Reactions of 5-dialkylamino-1,2,3-thiadiazole-4-carbaldehydes with amines as a method for the synthesis of 1,2,3-triazole-4-carbothioamides ✽

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A method for the synthesis of previously inaccessible 5-dialkylamino-substituted 1,2,3-thiadiazole-4-carbaldehydes was developed. Ring transformation in these compounds induced by primary aliphatic and aromatic amines, hydroxylamines, and *N*-substituted hydrazines resulted in the synthesis of a broad range of 1,2,3-triazole-4-carbothioamide.

Key words: 1,2,3-triazole, 1,2,3-thiadiazole, thioamides, Cornfort rearrangement, nucleophilic substitution, reduction, oxidation.

Thioamides are highly reactive compounds, which find extensive use in organic synthesis,[1] medicine,[2] and engineering.[3] However, the most popular methods for their synthesis such as thionation[4] or sulfhydration of nitriles[5] are inapplicable, in some cases, to heterocyclic thioamides, because under the reaction conditions, heterocycles can undergo various transformations.[6] The rearrangements of some heterocycles into other ones represent a convenient route to compounds that are difficult or impossible to prepare by other methods;[7] however, rearrangements are seldom used for targeted synthesis of heterocyclic systems.[8] As a continuation of our studies dealing with rearrangements of 1,2,3-thiadiazoles,[9] in this work, we present a method for the synthesis of 1,2,3-triazole-4-carbothioamides **1**.

We developed a synthetic route to 1,2,3-triazole-4-carbothioamides **1** whose key step was the rearrangement of imines **2**, which are produced in the reaction of 1,2,3-thiadiazole-4-carbaldehydes **3** with primary amines (Cornfort rearrangement). In a reported example where this method was used for the synthesis of 1,2,3-triazole-4-carbothioamide derivatives, 5-chloro- or 5-*tert*-butylthio-1,2,3-thiadiazole-4-carbaldehyde was taken as the starting compound.[10,11] However, this approach restricts the scope of the method to the triazoles with identical substituents in position 1 of the ring and the thioamide function, because the substitution occurs simultaneously at the two reaction centers. We used aldehydes **3** for the synthesis of triazoles with various substituents in position 1 and the thioamide group in position 4 of the ring. It should be noted that aldehydes **3** have not been reported. They can be prepared by oxidation of the CH_2OH group in 5-amino-4-hydroxymethyl-1,2,3-thiadiazoles **4**. This method has been used to synthesize ethyl 5-formyl-1,2,3-thiadiazole-4-carboxylate.[12] The existing methods for the preparation of 4-hydroxymethyl-1,2,3-thiadiazoles include nucleophilic substitution of an OH group for the halogen atom in the reaction of 4-bromomethyl-1,2,3-thiadiazole with NaOH and the reaction of 4-lithio-1,2,3-thiadiazole with formaldehyde.[13] The scope of both reactions is markedly limited as regards the structure of the starting compounds, and they have not found wide use for the synthesis of aldehydes of the 1,2,3-triadiazole series.

We synthesized compounds **4** in two steps from available[14] ethyl 5-chloro-1,2,3-thiadiazole-4-carboxylate (**5**).

The nucleophilic replacement of the chlorine atom in compound **5** in reactions with secondary amines gave 5-amino-1,2,3-thiadiazoles **6a—e** (Scheme 1). It is known that these reactions can be accompanied by side processes;[15—16] therefore, the reaction was carried out in ethanol with cooling. Under these conditions, the ester groups in compounds **6a—e** were not amidated, and these compounds were obtained in 50—85% yields.

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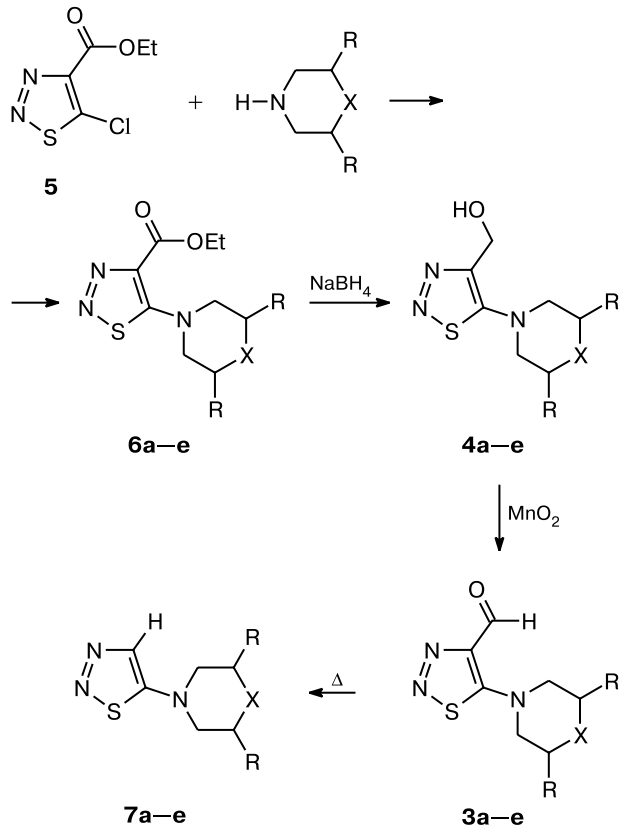
Scheme 1



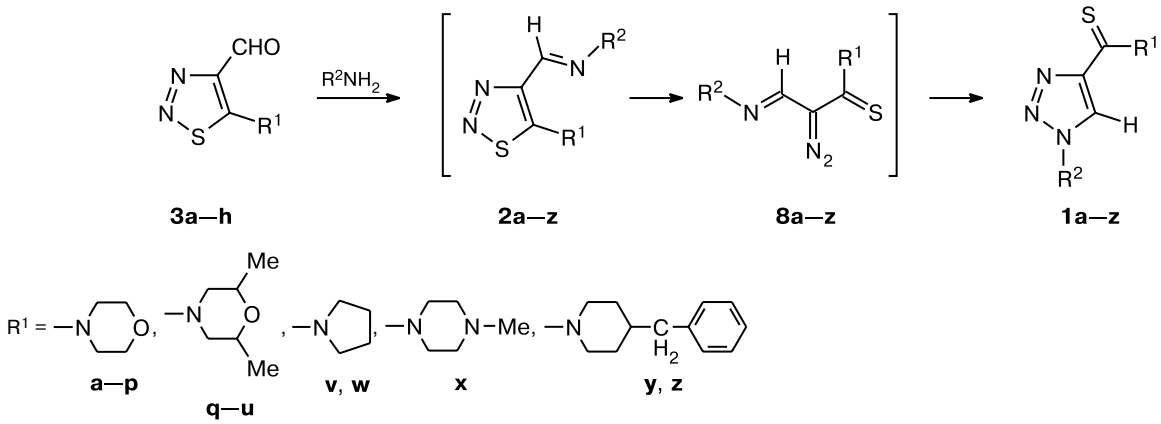
3, 4, 6, 7	a	b	c	d	e
R	H	Me	H	H	H
X	O	O	—	NMe	$CHCH_2Ph$

4-Hydroxymethyl-1,2,3-thiadiazoles **4a—e** were prepared in 44—80% yields by the reduction of the ethoxycarbonyl group in compounds **6a—e** with sodium borohydride.[17] According to our data, unlike those published previously,[18] the reduction involves only the ethoxycarbonyl group and does not affect the thiadiazole ring. The oxidation of the hydroxymethylene group of compounds **4a—e** to an aldehyde group was performed by active manganese dioxide in chloroform at ~20 °C. Note that aldehydes **3a—e** are thermally labile compounds and are easily deformylated: on heating in solvents such as benzene, toluene, or ethanol, 4*H*-1,2,3-thiadiazoles **7a—c** are formed.

The reactions of 1,2,3-thiadiazole-4-carbaldehydes **3a—h** with amines and hydrazines were carried out at ~20 °C in ethanol. However, imines **2** have not been isolated, as under these conditions, they underwent the Cornfort rearrangement through intermediate diazo compounds **8a—z** (Scheme 2). Thus, two successive condensations and ring transformation provided the target 1,2,3-triazole-4-carbothioamides **1a—z**.

The structure of the compounds obtained was confirmed by IR, ^1H NMR, and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis data. The main clues pointing to the triazole structure are the chemical shifts of the ^{13}C NMR signals of the thioamide carbon atom in the region of 184.8 ppm and the C(4) and C(5) atoms of the triazole ring at 147 and 122.8 ppm, respectively. The signal of the proton of the triazole ring occurs at 8.15 ppm as a singlet. The proton and carbon chemical shifts are consistent with published data for 1,2,3-triazole-4-carbothioamides.[19] In the case of 1,2,3-thiadiazole **2**, the signals for the C(4) and C(5) atoms of the thiadiazole ring should have been observed at 138—141 and 165—166 ppm, that for the carbon atom of the CH=N group would be at 140—142 ppm, and the proton signal for the CH=N group would be at 9.1—9.5 ppm.[19]

Scheme 2



R^2 = OH (**a**), OMe (**b**), $NHC_6H_3(NO_2)_2$-2,4 (**c**), C_6H_4OMe-2 (**d**, **q**, **v**, **t**), C_6H_4F-4 (**e**, **r**), Me (**f**), $C_6H_4CF_3$-2 (**g**), C_6H_4OMe-3 (**h**), C_6H_4OMe-4 (**i**), C_6H_{11} (**j**), C_6H_4F-2 (**k**), C_6H_4OH-2 (**l**, **s**), C_6H_4Br-4 (**m**), CH_2Ph (**n**, **t**, **w**, **y**), $NHSO_2C_6H_4Me$-4 (**o**), C_6H_4Me-4 (**p**, **u**, **z**), C_6H_4Me-3 (**x**)

Thus, by using a new approach to the synthesis of 5-dialkylamino-1,2,3-thiadiazole-4-carbaldehydes, we have developed a convenient method for the synthesis of a broad range of 1,2,3-triazole-4-carbothioamide derivatives.

Experimental

The course of the reactions was monitored and the purity of the synthesized compounds was checked by TLC on Silufol UV-254 plates in chloroform and in the chloroform—ethanol (9 : 1, 15 : 1, 20 : 1) and ethyl acetate—hexane (1.5 : 2, 1 : 2) solvent systems. IR spectra were measured on a UR-20 spectrophotometer in KBr pellets; and NMR spectra were recorded on Bruker WM-250 (250 MHz for ^{1}H) and Bruker DRX-400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) instruments with Me_4Si as the internal standard; and mass spectra were run on Varian MAT 311A and Finnigan MAT 8200 spectrometers with an ionizing voltage of 70 eV and with direct sample injection into the ion source. The solvents were purified by standard procedures. Ethyl 5-amino-1,2,3-thiadiazole-4-carboxylate[14] and

Table 1. Physicochemical characteristics of the synthesized compounds

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) N	Found / Calculated (%) S	Molecular formula	Mass spectrum, *m/z* (I_{rel} (%))
1a	89	112	26.03 26.15	14.42 14.97	$C_7H_{10}N_4O_2S$	214 (27)
1b	88	112	24.55 24.54	14.42 14.05	$C_8H_{12}N_4O_2S$	228 (59)
1c	76	182	25.5 25.85	8.50 8.45	$C_{13}H_{13}N_7O_5S$	379 (3)
1d	53	160	18.66 18.40	10.59 10.54	$C_{14}H_{16}N_4O_2S$	304 (12)
1e	38	146	18.82 19.17	11.30 10.97	$C_{13}H_{13}FN_3OS$	292 (47)
1f	40	114	26.11 26.39	14.93 15.11	$C_8H_{12}N_4OS$	212 (42)
1g	85	89	16.03 16.37	9.39 9.37	$C_{14}H_{16}N_4OS$	342 (70)
1h	92	128	19.03 18.41	10.39 10.53	$C_{14}H_{16}N_4O_2S$	304 (33)
1i	91	92	18.39 18.41	10.89 10.53	$C_{14}H_{16}N_4O_2S$	304 (76)
1j	62	92	19.79 19.98	11.99 11.44	$C_{13}H_{20}N_4OS$	280 (85)
1k	62	92	18.79 19.17	11.15 10.97	$C_{13}H_{13}FN_4OS$	292 (35)
1l	73	164	19.17 19.30	11.01 11.04	$C_{13}H_{14}N_4O_2S$	290 (12)
1m	85	180	16.03 15.86	9.25 9.08	$C_{13}H_{13}BrN_4OS$	—
1n	76	140	20.00 19.43	10.81 11.12	$C_{14}H_{16}N_4OS$	288 (16)
1o	57	112	19.55 19.06	17.42 17.45	$C_{14}H_{17}N_5O_3S_2$	—
1p	86	150	19.32 19.43	11.28 11.12	$C_{14}H_{16}N_4OS$	288 (25)
1q	92	112	17.58 17.71	10.22 10.13	$C_{16}H_{20}N_4OS$	316 (12)
1r	67	130	17.63 17.71	10.18 10.13	$C_{16}H_{20}N_4OS$	316 (25)
1s	52	114	16.72 16.85	9.43 9.65	$C_{16}H_{20}N_4O_2S$	332 (13)
1t	60	130	17.33 17.49	10.13 10.01	$C_{15}H_{17}FN_4OS$	320 (8)
1u	60	130	17.79 17.60	10.45 10.07	$C_{15}H_{18}N_4O_2S$	
1v	75	104	20.90 20.57	11.80 11.77	$C_{14}H_{16}N_4S$	272 (10)
1w	66	106	19.78 19.43	11.17 11.12	$C_{14}H_{16}N_4OS$	288 (12)
1x	95	102	23.08 23.23	10.55 10.64	$C_{15}H_{19}N_5S$	301 (13)
1y	82	110	14.65 14.88	8.73 8.52	$C_{12}H_{24}N_4S$	376 (5)
1z	28	130	14.35 14.88	8.46 8.52	$C_{22}H_{24}N_4S$	376 (33)
4a	73	120	21.10 20.88	15.80 15.93	$C_7H_{11}N_3O_2S$	201 (87)
4b	44	88	18.30 18.33	13.87 13.98	$C_9H_{15}N_3O_2S$	299 (36)
4c	80	90	22.58 22.68	17.47 17.31	$C_7H_{11}N_3OS$	185 (30)
4d	76	90	26.03 26.15	15.07 14.96	$C_8H_{14}N_4OS$	—
4e	69	105	15.05 14.52	10.78 11.08	$C_{15}H_{19}N_3OS$	289 (20)
6a	85	92	17.50 17.27	12.70 13.18	$C_9H_{13}N_3O_3S$	—
6b	61	82*	15.97 15.49	12.06 11.82	$C_{11}H_{17}N_3O_3S$	—
6c	47	76—78	18.53 18.49	14.09 14.11	$C_9H_{13}N_3O_2S$	—
6d	67	62—65	21.53 21.86	12.49 12.51	$C_{10}H_{16}N_4O_2S$	—
6e	64	84	12.78 12.68	9.44 9.67	$C_{17}H_{21}N_3O_2S$	—
7a	72	90	24.90 24.54	18.78 18.73	$C_6H_9N_3OS$	171 (65)
7b	77	136	21.39 21.09	16.12 16.09	$C_8H_{13}N_3OS$	199 (20)
7c	68	80	26.79 27.07	20.51 20.66	$C_6H_9N_3S$	155 (67)

* *cf.* Ref. 19: 82 °C.

Table 2. ^{1}H NMR spectra (DMSO-d_6) of 1,2,3-triazole-4-carbothioamides **1a—z**

Compound	δ (*J*/Hz)			
	C(5)H	R^2	R^1	
			NCH_2	Other signals
1a	8.40	13.94 (br.s, 1 H, OH)	3.76 (t, 2 H, NCH_2, *J* = 4.6); 3.68 (t, 2 H, NCH_2, *J* = 4.6)	4.30 (t, 2 H, OCH_2, *J* = 4.6); 4.07 (t, 2 H, OCH_2 *J* = 4.6)
1b	8.77	4.25 (s, 3 H, OCH_3)	3.77 (t, 2 H, NCH_2, *J* = 4.9); 3.67 (t, 2 H, NCH_2, *J* = 4.9)	4.20—4.35 (m, 2 H, OCH_2); 4.03 (t, 2 H, OCH_2, *J* = 4.9)
1c	8.83	11.88 (br.s, 1 H, NH); 8.92 (d, 1 H, ArH, *J* = 2.8); 8.35 (dd, 1 H, ArH, *J* = 9.5, *J* = 2.8); 6.46 (d, 1 H, ArH, *J* = 9.5)	3.81 (t, 2 H, NCH_2, *J* = 4.6); 3.75 (t, 2 H, NCH_2, *J* = 4.6)	4.35 (t, 2 H, OCH_2, *J* = 4.6); 4.12 (t, 2 H, OCH_2, *J* = 4.6)
1d	8.77	7.67 (dd, 1 H, ArH, *J* = 6.7, *J* = 1.8); 7.55 (ddd, 1 H, ArH, *J* = 7.6, *J* = 7.9, *J* = 1.5); 7.33 (ddd, 1 H, ArH, *J* = 7.6, *J* = 7.8, *J* = 1.6); 7.16 (dd, 1 H, ArH, *J* = 7.6, *J* = 1.2); 3.87 (s, 3 H, OMe)	3.79 (t, 2 H, NCH_2, *J* = 4.6); 3.71 (t, 2 H, NCH_2, *J* = 4.6)	4.35 (t, 2 H, OCH_2, *J* = 4.6); 4.12 (t, 2 H, OCH_2, *J* = 4.6)
1e	8.55	7.77—7.72 (m, 2 H, 2 ArH); 7.29—7.81 (m, 2 H, 2 ArH)	3.94—3.82 (m, 4 H, $N(CH_2)_2$)	4.48—4.38 (m, 4 H, $O(CH_2)_2$)
1f	8.14	4.09 (s, 3 H, Me)	3.89 (t, 2 H, NCH_2, *J* = 4.6); 3.82 (t, 2 H, NCH_2, *J* = 4.6)	4.42 (t, 2 H, OCH_2 *J* = 4.6); 4.35 (t, 2 H, OCH_2, *J* = 4.6)
1g	8.86	8.05—7.78 (m, 4 H, ArH)	3.82 (t, 2 H, $N(CH)_2$ *J* = 4.5); 3.75 (t, 2 H, $N(CH)_2$, *J* = 4.5)	4.37 (t, 2 H, $O(CH)_2$, *J* = 4.5); 4.10 (t, 2 H, $O(CH)_2$, *J* = 4.5)
1h	8.58	7.43 (dd, 1 H, ArH, *J* = 8.1, *J* = 8.1); 7.26—7.34 (m, 2 H, 2 ArH); 7.0 (dd, H, ArH, *J* = 6.3, *J* = 1.5); 3.93—3.84 (m, 7 H, OCH_3 and $N(CH_2)_2$)		4.46 (t, 2 H, $O(CH)_2$, *J* = 4.8); 4.40 (t, 2 H, $O(CH)_2$, *J* = 4.8); 3.93—3.84 (m, 7 H, Me and $N(CH_2)_2$)
1i	8.50	7.65 (d, 2 H, 2 ArH, *J* = 9.2); 7.03 (d, 2 H, 2 ArH, *J* = 9.2); 3.85 (s, 3 H, OCH_3)	3.80 (t, 2 H, $N(CH)_2$, *J* = 4.4); 3.72 (t, 2 H, $N(CH)_2$, *J* = 4.4)	3.75—3.88 (m, 4 H, $O(CH_2)_2$)
1j	8.52	4.40—4.55 (m, 1 H, CH); 2.00—2.20 (m, 2 H, CH_2); 1.20—2.00 (m, 8 H, 4 (CH_2))	3.76 (t, 2 H, $N(CH)_2$, *J* = 4.9); 3.68 (t, 2 H, $N(CH)_2$, *J* = 4.9)	4.31 (t, 2 H, $O(CH)_2$, *J* = 4.9); 4.10 (t, 2 H, $O(CH)_2$, *J* = 4.9)
1k	8.91	7.88 (ddd, 1 H, ArH, *J* = 6.4, *J* = 6.0, *J* = 1.6); 7.56—7.66 (m, 2 H, 2 ArH); 7.10 (dd, 1 H, ArH, *J* = 7.6, *J* = 7.6)	3.81 (t, 2 H, $N(CH)_2$, *J* = 4.8); 3.72 (t, 2 H, $N(CH)_2$, *J* = 4.8)	4.36 (t, 2 H, $O(CH)_2$, *J* = 4.8); 4.08 (t, 2 H, $O(CH)_2$, *J* = 4.8)
1l	8.74	10.53 (уш.s, 1 H, OH); 7.69 (dd, 1 H, ArH, *J* = 8.0, *J* = 1.2); 7.29 (ddd, ArH, *J* = 8.0, *J* = 8.0, *J* = 1.6); 7.12 (dd, 1 H, ArH, *J* = 7.2, *J* = 1.2); 6.97 (ddd, 1 H, ArH, *J* = 7.2, *J* = 8.0, *J* = 1.2)	3.83 (t, 2 H, $N(CH)_2$, *J* = 4.4); 3.77 (t, $N(CH)_2$, *J* = 4.8)	4.36 (t, 2 H, $O(CH)_2$, *J* = 4.8); 4.26 (t, 2 H, $O(CH)_2$, *J* = 4.4)
1m	8.55	7.96 (d, 2 H, 2 ArH, *J* = 8.8); 7.72 (d, 2 H, 2 ArH, *J* = 8.8)	3.83 (t, 2 H, $N(CH)_2$, *J* = 4.8); 3.75 (t, 2 H, NCH_2, *J* = 4.7)	4.36 (t, 2 H, $O(CH)_2$, *J* = 4.8); 4.15 (t, 2 H, $O(CH)_2$, *J* = 4.6)
1n	8.59	7.39—7.35 (m, 5 H, Ph); 5.62 (s, 2 H, CH_2)	3.76 (t, 2 H, $N(CH)_2$, *J* = 4.8); 3.67 (t, 2 H, $N(CH)_2$, *J* = 4.9)	4.31 (t, 2 H, $O(CH)_2$, *J* = 4.9); 4.11 (t, 2 H, $O(CH)_2$, *J* = 4.8)
1o	8.42	12.00 (br.s, 1 H, NH); 7.62 (d, 2 H, 2 ArH, *J* = 8.5); 7.44 (d, 2 H, 2 ArH, *J* = 8.5); 2.42 (s, 3 H, Me)	3.76 (t, 2 H, $N(CH)_2$, *J* = 4.9); 3.67 (t, 2 H, $N(CH)_2$, *J* = 4.9)	4.28 (t, 2 H, $O(CH)_2$, *J* = 4.9); 3.91 (t, 2 H, $O(CH)_2$, *J* = 4.9)
1p	8.55	7.65 (d, 2 H, 2 ArH, *J* = 8.0); 7.61 (d, 2 H, 2 ArH, *J* = 8.0); 2.43 (s, 3 H, Me)	3.83—3.93 (m, 4 H, $N(CH_2)_2$)	4.38—4.47 (m, 4 H, $O(CH_2)_2$)
1q	8.08	7.33—7.41 (m, 5 H, Ph); 5.45—5.43 (m, 3 H, CH_2 and NCH); 5.15 (d, 1 H, NCH, *J* = 6.5); 3.04 (dd, 1 H, NCH, *J* = 13.1, *J* = 10.7); 2.83 (dd, 1 H, NCH, *J* = 13.1, *J* = 10.7)		3.73—3.81 (m, 2 H, $O(CH)_2$); 1.21 (d, 3 H, Me, *J* = 6.1)
1r	9.11	7.84 (d, 2 H, 2 ArH, *J* = 8.2); 7.41 (d, 2 H, 2 ArH, *J* = 8.2); 2.39 (s, 3 H, Me)	5.36 (dd, 1 H, NCH, *J* = 13.2, *J* = 0.6); 4.54 (d, 1 H, NCH, *J* = 13.2); 3.13 (dd, 1 H, NCH, *J* = 12.8, *J* = 10.7); 2.93 (dd, 1 H,NCH, *J* = 12.8, *J* = 10.7)	3.63—3.72 (m, 2 H, $O(CH)_2$); 1.22 (d, 3 H, Me, *J* = 6.4); 1.19 (d, 3 H, Me, *J* = 6.1)

(*to be continued*)

Table 2 (*continued*)

Compound	δ (*J*/Hz)			
	C(5)H	R^2	R^1	
			NCH_2	Other signals
1s	8.63	7.73 (dd, 1 H, ArH, *J* = 7.6, *J* = 1.6); 7.49 (ddd, 1 H, ArH, *J* = 8.5, *J* = 8.9, *J* = 1.6); 7.27 (dd, 1 H, ArH, *J* = 8.5, *J* = 0.8); 7.13 (ddd, 1 H, ArH, *J* = 7.7, *J* = 8.7, *J* = 0.9); 3.95 (s, 3 H, OMe)	5.40 (d, 1 H, NCH, *J* = 13.0); 4.91 (d, 1 H, NCH, *J* = 13.2); 3.10 (dd, 1 H, NCH, *J* = 13.0, *J* = 10.6); 2.84 (dd, 1 H, NCH, *J* = 13.0, *J* = 10.8)	3.70—3.76 (m, 2 H, $O(CH)_2$); 1.27 (d, 3 H, Me, *J* = 6.2); 1.18 (d, 3 H, Me, *J* = 6.2)
1t	8.54	7.72—7.77 (m, 2 H, 2 ArH); 7.28—7.21 (m, 2 H, 2 ArH)	5.52 (d, 1 H, NCH, *J* = 13.2); 5.08 (dd, 1 H, NCH, *J* = 13.2, *J* = 2.2); 3.11 (dd, 1 H, NCH, *J* = 12.9, *J* = 11.0); 2.89 (dd, 1 H, NCH, *J* = 13.2, *J* = 11.0)	3.76—3.87 (m, 2 H, $O(CH)_2$); 1.32 (d, 3 H, Me, *J* = 5.9); 1.24 (d, 3 H, Me, *J* = 6.3)
1u	8.76	10.63 (br.s, 1 H, OH); 7.66 (dd, 1 H, ArH, *J* = 7.9, *J* = 1.5); 7.36 (ddd, 1 H, ArH, *J* = 9.2, *J* = 8.2, *J* = 1.7); 7.13 (dd, 1 H, ArH, *J* = 8.2, *J* = 0.9); 7.00 (ddd, 1 H, ArH, *J* = 7.9, *J* = 8.6, *J* = 1.2)	5.36 (d, 1 H, NCH, *J* = 13.1); 4.66 (d, 1 H, NCH, *J* = 13.1); 3.15 (dd, 1 H, NCH, *J* = 12.5, *J* = 10.7); 2.92 (dd, 1 H, NCH, *J* = 13.1, *J* = 11.0)	3.66—3.72 (m, 2 H, $O(CH)_2$); 1.22 (d, 3 H, Me, *J* = 6.1); 1.11 (d, 3 H, Me, *J* = 6.1)
1v	8.53	7.20—7.50 (m, 5 H, 5 ArH); 5.59 (s, 2 H, CH_2)	4.12 (t, 2 H, $N(CH)_2$, *J* = 6.4); 3.86 (t, 2 H, $N(CH)_2$, *J* = 6.4)	1.90—2.10 (m, 4 H, 2 CH_2)
1w	8.69	7.69 (d, 1 H, ArH, *J* = 7.3); 7.50 (dd, 1 H, ArH, *J* = 7.0, *J* = 7.3); 7.28 (d, 1 H, ArH, *J* = 8.2); 7.13 (dd, 1 H, ArH, *J* = 7.6, *J* = 7.6); 4.19 (t, 2 H, $N(CH)_2$, *J* = 6.4); 3.81—4.10 (m, 5 H, OMe and $N(CH)_2$)		1.90—2.25 (m, 4 H, 2 CH_2)
1x	8.83	7.40—7.54 (m, 4 H, ArH); 2.18 (s, 3 H, Me)	4.34 (t, 2 H, NCH_2, *J* = 4.9); 4.04 (t, 2 H, NCH_2, *J* = 4.9)	2.45—2.54 (m, 4 H, 2 $N(CH)_2$); 2.25 (s, 3 H, NMe)
1y	8.52	7.16—7.42* (m, 10 H, 2 Ph); 5.60 (s, 2 H, CH_2)	5.33 (dd, NCH, *J* = 6.7, *J* = 4.9); 4.58 (dd, 1 H, NCH, *J* = 14.3, *J* = 4.0); 3.12—3.67 (m, 2 H, $N(CH)_2$)	2.56 (d, 2 H, CH_2, *J* = 7.0); 1.80—2.02 (m, 1 H, CH); 1.65—1.75 (m, 2 H, 2 CH); 1.24—1.39 (m, 2 H, 2 CH);**
1z	9.03	7.82 (m, 2 H, 2 ArH); 7.40 (m, 2 H, 2 ArH); 2.39 (s, 3 H, Me)	5.35 (d, 1 H, NCH, *J* = 12.5); 4.46 (d, 1 H, NCH, *J* = 12.5); 3.20—3.42 (m, 2 H, $N(CH)_2$)	7.18—7.32 (m, 5 H, Ph); 2.57 (d, 2 H, CH_2, *J* = 7.3); 1.90—2.10 (m, 1 H, CH); 1.60—1.90 (m, 2 H, 2 CH); 1.20—1.50 (m, 2 H, 2 CH)

* The signals of the Ph groups occur together with the signals of the Ph group of R^1.
** The signals of the Ph groups occur together with the signals of the benzene groups of R^2.

Table 3. ^{1}H NMR spectra of 1,2,3-thiadiazoles **4a—e**

Compound	Solvent	δ (*J*/Hz)		
		CH_2O	OH	Other signals
4a	$CDCl_3$	5.00 (d, *J* = 5.5)	2.48 (t, *J* = 5.5)	3.34—3.39 (m, $N(CH_2)_2$); 3.35—3.88 (m, 4 H, $O(CH_2)_2$)
4b	$CDCl_3$	5.00 (d, *J* = 6.1)	2.34 (t, *J* = 6.1)	3.51 (dd, 2 H, 2NCH, *J* =11.9, *J* =1.5); 2.75 (dd, 2 H, 2 NCH, *J* = 11.9, *J* = 10.7); 33.77—3.89 (m, 2 H, $O(CH)_2$); 1.24 (d, 6 H, 2 Me, *J* = 6.4)
4c	DMSO-d_6	4.80 (d, *J* = 4.9)	5.24 (t, *J* = 4.9)	3.48—3.53 (m, 4 H, $N(CH_2)_2$); 1.98—2.03 (m, 4 H, 2 CH_2)
4d	DMSO-d_6	4.79 (s)	5.24 (br.s)	3.51 (t, 4 H, $N(CH_2)_2$, *J* = 5.2); 2.50 (t, 4 H, $N(CH_2)_2$, *J* = 5.2); 2.24 (s, 3 H, Me)
4e	$CDCl_3$	4.82 (br.s)	5.73 (br.s)	7.10—7.35 (m, 5 H, Ph); 5.30 (dd, 1 H, NCH, *J* = 12.2); 4.82 (br.s, 2 H, CH_2); 4.48 (dd, 1 H, NCH, *J* = 12.2); 3.20—3.43 (m, 2 H, CH_2)

Table 4. ^{1}H NMR spectra (DMSO-d_6) of 1,2,3-thiadiazoles **6a—e**

Compound	δ (*J*/Hz)		
	OCH_2	Me	Other signals
6a	4.35 (q, *J* = 7.0)	1.32 (t, *J* =7.0)	3.76 (t, 4 H, $O(CH_2)_2$, *J* = 4.8); 3.43 (t, 4 H, $N(CH_2)_2$, *J* = 4.8)
6b	4.32 (q, *J* = 7.0)	1.32 (t, *J* =7.0)	3.70—3.82 (m, 2 H, 2 CH); 3.67 (dd, 2 H, 2 CH, *J* = 12.2, *J* = 2.7); 2.81 (dd, 2 H, 2 CH, *J* = 12.2, *J* = 11.0); 1.32 (t, 3 H, $OCH_2C\underline{H}_3$, *J* = 7.0); 1.12 (d, 6 H, 2 Me, *J* = 6.4)
6c	4.33 (q, *J* = 7.0)	1.31 (t, *J* =7.0)	3.27—3.45 (t, 4 H, $N(CH_2)_2$, *J* = 6.7); 1.97—3.03 (pentete, 4 H, 2 CH_2, *J* = 6.7)
6d	4.34 (q, *J* = 7.0)	1.32 (t, *J* =7.0)	3.43 (t, 4 H, $O(CH_2)_2$, *J* = 5.0); 2.49 (t, 4 H, $N(CH_2)_2$, *J* = 5.0); 2.23 (s, 3 H, NCH_3)
6e	4.33 (q, *J* = 7.1)	1.32 (t, *J* =7.1)	7.26—7.23 (m, 2 H, ArH); 7.13—7.17 (m, 3 H, ArH); 3.70 (d, 2 H,$N(CH)_2$, *J* = 12.5); 3.13—3.05 (m, 2 H, $(CH)_2$); 2.57 (d, 2 H, CH_2, *J* = 7.1); 1.85—1.79 (m, 1 H, CH); 1.73 (dd, 2 H, $N(CH)_2$, *J* = 13.0); 1.48—1.50 (m, 2 H, $(CH)_2$)

Table 5. ^{13}C NMR spectra ($CDCl_3$) of 1,2,3-triazole-4-carbothioamides **1b—d**

Compound	δ					
	C=S	C(4)	C(5)	NCH_2	OCH_2	Other signals
1b	184.8	147.0	122.8	52.9, 50.7	66.8, 66.3	67.8 (OMe)
1c	185.6	146.4	115.8	52.6, 51.1	67.2, 66.7	140.4 ($ArNO_2$); 135.9 ($ArNO_2$); 132.8 (ArNH); 132.1 (ArH), 130.5 (ArH); 123.2 (ArH)
1d	185.1	147.7	130.3	52.8, 50.1	66.4, 65.8	151.6 (ArO); 131.1 (Ar); 125.7 (ArH); 125.0 (Ar); 120.8 (ArH); 113.0 (ArH); 56.20 (Me)

5-morpholino-1,2,3-thiadiazolecarbaldehydes **3a,b** were synthesized by known procedures.[9,20]

Synthesis of 1-substituted 1,2,3-triazole-4-carbothioamides (1) (general procedure). Amine (1 mmol) was added to a solution of 5-dialkylamino-1,2,3-thiadiazole-4-carbaldehyde **3** (1 mmol) in 2 mL of ethanol. The mixture was kept for 1 h at ~20 °C and cooled. The precipitate was filtered off and recrystallized from ethanol. The data of elemental analysis and physicochemical characteristics are given in Tables 1—5.

Synthesis of 5-dialkylamino-1,2,3-thiadiazole-4-carbaldehydes (3a—e) (general procedure). Freshly prepared active MnO_2 (10.5 g, 0.12 mmol) was added to a solution of 5-dialkylamino-4-hydroxymethyl-1,2,3-thiadiazole (**4)** (5 mmol) in 50 mL of CH_2Cl_2. The reaction mixture was stirred for 2 h at ~20 °C and filtered to remove the inorganic compounds. The solvent was evaporated *in vacuo* and the residue was triturated with hexane.

5-Pyrrolidino-1,2,3-thiadiazole-4-carbaldehyde (3c). Yield 0.47 g (47%), m.p. 46—47 °C. ^{1}H NMR (DMSO-d_6+CCl_4), δ: 10.33 (s, 1 H, CH); 3.33—3.45 (m, 4 H, $N(CH_2)_2$); 1.97—3.03 (m, 4 H, 2 CH_2). IR, ν/cm^{-1}: 1730 (C=O). MS, *m/z* (I_{rel} (%)): 199 $[M]^+$ (15). Found (%): N, 18.53; S, 14.09. $C_9H_{13}N_3O_2S$. Calculated (%): N, 18.49; S, 14.11.

5-(4-Methylpiperazino)-1,2,3-thiadiazole-4-carbaldehyde (3d). Yield 1.75 g (75%), m.p. 554 °C. ^{1}H NMR (DMSO-d_6+CCl_4), δ: 10.34 (s, 1 H, CH); 3.44 (t, 4 H, $O(CH_2)_2$, *J* = 5.0 Hz); 2.54 (t, 4 H, $N(CH_2)_2$, *J* = 5.0 Hz); 2.23 (s, 3 H, NCH_3). IR, ν/cm^{-1}: 1735 (C=O). MS, *m/z* (I_{rel} (%)): 212 $[M]^+$ (15). Found (%): N, 26.38; S, 14.94. $C_8H_{12}N_4OS$. Calculated (%): N, 26.39; S, 15.10.

5-(4-Benzylpiperidino)-1,2,3-thiadiazole-4-carbaldehyde (3e). Yield 0.98 g (64%), m.p. 78 °C. ^{1}H NMR (DMSO-d_6+CCl_4), δ: 10.27 (s, 1 H, CH); 7.25—7.28 (m, 2 H, ArH); 7.12—7.17 (m, 3 H, ArH); 3.72 (t, 2 H, $N(CH)_2$, *J* = 12.5 Hz); 3.13—3.05 (m, 2 H, $(CH)_2$); 2.57 (d, 2 H, CH_2, *J* = 7.1 Hz); 1.80—1.85 (m, 1 H, CH); 1.70 (t, 2 H, $N(CH)_2$, *J* = 13.0 Hz); 1.49—1.50 (m, 2 H, $(CH)_2$). IR, ν/cm^{-1}: 1735 (C=O). MS, *m/z* (I_{rel} (%)): 287 $[M]^+$ (15). Found (%): N, 15.08; S, 11.44. $C_{15}H_{17}N_3OS$. Calculated (%): N, 14.62; S, 11.16.

Synthesis of 5-dialkylamino-4-hydroxymethyl-1,2,3-thiadiazoles (4a—e) (general procedure). $NaBH_4$ (0.53 g, 14 mmol) was added to a solution of ethyl 5-dialkylamino-1,2,3-thiadiazole-4-carboxylate **6** (3.5 mmol) in 50 mL of anhydrous ethanol. The mixture was refluxed for 1 h and cooled. Water (100 mL) was added. The product was extracted with $CHCl_3$ (3×50 mL), the combined organic extract was dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. The product was recrystallized from benzene.

Synthesis of ethyl 5-dialkylamino-1,2,3-thiadiazole-4-carboxylates (6a—e) (general procedure). Dialkylamine (20 mmol) was added to a solution of ethyl 5-chloro-1,2,3-thiadiazole-4-carboxylate (1.97 g, 10 mmol) in 10 mL of ethanol. The mixture was stirred at ~20 °C for 30 min and cooled. The precipitate was filtered off.

Synthesis of 5-dialkylamino-1,2,3-thiadiazoles (7a—c) (general procedure). Aldehyde **3** (1.5 mmol) was dissolved in DMF (0.5 mL). The mixture was heated on a water bath for 2.5 h and cooled. The product was precipitated with water and filtered off.

5-Morpholino-1,2,3-thiadiazole (7a). Yield 0.18 g (72%), m.p. 90 °C. ^{1}H NMR (DMSO-d_6), δ: 8.17 (s, 1 H, CH); 3.71—3.76 (m, 4 H, $O(CH_2)_2$); 3.28—3.32 (m, 4 H, $N(CH_2)_2$). MS, *m/z* (I_{rel} (%)): 171 $[M]^+$ (65). Found (%): N, 24.90; S, 18.78. $C_6H_9N_3OS$. Calculated (%): N, 24.54; S, 18.73.

5-(2,6-Dimethylmorpholino)-1,2,3-thiadiazole (7b). Yield 0.23 g (77%), m.p. 136 °C. ^{1}H NMR (DMSO-d_6), δ: 8.16 (s, 1 H, CH); 3.66—3.79 (m, 2 H, $O(CH)_2$); 3.43 (dd, 2 H, $N(CH)_2$, J = 10.3 Hz, J = 2.4 Hz); 275 (dd, 2 H, $N(CH)_2$, J = 11.9 Hz, J = 10.7 Hz); 1.14 (d, 6 H, 2 CH_3, J = 6.1 Hz). MS, m/z (I_{rel} (%)): 199 $[M]^+$ (20). Found (%): N, 22.39; S, 17.12. $C_8H_{13}N_3OS$. Calculated (%): N, 22.21; S, 16.95.

5-Pyrrolidino-1,2,3-thiadiazole (7c). Yield 0.16 g (68%), m.p. 80 °C. ^{1}H NMR (DMSO-d_6), δ: 7.75 (s, 1 H, CH); 3.29—3.35 (m, 4 H, $N(CH_2)_2$); 2.01—2.06 (m, 4 H, 2 CH_2). MS, m/z (I_{rel} (%)): 155 $[M]^+$ (67). Found (%): N, 26.79; S, 20.51. $C_6H_9N_3S$. Calculated (%): N, 27.07; S, 20.66.

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