Reaction of 5-halo-1,2,3-thiadiazoles with arylenediamines as a new approach to tricyclic 1,3,6-thiadiazepines

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A multistep reaction of 5-halo-1,2,3-thiadiazoles and 1,2-phenylenediamines provides a new route to fused 1,3,6-thiadiazepines. The overall process consists of the known stepwise formation of 5-[1-(2-aminophenyl)-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole, and a novel ring transformation which involves the Smiles and Dimroth rearrangements followed by an intramolecular nucleophilic substitution of the thiol group, affording di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*]-[3,1,5]benzothiadiazepines. The influence of the substituents on the 1,2,3-thiadiazole and phenyl rings on this reaction was discussed.

Introduction

The recent surge of interest in the chemistry of medium sized heterocycles can be explained by their unusual properties and exotic structure. Many of them have been extensively investigated in view of their high biological activity, especially 1,4-benzodiazepines and oxazepines which are clinically used as CNS drugs (anti-anxiety, hypnotic agents, anticonvulsants, muscle relaxants, *etc*.). Dibenzo[*b*,*f*]thiepines were found to show similar properties and they are used as antidepressants, neuroleptic and psychosedative drugs.[1]

Seven-membered rings containing sulfur and two nitrogen atoms (thiadiazepines) have received less attention. Up to now information in this field has been limited to a few examples of synthesis, with no systematic study, and a few notes about pharmacological and other kinds of activity of 1,2,4-thiadiazepines, 1,2,7-thiadiazepines, 1,3,4-thiadiazepines, and 1,4,5-thiadiazepines.[2]

We now report our results for the synthesis of novel, fused 1,3,6-thiadiazepines.[3] Again, only limited data are available for this heterocyclic ring system. Thiadiazepines were obtained by a [6 + 1]cyclocondensation reaction,[4] ring formation by the reaction of thioimidates and diimines with dihalo-containing cyclization agents,[4d,5] and other miscellaneous methods.[6]

We have recently communicated that the condensation of 5-halo-1,2,3-thiadiazole-4-carboxylate **1** with *o*-phenylenediamine **2** affords thiadiazepine **6** *via* sulfide **5**.[3] The process seems to be an unusual cyclization and a promising method for the syntheses of novel heterocyclic systems. In this paper we present full data for this reaction, including its scope and limitations, details of the reaction mechanism and structural data for the new ring system.

Results and discussion

Nucleophilic substitution of 5-halo-1,2,3-thiadiazole-4-carboxylates and 4-carboxamides **1** with aliphatic and aromatic amines has been discussed in the literature. At the same time it is known that 5-amino-1,2,3-thiadiazoles can undergo the Dimroth rearrangement[7] in the presence of base. Thus, nucleophilic substitution of **1** with amines produces, depending on the reaction conditions, a variety of products including the initially formed 5-amino-1,2,3-thiadiazole, 5-mercapto-1,2,3-triazole after the Dimroth rearrangement and (1-substituted-1,2,3-triazol-5-yl)sulfanyl-1,2,3-thiadiazole as a product of hetarylation of the mercapto group.[8] In the case of *o*-phenylenediamine **2** we have succeeded in obtaining all these products **3**, **4**, and **5** (Scheme 1). The introduction of the vicinal amino group provides both an internal basic catalyst and an additional reaction center. For example, the usual procedure for the preparation of 5-amino-1,2,3-thiadiazoles from **1** and amines requires heating in DMF at 80 °C. Contrary to this, when **1a** and diamine **2** were used under these conditions we obtained a mixture of sulfide **5**, 1,4-diazepine **7** and 5-aminothiadiazole **3**. Thus, the additional amino group can react with the thiadiazole ester affording a novel benzo[*b*]-[1,4]-diazepine **7**. By an alternative pathway the amino group acts as an internal base, catalyzing the Dimroth rearrangement allowing the formation of sulfide **5**. We have found appropriate conditions for the selective preparation of each of the compounds **3**, **4**, and **5** in fair to good yields. Diazepine **7** was obtained as the major product (40% yield) upon refluxing **1** and phenylenediamine **2** in DMF. The NMR spectra of **3a** and **4a** are quite different although the mass spectra are similar. A test reaction of **4a** with $FeCl_3$ confirms the presence of the thiol group. The best results obtained in the synthesis of **5** were achieved by carrying out the reaction sequence with the isolation of 5-aminothiadiazole **3**. Compound **3** rearranged in refluxing ethanol in the presence of a base catalyst (Et_3N or dimethylaniline), and a second portion of 5-halo-1,2,3-thiadiazole **1** was added. This procedure also allows one to obtain sulfides **5d**–**f** with different substituents on the 1,2,3-triazole and 1,2,3-thiadiazole rings, by combining **3a**–**c** and 5-halo-1,2,3-thiadiazoles **1a**–**c**. The reactivity of the 5-chloro- and 5-bromo-1,2,3-thiadiazole derivatives **1** towards diamines is almost equal. Most of this work was carried out using the bromoester, which is the most convenient to obtain and to work with. However, for amides **1b**,**c** only chloro-substituted compounds were used because bromine in this case is not sufficiently active towards nucleophilic substitution. Higher reactivity for chloro compounds is normal since for aromatic nucleophilic substitution the rate determining step is the formation of the σ complex.

Interestingly, when the starting bromoester **1a** (two equivalents), *o*-phenylenediamine **2** and triethylamine (three

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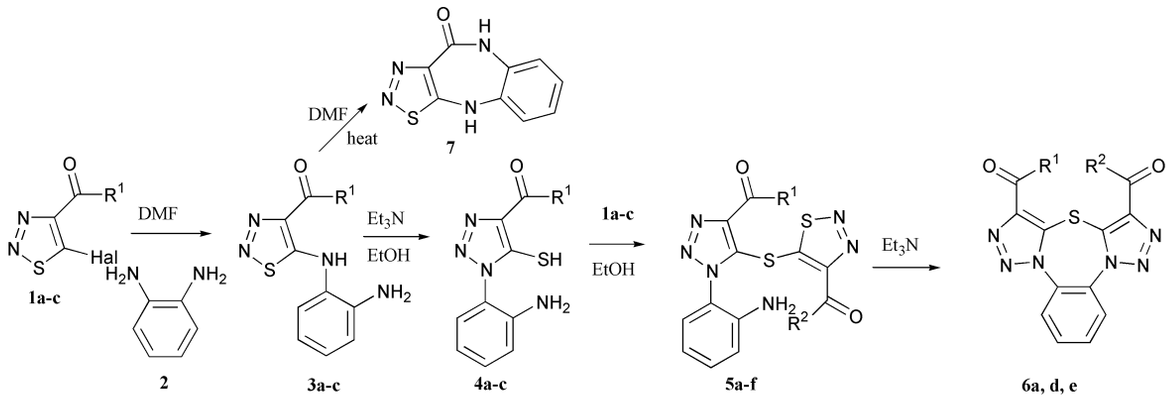
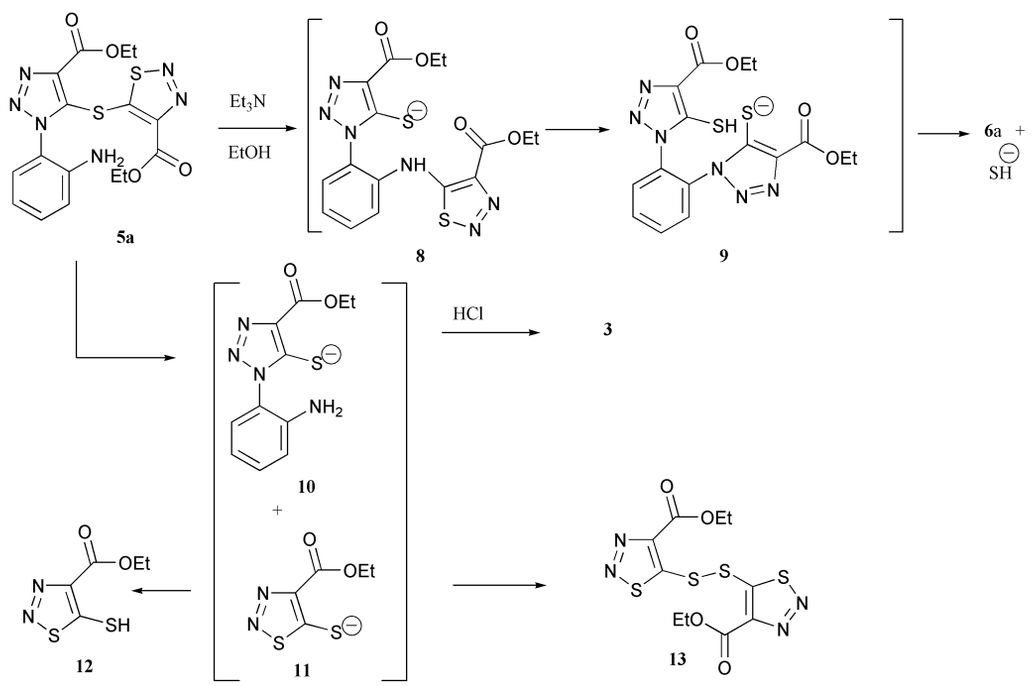


1, **3**, **4** (a) R^1 = OEt (b) R^1 = NH_2 (c) R^1= $NHCH_3$

5, **6** (a) R^1 = R^2 = OEt , (b) R^1 = R^2 = NH_2, (c) R^1 = R^2 = $NHCH_3$, (d) R^1 = NH_2, R^2 = OEt, (e) R^1 = $NHCH_3$, R^2 = OEt, (f) R^1 = OEt, R^2 = $NHCH_3$

Scheme 1



Scheme 2

equivalents) were refluxed in ethanol, the major reaction product appeared to be thiadiazepine **6a**. Sulfide **5a**, prepared in the presence of only one equivalent of triethylamine or a weaker base (dimethylaniline) again yielded thiadiazepine **6a** upon heating in ethanol with excess triethylamine. This fact confirms that sulfide **5** is an intermediate in the process leading to **6a**. The yield of the latter compound, starting from bromoester **1a** or sulfide **5a**, averages 50%.

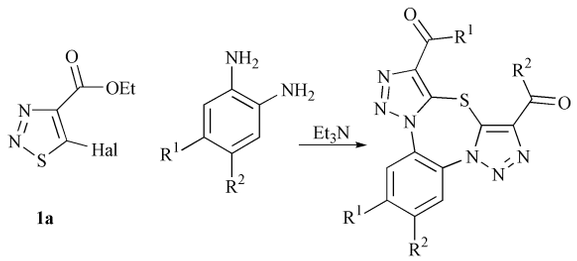
The yield of **6a**, calculated with respect to the diamine, can be increased to 70% when an excess of bromoester **1** is used. DMF and DMSO are also suitable solvents for the reaction, but it is necessary to maintain the temperature below 110 °C to avoid decomposition. The reaction in acetonitrile gives only sulfide **5**. In dichloromethane with Et_3N, sulfide **5** is formed very slowly.

The transformation of sulfides **5** into thiadiazepines **6** most probably proceeds as shown in Scheme 2. At first, an intramolecular substitution takes place and the 1,2,3-thiadiazole ring is transposed from the sulfur to the nitrogen atom. This can be seen as a heterocyclic example of a base catalyzed Smiles rearrangement.[9] In a second step, 5-amino-1,2,3-thiadiazole **8** undergoes the Dimroth rearrangement to form the bis(triazole) **9**, which immediately cyclizes to form the thiadiazepine ring **6** with the loss of hydrogensulfide.[10]

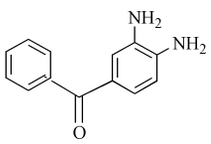
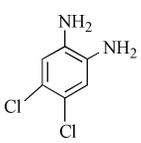
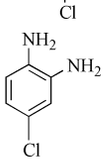
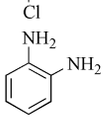
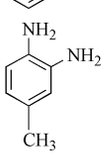
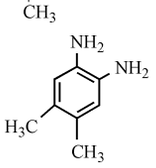
Taking into account the moderate yield of thiadiazepine **6** we tried to identify the by-products of this reaction. After acidification of the reaction mixture and separation by means of column chromatography, compounds **3**, **12**, and **13** were isolated from the reaction mixture. It appears logical that the hydrogensulfide ion, eliminated in the main reaction, can cleave the C–S bond of sulfide **5** to form thiolates **10** and **11**. The former, upon acidification, rearranged into 5-amino-1,2,3-thiadiazole **3** while the latter gave products **12** and **13** which were compared, for purposes of identification, with samples synthesized earlier by known procedures.[8a] This assumption was confirmed by the fact that **5** on treatment with sodium hydrogen sulfide yielded the same products **3** and **13**.[11]

The same reaction was observed when 5-(2-aminophenyl)-amino-1,2,3-thiadiazole-4-carboxamides **3b**,**c** were refluxed in ethanol with bromoester **1a** and triethylamine. It was clearly evident from TLC control after two days of heating that the initially formed sulfides **5d**,**e** had completely disappeared to give rise to the 1,3,6-thiadiazepines **6d**,**e** in about 50% yield. On the other hand, sulfides **5b**,**c** bearing amide groups on both the triazole and thiadiazole rings, as well as compound **5f** which has an amide function only in the thiadiazole moiety do not transform to the corresponding thiadiazepines **6b**,**c**,**f** even on

Table 1



1a **2a, g-k** **6a, g-k**

Diamine	Product[a]	Yield (%)	Mp/°C
	**6i**	15	185
	**6h**	30	220
	**6g**	27	174
	**6a**	54	164
	**6j**	47	212
	**6k**	35	237

[a] The products were crystallized from ethanol.

prolonged heating. This observation can be explained by the lower electron-withdrawing effect of the amide group that makes the 5-position of the 1,2,3-thiadiazole ring less reactive for nucleophilic attack.

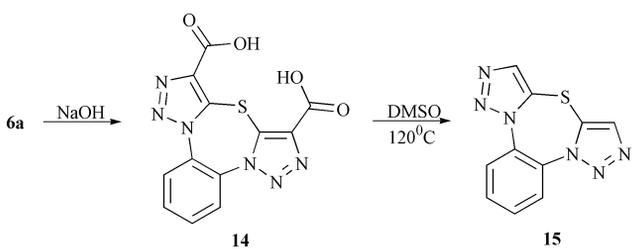
A number of diamines of different reactivity were involved in reactions with **1a** and the results are summarized in Table 1. It can be seen that the yield of thiadiazepine, which was not optimized, does not correlate with the electronic properties of the substituents. At the same time, the reaction outcome is strongly influenced by the reactivity of the diamine. This can be explained by the multistep character of the transformation. In the first step, nucleophilic substitution of the halogen, it is evident that electron-rich substituents on the amine would favor the process. Indeed, it takes about two days to obtain 5-amino-1,2,3-thiadiazole **3k** in 74% yield from a diamine carrying two methyl groups. On the other hand, when chloro-substituted aminothiadiazoles **3g**,**h** were formed, two weeks were not enough for the complete conversion of the starting material.

Contrary to this, the following Dimroth rearrangement is promoted by electron-withdrawing substituents.[12] The final transformation to thiadiazepine **6** is also promoted in this case. Several attempts to obtain sulfides **5g**,**h** according to the general procedure have failed and in all cases thiadiazepines **6g**,**h** have been isolated. Thus, upon lowering the electron density of the diamine, the first step becomes increasingly difficult. For example, the benzoyl derivative **6i** was formed in only 15% yield and most of the diamine remained unconverted after a week of heating.

Phenylenediamines **2j**,**k** with methyl substituents are more reactive towards bromoester **1a**, although the thiadiazepine yield does not increase. For compounds **3g**,**j** and **5g**,**j** the substituent is at the 4 position of the phenyl ring, but there is an impurity of approximately 10% of the 5-isomer.

The symmetrical structure of compounds **6** was completely supported by ^{1}H and ^{13}C NMR and mass spectra. The mass spectra of thiadiazepines **6** show prominent ion peaks and peaks due to the base, which can be attributed to the subsequent loss of two nitrogen molecules and ester or amide groups.

The parent system **15** was easily obtained by saponification of the ester groups with NaOH, following decarboxylation of the diacid **14** which occurs smoothly, below the melting point in DMSO at 120 °C (Scheme 3).



14 **15**

Scheme 3

X-Ray structural analysis confirms the symmetrical structure of compound **15** (Fig. 1). The asymmetric unit consists of a half molecule, the whole molecule is generated by a crystallographic mirror plane. The thiadiazepine ring occurs in a boat conformation with the benzene and triazole rings at different sides of the best plane through the seven-membered ring. This plane makes an angle of 28.4(1)° with the best plane through the six-membered ring, and 32.3(1)° with the best plane through the five-membered ring.

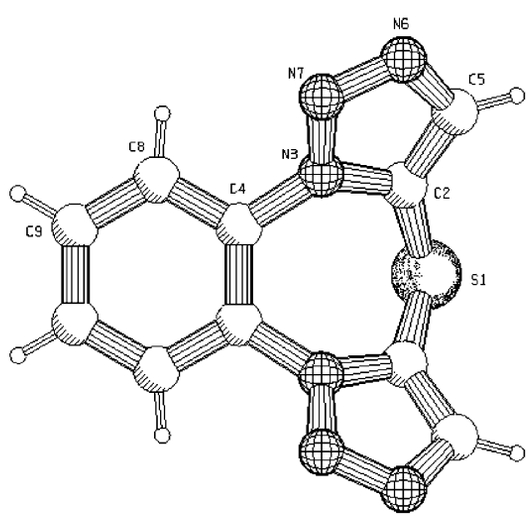


Fig. 1 The molecular structure of **15**.

Conclusions

In conclusion, various vicinal phenylenediamines react with 5-halo-1,2,3-thiadiazoles to form products **5**. On heating in the presence of excess base compounds **5** undergo a multistep transformation into the thiadiazepine system **6**. The electron

density of the phenylenediamines has different effects on the reaction steps, but the overall yield is not influenced. It is evident that in any case the last step of the process is a cyclization of a dithiol intermediate into the thiadiazepine with the elimination of hydrogensulfide. Experimental evidence for this has been given.

Experimental

Materials and methods

NMR spectra were obtained on Bruker WP-100 (100.68 MHz) and AMX 400 (400.14 MHz) spectrometers. Mass spectra were recorded on a Varian MAT 311 spectrometer or as previously described.[13]

General procedure for the preparation of [*N*-(2-aminophenyl)-amino]-1,2,3-thiadiazoles 3

A solution of ethyl 5-bromo-1,2,3-thiadiazole-4-carboxylate **1** and diamine **2** (2 equiv.) in DMF was stirred at room temperature, and the reaction was monitored with TLC. After the starting compound had disappeared, the reaction mixture was diluted with water. The precipitate was filtered off and crystallized from ethanol.

Ethyl 5-[*N*-(2-aminophenyl)amino]-1,2,3-thiadiazole-4-carboxylate 3a. Yield 76%, mp 125 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 400 MHz): 1.37 (3H, t, J = 7.12 Hz, CH_3), 4.42 (2H, q, J = 7.08 Hz, CH_2), 4.80–5.60 (br s, NH_2 + H_2O), 6.65 (1H, td, J = 7.92, 1.2 Hz, C5H), 6.86 (1H, dd, J = 8.04, 1.12 Hz, C3H), 7.07 (1H, td, J = 7.80, 1.32 Hz, C4H), 7.16 (1H, dd, J = 7.84, 1.20 Hz, C6H), 9.30 (1H, br s, NH). ^{13}C NMR (DMSO-D_6, δ (ppm), 100 MHz): 14.30 (q, J = 126.77 Hz, CH_3), 60.50 (t, J = 150.91 Hz, CH_2), 116.66 (dm, J = 157.0 Hz, CH), 117.07 (dd, J = 162.5, 9.0 Hz, CH), 124.03 (dd, J = 158.0, 8.0 Hz, CH), 127.87 (dd, J = 11.07, 7.04 Hz, C-*ipso*), 128.39 (dm, J = 155.0 Hz, CH), 132.66 (s, C4-thiadiaz.), 142.49 (t, J = 8.05 Hz, C-*ipso*), 162.12 (t, J = 4.02 Hz, CO), 170.16 (s, C5-thiadiaz.). EIMS *m*/*z* (rel. int.): 264 (M^+, 69), 162 (100). Anal. calcd for $C_{11}H_{12}N_4SO_2$: C, 49.98; H, 4.58; N, 21.20; S, 12.13. Found C, 49.79; H, 4.60; N, 21.64; S, 12.33%.

5-[*N*-(2-Aminophenyl)amino]-1,2,3-thiadiazole-4-carboxamide 3b. Yield 68%, mp 227 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 400 MHz): 3.50–5.50 (br s, NH_2 + H_2O), 6.69 (1H, td, J = 7.60, 1.4 Hz, C5H), 6.87 (1H, dd, J = 8.00, 1.32 Hz, C3H), 7.03 (1H, td, J = 8.04, 1.40 Hz, C4H), 7.18 (1H, dd, J = 7.88, 1.32 Hz, C6H), 7.68 (1H, s, N*H*H), 8.11 (1H, s, NH*H*), 10.02 (1H, s, NH). ^{13}C NMR (DMSO-D_6, δ (ppm), 100 MHz): 116.87 (dd, J = 159.5, 8.0 Hz, CH), 117.58 (dd, J = 162.0, 8.0 Hz, CH), 121.11 (dd, J = 158.0, 8.5 Hz, CH), 127.21 (dd, J = 150.0, 8.0 Hz, CH), 127.99 (m, C-*ipso* NH), 135.22 (d, J = 7.0 Hz, C4-thiadiazole), 141.30 (t, J 7.5, C-*ipso* NH_2), 164.63 (s, CO), 166.36 (s, C5-thiadiazole). EIMS *m*/*z* (rel. int.): 236 (MH^+, 100). Anal. calcd for $C_9H_9N_5SO$: C, 45.94; H, 3.86; N, 29.77; S, 13.63. Found C, 46.02; H, 3.85; N, 29.86; S, 13.57%.

***N*-Methyl-5-[*N*-(2-aminophenyl)amino]-1,2,3-thiadiazole-4-carboxamide 3c.** Yield 67%, mp 228 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 2.85 (3H, d, J = 4.9 Hz, CH_3), 5.05 (2H, br s, NH_2), 6.66 (1H, td, J = 7.5, 1.5 Hz, C5H), 6.85 (1H, dd, J = 7.9, 1.5 Hz, C3H), 7.01 (1H, td, J = 7.3, 1.5 Hz, C4H), 7.15 (1H, dd, J = 7.8, 1.5 Hz, C6H), 8.66 (1H, q, J = 4.6 Hz, NH), 9.98 (1H, s, NH). EIMS *m*/*z* (rel. int.): 249 (M^+, 92), 162 (100). Anal. calcd for $C_{10}H_{11}N_5SO$: C, 48.18; H, 4.45; N, 28.09; S, 12.86. Found C, 48.20; H, 4.50; N, 28.10; S, 12.95%.

Ethyl 5-[*N*-(2-amino-4,5-dimethylphenyl)amino]-1,2,3-thiadiazole-4-carboxylate 3k. Yield 74%, mp 123 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.42 (3H, t, J = 7.0 Hz, CH_3), 2.10 (3H, s, C5CH_3), 2.14 (3H, s, C4CH_3), 4.43 (2H, q, J = 7.0 Hz, CH_2), 4.70 (2H, br s, NH_2), 6.62 (1H, s, C3H), 6.85 (1H, s, C6H), 9.15 (1H, br s, NH). EIMS *m*/*z* (rel. int.): 292 (M^+, 73), 190 (100). Anal. calcd for $C_{13}H_{16}N_4SO_2$: C, 53.41; H, 5.52; N, 19.16; S, 10.97. Found C, 53.55; H, 5.50; N, 19.21; S, 11.00%.

Ethyl 5-[*N*-(2-amino-4-methylphenyl)amino]-1,2,3-thiadiazole-4-carboxylate 3j. Yield 69%, mp 123 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.42 (3H, t, J = 7.0 Hz, CH_3), 2.23 (3H, s, CH_3), 4.42 (2H, q, J = 7.0 Hz, CH_2), 4.90 (2H, br s, NH_2), 6.41 (1H, dd, J = 7.9, 1.1 Hz, C5H), 6.62 (1H, d, J = 0.7 Hz, C3H), 6.96 (1H, d, J = 7.7 Hz, C6H), 9.13 (1H, br s, NH). EIMS *m*/*z* (rel. int.): 278 (M^+, 46), 176 (100). Anal. calcd for $C_{12}H_{14}N_4SO_2$: C, 51.78; H, 5.07; N, 20.13; S, 11.52. Found C, 51.83; H, 5.10; N, 20.05; S, 11.53%.

Ethyl 5-[*N*-(2-amino-4-chlorophenyl)amino]-1,2,3-thiadiazole-4-carboxylate 3g. Yield 54%, mp 148 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 400 MHz): 1.37 (3H, t, J = 7.1 Hz, CH_3), 4.40 (2H, q, J = 7.1 Hz, CH_2), 5.57 (2H, br s, NH_2), 6.60 (1H, dd, J = 8.4, 2.4 Hz, C5H), 6.84 (1H, d, J = 2.4 Hz, C3H), 7.15 (1H, d, J = 8.4 Hz, C6H), 9.28 (1H, br s, NH). EIMS *m*/*z* (rel. int.): 298 (M^+, 66), 196 (100). Anal. calcd for $C_{11}H_{11}N_4SClO_2$: C, 44.22; H, 3.71; N, 18.75; S, 10.73; Cl, 11.87. Found C, 44.27; H, 3.65; N, 18.70; S, 10.91; Cl, 11.92%.

Ethyl 5-[*N*-(2-amino-4,5-dichlorophenyl)amino]-1,2,3-thiadiazole-4-carboxylate 3h. Yield 51%, mp 151 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 1.37 (3H, t, J = 7.1 Hz, CH_3), 4.41 (2H, q, J = 7.1 Hz, CH_2), 5.60 (2H, br s, NH_2), 7.15 (1H, s, C3H), 7.36 (1H, s, C6H). EIMS *m*/*z* (rel. int.): 332 (M^+, 37), 230 (100). Anal. calcd for $C_{11}H_{10}N_4SCl_2O_2$: C, 39.65; H, 3.03; N, 16.81; S, 9.62; Cl, 21.28. Found C, 39.80; H, 3.08; N, 16.91; S, 9.60; Cl, 21.51%.

Ethyl 1-(2-aminophenyl)-5-sulfanyl-1,2,3-triazole-4-carboxylate 4a

To a solution of **3a** (0.87 g, 3.29 mmol) in ethanol (20 mL), triethylamine (1.38 mL, 11.7 mmol) was added and the mixture was refluxed for 3 hours, cooled to room temperature and acidified with 1 mL of hydrochloric acid. The precipitate was filtered off, yielding 0.81 g (93%) of colourless crystals, mp 144 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.43 (3H, t, J = 7.0 Hz, CH_3), 4.48 (2H, q, J = 7.0 Hz, CH_2), 7.31–7.38 (2H, m, CH-arom.), 7.51–7.59 (2H, m, CH-arom.), 9.00–9.40 (br s, NH_2 + H_2O), 9.61 (1H, br s, SH). EIMS *m*/*z* (rel. int.): 264 (M^+, 37), 86 (100). Anal. calcd for $C_{11}H_{12}N_4SO_2$: C, 49.98; H, 4.58; N, 21.20; S, 12.13. Found C, 50.00; H, 4.61; N, 21.18; S, 12.04%.

Ethyl 5-[1-(2-aminophenyl)-4-ethoxycarbonyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxylate 5a

A solution of **1a** (0.5 g, 2.1 mmol) and *o*-phenylenediamine **2a** (0.23 g, 2.1 mmol) in ethanol (40 mL) was refluxed for 2 hours, then triethylamine (0.3 mL, 2.1 mmol) and bromoester **1a** (0.5 g) were added. The reaction mixture was refluxed for an hour, and half of the solvent was removed. The product which precipitated from the solution upon cooling was filtered off and recrystallized from ethanol. This gave **5a** (0.82 g, 93%), mp 143–145 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 400 MHz): 1.15 (3H, t, J = 7.08 Hz, CH_3-triazole), 1.33 (3H, t, J = 7.12 Hz, CH_3-thiadiazole), 4.30 (2H, q, J = 7.08 Hz, CH_2-triazole), 4.41 (2H, q, J = 7.12 Hz, CH_2-thiadiazole), 5.44 (2H, s, NH_2), 6.61 (1H, td, J = 7.52, 1.12 Hz, C5H), 6.72 (1H, dd, J = 8.28, 0.92 Hz, C3H), 6.75 (1H, dd, J = 7.92, 1.36 Hz, C6H), 7.19 (1H, td, J = 7.72, 1.44 Hz, C4H). ^{13}C NMR (DMSO-D_6, δ (ppm),

100 MHz): 13.70 (CH_3), 13.95 (CH_3), 61.25 (CH_2), 62.15 (CH_2), 115.69 (dd, J = 165.00, 9.05 Hz, CH), 116.39 (dd, J = 159.97, 7.04 Hz, CH), 118.60 (m, C-*ipso* N-triazole), 127.73 (dd, J = 161.98, 7.04 Hz, CH), 131.94 (dd, J = 159.97, 8.05 Hz, CH), 133.95 (s, C5-triazole), 140.33 (s, C4-triazole), 144.65 (ddd, J = 8.55, 6.04, 1.1 Hz, C-*ipso* NH_2), 146.18 (s, C4-thiadiazole), 159.06 (t, J = 4.02 Hz, CO), 159.97 (t, J = 3.02 Hz, CO), 162.10 (s, C5-thiadiazole). EIMS *m*/*z* (rel. int.): 420 (M^+, 1), 161 (100). Anal. calcd for $C_{16}H_{16}N_6S_2O_4$: C, 45.71; H, 3.84; N, 19.99; S, 15.25. Found C, 45.69; H, 3.83; N, 20.03; S, 15.10%.

5-[1-(2-Aminophenyl)-4-carbamoyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxamide 5b

Prepared from 5-chloro-1,2,3-thiadiazole-4-carboxamide **1b** as described for **5a**. Yield 40%, mp 182 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 400 MHz): 4.50–5.50 (2H, br s, NH_2), 6.60 (1H, dt, J = 8.13, 0.93 Hz, C5H), 6.87(1H, dd, J = 7.60, 0.92 Hz, C3H), 7.00 (1H, dd, J = 7.87, 1.28 Hz, C6H), 7.21 (1H, td, J = 8.49, 1.39 Hz, C4H). ^{13}C NMR (DMSO-D_6 + CCl_4, δ (ppm), 100 MHz): 115.75, 116.59, 119.11, 127.38, 131.53, 132.54, 142.77, 144.49, 148.65, 160.03, 160.46, 161.47. EIMS *m*/*z* (rel. int.): 362 (M^+, 13), 161 (100). Anal. calcd for $C_{12}H_{10}N_8S_2O_2$: C, 39.77; H, 2.78; N, 30.92; S, 17.69. Found C, 39.84; H, 2.75; N, 31.26; S, 17.23%.

N-Methyl-5-[1-(2-aminophenyl)-4-(*N*-methylcarbamoyl)-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxamide 5c

Prepared from **1c** as described for **5a**. Yield 65%, mp 165 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 2.78 (3H, d, J = 4.6 Hz, CH_3), 2.81 (3H, d, J = 4.9 Hz, CH_3), 5.35 (2H, s, NH_2), 6.59 (1H, td, J = 7.3, 1.2 Hz, C5H), 6.85 (1H, dd, J = 7.9, 0.9 Hz, C3H), 7.06 (1H, dd, J = 7.9, 1.5 Hz, C6H), 7.24 (1H, td, J = 7.5, 1.5 Hz, C4H), 8.77 (1H, q, J = 4.9 Hz, NH), 8.99 (1H, q, J = 4.6 Hz, NH). EIMS *m*/*z* (rel. int.): 390 (M^+, 8), 161 (100). Anal. calcd for $C_{14}H_{14}N_8S_2O_2$: C, 43.06; H, 3.61; N, 28.70; S, 16.42. Found C, 42.96; H, 3.63; N, 28.64; S, 16.25%.

Ethyl 5-[1-(2-aminophenyl)-4-carbamoyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxylate 5d

A solution of **3b** (0.5 g, 2.1 mmol) and triethylamine (0.3 mL, 2.1 mmol) in ethanol (50 mL) was refluxed for 3 hours, then cooled to room temperature and bromoester **1a** (0.5 g, 2.1 mmol) was added. The reaction mixture was stirred for an hour, and half of the solvent was removed. The product which precipitated from the solution upon cooling was filtered off and recrystallized from ethanol (0.76 g) 92%, mp 99 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 1.33 (3H, t, J = 7.1 Hz, CH_3), 4.40 (2H, q, J = 6.9 Hz, CH_2), 5.37 (2H, br s, NH_2), 6.63 (1H, t, J = 7.2 Hz, C5H), 6.85 (1H, d, J = 7.3 Hz, C3H), 7.08 (1H, dd, J = 7.8, 1.3 Hz, C6H), 7.24 (1H, td, J = 7.8, 1.5 Hz, C4H), 7.74 (1H, s, N*H*H), 8.18 (1H, s, NH*H*). EIMS *m*/*z* (rel. int.): 391 (M^+, 4), 161 (100). Anal. calcd for $C_{14}H_{13}N_7S_2O_3$: C, 42.96; H, 3.35; N, 25.05; S, 16.38. Found C, 43.05; H, 3.40; N, 24.97; S, 15.92%.

Ethyl 5-[1-(2-aminophenyl)-4-(*N*-methylcarbamoyl)-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxylate 5e

Prepared from **3c** and **1a** as described for **5d**. Yield 49%, mp 179–181 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 1.39 (3H, t, J = 7.0 Hz, CH_3), 2.80 (3H, d, J = 4.6 Hz, CH_3), 4.41 (2H, q, J = 7.0 Hz, CH_2), 5.22 (2H, br s, NH_2), 6.59 (1H, td, J = 7.5, 0.9 Hz, C5H), 6.86 (1H, dd, J = 8.2, 0.9 Hz, C3H), 7.00 (1H, dd, J = 7.9, 1.5 Hz, C6H), 7.21 (1H, td, J = 7.8, 1.5 Hz, C4H), 8.67 (1H, q, J = 4.6 Hz, NH). EIMS *m*/*z* (rel. int.): 405 (M^+, 6), 161 (100). Anal. calcd for $C_{15}H_{15}N_7S_2O_3$: C, 44.43; H, 3.73; N, 24.18; S, 15.81. Found C, 44.51; H, 3.70; N, 24.06; S, 15.57%.

N-Methyl-5-[1-(2-aminophenyl)-4-ethoxycarbonyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxamide 5f

Prepared from **3a** and **1c** as described for **5d**. Yield 73%, mp 196 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.22 (3H, t, J = 7.0 Hz, CH_3), 2.83 (3H, d, J = 4.6 Hz, CH_3), 4.30 (2H, q, J = 7.0 Hz, CH_2), 5.26 (2H, s, NH_2), 6.59 (1H, t, J = 7.6 Hz, C5H), 6.86 (1H, d, J = 8.2 Hz, C3H), 7.02 (1H, d, J = 7.9 Hz, C6H), 7.21 (1H, t, J = 7.3 Hz, C4H), 8.87 (1H, q, J = 3.3 Hz, NH). EIMS *m*/*z* (rel. int.): 405 (M^+, 4), 161 (100). Anal. calcd for $C_{15}H_{15}N_7S_2O_3$: C, 44.43; H, 3.73; N, 24.18; S, 15.81. Found C, 44.40; H, 3.69; N, 24.22; S, 15.54%.

Ethyl 5-[1-(2-amino-4-methylphenyl)-4-ethoxycarbonyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxylate 5j

Prepared from **3j** and **1a** as described for **5d**. Yield 87%, mp 140 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.22 (3H, t, J = 7.0 Hz, CH_3), 1.40 (3H, t, J = 7.0 Hz, CH_3), 2.25 (3H, s, CH_3), 4.30 (2H, q, J = 7.0 Hz, CH_2), 4.43 (2H, q, J = 7.0 Hz, CH_2), 5.18 (2H, br s, NH_2), 6.41 (1H, d, J 8.4, C5H), 6.66 (1H, s, C3H), 6.93 (1H, d, J = 8.2 Hz, C6H). EIMS *m*/*z* (rel. int.): 434 (M^+, 1), 175 (100). Anal. calcd for $C_{17}H_{18}N_6S_2O_4$: C, 46.99; H, 4.18; N, 19.34; S, 14.76. Found C, 47.12; H, 4.20; N, 19.51; S, 14.74%.

Ethyl 5-[1-(2-amino-4,5-dimethylphenyl)-4-ethoxycarbonyl-1,2,3-triazol-5-ylsulfanyl]-1,2,3-thiadiazole-4-carboxylate 5k

Prepared from **3k** and **1a** as described for **5d**. Yield 89%, mp 158 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.22 (3H, t, J = 7.0 Hz, CH_3), 1.40 (3H, t, J = 7.0 Hz, CH_3), 2.08 (3H, s, C5CH_3), 2.18 (3H, s, C4CH_3), 4.30 (2H, q, J = 7.3 Hz, CH_2), 4.43 (2H, q, J = 7.0 Hz, CH_2), 4.94 (2H, br s, NH_2), 6.66 (1H, s, C3H), 6.81 (1H, s, C6H). EIMS *m*/*z* (rel. int.): 448 (M^+, 9), 189 (100). Anal. calcd for $C_{18}H_{20}N_6S_2O_4$: C, 48.20; H, 4.49; N, 18.74; S, 14.30. Found C, 48.28; H, 4.50; N, 19.06; S, 14.63%.

General procedure for the preparation of di[1,2,3]triazolo-[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepines 6

To a solution of **1a** and diamine **2** (0.5 equiv.) in ethanol (50 mL for 0.5 g of bromoester) triethylamine (1 equiv.) was added and the reaction mixture was refluxed overnight. After this time the second portion of triethylamine (2 equiv.) was added. Soon after this the product precipitated from the boiling solution. After refluxing for an additional hour the reaction mixture was cooled, the thiadiazepine was filtered off and recrystallized from ethanol.

Diethyl di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine-8,10-dicarboxylate 6a. Yield 54%, mp 164 °C. ^{1}H NMR ($CDCl_3$, δ (ppm), 400 MHz): 1.48 (6H, t, J = 7.1 Hz, $2CH_3$), 4.51 (4H, q, J = 7.1 Hz, $2CH_2$), 7.79–7.81 (2H, m, CH-arom.), 8.08–8.10 (2H, m, CH-arom.). ^{13}C NMR ($CDCl_3$, δ (ppm), 100 MHz): 14.20 (qt, J = 127.79, 3.02 Hz, CH_3), 62.07 (tq, J = 147.89, 4.02, CH_2), 126.28 (dm, J = 167.0 Hz, C-*ortho*), 128.21 (m, C-*ipso*), 131.36 (dd, J = 166.0, 8.0 Hz, C-*meta*), 133.47 (s, C-triazole), 139.71 (s, C-triazole), 159.17 (t, J = 3.0 Hz, CO). EIMS *m*/*z* (rel. int.): 386 (M^+, 25), 286 (13), 258 (82), 229 (23), 214 (71), 186 (100), 102 (44), 57 (19), 29 (97). Anal. calcd for $C_{16}H_{14}N_6SO_4$: C, 49.74; H, 3.65; N, 21.75; S, 8.30. Found C, 49.33; H, 3.99; N, 21.59; S, 8.32%.

Procedure with isolation of the side products. To a solution of **5a** (2 g, 4.67 mmol) in ethanol (20 mL) triethylamine (0.7 mL, 5.0 mmol) was added. The reaction mixture was refluxed for 2 hours and another portion of triethylamine (0.7 mL) was added. After three hours of refluxing the solution was cooled and 0.95 g (52%) of thiadiazepine **6a** was filtered off and washed with ethanol. The filtrate was acidified with HCl, dried under reduced pressure, the residue dissolved in dichloromethane and washed with water. The organic layer was

separated by means of column chromatography on silica gel with dichloromethane to give 0.45 g (25%) bis(4-ethoxycarbonyl-1,2,3-thiadiazol-5-yl) disulfide **13**. Mp 165 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 400 MHz):1.39 (6H, t, J = 7.20 Hz, $2CH_3$), 4.48 (4H, q, J = 7.20 Hz, $2CH_2$). ^{13}C NMR (DMSO-D_6, δ (ppm), 100 MHz): 13.94, 62.23, 146.27, 149.56, 157.51, 158.88, 160.02. EIMS m/z (rel. int.): 379 (MH^+). Anal. calcd for $C_{10}H_{10}N_4S_4O_4$: C, 31.74; H, 2.66; N, 14.80; S, 33.89. Found C, 32.03; H, 2.90; N, 14.74; S, 33.90%. Compound **3a** ethyl 5-[*N*-(2-aminophenyl)amino]-1,2,3-thiadiazole-4-carboxylate was also obtained (0.40 g, 32%). The aqueous layer gave 0.12 g (13%) of **12**. EIMS m/z (rel. int.): 190 (M^+, 55), 116 (100). Melting point and TLC data were identical to those given in the literature.[8a]

Ethyl 8-carbamoyldi[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]-benzothiadiazepine-10-carboxylate 6d. Prepared from **3b** and **1a** according to the general procedure. Yield 48%, mp 205 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 1.39 (3H, t, J = 7.0 Hz, CH_3), 4.39 (2H, q, J = 7.3 Hz, CH_2), 7.77 (1H, br s, N*H*H), 7.90–7.96 (2H, m, CH-arom.), 8.08–8.13 (3H, m, CH-arom. + NH*H*). EIMS m/z (rel. int.): 357 (M^+, 12), 312 (4), 285 (3), 256 (12), 229 (100), 213 (43), 201 (25), 186 (52), 161 (23), 129 (24), 114 (26), 102 (71). Anal. calcd for $C_{14}H_{11}N_7SO_3$: C, 47.05; H, 3.10; N, 27.44; S, 8.97. Found C, 47.29; H, 3.43; N, 27.62; S, 9.01%.

Ethyl 8-(*N*-methylcarbamoyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*]-[3,1,5]benzothiadiazepine-10-carboxylate 6e. Prepared from **3c** and **1a** according to the general procedure. Yield 50%, mp 190 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 1.39 (3H, t, J = 7.0 Hz, CH_3), 2.81 (3H, d, J = 4.9 Hz, CH_3), 4.40 (2H, q, J = 7.3 Hz, CH_2), 7.89–7.95 (2H, m, CH-arom.), 8.09–8.13 (2H, m, CH-arom.), 8.68 (1H, q, J = 4.6 Hz, NH). EIMS m/z (rel. int.): 371 (M^+, 5), 258 (54), 243 (20), 214 (66), 186 (100), 114 (24), 102 (52), 58 (28). Anal. calcd for $C_{15}H_{13}N_7SO_3$: C, 48.51; H, 3.53; N, 26.40; S, 8.63. Found C, 48.32; H, 3.69; N, 26.78; S, 8.20%.

2-Chloro-8,10-bis(ethoxycarbonyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 6g. Yield 27%, mp 174 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.43 (6H, 2t, J = 7.3 Hz, $2CH_3$), 4.41 (4H, 2q, J = 7.0 Hz, $2CH_2$), 7.94 (1H, dd, J = 8.8, 2.1 Hz, C5H), 8.13 (1H, d, J = 1.2 Hz, C3H), 8.15 (1H, d, J = 5.2 Hz, C6H). EIMS m/z (rel. int.): 420 (M^+, 15), 366 (5), 320 (13), 292 (58), 264 (19), 248 (56), 220 (100), 136 (22), 100 (15). Anal. calcd for $C_{16}H_{13}N_6SClO_4$: C, 45.66; H, 3.11; N, 19.97; S, 7.62; Cl, 8.42. Found C, 45.70; H, 3.17; N, 20.03; S, 7.44%.

2,3-Dichloro-8,10-bis(ethoxycarbonyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 6h. Yield 30%, mp 220 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.38 (6H, t, J = 7.0 Hz, $2CH_3$), 4.36 (4H, q, J = 7.0 Hz, $2CH_2$), 8.31 (2H, s, 2CH-arom.). EIMS m/z (rel. int.): 454 (M^+, 9), 400 (5), 356 (8), 354 (12), 326 (45), 298 (23), 284 (46), 282 (68), 256 (67), 254 (100), 134 (15), 57 (32). Anal. calcd for $C_{16}H_{12}N_6SCl_2O_4$: C, 42.21; H, 2.66; N, 18.46; S, 7.04; Cl, 15.57. Found C, 42.19; H, 2.70; N, 18.80; S, 7.27%.

2-Benzoyl-8,10-bis(ethoxycarbonyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 6i. Yield 15%, mp 185 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.43 (3H, t, J = 7.0 Hz, CH_3), 1.44 (3H, t, J = 7.0 Hz, CH_3), 4.42 (2H, q, J = 7.0 Hz, CH_2), 4.43 (2H, q, J = 7.0 Hz, CH_2), 7.57–7.75 [7.60 (2H, t, J = 7.0 Hz, 2CH-*meta* benzoyl), 7.72 (1H, m, CH-*para* benzoyl)], 7.88 (2H, dd, J = 7.0, 1.5 Hz, CH-*ortho* benzoyl), 8.20 (1H, dd, J = 8.5, 1.8 Hz, C3H), 8.29 (1H, d, J = 8.2 Hz, C4H), 8.35 (1H, d, J = 1.5 Hz, C1H). EIMS m/z (rel. int.): 490 (M^+, 4), 390 (11), 362 (30), 318 (39), 290 (39), 241 (15), 213 (28), 105 (100), 77 (71). Anal. calcd for $C_{23}H_{18}N_6SO_5$: C, 56.32; H, 3.70; N, 17.13; S, 6.54. Found C, 56.38; H, 3.65; N, 17.18; S, 6.84%.

2-Methyl-8,10-bis(ethoxycarbonyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 6j. Yield 47%, mp 212 °C. ^{1}H NMR ($CDCl_3$, δ (ppm), 400 MHz): 1.47 (6H, 2t, J = 7.20 Hz, $2CH_3$), 2.59 (3H, s, CH_3), 4.51 (4H, 2q, J = 6.80 Hz, $2CH_2$), 7.58 (1H, dd, J = 8.40, 1.52 Hz, C3H), 7.89 (1H, d, J = 1.50 Hz, C1H), 7.96 (1H, d, J = 8.28 Hz, C4H). ^{13}C NMR ($CDCl_3$, δ (ppm), 100 MHz): 14.21 ($2CH_3$), 21.25 (CH_3), 62.03 (CH_2), 62.06 (CH_2), 125.80 (C-*ipso*), 125.99 (CH), 126.45 (CH), 127.89 (C-*ipso*), 132.07 (CH), 133.18, 133.40, 139.60, 139.64, 142.51 (CCH_3), 159.24 (2CO). EIMS m/z (rel. int.): 400 (M^+, 14), 272 (52), 228 (77), 200 (100), 187 (12), 116 (15), 89 (28), 84 (26), 51 (17), 49 (41). Anal. calcd for $C_{17}H_{16}N_6SO_4$: C, 50.99; H, 4.03; N, 20.99; S, 8.01. Found C, 51.16; H, 4.10; N, 21.18; S, 8.16%.

2,3-Dimethyl-8,10-bis(ethoxycarbonyl)di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 6k. Yield 35%, mp 237 °C. ^{1}H NMR (DMSO-D_6 + CCl_4, δ (ppm), 250 MHz): 1.43 (6H, t, J = 7.0 Hz, $2CH_3$), 2.49 (6H, s, $2CH_3$), 4.41 (4H, q, J = 7.0 Hz, $2CH_2$), 7.87 (2H, s, 2CH). EIMS m/z (rel. int.): 414 (M^+, 19), 286 (51), 242 (57), 214 (100), 103 (26), 77 (23). Anal. calcd for $C_{18}H_{18}N_6SO_4$: C, 52.17; H, 4.38; N, 20.28; S, 7.74. Found C, 52.20; H, 4.39; N, 20.24; S, 7.87%.

[1,2,3]Thiadiazolo[5,4-*b*][1,5]benzodiazepin-10-one 7

A solution of **3a** (0.5 g, 1.89 mmol) in DMF (10 mL) was refluxed overnight. After the starting material disappeared, the reaction mixture was evaporated under reduced pressure and the residue was washed with CH_2Cl_2, and purified by silica gel column chromatography with ethyl acetate to give 0.165 g (40%) of **7** as a yellow solid with mp 260 °C. ^{1}H NMR ($CDCl_3$, δ (ppm), 400 MHz): 6.81–7.01 (4H, m, CH-arom.), 9.61 (1H, s, NHCO), 10.32 (1H, s, NH). ^{13}C NMR (DMSO-D_6, δ (ppm), 100 MHz): 119.57 (dm, J = 158.0 Hz, CH), 122.10 (dm, J = 160.0 Hz, CH), 124.51 (dd, J = 165.0, 8.0 Hz, CH), 124.98 (dd, J = 164.0, 9.0 Hz, CH), 128.23 (m, C-*ipso* NHCO), 133.47 (m, C-*ipso* NH), 140.03 (dd, J = 7.0, 6.0 Hz, C4-thiadiazole), 160.57 (d, J = 3.0 Hz, CO), 165.36 (d, J = 2.0 Hz, C5-thiadiazole). EIMS m/z (rel. int.): 218 (M^+, 85), 118 (100). Anal. calcd for $C_9H_6N_4SO$: C, 49.53; H, 2.77; N, 25.67; S, 14.69. Found C, 49.78; H, 2.57; N, 25.90; S, 14.70%.

Di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine-8,10-dicarboxylic acid 14

To an aqueous solution of NaOH (0.2 g, 5 mmol in 100 mL), thiadiazepine **6a** (1 g, 2.5 mmol) was added and the suspension was refluxed until a clear solution formed, then this was acidified with conc. HCl and the precipitated acid filtered off as colourless crystals (0.76 g, 89%). Decarboxylation occurs at 120 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 7.89–7.95 (2H, m, CH-arom.), 8.08–8.14 (2H, m, CH-arom.), 13.72 (2H, br s, 2OH). Anal. calcd for $C_{12}H_6N_6SO_4$: C, 43.63; H, 1.83; N, 25.45; S, 9.71. Found C, 43.57; H, 1.90; N, 25.33; S, 9.73%.

Di[1,2,3]triazolo[1,5-*a*:5′,1′-*d*][3,1,5]benzothiadiazepine 15

Acid **14** (0.76 g, 2.3 mmol) was heated at 120 °C in DMSO (20 mL) for 2 hours. After the evolution of gas ceased, the solution was diluted with water and the decarboxylation product filtered off. This gave **15** (0.49 g, 88%), mp 253–255 °C. ^{1}H NMR (DMSO-D_6, δ (ppm), 250 MHz): 7.89–7.94 (2H, m, 2CH-arom.), 8.08–8.15 (2H, m, 2CH-arom.), 8.17 (2H, s, 2CH-triazole). ^{13}C NMR (DMSO-D_6 + $CDCl_3$, δ (ppm), 100 MHz): 126.08 (C-*ortho*), 127.82 (C-*ipso*), 130.02 (C4-triazole), 131.31 (C-*meta*), 135.65 (C5-triazole). EIMS m/z (rel. int.): 242 (M^+, 61), 186 (100), 159 (37), 142 (32), 129 (17), 115 (27), 102 (76), 88 (19), 82 (23), 76 (52), 58 (42). Anal. calcd for $C_{10}H_6N_6S$: C,

49.57; H, 2.50; N, 34.69; S, 13.23. Found C, 49.68; H, 2.81; N, 34.43; S, 13.31%.

X-Ray diffraction study of 15. †Crystals were grown from DMSO. All measurements were made with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å); orthorhombic space group *Pnma*, a = 17.923(5), b = 14.449(2), c = 4.0860(10) Å, Z = 4, V = 1058.1(4) Å^3, D_c = 1.521 g cm^{-3}, $F(000)$ = 496, crystal size: 0.20 × 0.35 × 0.40 mm, μ(Mo-Kα) = 0.290 mm^{-1}, T = 289 K, 4.2 ≤ 2θ ≤ 50.0°, 1713 reflections collected, 964 unique reflections, R_{int} = 0.021. Final R indices: R_1 = 0.0339 for 839 reflections with $F > 4\sigma(F)$ and R_1 = 0.0410, wR_2 = 0.0954 for all data.

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† CCDC reference number 182868. See http://www.rsc.org/suppdata/p1/b2/b203072a/ for crystallographic files in .cif or other electronic format.

References

1 *Comprehensive Heterocyclic Chemistry II: a review of the literature 1982–1995*, eds. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon Press, London, 1996, Vol. 9.

2 See for instance: (*a*) M.-C. Forest, P. Lahouratate, M. Martin, G. Nadler, M. J. Quiniou and R. G. Zimmermann, *J. Med. Chem.*, 1992, **35**, 163–172; (*b*) M. Kuroda, M. Amano and F. Noboru, *Ger. Offen. DE 4 028 184* (*Chem. Abstr.*,1992, **116**, P31303u); (*c*) C. N. Hodge, C. H. Fernandez, P. K. Jadhav and P. Y.-S. Lam, *PCT Int. Appl.* WO 94 22 840 (*Chem. Abstr.*, 1995, **123**, P33104y); (*d*) P. K. Jadhav, W. F. Daneker and F. J. Woerner, USP 5 506 355 (*Chem. Abstr.*, 1996, **125**, P34038h).

3 N. N. Volkova, E. V. Tarasov, W. Dehaen and V. A. Bakulev, *Chem. Commun.*, 1999, 2273–2274.

4 (*a*) M. P. Mahajan, S. M. Sondhi and N. K. Ralhan, *Aust. J. Chem.*, 1977, **30**, 2057–2061; (*b*) S. M. Sondhi, M. P. Mahajan, A. K. Ganda and N. K. Ralhan, *J. Indian Chem. Soc.*, 1978, **16B**, 433–435; (*c*) P. Molina, J. Lindon and A. Tarraga, *Tetrahedron*, 1994, **50**(33), 10029–10036; (*d*) A. N. Krasovsky, P. M. Kochergin and A. B. Roman, *Khim. Geterotsikl. Soedin.*, 1976, **6**, 856.

5 (*a*) D. Hesek and A. Rybar, *Monatsh. Chem.*, 1994, **125**(11), 1273–1278; (*b*) W. Schulze and G. Letsch, *Pharmazie*, 1973, **28**, 367–371; (*c*) L. A. Sammers, *Angew. Chem.*, 1966, **78**(12), 644.

6 (*a*) R. A. Donia, J. A. Shotton, L. O. Bentz and G. E. P. Smith, *J. Org. Chem.*, 1949, **14**, 952–961; (*b*) D. O. Spry, A. R. Bhala, W. A. Spitzer, N. D. Jones and J. K. Swartzendruber, *Tetrahedron Lett.*, 1984, **25**(24), 2531–2534; (*c*) R. J. P. Corriu, G. F. Lanneau and V. D. Mehta, *J. Organomet. Chem.*, 1991, **419**, 9–26.

7 G. L'abbé, *J. Heterocycl. Chem.*, 1984, **21**, 627.

8 (*a*) Yu. Yu. Morzherin, E. V. Tarasov and V. A. Bakulev, *Khim. Geterotsikl. Soedin.*, 1994, **4**, 554–559; (*b*) G. L'abbé and E. Vanderstede, *J. Heterocycl. Chem.*, 1989, **26**, 1811–1814.

9 (*a*) J. R. Proudfoot, U. R. Patel and S. J. Campbell, *J. Org. Chem.*, 1993, **58**, 6996–7000; (*b*) W. R. Erickson and M. J. McKennon, *Tetrahedron Lett.*, 2000, **41**, 4541–4544.

10 (*a*) S. Ito, A. Ohta, H. Suhara, K. Tabashi and Y. Kawashima, *Chem. Pharm. Bull.*, 1993, **41**, 1066–1073; (*b*) D. Kotkar, S. W. Mahajan, A. K. Mandal and P. K. Ghosh, *J. Chem. Soc., Perkin Trans 1*, 1988, 1749–1752.

11 (*a*) V. A. Usov, L. V. Timokhina, L. I. Lavlinskaya and M. G. Voronkov, *Zh. Org. Khim.*, 1979, **15**, 2598–2599; (*b*) R. J. Anderson, C. A. Henrick and L. D. Rosenblum, *J. Am. Chem. Soc.*, 1974, **96**, 3654–3655.

12 M. Uher, V. Knoppova and A. Martvon, *Chem. Zvesti*, 1976, **30**(4), 514–519.

13 S. Smeets, C. V. Asokan, F. Motmans and W. Dehaen, *J. Org. Chem.*, 2000, **65**, 5882–5885.