azide **2b** in ratio 1:1, ethanol as a solvent and 5.0 equiv of sodium ethoxide at –10 °C. The desired product **4b** was obtained in 83% yield (Table 2, Entry 9). As follows from Table 2, the **4b**/**5b** ratio depends little on temperature, but it increases significantly when changing the alcohol solvent. It can be explained by a much larger decrease in solubility of triazole **4b** than thiadiazole **5b** in less polar solvents, which leads to a shift in the equilibrium in favor of the triazole).

Inspired by this result we used the optimized reaction conditions for reactions of azides **2a–d** with the *tert*-thioacetamides. Thus, we have demonstrated a method for the synthesis of novel 5-sulfonylamino-1,2,3-triazole-4-carbothioamides **4** and have prepared a series of 19 compounds bearing various *tert*-thioamide and sulfonylamino groups in good to excellent yields (57–93%) (Table 3). The reaction tolerates various tertiary amine moieties in thioamide function and substitutes in sulfonyl azides. However, in contrast to other reactions mesyl azide (**2e**) reacts with thioacetamide **1d** to give 5-(pyrrolidin-1-yl)-1,2,3-thiadiazole-4-carbonitrile (**3d**) in 70% yield (Table 3). Furthermore, the reaction of primary and secondary cyanothioacetamides **1h,i** under these conditions also affords 5-amino-4-cyanothiadiazoles **3h,i** (Table 1).

Table 3. Synthesis of triazoles 4a–s[a]



[a]Isolated yield. Reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), EtONa (5.0 mmol), EtOH (4 mL), –10°C, 1h.

To gain deeper insight into the effect of the amount of base and the nature of thioamides on the course of the process the products ratios in the reactions of tosyl azide (**2a**) with thioamides **1a** and **1d** in the presence of sodium ethoxide at 2, 5, 10, 30 and 45 min have been examined

(Figures 2,3). The formation of all three products **3**–**5** under these conditions is observed. In the reaction of thioamide **1d** with tosyl azide (**2a**) in the presence of 1.0 equiv of sodium ethoxide at 0 °C the constant **3d**/**4g**+**5g** ratio as 5:1 was registered after 5 min (Figure 2). The use of 2 equiv of sodium ethoxide at 0 °C dramatically changes the ratio of these products in favor of adducts **4g**/**5g** (ratio **3**:**4**:**5** achieved 4:65:20) (Figure S3 of Supporting Information). The NMR monitoring of the reaction of thioamide **1a** with azide **2a** (1.0 equiv of EtONa, –10 °C) revealed the sharp increase of thiadiazole **5a** concentration at very early stage of the process. Further the reduction of a share of thiadiazole **5a** with the simultaneous growth of a share of triazole **4a** was observed, proving that triazole **4a** originates from thiadiazole **5a**.

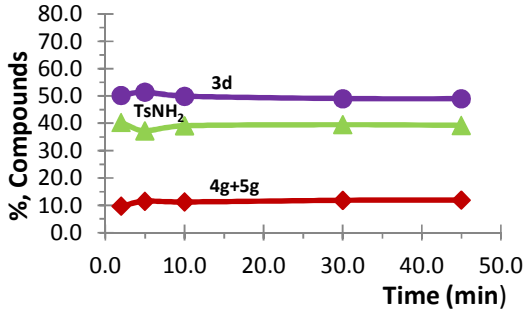


Figure 2. Content of the products **3d**,**4g**+**5g** in the course of the reaction of thioamide **1d** with tosyl azide (**2a**) according to ^{1}H NMR spectra. Reaction conditions: **1d** (1.0 equiv, 2.0 mmol, 308 mg), **2a** (1.0 equiv, 2.0 mmol, 394 mg), EtONa (1.0 equiv, 2.0 mmol), EtOH (5 mL), 0 °C. Aliquots of reaction mixture (1 mL) were taken off in 2, 5, 10, 30 and 45 min and precipitates were filtered off.

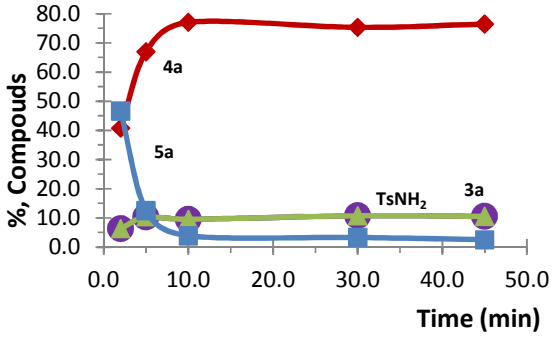
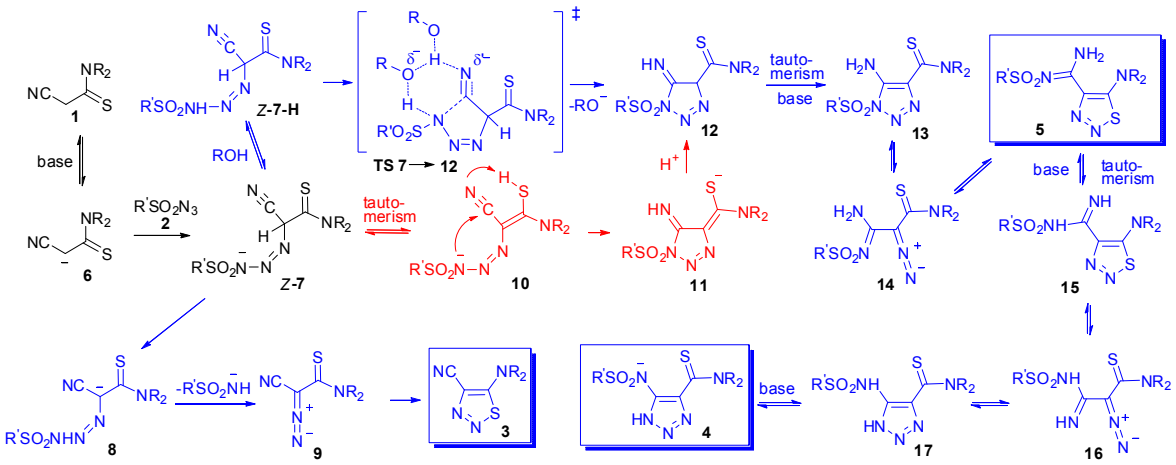


Figure 3. Content of the products **3a,4a,5a** in the course of the reaction of thioamide **1a** with tosyl azide (**2a**) according to ^{1}H NMR spectra. Reaction conditions: **1a** (1.0 equiv, 2.0 mmol, 340 mg), **2a** (1.0 equiv, 2.0 mmol, 394 mg), EtONa (1.0 equiv, 2.0 mmol), EtOH (5 mL), 0 °C. Aliquots of reaction mixture (1 mL) were taken off in 2, 5, 10, 30 and 45 min and precipitates were filtered off.

Thus, the direction of the reactions of thioamides **1** with azides **2** either to 4-cyanothiazoles **3** or to triazoles **4** depends whether weak or strong bases and protonic or aprotonic solvents are used. The factors govern the directions of the reaction of thioamides **1** with azides **2** in favor of thiadiazoles **3** or salts **4** are nature of starting reagent, type of a solvent and amount and strength of a base (Scheme 2, Table 2). The use of either aprotonic solvents in the presence of any base or protic solvents in the presence of a weak base leads to thiadiazoles **3** as exclusive products. Conversely, the use of an excess of a strong base in a protic solvent favors the formation of 1,2,3-triazol-4-carbothioamides **4**.

The reaction of triazoles **4** formation proceeding with retention of all atoms of starting compounds can be referred to the family of atom economic process[14] and can be used for elaboration of a new green chemistry process.[15]

A possible mechanism for the formation of compounds **3–5** is depicted in Scheme 3. We assumed that triazenyl anion *Z*-**7** generated by the addition of carbanion **6** to sulfonyl azide **2** is a common intermediate on the pathways to all products. 1,4-Prototropic shift in anion *Z*-**7** leading to carbanion **8** and cyclization across the cyano group to triazolidine **12**, are those competitive transformations that provides finally thiadiazole **3** and triazole **4**, respectively. According to the calculations performed for model triazenyl anion *Z*-**7a** (Scheme 3, Fig. 4, NR_2 = pyrrolidin-1-yl, R′ = Me) at DFT B3LYP/6-311+G(d,p)[16] level with PCM solvation model for methanol *Z*-**7a** is by 1.7 kcal/mol more stable than its *E* isomer and can undergo intramolecular 1,4-prototropic shift (**TS1**) into anion **8a** (Fig. 4) even at room temperature ($\Delta G^{\neq}$ 21.3 kcal/mol).



Scheme 3. Plausible mechanism for the reaction of thioamides **1** with azides **2**.

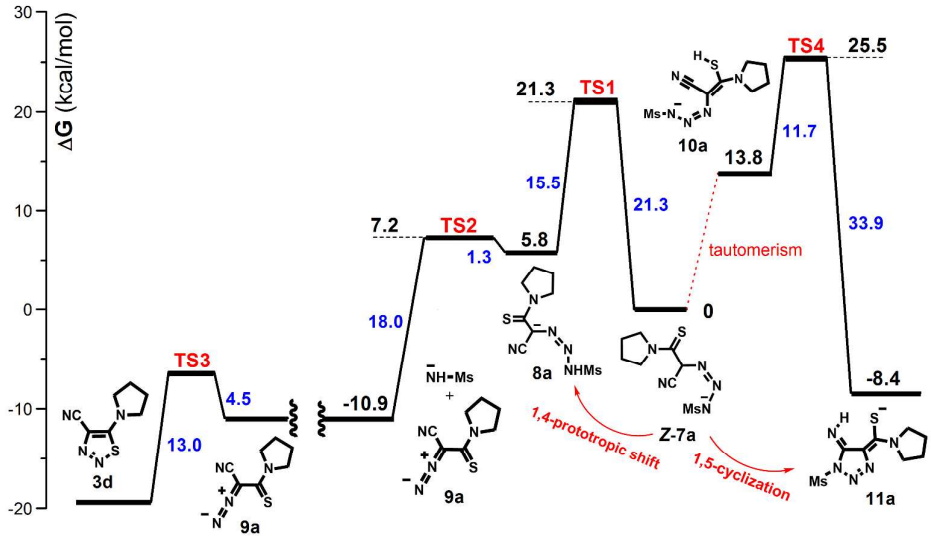


Figure 4. Relative free Gibbs energies (in kcal/mol, 298K, PCM model for the MeOH) of compounds **3d**,*Z*-**7a**–**11a** and the transition states **TS1**–**TS4** computed at the B3LYP/6-311+g(d,p) level.

The latter proved to be very unstable due to the fast elimination of sulfonylamide anion (**TS2**, $\Delta G^{\neq}$ 1.3 kcal/mol) to give diazo thioamide **9a** followed by low-barrier cyclization (**TS3**, $\Delta G^{\neq}$ 4.5 kcal/mol) into thiadiazole **3** via heteroelectrocyclic (pseudopericyclic)[17] mechanism. We have also supposed that triazole **4** and thiadiazole **5** originate from triazole intermediate **13**, the tautomer of triazoline **12** (Scheme 3). The latter is the cyclization product of triazenyl-anion *Z*-**7** across the cyano group. Intramolecular triazoline ring formation cannot occur directly in anion *Z*-

7 because there is no local minimum on the reaction **P**otential **E**nergy **S**urface (PES) corresponding to 1,5-*exo*-*dig*-cyclization product (not shown in Scheme 3). An alternative pathway to triazole **12** involves prior intermolecular tautomerization of anion *Z*-**7** to anion **10** followed by one-step cyclization/proton-transfer to give thiolate **11** precursor of triazole **12**. However this transformation is unlikely to occur as the barrier for cyclization of model system **11a** (**TS4**, Fig. 4) is much higher than for competitive proton transfer *Z*-**7a**→**8a** (**TS1**). Evidently the protonation of *Z*-7 with protic solvent to give triazene *Z*-**7-H** is the sole reaction which is capable of competing with intramolecular 1,4-proton transfer leading to thiadiazole **3**. Deprotonation of triazene *Z*-**7-H** with a weak base, such as triethylamine, triggered the reverse reaction sequence leading to thiadiazole **3**, while in alkoxide/alcohol system 1,5-*exo*-*dig*-cyclization onto C≡N bond via 6-memebered transition state **TS7→12** with the formation triazoline **12** as the first cyclic intermediate on the route to triazoles **4** occurs. In this case the formation of the five-membered ring of compound **12** is a concerted process which is facilitated by concurrent protonation of the nitrile nitrogen by an alcohol molecule. We propose that triazole **12** easily transforms in basic solution to aromatic triazole **13,** and this is in agreement with the isolation of stable 5-amino-1-aryl-1,2,3-triazole-4-carbothioamides in reaction of thioamides **1a,b** with aryl azides.[12] Then triazole **13**, bearing strong withdrawing sulfonyl group destabilizing the ring,[1b] rearranges to thiadiazole **5** via transient formation of diazo compound **14**. This is in good agreement with the experimentally observed high values of **5/4** ratio at an early stage of the reaction and decrease in share of thiadiazoles **5** by the end of the reaction.

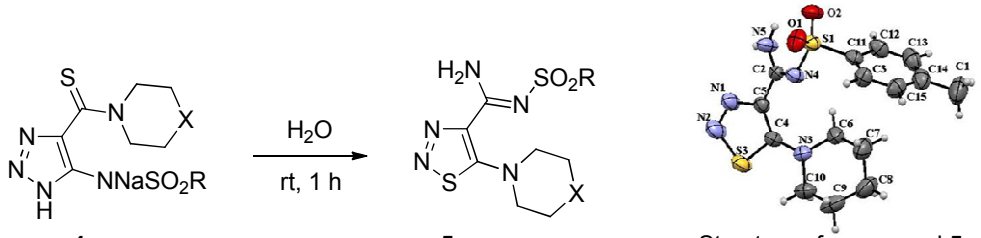
The further transformation of thiadiazole **5** to salt **4** involves base-catalyzed tautomerization to thiadiazole **15**, ring opening to diazo compound **16**, cyclization to triazole **17** followed by the sodium salt formation.

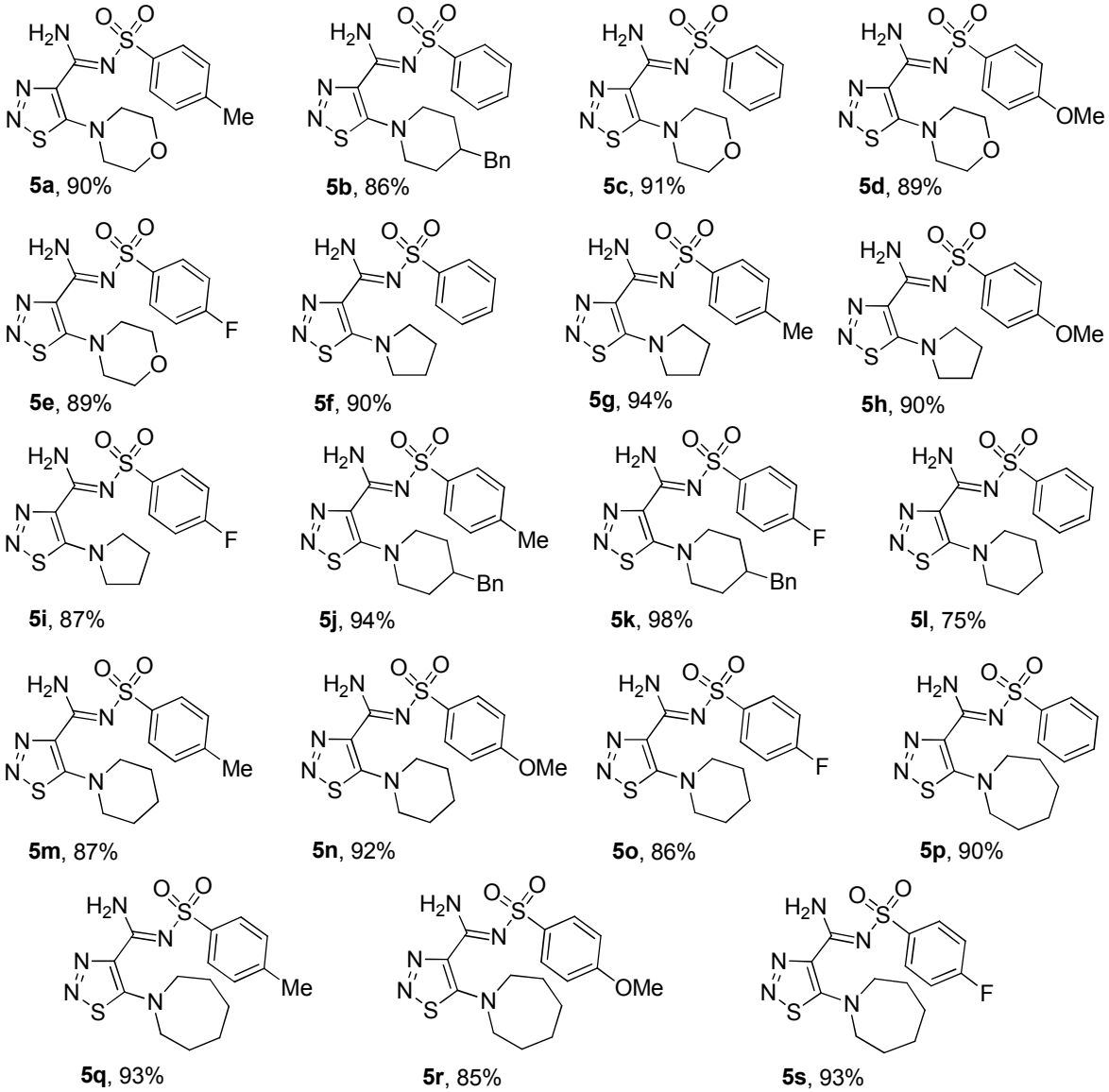
The calculation results well explain the change in the reaction pathway when EtONa/EtOH system is replaced with pyridine. In the absence of the alcohol molecules, e.g. in 1,5-cyclization of triazenyl-anion *Z*-**7**, 1,4-H-shift leading to diazo transfer product **3** becomes the fastest process

which, importantly, occurs irreversibly. The replacement of alkoxide/alcohol system with a solution of weak nitrogen base in alcohol leads to the decrease of concentration of alkoxide, which promotes cyclization of *Z*-**7-H** to **12**. As the result, 1,4-prototropic shift in anion *Z*-**7** that is rate limited step of transformation of *Z*-**7a** to thiadiazole **3** should become more preferable than 1,5-cyclization. This should inhance the formation of the latter that was observed experimentally.

5-Sulfonylamino-1,2,3-triazoles **4a–s** are stable as solids under storage during many days. However they are not very stable in the presence of water and in solutions of various solvents containing water traces. They were characterized as sodium salts hydrates. These compounds were found to undergo rearrangement to isomeric thiadiazoles **5** when treated with water. Reactions in water are completed within 1 h, in the presence of silica gel for 30 min and in the presence of hydrochloric acid it takes less than 10 min. The rearrangement occurs even in solid state (50% conversion of **4p** in 1 month storage in a closed flask). The scope of the reaction is shown in Table 4. All 5-sulfonamido-1,2,3-triazole-4-thiocarboxamides **4** undergo the rearrangement to form thiadiazoles **5** in good to excellent yields. This reaction represents a new practically useful, economic method for the synthesis of 5-amino-1,2,3-thiadiazole-4-*N*-sulfonylcarbamidines **5** presented in the literature by only two compounds prepared by other method.[12]

Table 4. Synthesis of Thiadiazoles 5a–s[a]



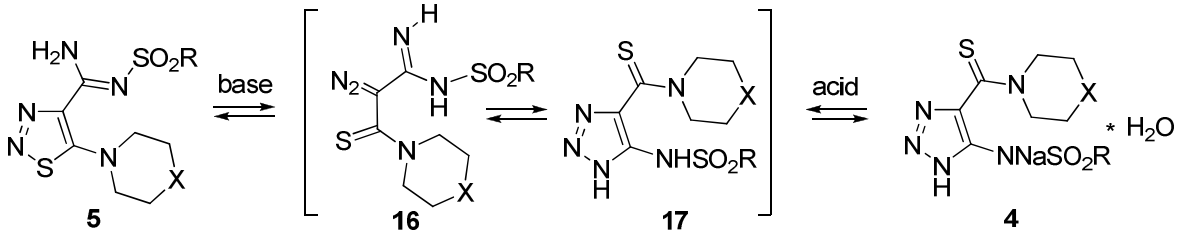


[a]Isolated yield. Reaction conditions: **4** (1.0 mmol), H_2O (4 mL), rt, 1 h.

The structures of compounds **4** and **5** are consistent with NMR and mass-spectra, including HRMS and confirmed by X-ray data for single-crystal of compound **5m**. Signals of carbon atoms of thiocarbonyl group are displayed at 194.7–194.9, atom C^5 of 1,2,3-triazole ring at 146.0–147.6 and atom C^4 at 137.1–138.5 ppm. Signal of ^1H in NMR spectra at 12.96–13.11 is

characteristic of compounds **4** as 1-NH-1,2,3-triazole tautomeric form.[18] Signals of the ring and 4-substituents in ^{1}H NMR spectra of compound **5** are slightly differed from those for triazole **4** allowing to estimate their ratio in reaction mixture. ^{13}C NMR spectra of thiadiazoles **5** exhibit signals of carbons: of amidino group at 156.5–157.4, of C^4 at 134.1–136.3 and C^5 at 164.7–170.2 ppm.

All amidines **5a-s** rearrange back to 5-sulfonylamino-1,2,3-thiadiazole-4-carbothioamides **4a-s** at ambient temperature in protic solvents in the presence of 5 equiv of sodium ethoxide, triethylamine or DBU in good yields. This novel rearrangement represents a base-acid catalyzed process between acidic (5-sulfonylamino-1,2,3-triazoles **4**) and basic (1,2,3-thiadiazole-4-carbamidines **5**) isomeric forms. Compounds **4** are stable as sodium salts, while compounds **5** being stable in neutral and acidic mediums undergo conversion to triazoles **4** in the presence of a sodium ethoxide. The NH-forms of triazoles **4** are not stable. Nevertheless ^{1}H NMR spectrum of NH-form of triazole **17** (X = CH_2, R = Tos) was successfully recorded in solution of CD_3OD (Scheme 4).



Scheme 4. Reversible transformation of 1,2,3-thiadiazole **5** and 1,2,3-triazole **4**.

The effect of a type and amount of a base on the process of rearrangement was studied by ^{1}H NMR spectrometry for transformation of thiadiazole **5m** to triazole **17/4m** in methanol in the presence of triethylamine and sodium ethoxide (Table 5).

It was shown that the conversion of **5m** achieved 10% in 24 hr after treatment with 5.0 equiv triethylamine to form mixture of **5m** and **17** (R = *p*-Tolyl, X = CH_2). The use of stronger base (0.1 equiv of sodium ethoxide) increased the conversion to 97%, respectively. The complete conversion **5m** to **4m** was observed when 5.0 equiv of CD_3ONa was used. The half-time of the

rearrangement of **4m** in methanol in the presence of 1.0 equiv of DBU, 1.0 equiv or 5.0 equiv of sodium ethylate was determined by ^{1}H NMR spectrometry as 95, 53 and 22 min, respectively (Figure S4 of Supporting Information). These data reveal that the time of reaction decreases with the increase of strength and amount of the base.

Table 5. Ratio of 17:4m:5m in 24 h after treatment of 5m with a base according to ^{1}H NMR spectroscopy[a]

base	amount of base		
	0.1 equiv	1.0 equiv	5.0 equiv
Et_3N	8/0/92	7/0/93	10/0/90
CD_3ONa	97/0/3[b]	0/100/0	0/100/0

[a]Reaction conditions: thiadiazole **5m** (0.027 mmol), CD_3OD (0.5 mL), Et_3N or CD_3ONa (0.1 equiv; 1.0 equiv; 5.0 equiv), 25 °C, 24 h.

The both rearrangements processes involve two atoms of 4-substituents, opening of the ring to form intermediate diazo compounds and concurrent cyclization of the latter by C=N or C=S bonds to form isomeric heterocyclic compounds **4** and **5** and reffered to Cornforth type rearrangement.[1a,b,k,19] The transformation of compounds **4** to **5** represents a first example of novel rearrangement of 1,2,3-triazoles containing C=S bond in the chain to isomeric 1,2,3-thiadiazole bearing C=N bond in the chain. The reverse rearrangement of 1,2,3-thiadiazoles **5** to 1,2,3-triazoles **4** represents first example of interchange of cyclic thioamide group by carbamidine group of the chain. A few examples of rearrangements of 1,2,3-thiadiazoles containing aldimine group to 1,2,3-triazoles with C=S group in the chain are used to describe the mechanism of multi-step reactions. Either starting 1,2,3-thiadiazoles[1h] or final 1,2,3-triazoles[1c,i] were not isolated in these reaction and used in situ. In contrast to previously studied rearrangements in 1,2,3-triazole and 1,2,3-thiadiazole series[1a–d] the reversible rearrangement of 1,2,3-triazoles **4** and 1,2,3-thiadiazoles **5** represent transformations where both participants are isolated and

identified that allowed to elucidate factors govern the direction of the rearrangement. Their directions can be switched by the change in acidity of the medium. There are any example of that kind effect for Cornforth rearrangement between 1,2,3-triazoles and 1,2,3-thiadiazoles published in the literature.

To clarify the role of an acid that can operate either as a neutralizing agent or as a catalyst in Cornforth-type rearrangement of **5** to **4**, quantum-chemical calculations of possible isomerization routes for model triazole **18** were carried out. Calculations demonstrate (Fig. 5) that 1,2,3-triazole ring opening in **18** with the formation of diazo compound **19** is a rate determining step with activation barrier 23.8 kcal/mol (**TS5**) (Fig. 5, blue line).

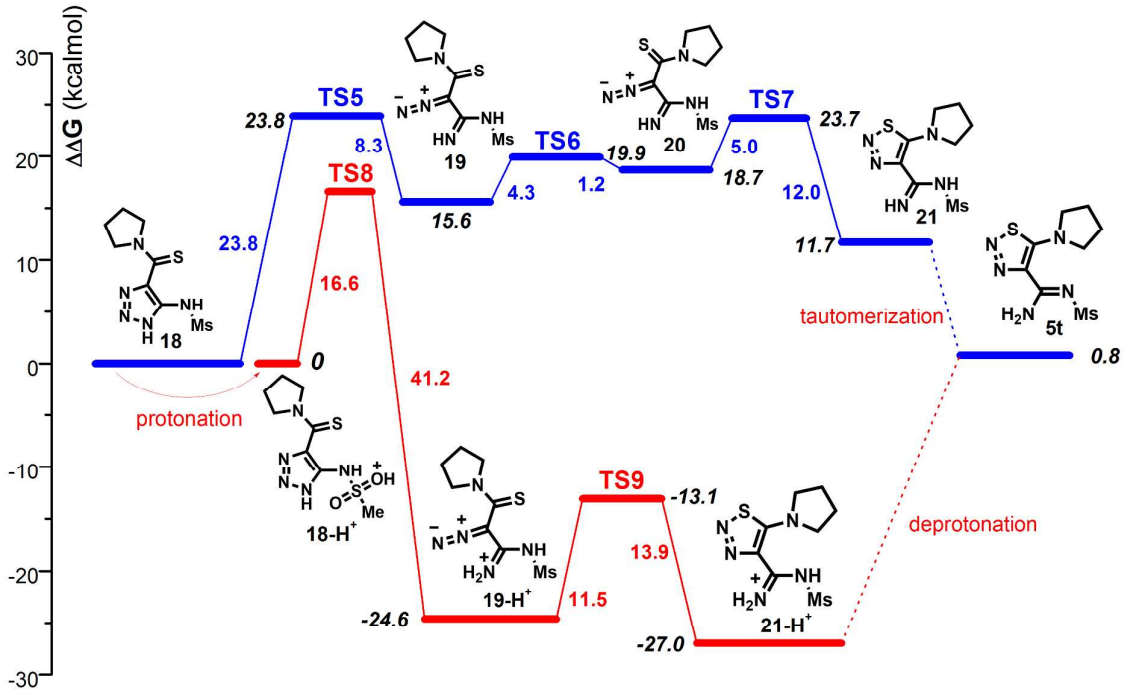


Figure 5. Relative free Gibbs energies (in kcal/mol, 298K, PCM model for the MeOH) of compounds **5t**,**18–21** and the transition states **TS5**–**TS9** computed at the B3LYP/6-311+g(d,p) level.

The subsequent steps involve rotation around single C–C bond (**TS6**) and cyclyzation to thiadiazole **21** (**TS7**). The energies of the corresponding transition states do not exceed that for

TS5. Thiadiazole **21** resulted from this sequence is less stable than final tautomer **5t** by 11.7 kcal/mol. We also evaluated the activation barrier for ring opening of protonated triazole **18** cation **18-H**$^+$ (**TS8**, red line) which can be generated under acidic conditions. The ring opening of cation **18-H**$^+$, resulting in the formation of N-protonated diazo compound **19-H**$^+$, has much lower barrier (**TS8** 16.6 kcal/mol) than that for neutral molecule (**TS5** 23.8 kcal/mol). Low-barrier cyclization (**TS12** 11.5 kcal/mol) followed by deprotonation gives thiadiazole **5t**. These data give reasons to believe that neutral forms of thiocarbamoyltriazoles **4** kinetically are less stable than their salts and can undergo Cornforth-type rearrangement even at room temperature via intermediate formation of the diazo compounds to give more stable in acidic medium thiadiazoles **5**. Acids catalyze this isomerization facilitating the triazole ring opening by protonation of sulfonamide oxygen atom.

Conclusions

A flexible and convenient method for the preparation of 4,5-functionalized 1,2,3-thiadiazoles and 1,2,3-triazoles from cyanothioacetamides and sulfonyl azides is described. The change of the solvent and base enables the use a 2-cyanothioacetamide both as C–C–S and C–C–N building blocks for the construction either of 1,2,3-thiadiazole or 1,2,3-triazole system, respectively, from the same precursors. The reaction of benzenesulfonyl azide with primary, secondary and tertiary cyanothioacetamides in pyridine gives 5-amino-4-cyano-1,2,3-thiadiazoles in good yields. The excess of sodium alkoxide in alcohol completely switches the reaction course resulting in the formation of 5-sulfonamido-1,2,3-triazole-4-carbothioamide sodium salts as the only products. This dramatic redirection of the reaction pathway is explained in terms of the competing transformations of triazenide-anion resulting from base-induced addition of 2-cyanothioacetamide to sulfonyl azide: intramolecular 1,4-prototropic shift versus alcohol-mediated 1,5-cyclization to triazoline derivative. The synthesized 1,2,3-triazole-4-carbothioamide sodium salts serve as good precursors for 5-amino-1,2,3-thiadiazole-4-carboximidamides, the products of Cornforth-type rearrangement occurring in neutral protic

medium or under acid conditions. According to DFT calculations the rearrangement proceeds via intermediate formation of a diazo compound, and can be catalyzed by acids via the protonation of oxygen atom of the sulfonamide group.

Experimental

General

Starting materials and reagents were purchased from commercial sources and used without further purification. Ethanol (EtOH) was dried and distilled over CaO prior to use. Pyridine and triethylamine (Et_3N) were distilled over KOH prior to use. THF was dried over sodium benzophenone ketyl and distilled. 1,4-Dioxane was dried and distilled over Na prior to use. Solvents used for silica gel chromatography (EtOAc/petroleum ether (40–70) (PE)) and crystallization (EtOH, Et_2O) were used without purification or removal of water. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, with $SiMe_4$ as internal reference in DMSO-d_6, DMSO-d_6/$CHCl_3$, $CDCl_3$ or CD_3OD-d_4; the chemical shifts (δ) were expressed in ppm, and J values were given in Hz. Mass spectra were obtained with a mass-spectrometer using electron ionisation (EI) technique (40–200 °C, 70 eV) with direct sample introduction into the ion source. High-resolution mass spectra (HRMS) were obtained with electrospray ionization (ESI-TOF). The compounds were analyzed in positive ion detection mode. The IR spectra were recorded with a FT-IR ATR (attenuated total reflection, ZnSe) spectrometer in the 4000−400 cm^{-1} region. The reactions were monitored by analytical TLC on aluminium foil plates with 0.2 mm silica gel with a fluorescent indicator visualed under UV light. The column chromatography was performed with 60−120 mesh silica gel. Melting points were determined on a melting point apparatus and are uncorrected.

Preparation of thioamides. 3-Morpholino-3-thioxopropanenitrile[20] (**1a**), 3-(piperidin-1-yl)-3-thioxopropanenitrile[20] (**1c**), 3-(pyrrolidin-1-yl)-3-thioxopropanenitrile[20] (**1d**), 2-cyano-N-p-tolylethanethioamide[21] (**1i**) were synthesized according to previously reported procedures. 2-

Cyano-*N*,*N*-dimethylethanethioamide (**1f**) and cyanoethanethioamide (**1h**) were commercially available. New 3-(4-benzylpiperidin-1-yl)-3-thioxopropanenitrile (**1b**), 3-(azepan-1-yl)-3-thioxopropanenitrile (**1e**) and 2-cyano-*N*,*N*-diphenylethanethioamide (**1g**) were prepared using modified literature procedure from appropriate amides.[22]

Preparation of Sulfonyl Azides. Sulfonyl azides were prepared from the corresponding sulfonyl chlorides[23] following the literature procedures. Warning! Sulfonyl azides are potentially explosive, and all reactions should be carried out behind blast shields. We recommend the use of plastic spatulas for the handling of solid material.

*3-(4-Benzylpiperidin-1-yl)-3-thioxopropanenitrile (**1b**).* 3-(4-Benzylpiperidin-1-yl)-3-oxopropanenitrile (7.27 g, 30.0 mmol) was dissolved in anhydrous 1,4-dioxane (50 mL), and Lowesson's reagent (6.10 g, 15.0 mmol) was added. Reaction mixture was stirred at 40−50 °C for 5 h. Then the solvent was removed under reduced pressure and EtOH (10 mL) was added to the residue. The precipitate was formed after the reaction mixture was maintained at +8 °C for 12 h. Then it was filtered off and washed with Et_2O to obtain **1b** as a colorless powder (6.60 g, 85%); mp: 115–117 °C; R_f = 0.57 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 1.13−1.32 (m, 2H), 1.66–1.70 (m, 2H), 1.88−1.97 (m, 1H), 2.52–2.54 (m, 2H), 3.05–3.06 (m, 1H), 3.23–3.29 (m, 1H), 4.11 (d, J = 12.0 Hz, 1H), 4.36 (s, 2H), 5.22 (d, J = 12.0 Hz, 1H), 7.17−7.21 (m, 3H), 7.27−7.31 (m, 2H). ^{13}C NMR (DMSO-d_6): δ 30.8, 31.9, 33.7, 36.4, 41.4, 50.1, 50.3, 116.3, 125.9, 128.2, 129.0, 139.8, 187.0. IR (ATR, ZnSe, cm^{-1}): ν 3063, 3025, 2944, 2912, 2883, 2848, 2252. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{19}N_2S$ 259.1264; Found 259.1264.

*3-(Azepan-1-yl)-3-thioxopropanenitrile (**1e**).* 3-(Azepan-1-yl)-3-oxopropanenitrile (2.0 g, 12.0 mmol) was dissolved in anhydrous 1,4-dioxane (15 mL), and Lowesson's reagent (2.43 g, 6.0 mmol) was added. Reaction mixture was stirred at 75 °C for 1.5 h. Then the solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (1:2) mixture to give **1e** as pale yellow crystals (1.30 g,

59%); mp: 58–59 °C; R_f = 0.40 (EtOAc/PE, 2:1). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 1.55−1.62 (m, 4H), 1.78−1.85 (m, 4H), 3.76−3.79 (m, 2H), 4.04−4.07 (m, 2H), 4.23 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 24.6, 25.5, 26.1, 27.3, 33.7, 52.8, 53.9, 116.5, 185.6. IR (ATR, ZnSe, cm^{-1}): ν 2984, 2941, 2920, 2856, 2252, 1512. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_{15}N_2S$ 183.0951; Found 183.0950.

2-Cyano-N,N-diphenylethanethioamide (***1g***). 2-Cyano-*N*,*N*-diphenylacetamide (709 mg, 3.0 mmol) was dissolved in anhydrous 1,4-dioxane (20 mL), and Lowesson's reagent (667 mg, 1.65 mmol) was added. Reaction mixture was stirred at 90 °C for 2 h. Then the solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE mixture. To achieve better separation, a composition of the eluent was gradually changed from 1:6 to 1:4 EtOAc/PE. Pale yellow needles (524 mg, 69%); mp: 131–133 °C; R_f = 0.40 (EtOAc/PE, 1:4). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 3.99 (s, 2H), 7.27–7.31 (m, 1H), 7.40–7.49 (m, 7H), 7.56 (d, J = 8.0 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 35.5, 116.1, 126.9, 127.0, 127.8, 129.0, 129.6, 130.1, 134.6, 142.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_2S$ 253.0794; Found 253.0790.

Experimental procedures for preliminary study of interaction of thioamide 1a with tosyl azide 2a (Scheme 2). (A) Thioamide **1a** (170 mg, 1.0 mmol) was added into cooled (+10 °C) solution of sodium ethoxide, freshly prepared from sodium (23 mg, 1.0 mmol) and anhydrous ethanol (4 mL), and the resulting solution was stirred at this temperature for 5–10 min. Then the reaction mixture was cooled till 0 °C and azide **2a** (197 mg, 1.0 mmol) was added to the reaction mixture portion by portion and the resulting mixture were stirred at 0 °C for 1 h. The formed precipitate (346 mg) was filtered off, washed with cold ethanol and diethyl ether and dried in a desiccator over P_4O_{10}. According to ^{1}H NMR spectrum the mixture consists of 4 products: thiadiazole **3a**, triazole **4a**, thiadiazole **5a** and tosyl amide in ratio/yield 11/10% : 73/67% : 3/2.5% : 11/10% (^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 2.34 (s, 3H, Me, **4a**), 2.41 (s, 3H, Me, $TsNH_2$), 2.43 (s, 3H, Me, **5a**), 3.06 (br. s, 2H, CH_2, **4a**), 3.27−3.30 (m, 4H, CH_2, **5a**), 3.55 (br. s, 2H, CH_2,

4a) + **5a** (m, 4H, CH_2), 3.62−3.64 (m, 4H, CH_2, **3a**), 3.68 (br. s, 2H, CH_2, **4a**), 3.78−3.81 (m, 4H, CH_2, **3a**), 4.18 (br. s, 2H, CH_2, **4a**), 7.04 (s, 2H, NH_2, $TsNH_2$), 7.15 (d, J = 8.0 Hz, 2H, Ar, **4a**), 7.29 (d, J = 8.0 Hz, 2H, Ar, $TsNH_2$), 7.34 (d, J = 8.2 Hz, 2H, Ar, **5a**), 7.65 (d, J = 8.1 Hz, 2H, Ar, **4a**), 7.71 (d, J = 8.2 Hz, 2H, Ar, $TsNH_2$), 7.77 (d, J = 8.1 Hz, 2H, Ar, **5a**), 8.24 (s, 1H, NH_2, **5a**), 8.97 (s, 1H, NH_2, **5a**), 12.96 (s, 1H, NH, **4a**).

(B) A mixture of tosyl azide **2a** (170 mg, 1.0 mmol) and thioamide **1a** (197 mg, 1.0 mmol) in anhydrous pyridine (2 mL) was stirred at room temperature for 5 h. The reaction mixture was poured on ice, the formed precipitate was filtered off, dried in desiccator over P_4O_{10} overnight and crystallized from EtOH−Et_2O mixture to give aminonitrile **3a** (157 mg, 80%) as a colorless crystals, mp: 80–82 °C; R_f = 0.5 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 3.62−3.64 (m, 4H), 3.78−3.81 (m, 4H).

General Procedure (A) for the Synthesis of 4-Cyanothiadiazoles 3a-h. A mixture of benzenesulfonyl azide **2b** (238 mg, 1.3 mmol) and corresponding thioamide **1** (1.3 mmol) in anhydrous pyridine (2 mL) was stirred at room temperature for 1−5 h. The reaction mixture was poured on ice, the formed precipitate was filtered off, dried in desiccator over P_4O_{10} overnight and crystallized from EtOH−Et_2O mixture to give aminonitriles **3a,b,d,f,g**. In the case of reaction of thioamides **1c,e** pyridine was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (2:1) mixture to give aminonitriles **3c,e**.

*5-Morpholino-1,2,3-thiadiazole-4-carbonitrile (**3a**).* Compound **3a** was obtained in 85% yield (217 mg) according to the general procedure **A** (thioamide **1a**: 221 mg; 2 h) as a colorless crystals; mp: 80–82 °C; R_f = 0.5 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 3.62−3.64 (m, 4H), 3.78−3.81 (m, 4H). ^{13}C NMR (DMSO-d_6): δ 51.9, 64.8, 113.6, 114.4, 172.2. IR (ATR, ZnSe, cm^{-1}): ν 2914, 2862, 2218, 1549, 1444, 1308, 1276, 1111. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_7H_9N_4OS$ 197.0492; Found 197.0488.

*5-(4-Benzylpiperidin-1-yl)-1,2,3-thiadiazole-4-carbonitrile (**3b**).* Compound **3b** was obtained in 86% yield (318 mg) according to the general procedure **A** (thioamide **1b**: 336 mg; 4 h) as a colorless crystals, mp: 97–99 °C; R_f = 0.2 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 1.36−1.46 (m, 2H), 1.77−1.81 (m, 2H), 1.85−1.91 (m, 1H), 2.57 (d, J = 8.0 Hz, 2H), 3.37−3.44 (m, 2H), 3.85 (br. s, 1H), 3.89 (br. s, 1H), 7.13−7.17 (m, 3H), 7.23−7.27 (m, 2H). ^{13}C NMR (DMSO-d_6): δ 30.4, 35.4, 41.3, 53.2, 113.3, 114.3, 125.8, 128.1, 128.8, 139.5, 171.0. IR (ATR, ZnSe, cm^{-1}): ν 2937, 2917, 2849, 2218, 1517, 1438, 1250. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}N_4S$ 285.1168; Found 285.1171.

*5-(Piperidin-1-yl)-1,2,3-thiadiazole-4-carbonitrile (**3c**).* Compound **3c** was obtained in 90% yield (228 mg) according to the general procedure **A** (thioamide **1c**: 219 mg; 2 h) as a pale brownish oil; R_f = 0.42 (EtOAc/PE, 1:2). ^{1}H NMR ($CDCl_3$): δ 1.70−1.83 (m, 6H), 3.63−3.66 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 22.9, 25.1, 54.6, 114.2, 114.4, 171.8. IR (NPVO, ZnSe, cm^{-1}): ν 2946, 2860, 2219, 1535, 1449, 1283. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_8H_{11}N_4S$ 195.0699; Found 195.0670.

Method B. A mixture of thioamide **1c** (530 mg, 3.15 mmol) and Et_3N (319 mg, 0.41 mL, 3.15 mmol) in EtOH (15 mL) was stirred at ambient temperature for 0.5 h. Then the reaction mixture was cooled down to +10 °C and tosyl azide (**2a**) (621 mg, 3.15 mmol) was added portion by portion. The resulting solution was stirred at +10 °C for 1.5 h, the solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (1:5) mixture to give aminonitrile **3c** in 75% yield (450 mg) as a pale brownish oil; R_f = 0.2 (EtOAc/PE, 1:5).

*5-(Pyrrolidin-1-yl)-1,2,3-thiadiazole-4-carbonitrile (**3d**).* Compound **3d** was obtained in 81% yield (188 mg) according to the general procedure **A** (thioamide **1d**: 200 mg; 1 h) as a colorless crystals; mp: 96–97 °C; R_f = 0.56 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 2.10−2.18 (m, 4H), 3.61 (br. s, 4H). ^{13}C NMR (DMSO-d_6): δ 25.2, 53.4, 112.3, 113.9, 166.9. IR (ATR,

ZnSe, cm^{-1}): ν 2952, 2857, 2212. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_7H_9N_4S$ 181.0542; Found 181.0542.

*5-(Azepan-1-yl)-1,2,3-thiadiazole-4-carbonitrile (**3e**).* Compound **3e** was obtained in 69% yield (187 mg) according to the general procedure **A** (thioamide **1e**: 237 mg; 3.5 h) as a yellow oil; R_f = 0.4 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 1.56−1.63 (m, 4H), 1.84 (br. s, 4H), 3.61−3.72 (m, 4H). ^{13}C NMR (DMSO-d_6): δ 26.3, 26.7, 55.6, 112.2, 114.5, 170.2. IR (ATR, ZnSe, cm^{-1}): ν 2934, 2859, 2218, 1540, 1449, 1305. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_{12}N_4S$ 209.0855; Found 209.0876.

Method C. The solution of thioamide **1e** (456 mg, 2.5 mmol), azide **2b** (183.0 mg, 1.0 mmol) and sodium ethoxide (68 mg, 1.0 mmol) in pyridine (1 mL) was stirred at room temperature for 5 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (1:2) mixture to give aminonitrile **3e** in 91% yield (190 mg) as a yellow oil; R_f = 0.4 (EtOAc/PE, 1:2).

Method D. The solution of thioamide **1e** (456 mg, 2.5 mmol), azide **2b** (183 mg, 1.0 mmol) in pyridine/water (1:0.4 mL) mixture was stirred at room temperature for 5 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (1:2) mixture to give aminonitrile **3e** in 85% yield (177 mg) as a yellow oil; R_f = 0.4 (EtOAc/PE, 1:2).

Method E. The solution of thioamide **1e** (456 mg, 2.5 mmol), azide **2b** (183 mg, 1.0 mmol) and Et_3N (101 mg, 1.0 mmol) in anhydrous EtOH (5 mL) was stirred at room temperature for 5 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography over silica gel (60−120) using EtOAc/PE (1:2) mixture to give aminonitrile **3e** in 90% yield (187 mg) as a yellow oil; R_f = 0.4 (EtOAc/PE, 1:2).

*5-(Dimethylamino)-1,2,3-thiadiazole-4-carbonitrile (**3f**).* Compound **3f** was obtained in 74% yield (148 mg) according to the general procedure **A** (thioamide **1f**: 167 mg; 4 h) as a yellow powder; mp: 62–64 °C; R_f = 0.33 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 3.33 (s, 6H).

^{13}C NMR (DMSO-d_6): δ 44.9, 112.8, 114.3, 171.2. IR (ATR, ZnSe, cm^{-1}): ν 2930, 2219, 1558, 1455, 1330. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_5H_7N_4S$ 155.0373; Found 155.0386.

*5-(Diphenylamino)-1,2,3-thiadiazole-4-carbonitrile (**3g**).* Compound **3g** was obtained in 81% yield (293 mg) according to the general procedure **A** (thioamide **1g**: 328 mg; 5 h) as a light yellow powder; mp: 122–124 °C; R_f = 0.72 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 7.39−7.44 (m, 2H), 7.47−7.52 (m, 8H). ^{13}C NMR (DMSO-d_6): δ 111.2, 117.5, 126.0, 129.0, 130.4, 145.3, 172.1. IR (ATR, ZnSe, cm^{-1}): ν 3057, 2227, 1587, 1484, 1454, 1374, 1289, 1267. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}N_4S$ 279.0699; Found 279.0699.

*5-Amino-1,2,3-thiadiazole-4-carbonitrile (**3h**).* Compound **3h** was obtained in 77% yield (124 mg) according to the general procedure **A** (thioamide **1h**: 130 mg; 5 h) as a colorless crystals; mp: 166−168 °C (lit.[21] 168−171 °C); R_f = 0.4 (EtOAc/PE, 1:2). ^{1}H NMR ($CDCl_3$): δ 8.33 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 112.8, 115.8, 170.8. IR (ATR, ZnSe, cm^{-1}) ν 3400, 3356, 2922, 2888, 2260, 1623, 1510 1447, 1301. MS (EI), m/z (%): 126 ($[M]^+$, 17), 98 (59), 71 (100), 45 (65), 38 (48).

*5-(p-Tolylamino)-1,2,3-thiadiazole-4-carbonitrile (**3i**).* Compound **3i** was obtained in 78% yield (219 mg) according to the general procedure **A** (thioamide **1i**: 247 mg; 5.5 h) as a red crystals; mp: 187–189 °C (lit.[11] 185 °C); R_f = 0.8 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6/$CHCl_3$): δ 2.34 (s, 3H), 7.19−7.24 (m, 4H), 10.99 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.3, 112.5, 117.1, 119.8, 130.1, 135.3, 138.7 167.8. IR (ATR, ZnSe, cm^{-1}): ν 3225, 2229, 1605, 1591, 1550, 1509, 1435, 1369, 1304, 1259.

General Procedure for the Synthesis of Triazoles 4a-s, Exemplified by Sodium (4-(morpholine-4-carbonothioyl)-1*H*-1,2,3-triazol-5-yl)(tosyl)amide hydrate (4a). Thioamide **1a** (170 mg, 1.0 mmol) was added into cooled to +10 °C solution of sodium ethoxide, freshly prepared from sodium (115 mg, 5.0 mmol) and anhydrous ethanol (4 mL), and the resulting solution was stirred at +10 °C for 5–10 min. Then the reaction mixture was cooled to –10 °C and

azide **2a** (197 mg, 1.00 mmol) was added to the reaction mixture portion by portion and the resulting mixture were stirred at –10 °C for 1 h. The formed precipitate was filtered off, washed with cold ethanol and diethyl ether and dried in a desiccator over P_4O_{10}. Triazole **4a** was obtained as colorless powder in 91% (370 mg) yield; mp: 263–265 °C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 2.31 (s, 3H), 3.52−3.62 (m, 4H), 3.74 (br. s, 2H), 4.23 (br. s, 2H), 5.12 (CD_3OD-d_4 + NH), 7.12 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 21.3, 50.6, 54.1, 67.3, 68.0, 127.8, 129.4, 137.1, 141.1, 144.7, 147.0, 194.5. IR (ATR, ZnSe, cm^{-1}): ν 3298, 2960, 2918, 1566, 1499, 1398, 1265, 1154. MS (EI), m/z (%): 367 ([M–NaOH]$^+$, 17), 212 (52), 184 (23), 127 (53), 91 (86), 87 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{16}N_5NaO_3S_2$ 390.0665; Found 390.0668.

*Sodium (4-(4-benzylpiperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(phenylsulfonyl)amide hydrate (**4b**)*. Compound **4b** was obtained in 82% yield (790 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1b**: 517 mg, 2.0 mmol; azide **2b**: 366 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 225–227 °C (decomp.). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.16−1.32 (m, 2H), 1.38−1.40 (m, 1H), 1.70−1.73 (m, 1H), 1.81−1.84 (m, 1H), 2.50−2.52 (m, 2H), 2.90−3.01 (m, 2H), 3.55–4.00 (m, 1H), 5.35 (d, J = 12.0 Hz, 1H), 7.12−7.17 (m, 3H), 7.23−7.26 (m, 2H), 7.30−7.32 (m, 3H), 7.74−7.76 (m, 2H), 13.06 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.10−1.20 (m, 1H), 1.29−1.39 (m, 2H), 1.70−1.73 (m, 1H), 1.78−1.88 (m, 1H), 2.48−2.57 (m, 2H), 2.94−3.00 (m, 2H), 3.89 (d, J = 12.0 Hz, 1H), 4.91 (CD_3OD-d_4 + NH), 5.37 (d, J = 12.0 Hz, 1H), 7.14−7.18 (m, 3H), 7.24−7.32 (m, 5H), 7.84−7.86 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 32.6, 33.8, 39.2, 43.5, 50.6, 53.6, 126.9, 127.7, 128.9, 129.2, 130.1, 130.8, 137.5, 141.6, 146.6, 147.6, 193.2. IR (ATR, ZnSe, cm^{-1}): ν 3294, 3061, 2928, 1566, 1497, 1442, 1400, 1268, 1139. MS (EI), m/z (%): 441 ([M−NaOH]$^+$, 2), 300 (21), 272 (12), 242 (27), 174 (100), 117 (25), 91 (91). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{23}N_5NaO_2S_2$ 464.1185; Found: 464.1187.

*Sodium (4-(morpholine-4-carbonothioyl)-1H-1,2,3-triazol-5-yl)(phenylsulfonyl)amide hydrate (**4c**)*. Compound **4c** was obtained in 84% yield (330 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1a**: 170 mg, 1.0 mmol; azide **2b**: 183 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 254–256 °C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 3.48−3.60 (m, 4H), 3.73 (br. s, 2H), 4.23 (br. s, 2H), 5.12 (CD_3OD-d_4 + NH), 7.28−7.34 (m, 3H), 7.83−7.85 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 50.8, 53.8, 67.3, 68.0, 127.7, 129.0, 130.9, 137.0, 146.8, 147.6, 194.5. IR (ATR, ZnSe, cm^{-1}): ν 3337, 2971, 2945, 1597, 1124. MS (EI), m/z (%): 353 ($[M-NaOH]^+$, 17), 212 (40), 184 (19), 127 (52), 113 (29), 86 (100), 77 (80). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}N_5NaO_3S_2$ 376.0509; Found 376.0511.

*Sodium ((4-methoxyphenyl)sulfonyl)(4-(morpholine-4-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4d**)*. Compound **4d** was obtained in 81% yield (342 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1a**: 170 mg, 1.0 mmol; azide **2c**: 213 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 282–284°C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 3.52−3.59 (m, 4H), 3.75−3.78 (m, 5H), 4.25 (br. s, 2H), 5.16 (CD_3OD-d_4 + NH), 6.83 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 50.8, 54.1, 55.9, 67.1, 68.1, 114.2, 129.4, 137.1, 139.4, 146.7, 162.3, 194.5. IR (ATR, ZnSe, cm^{-1}): ν 3298, 2960, 2907, 1598, 1562, 1499, 1440, 1399, 1309, 1264, 1168. MS (EI), m/z (%): 383 ($[M-NaOH]^+$, 11), 212 (52), 189 (21), 113 (32), 107 (29), 86 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}N_5NaO_4S_2$ 406.0614; Found 406.0611.

*Sodium ((4-fluorophenyl)sulfonyl)(4-(morpholine-4-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4e**)*. Compound **4e** was obtained in 78% yield (321 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1a**: 170 mg, 1.0 mmol; azide **2d**: 201 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 268–270°C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 3.60−3.65 (m, 4H), 3.77 (br. s, 2H), 4.26 (br. s, 2H), 5.13 (CD_3OD-d_4 + NH), 6.99−7.04 (m, 2H), 7.84−7.88 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 50.4, 53.8, 67.3, 68.1, 115.7 (d, J = 22.0 Hz), 130.3 (d, J = 8.0 Hz), 137.1, 143.8 (d, J = 3.0 Hz), 146.8, 165.0 (d, J = 267.0 Hz), 194.2. IR

(ATR, ZnSe, cm^{-1}): ν 3298, 2971, 2945, 1569, 1495, 1443, 1369, 1267, 1223, 1155. MS (EI), m/z (%): 371 ($[M-NaOH]^+$, 17), 212 (39), 184 (16), 127 (61), 95 (61), 86 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}FN_5NaO_3S_2$ 394.0414; Found: 394.0413.

*Sodium (phenylsulfonyl)(4-(pyrrolidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide (**4f**).* Compound **4f** was obtained in 77% yield (292 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1d**: 154 mg, 1.0 mmol; azide **2b**: 183 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 272–274°C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 1.76−1.82 (m, 2H), 1.90−1.97 (m, 2H), 3.45−3.48 (m, 2H), 3.71−3.75 (m, 2H), 5.09 (CD_3OD-d_4 + NH), 7.28−7.34 (m, 3H), 7.83−7.85 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 25.6, 27.3, 53.8, 54.1, 127.9, 128.9, 130.9, 138.4, 147.0, 147.4, 190.7. IR (ATR, ZnSe, cm^{-1}): ν 3337, 2971, 2945, 1597, 1124. MS (EI), m/z (%): 337 ($[M-NaOH]^+$, 3), 176 (12), 134 (13), 117 (21), 97 (19), 70 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}N_5NaO_2S_2$ 360.0559; Found: 360.0558.

*Sodium (4-(pyrrolidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(tosyl)amide hydrate (**4g**).* Compound **4g** was obtained in 89% yield (350 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1d**: 154 mg, 1.0 mmol; azide **2a**: 197 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 268–270°C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 1.77−1.84 (m, 2H), 1.92−1.98 (m, 2H), 2.33 (s, 3H), 3.50 (t, J = 8.0 Hz, 2H), 3.73 (t, J = 8.0 Hz, 2H), 4.90 (CD_3OD-d_4 + NH), 7.13 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 11.8, 15.9, 17.5, 44.4, 44.6, 118.6, 120.0, 128.9, 131.9, 134.2, 137.3, 180.8. IR (ATR, ZnSe, cm^{-1}): ν 3301, 2968, 2870, 1572, 1517, 1430, 1350, 1322, 1229, 1150. MS (EI), m/z (%): 351 ($[M-NaOH]^+$, 21), 196 (100), 168 (22), 127 (16), 70 (64). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}N_5NaO_2S_2$ 374.0716; Found 374.0712.

*Sodium ((4-methoxyphenyl)sulfonyl)(4-(pyrrolidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4h**).* Compound **4h** was obtained in 82% yield (333 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1d**: 154 mg, 1.0 mmol; azide **2c**: 213 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 270–272 °C (decomp.). ^{1}H NMR

(CD_3OD-d_4): δ 1.79−1.85 (m, 2H), 1.92−1.99 (m, 2H), 3.51 (t, J = 8.0 Hz, 2H), 3.74 (t, J = 8.0 Hz, 2H), 3.79 (s, 3H), 4.90 (CD_3OD-d_4 + NH), 6.84 (d, J = 8.0 Hz, 2H), 7.75 (t, J = 8.0 Hz, 2H). ^{13}C NMR (DMSO-d_6): δ 15.9, 17.5, 44.5, 44.6, 46.3, 104.7, 120.4, 128.8, 129.0, 137.2, 153.1, 180.7. IR (ATR, ZnSe, cm^{-1}): ν 3301, 3221, 2971, 2879, 1596, 1571, 1518, 1497, 1433, 1325, 1221, 1125. MS (EI), m/z (%): 367 ($[M-NaOH]^+$, 8), 196 (48), 187 (39), 171 (52), 123 (38), 70 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}N_5NaO_3S_2$ 390.0665; Found 390.0681.

*Sodium ((4-fluorophenyl)sulfonyl)(4-(pyrrolidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4i**)*. Compound **4i** was obtained in 68% yield (270 mg) according to the general procedure (sodium: 115 mg, 5.0 mmol; thioamide **1d**: 154 mg, 1.0 mmol; azide **2d**: 201 mg, 1.0 mmol; ethanol (4 mL)) as a colorless powder; mp: 274–276 °C (decomp.). ^{1}H NMR (CD_3OD-d_4): δ 1.81−1.87 (m, 2H), 1.94−2.01 (m, 2H), 3.55 (t, J = 7.0 Hz, 2H), 3.76 (t, J = 7.0 Hz, 2H), 5.03 (CD_3OD-d_4 + NH), 6.99−7.03 (m, 2H), 7.84−7.87 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 25.5, 27.1, 53.8, 54.1, 115.6 (d, J = 22.0 Hz), 130.5 (d, J = 9.0 Hz), 138.5, 134.6 (d, J 3.0 Hz), 146.9, 164.9 (d, J = 241.0 Hz), 190.8. IR (ATR, ZnSe, cm^{-1}): ν 3337, 2971, 2945, 1597, 1442, 1361, 1335, 1124. MS (EI), m/z (%): 355 ($[M-NaOH]^+$, 4), 241 (12), 159 (4), 111 (13), 84 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}FN_5NaO_2S_2$ 378.0465; Found 378.0468.

*Sodium (4-(4-benzylpiperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(tosyl)amide hydrate (**4j**)*. Compound **4j** was obtained in 75% yield (740 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1b**: 517 mg, 2.0 mmol; azide **2a**: 394 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 205–206 °C (decomp.). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.16−1.33 (m, 2H), 1.38−1.41 (m, 1H), 1.72−1.75 (m, 1H), 1.82−1.86 (m, 1H), 2.30 (s, 3H), 2.51−2.53 (m, 2H), 2.91−3.01 (m, 2H), 3.46−4.04 (m, 1H), 5.36 (d, J = 12.0 Hz, 1H), 7.10−7.18 (m, 5H), 7.24−7.27 (m, 2H), 7.64 (d, J = 8.0 Hz, 2H), 13.02 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.03−1.13 (m, 1H), 1.29−1.39 (m, 2H), 1.71−1.74 (m, 1H), 1.77−1.87 (m, 1H), 2.26 (s, 3H), 2.45−2.58 (m, 2H), 2.86−3.01 (m, 2H), 3.80 (d, J = 12.0 Hz, 1H), 5.26 (CD_3OD-d_4 + NH), 5.37 (d, J = 12.0 Hz, 1H), 7.06 (d, J = 8.0 Hz, 2H), 7.13−7.18 (m, 3H), 7.24−7.28 (m, 2H), 7.71 (d, J

= 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 21.3, 32.7, 33.7, 39.3, 43.5, 50.6, 53.7, 127.0, 127.8, 129.3, 129.5, 130.1, 137.4, 141.2, 141.5, 144.6, 146.7, 193.1. IR (ATR, ZnSe, cm^{-1}): ν 3302, 3066, 2919, 1569, 1501, 1450, 1265, 1137. MS (EI), m/z (%): 455 ($[M–NaOH]^+$, 3), 174 (37), 155 (11), 117 (10), 91 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{25}N_5NaO_2S_2$ 478.1342; Found 478.1345.

*Sodium (4-(4-benzylpiperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)((4-fluorophenyl)sulfonyl)amide hydrate (**4k**).* Compound **4k** was obtained in 76% yield (760 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1b**: 517 mg, 2.0 mmol; azide **2d**: 402 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 204–205 °C (decomp.). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.19−1.34 (m, 2H), 1.42−1.45 (m, 1H), 1.72−1.75 (m, 1H), 1.81−1.92 (m, 1H), 2.52−2.54 (m, 2H), 2.92−3.06 (m, 2H), 3.62−4.06 (m, 1H), 5.36 (d, J = 12.0 Hz, 1H), 7.03−7.07 (m, 2H), 7.13−7.17 (m, 3H), 7.23−7.27 (m, 2H), 7.78−7.82 (m, 2H), 13.11 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.10−1.21 (m, 1H), 1.29−1.43 (m, 2H), 1.72−1.75 (m, 1H), 1.80−1.91 (m, 1H), 2.49−2.58 (m, 2H), 2.96−3.07 (m, 2H), 3.93 (d, J = 12.0 Hz, 1H), 5.20 (CD_3OD-d_4 + NH), 5.38 (d, J = 12.0 Hz, 1H), 6.95−7.01 (m, 2H), 7.14−7.18 (m, 3H), 7.24−7.28 (m, 2H), 7.84−7.89 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 32.6, 33.9, 39.3, 43.5, 50.6, 53.7, 115.7 (d, J = 22.0 Hz), 127.0, 129.3, 130.1, 130.4 (d, J = 8.0 Hz), 137.5, 141.5, 143.8 (d, J = 3.0 Hz), 146.5, 164.9 (d, J = 247.0), 193.1. IR (ATR, ZnSe, cm^{-1}): ν 3295, 2927, 2851, 1569, 1491, 1450, 1403, 1266, 1220, 1138. MS (EI), m/z (%): 459 ($[M–NaOH]^+$, 3), 300 (12), 242 (12), 175 (27), 174 (68), 173 (21), 129 (14), 127 (11), 117 (17), 115 (15), 97 (13), 96 (13), 95 (46), 92 (10), 91 (100). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}FN_5NaO_2S_2$ 482.1091; Found 482.1092.

*Sodium (phenylsulfonyl)(4-(piperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4l**).* Compound **4l** was obtained in 61% yield (476 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1c**: 337 mg, 2.0 mmol; azide **2b**: 366 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 205–206 °C (decomp.).^{1}H NMR (DMSO-d_6:$CHCl_3$):

δ 1.45 (br. s, 2H), 1.65 (br. s, 4H), 3.51 (br. s, 2H), 4.16 (br. s, 2H), 7.32−7.35 (m, 3H), 7.75−7.78 (m, 2H), 13.02 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.39 (br. s, 2H), 1.64−1.68 (m, 4H), 3.41−3.43 (m, 2H), 4.17−4.18 (m, 2H), 5.24 (CD_3OD-d_4 + NH), 7.26−7.36 (m, 3H), 7.85−7.87 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 25.4, 26.6, 27.8, 51.5, 54.6, 127.8, 129.0, 130.9, 137.4, 146.6, 147.5, 193.0. IR (ATR, ZnSe, cm^{-1}): ν 3298, 2933, 2856, 2119, 1618, 1569, 1499, 1443, 1271, 1227, 1161. MS (EI), m/z (%): 351 ([M–NaOH]$^+$, 4), 210 (17), 127 (11), 111 (12), 84 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{17}N_5NaO_2S_2$ 374.0716; Found 374.0721.

*Sodium (4-(piperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(tosyl)amide hydrate (**4m**).* Compound **4m** was obtained in 69% yield (560 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1c**: 337 mg, 2.0 mmol; azide **2a**: 394 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 214–215 °C (decomp.). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.45 (br. s, 2H), 1.65 (br. s, 4H), 2.32 (s, 3H), 3.56 (br. s, 2H), 4.15 (br. s, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 13.00 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.34−1.41 (m, 2H), 1.60−1.70 (m, 4H), 2.31 (s, 3H), 3.40−3.42 (m, 2H), 4.16−4.21 (m, 2H), 5.22 (CD_3OD-d_4 + NH), 7.11 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 21.3, 25.5, 26.6, 27.8, 51.4, 54.6, 127.9, 129.5, 137.4, 141.2, 144.6, 146.7, 193.0. IR (ATR, ZnSe, cm^{-1}): ν 3296, 2958, 2854, 2130, 1619, 1568, 1442, 1229, 1176, 1128. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{19}N_5NaO_2S_2$ 388.0872; Found 388.0871.

*Sodium ((4-methoxyphenyl)sulfonyl)(4-(piperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4n**).* Compound **4n** was obtained in 57% yield (480 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1c**: 337 mg, 2.0 mmol; azide **2c**: 426 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 209–210 °C (decomp.). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.47 (br. s, 2H), 1.66 (br. s, 4H), 3.59 (br. s, 2H), 3.77 (s, 3H), 4.15 (br. s, 2H), 6.84 (d, 2H, J = 8.0 Hz), 7.68 (d, 2H, J = 8.0 Hz), 12.96 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.36−1.44 (m, 2H), 1.63−1.73 (m, 4H), 3.43−3.46 (m, 2H), 3.78 (s, 3H), 4.18−4.22 (m, 2H), 5.21

(CD$_3$OD-d_4 + NH), 6.82 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H). ^{13}C NMR (CD$_3$OD-d_4): δ 25.5, 26.6, 27.8, 51.5, 54.6, 55.9, 114.1, 129.7, 137.4, 139.4, 146.8, 162.4, 193.0. IR (ATR, ZnSe, cm^{-1}): ν 3303, 2936, 2835, 1597, 1567, 1497, 1443, 1396, 1290, 1253, 1159. MS (EI), m/z (%): 381 ([M–NaOH]$^+$, 3), 224 (53), 210 (11), 171 (15), 155 (14), 141 (95), 128 (27), 123 (19), 107 (23), 84 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{19}N_5NaO_3S_2$ 404.0822; Found 404.0824.

*Sodium ((4-fluorophenyl)sulfonyl)(4-(piperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)amide hydrate (**4o**)*. Compound **4o** was obtained in 68% yield (560 mg) according to the general procedure (sodium: 230 mg, 10.0 mmol; thioamide **1c**: 337 mg, 2.0 mmol; azide **2d**: 402 mg, 2.0 mmol; ethanol (8 mL)) as a colorless powder; mp: 200–201 °C (decomp.). ^{1}H NMR (DMSO-d_6:CHCl$_3$): δ 1.48 (br. s, 2H), 1.65 (br. s, 4H), 3.47 (br. s, 2H), 4.16 (br. s, 2H), 7.08 (t, J = 8.0 Hz, 2H), 7.78−7.81 (m, 2H), 13.07 (br. s, 1H). ^{1}H NMR (CD$_3$OD-d_4): δ 1.42−1.47 (m, 2H), 1.62−1.72 (m, 4H), 3.49−3.51 (m, 2H), 4.18−4.22 (m, 2H), 5.24 (CD$_3$OD-d_4 + NH), 6.98−7.03 (m, 2H), 7.85−7.90 (m, 2H). ^{13}C NMR (CD$_3$OD-d_4): δ 25.5, 26.6, 27.9, 51.5, 54.6, 115.6 (d, J = 22.0 Hz), 130.4 (d, J = 9.0 Hz), 137.5, 143.8 (d, J = 3.0 Hz), 146.4, 164.9 (d, J = 246.0 Hz), 193.0. IR (ATR, ZnSe, cm^{-1}): ν 3299, 2934, 2813, 1592, 1565, 1495, 1400, 1269, 1234, 1140. MS (EI), m/z (%): 369 ([M–NaOH]$^+$, 5), 210 (19), 152 (10), 127 (16), 111 (13), 95 (42), 84 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{16}FN_5NaO_2S_2$ 392.0622; Found 392.0621.

*Sodium (4-(azepane-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(phenylsulfonyl)amide hydrate (**4p**)*. Compound **4p** was obtained in 87% yield (296 mg) according to the general procedure (sodium: 97 mg, 4.2 mmol; thioamide **1e**: 153 mg, 0.84 mmol; azide **2b**: 154 mg, 0.84 mmol; ethanol (8 mL)) as a colorless powder; mp: 207−211 (decomp.). °C. ^{1}H NMR (DMSO-d_6:CHCl$_3$): δ 1.44−1.54 (m, 6H), 1.83−1.86 (m, 2H), 3.60 (br. s, 2H), 4.01−4.04 (m, 2H), 7.32−7.34 (m, 3H), 7.73−7.75 (m, 2H), 13.01 (br. s, 1H). ^{1}H NMR (CD$_3$OD-d_4): δ 1.40−1.47 (m, 4H), 1.57−1.59 (m, 2H), 1.87−1.93 (m, 2H), 3.48−3.51 (m, 2H), 4.00−4.03 (m, 2H), 5.28 (CD$_3$OD-d_4 + NH),

7.28−7.36 (m, 3H), 7.85−7.88 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 27.1, 27.4, 28.6, 29.6, 54.1, 55.4, 127.8, 129.0, 130.9, 137.9, 146.0, 147.6, 194.9. IR (ATR, ZnSe, cm^{-1}): ν 3444, 3318, 3240, 2900, 2848, 1130, 1546, 1508, 1439, 1269, 1139, 1081. MS (EI), m/z (%): 365 ([M–NaOH]$^+$, 5), 241 (20), 196 (18), 125 (19), 98 (100), 77 (49). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{19}N_5NaO_2S_2$ 388.0872; Found 388.0878.

*Sodium (4-(azepane-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)(tosyl)amide hydrate (**4q**).* Compound **4q** was obtained in 90% yield (317 mg) according to the general procedure (sodium: 97 mg, 4.2 mmol; thioamide **1e**: 153 mg, 0.84 mmol; azide **2a**: 166 mg, 0.84 mmol; ethanol (8 mL)) as a colorless powder; mp: 199−203 (decomp.) °C. ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.46−1.54 (m, 6H), 1.81−1.88 (m, 2H), 2.31 (s, 3H), 3.67 (br. s, 2H), 4.01−4.04 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 12.97 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.41−1.47 (m, 4H), 1.57−1.59 (m, 2H), 1.87−1.93 (m, 2H), 2.31 (s, 3H), 3.49−3.52 (m, 2H), 3.99−4.02 (m, 2H), 5.05 (CD_3OD-d_4 + NH), 7.11 (d, J = 8.0 Hz, 2H), 7.73 (m, J = 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 21.3, 27.1, 27.5, 28.7, 29.5, 54.2, 55.4, 127.9, 129.5, 137.9, 141.1, 144.7, 146.0, 194.9. IR (ATR, ZnSe, cm^{-1}): ν 3447, 3325, 2930, 2854, 1714, 1614, 1597, 1531, 1436, 1386, 1364, 1252, 1139. MS (EI), m/z (%): 379 ([M–NaOH]$^+$, 7), 255 (18), 224 (29), 196 (17), 125 (15), 98 (100), 91 (52). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{20}N_5NaO_2S_2$ 402.1029; Found 402.1029.

*Sodium (4-(azepane-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)((4-methoxyphenyl)sulfonyl)amide hydrate (**4r**).* Compound **4r** was obtained in 84% yield (307 mg) according to the general procedure (sodium: 97 mg, 4.2 mmol; thioamide **1e**: 153 mg, 0.84 mmol; azide **2c**: 179 mg, 0.84 mmol; ethanol (8 mL)) as a colorless powder; mp: 206−210 (decomp.) °C. ^{1}H NMR (CD_3OD-d_4): δ 1.43−1.47 (m, 4H), 1.57−1.62 (m, 2H), 1.87−1.93 (m, 2H), 3.51−3.54 (m, 2H), 3.78 (s, 3H), 4.01−4.04 (m, 2H), 5.28 (CD_3OD-d_4 + NH), 6.84 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H). ^{13}C NMR (CD_3OD-d_4): δ 27.1, 27.4, 28.7, 29.6, 54.2, 55.4, 55.9, 114.1, 129.8, 137.9, 139.5, 146.2, 162.4, 194.7. IR (ATR, ZnSe, cm^{-1}): ν 3307, 2926, 2855, 1570, 1510, 1424, 1346, 1156.

MS (EI), m/z (%): 395 ([M–NaOH]$^+$, 8), 238 (21), 224 (60), 141 (33), 127 (19), 98 (100), 77 (32). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{21}N_5NaO_3S_2$ 418.0978; Found 418.0985.

*Sodium (4-(azepane-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)((4-fluorophenyl)sulfonyl)amide hydrate (**4s**).* Compound **4s** was obtained in 90% yield (319 mg) according to the general procedure (sodium: 97 mg, 4.2 mmol; thioamide **1e**: 153 mg, 0.84 mmol; azide **2d**: 169 mg, 0.84 mmol; ethanol (8 mL)) as a colorless powder; mp: 213−217 (decomp.) °C. ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.47−1.56 (m, 6H), 1.83−1.88 (m, 2H), 3.60 (br. s, 2H), 4.02−4.05 (m, 2H), 7.05−7.09 (m, 2H), 7.77−7.80 (m, 2H), 13.05 (br. s, 1H). ^{1}H NMR (CD_3OD-d_4): δ 1.45−1.49 (m, 4H), 1.58−1.63 (m, 2H), 1.89−1.93 (m, 2H), 3.56−3.59 (m, 2H), 4.02−4.05 (m, 2H), 5.44 (CD_3OD-d_4 + NH), 6.98−7.02 (m, 2H), 7.85−7.88 (m, 2H). ^{13}C NMR (CD_3OD-d_4): δ 27.1, 27.4, 28.6, 29.6, 54.2, 55.5, 115.6 (d, J = 22.0 Hz), 130.4 (d, J = 8.0 Hz), 138.0, 143.8 (d, J = 3.0 Hz), 146.0, 165.0 (d, J = 253.0 Hz), 194.9. IR (ATR, ZnSe, cm^{-1}): ν 3445, 2926, 2856, 1640, 1538, 1440, 1329, 1270, 1140. MS (EI), m/z (%): 383 ([M–NaOH]$^+$, 6), 255 (32), 125 (13), 98 (100), 91 (41). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{18}FN_5NaO_2S_2$ 406.0778; Found 406.0774.

General Methods for the Synthesis of Thiadiazoles 5.

*General Procedure **A** for the Synthesis of Thiadiazoles **5a-s** in Water.* A suspension of triazole **4** (0.47−1.0 mmol) in water (4 mL) was stirred at ambient temperature during 1 h. The precipitate was filtered off and washed with water (2−3 times per 1 mL) till neutral pH of wash water. The precipitate was dried in a desiccator over P_4O_{10} to give thiadiazole **5**.

*General Procedure **B** for the Synthesis of Thiadiazoles **5a,c,d-i** in Acidic Medium.* A suspension of triazole **4** (1.0 mmol) in water solution (10 mL) of 0.5% hydrochloric acid was stirred at ambient temperature for 15 min. The precipitate was filtered off and washed with water (2−3 times per 1 mL) till neutral pH of wash water. The product was dried in a desiccator over P_4O_{10} to give thiadiazole **5**.

*General Procedure **C** for the Synthesis of Thiadiazoles **5j,k-o** under Silica Gel Action.* To a stirred solution of triazole **4** (200 mg, 0.40−0.51 mmol) in ethyl acetate (25 mL) at ambient temperature was added silica gel (1.0 g). The reaction mixture was stirred for 0.5 h. Then silica gel was filtered off and washed with ethyl acetate (5 mL). The filtrate was concentrated under reduced pressure. The precipitate was filtered off and dried under vacuum to obtain the product **5l**.

*(Z)-5-Morpholino-N'-tosyl-1,2,3-thiadiazole-4-carboximidamide (**5a**)*. Compound **5a** was obtained in 90% yield (330 mg) from triazole **4a** (407 mg, 1.0 mmol) according to the general *procedure A* as a colorless crystals; mp: 123−125°C (lit.[12] 123−125 °C); R_f = 0.62 ($CHCl_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6): δ 2.45 (s, 3H), 3.26−3.34 (m, 4H), 3.53−3.62 (m, 4H), 7.37 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 8.28 (s, 1 H), 9.03 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 20.9, 53.0, 64.9, 126.2, 129.5, 136.1, 142.8, 156.6, 170.2. IR (ATR, ZnSe, cm^{-1}): ν 3400, 3291, 3222, 2918, 2714, 1642, 1549, 1496, 1442, 1273, 1143. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}N_5O_3S_2$ 368.0846; Found 368.0848.

Compound **5a** was obtained in 83% yield (305 mg) from triazole **4a** (407 mg, 1.0 mmol) according to the general *procedure B*.

*(Z)-5-(4-Benzylpiperidin-1-yl)-N'-(phenylsulfonyl)-1,2,3-thiadiazole-4-carboximidamide (**5b**)*. Compound **5b** was obtained in 86% yield (190 mg) from triazole **4b** (241 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 128–129 °C; R_f = 0.60 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.17−1.27 (m, 2H), 1.46 (d, J = 12.0 Hz, 2H), 1.60−1.71 (m, 1H), 2.47−2.49 (m, 2H), 2.86−2.93 (m, 2H), 3.53 (br. s, 1H), 3.56 (br. s, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 8.0 Hz, 1H), 7.27 (t, J = 8.0 Hz, 2H), 7.47−7.56 (m, 3H), 7.87−7.89 (m, 2H), 8.27 (br. s, 1H), 8.97 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 30.5, 35.6, 41.6, 53.9, 125.9, 126.2, 128.2, 128.9, 129.0, 132.4, 135.7, 139.7, 141.9, 157.3, 169.6. IR (ATR, ZnSe,

cm^{-1}): ν 3437, 3328, 2940, 1601, 1528, 1492, 1444, 1215, 1137. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{24}N_5O_2S_2$ 442.1366; Found 442.1364.

(Z)-N'-(Phenylsulfonyl)-5-(morpholin-1-yl)-1,2,3-thiadiazole-4-carboximidamide ***(5c)***.

Compound **5c** was obtained in 85% yield (353 mg) from triazole **4c** (393 mg, 1.0 mmol) according to the general *procedure A* as a colorless crystals; mp: 190–192 °C; R_f = 0.59 ($CHCl_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 3.23−3.28 (m, 4H), 3.49−3.54 (m, 4H), 7.54−7.63 (m, 3H), 7.89−7.91 (m, 2H), 8.76 (s, 1 H), 9.07 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 52.9, 65.0, 126.2, 129.1, 132.5, 136.3, 141.8, 156.8, 170.2. IR (ATR, ZnSe, cm^{-1}): ν 3437, 3327, 2989, 2922, 1617, 1543, 1496, 1442, 1214, 1163. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{16}N_5O_3S_2$ 354.0689; Found 354.0691.

Compound **5c** was obtained in (91% yield, 321 mg) from triazole **4c** (393 mg, 1.0 mmol) according to the general *procedure B*.

(Z)-N'-((4-Methoxyphenyl)sulfonyl)-5-(morpholin-1-yl)-1,2,3-thiadiazole-4-carboximidamide ***(5d)***. Compound **5d** was obtained in 84% yield (322 mg) from triazole **4d** (423 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 165−167 °C; R_f = 0.59 ($CHCl_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6): δ 3.22−3.27 (m, 4H), 3.53−3.59 (m, 4H), 3.84 (s, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.0 Hz, 2H), 8.36 (s, 1 H), 9.14 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 53.0, 55.7, 65.0, 114.2, 128.4, 133.7, 136.4, 156.4, 162.3, 170.2. IR (ATR, ZnSe, cm^{-1}): ν 3418, 3320, 3220, 2939, 2870, 1620, 1552, 1496, 1255, 1084. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{18}N_5O_4S_2$ 384.0795; Found 384.0793.

Compound **5d** was obtained in 89% yield (343 mg) from triazole **4d** (423 mg, 1.0 mmol) according to the general *procedure B*.

(Z)-N'-((4-Fluorophenyl)sulfonyl)-5-(morpholin-1-yl)-1,2,3-thiadiazole-4-carboximidamide ***(5e)***.

Compound **5e** was obtained in 89% yield (332 mg) from triazole **4e** (411 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 180−182 °C; R_f = 0.65

(CHCl$_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6:CHCl$_3$): δ 3.24−3.36 (m, 4H), 3.54−3.65 (m, 4H), 7.27−7.38 (m, 2H), 7.91−8.01 (m, 2H), 8.30 (s, 1 H), 9.10 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 53.0, 65.0, 116.3 (d, J = 22.0 Hz), 129.3 (d, J = 10.0 Hz), 136.2, 138.4 (d, J = 3.0 Hz), 156.9, 164.2 (d, J = 250.0 Hz), 170.3. IR (ATR, ZnSe, cm^{-1}): ν 3400, 3292, 3200, 2945, 2880, 1632, 1552, 1489, 1440, 1273, 1221, 1110. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{15}FN_5O_3S_2$ 372.0595; Found 372.0594.

Compound **5e** was obtained in 83% yield (308 mg) from triazole **4e** (411 mg, 1.0 mmol) according to the general *procedure B*.

(Z)-N'-(Phenylsulfonyl)-5-(pyrrolidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide ***(5f)***. Compound **5f** was obtained in 90% yield (304 mg) from triazole **4f** (377 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 196−198 °C; R_f = 0.77 (CHCl$_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6): δ 1.86−2.01 (m, 4H), 3.22−3.34 (m, 4H), 7.51−7.60 (m, 3H), 7.88−7.99 (m, 2H), 8.17 (s, 1 H), 8.96 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 25.7, 55.5, 126.2, 129.0, 132.3, 134.1, 142.1, 157.0, 164.9. IR (ATR, ZnSe, cm^{-1}): ν 3427, 3315, 3220, 3025, 2857, 1629, 1553, 1514, 1446, 1279, 1140. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{16}N_5O_2S_2$ 338.0740; Found 338.0741.

Compound **5f** was obtained in 85% yield (286 mg) from triazole **4f** (377 mg, 1.0 mmol) according to the general *procedure B*.

(Z)-5-(Pyrrolidin-1-yl)-N'-tosyl-1,2,3-thiadiazole-4-carboximidamide ***(5g)***. Compound **5g** was obtained in 90% yield (316 mg) from triazole **4g** (391 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 163−165 °C (lit. 163−165°C); R_f = 0.79 (CHCl$_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6): δ 1.83−2.03 (m, 4H), 2.41 (s, 3H), 3.21−3.43 (m, 4H), 7.31 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 8.11(s, 1 H), 8.84 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 20.9, 25.7, 55.5, 126.2, 129.3, 134.1, 139.3, 142.6, 156.8, 164.9. IR (ATR, ZnSe, cm^{-1}): ν 3407, 3311,

3196, 2938, 1631, 1550, 1512, 1454, 1259, 1140, 1084. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}N_5O_2S_2$ 352.0896; Found 352.0896.

Compound **5g** was obtained in 94% yield (330 mg) from triazole **4g** (391 mg, 1.0 mmol) according to the general *procedure B*.

*(Z)-N'-(4-Methoxyphenylsulfonyl)-5-(pyrrolidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide (**5h**).* Compound **5h** was obtained in 88% yield (323 mg) from triazole **4h** (407 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 225−227 °C; R_f = 0.77 ($CHCl_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.93−1.95 (m, 4H), 3.27−3.30 (m, 4H), 3.84 (s, 3H), 7.01 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 8.10 (s, 1 H), 8.87 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 25.5, 55.4, 55.5, 113.9, 128.2, 134.0, 134.1, 156.5, 162.0, 164.7. IR (ATR, ZnSe, cm^{-1}): ν 3300, 2971, 1580, 1510, 1453, 1237, 1150. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}N_5O_3S_2$ 368.0846; Found 368.0842.

Compound **5h** was obtained in 90% yield (332 mg) from triazole **4h** (407 mg, 1.0 mmol) according to the general procedure **B**.

*(Z)-N'-(4-Fluorophenylsulfonyl)-5-(pyrrolidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide (**5i**).* Compound **5i** was obtained in 85% yield (302 mg) from triazole **4i** (395 mg, 1.0 mmol) according to the general *procedure A* as a colorless powder; mp: 168−170 °C; R_f = 0.78 ($CHCl_3$/EtOAc, 6:1). ^{1}H NMR (DMSO-d_6): δ 1.87−1.90 (m, 4H), 3.22−3.24 (m, 4H), 7.39−7.43 (m, 2H,), 7.96−7.99 (m, 2H), 8.33 (s, 1 H), 9.14 (s, 1 H). ^{13}C NMR (DMSO-d_6): δ 25.6, 55.4, 115.9 (d, J = 23.0 Hz), 129.1 (d, J = 9.0 Hz), 133.9, 138.6 (d, J = 3.0 Hz), 157.1, 164.0 (d, J = 249.0 Hz), 164.9. IR (ATR, ZnSe, cm^{-1}): ν 3427, 3264, 3025, 2857, 1632, 1551, 1514, 1490, 1452, 1279, 1235, 1140, 1013. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}FN_5O_2S_2$ 356.0646; Found 356.0643.

Compound **5i** was obtained in 87% yield (310 mg) from triazole **4i** (395 mg, 1.0 mmol) according to the general *procedure B*.

*(Z)-5-(4-Benzylpiperidin-1-yl)-N'-tosyl-1,2,3-thiadiazole-4-carboximidamide (**5j**)*. Compound **5j** was obtained in 94% yield (215 mg) from triazole **4j** (205 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 137–138 °C; R_f = 0.57 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.19−1.29 (m, 2H), 1.47−1.50 (m, 2H), 1.62−1.72 (m, 1H), 2.36 (s, 3H), 2.48−2.49 (m, 2H), 2.86−2.93 (m, 2H), 3.52 (br. s, 1H), 3.55 (br. s, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.17 (t, J = 8.0 Hz, 1H,), 7.27 (t, J = 8.0 Hz, 4H), 7.76 (d, J = 8.0 Hz, 2H), 8.23 (br. s, 1H), 8.94 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.9, 30.5, 35.6, 41.7, 53.9, 125.9, 126.3, 128.2, 128.9, 129.3, 135.8, 139.1, 139.7, 142.6, 157.2, 169.6. IR (ATR, ZnSe, cm^{-1}): ν 3420, 3302, 2941, 2907, 2844, 1612, 1529, 1494, 1452, 1282, 1253, 1154, 1106. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{26}N_5O_2S_2$ 456.1522; Found 456.1522.

Compound **5j** was obtained in 72% yield (132 mg) from triazole **4j** (200 mg, 0.40 mmol) according to the general *procedure C.*

*(Z)-5-(4-Benzylpiperidin-1-yl)-N'-((4-fluorophenyl)sulfonyl)-1,2,3-thiadiazole-4-carboximidamide (**5k**)*. Compound **5k** was obtained in 98% yield (226 mg) from triazole **4k** (250 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 148–149 °C; R_f = 0.60 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.10−1.21 (m, 2H), 1.41−1.44 (m, 2H), 1.60−1.71 (m, 1H), 2.46 (d, J = 8.0 Hz, 2H), 2.98−2.98 (m, 2H), 3.42 (br. s, 1H), 3.45 (br. s, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 8.0 Hz, 1H), 7.30 (t, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.95−7.98 (m, 2H), 8.45 (br. s, 1H), 9.20 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 30.5, 35.7, 41.7, 54.0, 116.1 (d, J = 22.0 Hz), 125.0, 128.2, 129.0, 129.2 (d, J = 10.0 Hz), 135.7, 138.1 (d, J = 3.0 Hz), 157.4, 164.1 (d, J = 249.0 Hz), 169.6. IR (ATR, ZnSe, cm^{-1}): ν 3406, 3307, 3222, 2937, 2920, 2845, 1635, 1491, 1445, 1224, 1172, 1083, 1056. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{23}FN_5O_2S_2$ 460.1272; Found 460.1271.

Compound **5k** was obtained in 71% yield (130 mg) from triazole **4k** (200 mg, 0.40 mmol) according to the general *procedure C*.

*(Z)-N'-(Phenylsulfonyl)-5-(piperidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide (**5l**)*. Compound **5l** was obtained in 75% yield (132 mg) from triazole **4l** (196 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 163–164 °C; R_f = 0.42 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.53 (br. s, 6H), 3.25 (br. s, 4H), 7.51−7.60 (m, 3H), 7.89−7.91 (m, 2H), 8.28 (br. s, 1H), 8.98 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 22.3, 24.5, 54.7, 126.2, 129.0, 132.4, 135.6, 142.0, 157.5, 169.7. IR (ATR, ZnSe, cm^{-1}): ν 3428, 3314, 3220, 2943, 2923, 2842, 1630, 1500, 1442, 1140. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}N_5O_2S_2$ 352.0896; Found 352.0894.

Compound **5l** was obtained in 72% yield (130 mg) from triazole **4l** (200 mg, 0.40 mmol) according to the general *procedure C*.

*(Z)-5-(Piperidin-1-yl)-N'-tosyl-1,2,3-thiadiazole-4-carboximidamide (**5m**)*. Compound **5m** was obtained in 87% yield (159 mg) from triazole **4m** (203 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 147–148 °C; R_f = 0.35 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.55 (br. s, 6H), 2.41 (s, 3H), 3.26 (br. s, 4H), 7.32 (d, 2H, J = 8.0 Hz), 7.78 (d, 2H, J = 8.0 Hz), 8.22 (br. s, 1H), 8.92 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 21.0, 22.3, 24.5, 54.7, 126.3, 129.4, 135.7, 139.2, 142.7, 157.3, 169.7. ^{1}H NMR (CD_3OD-d_4): δ 1.57 (br. s, 6H), 2.43 (s, 3H), 3.27 (br. s, 4H), 4.83 (s, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.2 Hz, 2H). IR (ATR, ZnSe, cm^{-1}): ν 3418, 3301, 3215, 2944, 2850, 1627, 1548, 1494, 1441, 1278, 1256, 1210, 1138, 1105. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_5O_2S_2$ 366.1053; Found 366.1050.

Compound **5m** was obtained in 78% yield (140 mg) from triazole **4m** (200 mg, 0.49 mmol) according to the general *procedure C*.

*(Z)-N'-((4-Methoxyphenyl)sulfonyl)-5-(piperidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide (**5n**)*. Compound **5n** was obtained in 92% yield (176 mg) from triazole **4n** (211 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 150–151 °C; R_f = 0.40

(EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.49 (br. s, 6H), 3.20 (br. s, 4H), 3.83 (s, 3H), 7.10 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 8.33 (br. s, 1H), 9.07 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 22.3, 24.4, 54.7, 55.6, 114.0, 128.3, 133.9, 135.6, 156.9, 162.1, 169.6. IR (ATR, ZnSe, cm^{-1}): ν 3417, 3306, 3222, 2939, 2844, 1633, 1549, 1495, 1441, 1380, 1275, 1181, 1109. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_5O_3S_2$ 382.1002; Found 382.1003.

Compound **5n** was obtained in 80% yield (146 mg) from triazole **4n** (200 mg, 0.47 mmol) according to the general *procedure C.*

*(Z)-N'-((4-Fluorophenyl)sulfonyl)-5-(piperidin-1-yl)-1,2,3-thiadiazole-4-carboximidamide (**5o**).* Compound **5o** was obtained in 86% yield (159 mg) from triazole **4o** (205 mg, 0.50 mmol) according to the general *procedure A* as a colorless crystals; mp: 158–159 °C; R_f = 0.51 (EtOAc/PE, 1:1). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.57 (br. s, 6H), 3.27 (br. s, 4H), 7.26−7.32 (m, 2H), 7.93−7.98 (m, 2H), 8.27 (br. s, 1H), 9.01 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 22.3, 24.5, 54.7, 116.1 (d, J = 22.0 Hz), 129.3 (d, J = 9.0 Hz), 135.5, 138.5 (d, J = 3.0 Hz), 157.6, 164.2 (d, J = 249.0 Hz), 169.7. IR (ATR, ZnSe, cm^{-1}): ν 3441, 3333, 2949, 3091, 2931, 2840, 1603, 1537, 1491, 1440, 1327, 1306, 1130, 1090. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}FN_5O_2S_2$ 370.0802; Found 370.0802.

Compound **5o** was obtained in 75% yield (135 mg) from triazole **4o** (200 mg, 0.49 mmol) according to the general *procedure C.*

*(Z)-5-(Azepan-1-yl)-N'-(phenylsulfonyl)-1,2,3-thiadiazole-4-carboximidamide (**5p**).* Compound **5p** was obtained in 93% yield (167 mg) from triazole **4p** (200 mg, 0.49 mmol) according to the general *procedure A* as a colorless crystals; mp: 153–155 °C; R_f = 0.34 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.49 (br. s, 4H), 1.63 (br. s, 4H), 3.39−3.42 (m, 4H), 7.51−7.61 (m, 3H), 7.87−7.89 (m, 2H), 8.32 (br. s, 1H), 9.03 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 26.1, 26.6, 55.8, 126.1, 128.8, 132.2, 134.3, 142.2, 158.4, 166.7. IR (ATR, ZnSe, cm^{-1}): ν 3408, 3313, 3218, 2944, 2917, 2856, 1628, 1543, 1511, 1443, 1274, 1080. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_5O_2S_2$ 366.1053; Found 366.1052.

(Z)-5-(Azepan-1-yl)-N'-tosyl-1,2,3-thiadiazole-4-carboximidamide ***(5q)***. Compound **5q** was obtained in 93% yield (168 mg) from triazole **4q** (200 mg, 0.48 mmol) according to the general *procedure A* as a colorless crystals; mp: 132–135 °C; R_f = 0.31 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.47 (br. s, 4H), 1.62 (br. s, 4H), 2.40 (s, 3H), 3.41−3.43 (m, 4H), 7.33 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 8.29 (br. s, 1H), 9.03 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.9, 26.1, 26.7, 55.8, 126.3, 129.3, 134.4, 139.2, 142.6, 158.3, 166.7. IR (ATR, ZnSe, cm^{-1}): ν 3453, 3315, 3219, 2932, 2852, 1600, 1515, 1435, 1268, 1046. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}N_5O_2S_2$ 380.1209; Found 380.1210.

(Z)-5-(Azepan-1-yl)-N'-(4-methoxyphenylsulfonyl)-1,2,3-thiadiazole-4-carboximidamide ***(5r)***. Compound **5r** was obtained in 90% yield (163 mg) from triazole **4r** (200 mg, 0.46 mmol) according to the general *procedure A* as a colorless crystals; mp: 129–131 °C; R_f = 0.20 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.49−1.53 (m, 4H), 1.65 (br. s, 4H), 3.40−3.43 (m, 4H), 3.84 (s, 3H), 7.01 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 8.23 (br. s, 1H), 8.93 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 26.1, 26.6, 55.5, 55.8, 114.0, 128.3, 133.9, 134.4, 157.9, 162.2, 166.7. IR (ATR, ZnSe, cm^{-1}): ν 3433, 3306, 3200, 2930, 1631, 1564, 1513, 1449, 1254, 1196. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}N_5O_3S_2$ 396.1159; Found 396.1158.

(Z)-5-(Azepan-1-yl)-N'-(4-fluorophenylsulfonyl)-1,2,3-thiadiazole-4-carboximidamide ***(5s)***. Compound **5s** was obtained in 85% yield (154 mg) from triazole **4s** (200 mg, 0.47 mmol) according to the general *procedure A* as a colorless crystals; mp: 137–139 °C; R_f = 0.22 (EtOAc/PE, 1:2). ^{1}H NMR (DMSO-d_6:$CHCl_3$): δ 1.50−1.53 (m, 4H), 1.67 (br. s, 4H), 3.42−3.45 (m, 4H), 7.26−7.31 (m, 2H), 7.91−7.96 (m, 2H), 8.32 (br. s, 1H), 9.05 (br. s, 1H). ^{13}C NMR (DMSO-d_6): δ 26.1, 26.6, 55.8, 115.9 (d, J = 22.0 Hz), 129.1 (d, J = 8.0 Hz), 134.2, 138.6 (d, J = 3.0 Hz), 158.6, 164.0 (d, J = 250.0 Hz), 166.8. IR (ATR, ZnSe, cm^{-1}): ν 3411, 3312, 3219, 2921, 2853, 1629, 1539, 1509, 1436, 1272, 1180. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{19}N_5FO_2S_2$ 384.0959; Found 384.0959.

General Procedure for the Rearrangement of Thiadiazoles 5a-s to 1,2,3-triazoles 4a-s by EtONa Action. To a stirred solution of sodium ethoxide, freshly prepared from Na (59 mg, 2.5 mmol) and anhydrous EtOH (2 mL) at ambient temperature corresponding thiadiazole **5** (0.50 mmol) was added. The resulting solution was stirred for 1 h. The formed precipitate was filtered off, washed with Et_2O (2 mL) and dried at 80°C during 8 h to obtain corresponding triazole **4** as colorless powder (see Table S2 in Supporting Information).

*Determination of **17/4m/5m** ratio in CD_3OD in the presence of bases.* To solution of compound **5m** (10 mg, 0.027 mmol) in CD_3OD (0.5 mL) was added an appropriate amount of a base in 0.5 mL of CD_3OD: (a) 3.0 (0.1 equiv); 31.5 (1.0 equiv); 157.0 (5.0 equiv) μL of 12.1% solution of Et_3N; (b) 2.0 (0.1 equiv); 16.0 (1.0 equiv); 80.0 (5.0 equiv) μL of 10.8% solution of CD_3ONa and the mixture was maintained at 25 °C for 24 h. Then the ratios of **17**:**4m:5m** were determined from integral intensity of signals in ^{1}H NMR spectra at 7.22 (**17**) (d, J = 8.0 Hz, $2H_{Ar}$) / 7.11 (**4m**) (d, J = 8.0 Hz, $2H_{Ar}$) / 7.38 (**5m**) (d, J = 8.0 Hz, $2H_{Ar}$) or 7.65 (**17**) (d, J = 8.0 Hz, $2H_{Ar}$) / 7.73 (**4m**) (d, J = 8.0 Hz, $2H_{Ar}$) / 7.86 (**5m**) (d, J = 8.0 Hz, $2H_{Ar}$). Compound **4m** is registered in experiments with 5.0 equiv of sodium ethoxide and compound **17** is registered in experiment with triethylamine and 0.1 or 1.0 equiv of sodium ethoxide. The ratios of the products are listed in Table 5.

*4-Methyl-N-(4-piperidine-1-carbonothioyl)-1H-1,2,3-triazol-5-yl)benzenesulfonamide (**17**).*

To solution of compound **5m** (10 mg, 0.027 mmol) in CD_3OD (0.5 mL) in NMR tube was added 26 μL of 10% solution of CF_3COOH in 0.5 mL of CD_3OD after 4 h passed the protons signals of compound **17** was registered.

^{1}H NMR (CD_3OD-d_4, 400 MHz): δ 1.38 (br. s, 2H), 1.66 (br. s, 4H), 2.36 (s, 3H), 3.60 (br. s, 2H), 4.14 (br. s, 2H), 4.84 (s, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H).

*Determination of half-time of transformation of **5m** to **4m/17** in CD_3OD in the presence of DBU or* CD_3ONa*.* To solution of compound **5m** (10 mg, 0.027 mmol) in CD_3OD (0.5 mL) was added

an appropriate amount of a base in 0.5 mL of CD_3OD: (a) 45.0 (1.0 equiv) μL of 9.1% solution of DBU; (b) 16.0 (1.0 equiv); 80.0 (5.0 equiv) μL of 10.8% solution of CD_3ONa. Then ^1H NMR spectra were recorded in 0; 6; 8; 9; 15; 20; 54; 161; 219; 384; 1469 min for reaction in the presence of 1.0. equiv DBU; in 0; 5; 9; 14; 19; 52; 87; 123; 201; 250; 466; 1450 min for reaction in the presence of 1.0 equiv of CD_3ONa and in 7; 10; 16; 21; 51; 94; 172 min for reaction in the presence of 5.0 equiv of CD_3ONa. Concentrations of **5m** were determined from integral intensity of signal at 7.38 (2H, Ar) or at 7.86 (2H, Ar) in ^1H NMR spectra. The half time of the reactions were calculated from the chart of change of concentration of **5m** as 22 (5.0 equiv of CD_3ONa), 53 (1.0 equiv of CD_3ONa), 95 (1.0 equiv of DBU) depending on the time of reaction in minutes (see p. 17 and Figure S4 in Supporting Information).

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Supporting Information: ^1H and ^{13}C spectra of all new compounds, X-ray diffraction study of **3a** and **5m**, rearrangement of **5a–s** to **4a–s** by treatment with EtONa, calculation details (PDF).

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