

On the Reaction of Thiazole-2,4-diamines with Isothiocyanates – Preparation and Transformation of 2,4-Diaminothiazole-5-carbothioamides

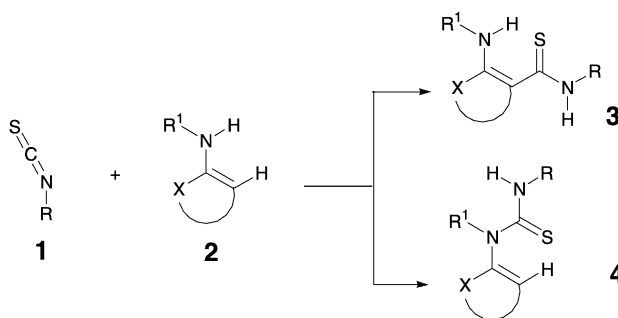
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In the reaction of thiazole-2,4-diamines **8** with isothiocyanates **1**, 2,4-diaminothiazole-5-carbothioamides **9**, **10**, **18**, and **19** as well as thiazolo[4,5-*d*]pyrimidine-7(6*H*)-thiones **21** were formed. The carbothioamides **9**, **10**, and **18** were transformed by reaction with different types of monofunctional and bifunctional electrophiles into hitherto unknown acceptor-substituted 4,4'-([2,5'-bithiazole]-2',4'-diyl)bis[morpholines] **24** and **29**, the 2',4'-bis(dialkylamino)[2,5'-bithiazol]-4-(5*H*)-ones **30**, and the 4-substituted 2',4'-bis(dialkylamino)-2,5'-bithiazoles **31**. From **30** and **31** new 4-mono- or 4,5-disubstituted 2',4'-bis(dialkylamino)-2,5'-bithiazoles **34**, **35**, **38**, and **39** as well as 5-substituted 2',4'-bis(dialkylamino)[2,5'-bithiazol]-4(5*H*)-ones **33**, **36**, and **37** were prepared.

Introduction. – Isothiocyanates **1** are, similar to other heterocumulenes, electrophilic compounds able to react with different types of nucleophiles [1]. For example, they can react with a series of electron-rich olefinic compounds **2**, such as enamines [2] or ketene *N,S*-acetals [3]. Independently of the substitution degree at the amino group, they usually react with the nucleophilic C-atom of compounds **2** to yield 3-amino-substituted thioacrylamides **3** [4] (*Scheme 1*). In contrast, with simple aromatic amines, isothiocyanates **1** react at their nucleophilic N-atom, as long as the amino moiety is not disubstituted, yielding corresponding thiourea derivatives **4** [5]. With *N,N*-disubstituted anilines, however, the reaction usually fails. The same is also observed for the reaction with *N,N*-disubstituted heteroaromatic amines such as thiazol-2-amines, whereas, *e.g.*, *N*-unsubstituted or *N*-monosubstituted thiazol-2-amines are able to react at the amino group with isothiocyanates giving rise to the formation of the corresponding thiourea derivatives [6].

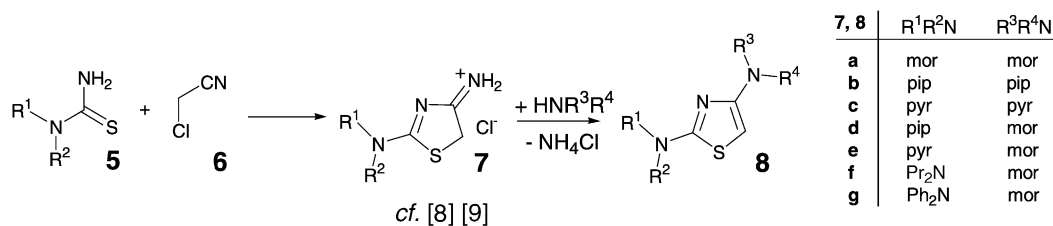
Scheme 1



The situation is significantly different in the case of thiazole-2,4-diamines **8**. As documented in the literature for one example so far, these compounds are able to react with aryl isothiocyanates **1** (R = Aryl) at C(5) of the heterocyclic system to yield 2,4-diaminothiazole-5-carbothioamides **9** [7]. Because this reaction was not generalized hitherto and the product obtained was not used for other reactions, we studied the reaction thiazole-2,4-diamines **8** with a series of different isothiocyanates **1** in more detail.

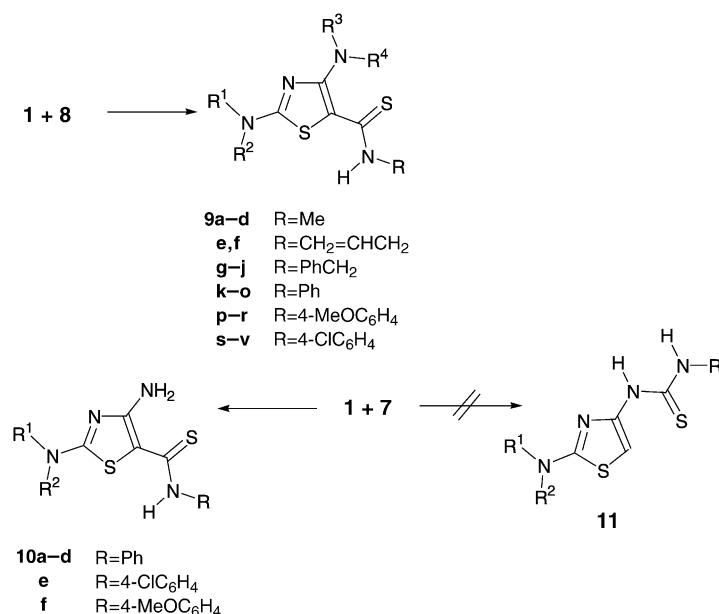
Results and Discussion. – The required substituted thiazole-2,4-diamines **8** were easily prepared starting from *N,N*-disubstituted thioureas **5** and chloroacetonitrile (**6**) [8] (Scheme 2). In a first step, 2-aminothiazol-4(5*H*)-iminium chlorides **7** were formed. These salts could be transformed, subsequently, by reaction with primary or secondary amines into the *N*²,*N*²,*N*⁴,*N*⁴-tetrasubstituted thiazole-2,4-diamines **8** [9].

Scheme 2



mor=morpholin-4-yl, pip=piperidin-1-yl, pyr=pyrrolidin-1-yl

Advantageously, the highly reactive heteroaromatic diamines **8** had to be stored as their mineral-acid adducts **8**·HX and generated from those by addition of a base before their use in the reaction with the isothiocyanates **1**. This reaction was performed, in general, by heating the mixture of **1** and **8** in MeOH, from which the products of the general structure **9** separated on cooling (Scheme 3). The yields of the thus prepared 2,4-diaminothiazol-5-carbothioamides **9a–v** ranged from 25 to 93% (see Table 1 in the Exper. Part). Their structures were elucidated from elemental analyses and spectroscopic data. Whereas there is no doubt about the structure of the products **9** obtained from *N*²,*N*²,*N*⁴,*N*⁴-tetrasubstituted thiazole-2,4-diamines **8**, some doubt is legitimated regarding the structure of the products **10** obtained from the reaction of isothiocyanates **1** with thiazole-2,4-diamines which bear a monosubstituted or unsubstituted amino group at C(4) and were generated *in situ* from their iminium salts **7**; alternatively to the formation of 2,4-diaminothiazole-5-carbothioamides **10** with a primary amino group at C(4), thiourea derivatives **11** might have been generated by the attack of isothiocyanates **1** at the 4-amino group of **7**. However, the ¹H-decoupled ¹³C-NMR spectra unambiguously established the general structure **10** for the products obtained from **1** and **7** (see also data in Tables 1 and 2 in the Exper. Part). It is worth mentioning that the formation of compounds **10** was not accompanied by the simultaneous or exclusive formation of *N*²,*N*²,*N*^{2'},*N*^{2'}-tetraalkyl[4,5'-bithiazole]-2,2',4'-triamines, the self-condensation products of the free thiazole-2,4-diamines primarily formed from their 2-aminothiazol-4(5*H*)-iminium precursors **7** [10].

Scheme 3^{a)}

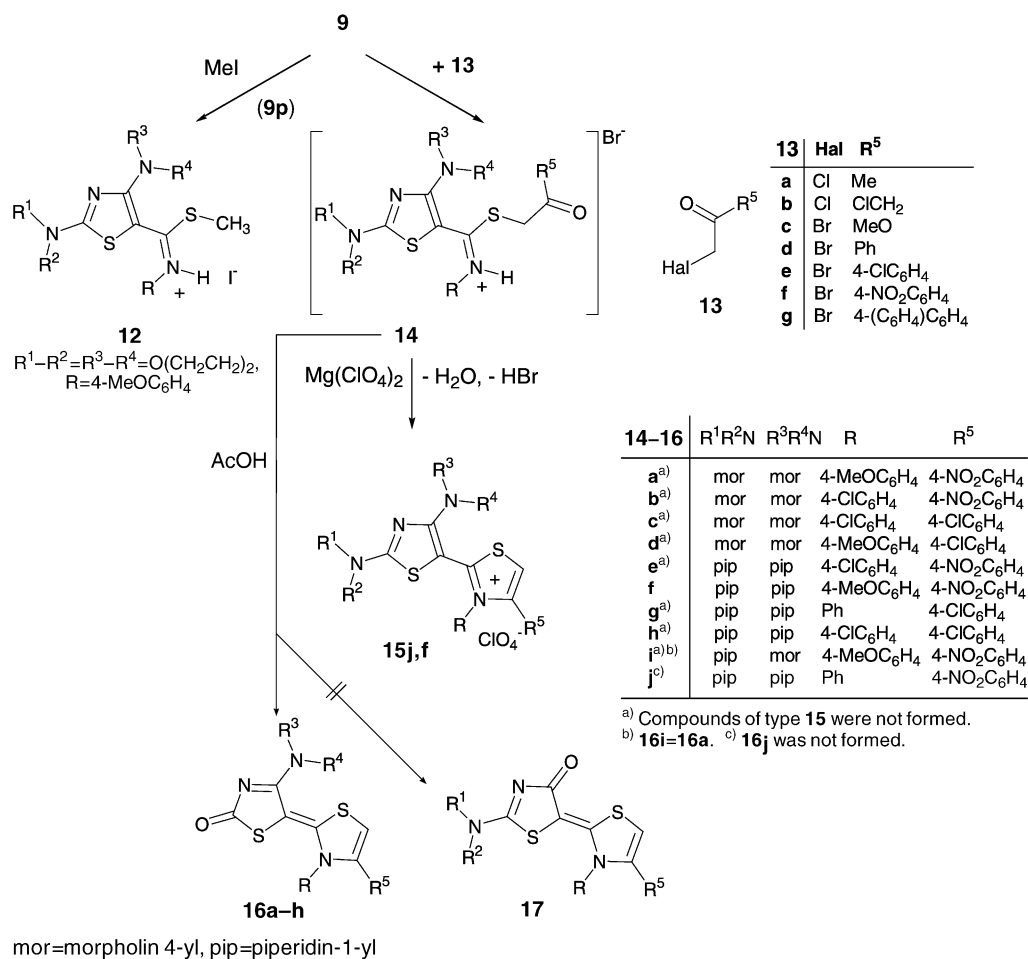
^{a)} For R¹–R⁴, see Table 1.

The 2,4-diaminothiazole-5-carbothioamides **9** and **10** are yellow or orange solids that are highly reactive towards alkylating reagents. As exemplified with **9p** and MeI, alkylation at the thiocarbonyl group occurred, and the *N*-[(diaminothiazolyl)-(methylthio)methylene]benzenaminium iodide **12** was formed (Scheme 4). Its structure was unambiguously elucidated from analytic and spectroscopic data.

With halomethyl carbonyl compounds **13**, which are also strong electrophilic reagents and, moreover, versatile synthons for preparing thiazoles *via* a *Hantzsch* reaction [11], the 2,4-diaminothiazole-5-carbothioamides **9** also reacted. However, the products could be isolated only under special conditions and in the case of specially substituted starting materials, *e.g.*, from chloro- or nitro-substituted phenacylmethyl halides **13e** and **13f**. Thus, by heating an equimolar mixture of 2,4-diaminothiazole-5-carbothioamides **9l** or **9g**, 2-bromo-2-(4-nitrophenyl)ethanone (**13f**), and Mg(ClO₄)₂ in Ac₂O, the corresponding 2',4'-bis(dialkylamino)-3,4-diaryl[2,5'-bithiazol]-3-ium perchlorates **15j** and **15f** were isolated (Scheme 4). These compounds result, obviously, *via* the primarily formed **14** by a ring-closure reaction between the carbonyl and iminium groups.

However, a mixture of **9** and **13e** or **13f** in AcOH at reflux temperature reacted to give products **16** having lost the amino group of the starting compound **9** (Scheme 4). The alternative formation of **17** was excluded by the fact that **9r** containing a piperidin-1-yl group at C(2) and a morpholin-4-yl group at C(4) yielded **16a** containing only a morpholin-4-yl group, as established by its characteristic ¹H-NMR signals. Thus, the piperidin-1-yl moiety at C(2) of the putative intermediate **15i** was selectively hydrolyzed to give **16a**. The 2',4'-bis(dialkylamino)-3,4-diaryl[2,5'-bithiazol]-3-ium

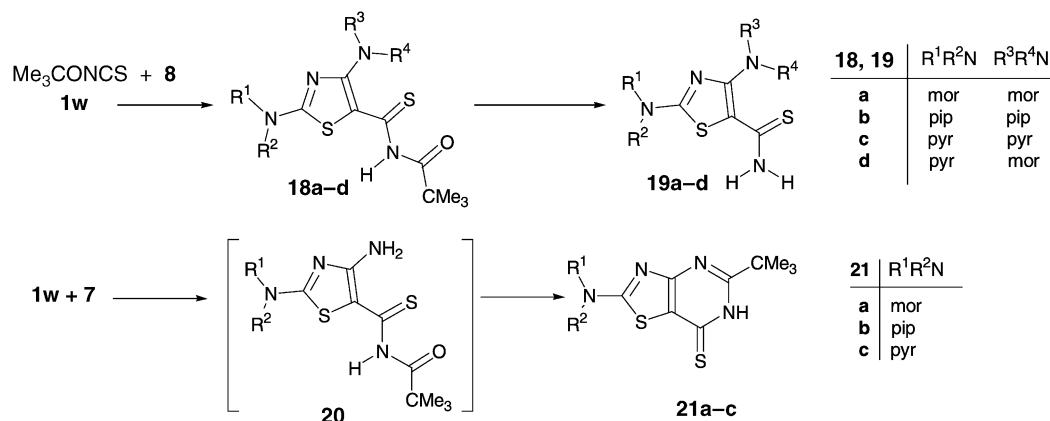
Scheme 4



perchlorates **15** and the 5-[3-aryl-4-aryl'-thiazol-2(3*H*)-ylidene]-4-(dialkylamino)thiazol-2(5*H*)-ones **16** are deep red compounds which absorb in CH_2Cl_2 at *ca.* 470 and 420 nm, respectively.

The reaction of thiazole-2,4-diamines **8** with isothiocyanates can also be extended to acyl isothiocyanates, as exemplified with pivaloyl isothiocyanate (**1w**). In this case, new *N*⁵-pivaloyl-substituted 2,4-diaminothiazole-5-carbothioamides **18** were obtained (Scheme 5). When *N*⁴-unsubstituted thiazole-2,4-diamines, generated *in situ* from the corresponding hydrochlorides **7**, were used for this reaction, fused thiazolo[4,5-*d*]pyrimidine-7(6*H*)-thiones **21** were obtained instead of the corresponding *N*⁵-pivaloyl-substituted 2,4-diaminothiazole-5-carbothioamides **20**. Obviously, these compounds result from the primarily formed **20** by a condensation reaction between the pivaloyl group and the free amino group at C(4). In contrast to compounds **18**,

Scheme 5



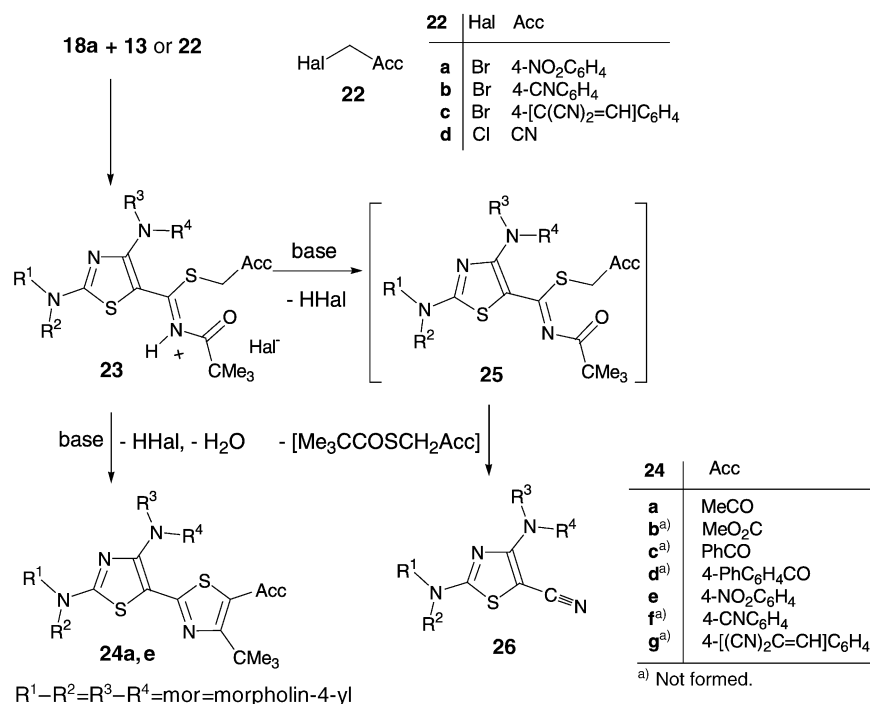
mor=morpholin-4-yl, pip=piperidin-1-yl, pyr=pyrrolidin-1-yl

which are deep yellow, the fused thiones **21** are nearly colorless. Their structures were determined from elemental analysis, NMR, and MS data.

Similarly to other *N*-acylthioureas [12], the *N*⁵-pivaloyl-substituted 2,4-diaminothiazole-5-carbothioamides **18** formally vinylogous *N*-acylthioureas, react with acceptor-substituted halomethyl compounds **13** or **22** (Scheme 6). The reaction was performed with **18a** and some halomethyl compounds in analogy to the previously mentioned alkylations of the *N*⁵-alkyl- or *N*⁵-aryl-substituted 2,4-diaminothiazole-5-carbothioamides **9** (see Scheme 4) by heating the components in MeCN and subsequent addition of Et₃N to the hot mixture. In contrast to the reaction with chloroacetone (**13a**) and 4-nitrobenzyl bromide (**22a**), from which the expected acetyl-(*tert*-butyl)- and (*tert*-butyl)-(4-nitrophenyl)-substituted 4,4'-([2,5'-bithiazole]-2',4'-diyl)bis[morpholines] **24a** and **24e**, respectively, were obtained, unexpected products could be isolated with other halomethyl compounds, such as from chloroacetonitrile (**22d**) or phenacyl bromide (**13d**). In these cases, 2,4-di(morpholin-4-yl)thiazole-5-carbonitrile (**26**) was obtained as the sole product. This compound was unambiguously identified by an IR absorption band at 2200 cm⁻¹ and was obviously formed by base-initiated splitting of a pivaloyl and a phenacylthio or mercaptoacetonitrile (Acc = CN) moiety from the intermediate **25** similar to other compounds of comparable structures recently described [13].

The *N*⁵-pivaloyl-substituted 2,4-diaminothiazole-5-carbothioamides **18** decomposed, analogously to other *N*-acylthioamides and thioureas [14], into the *N*⁵-unsubstituted 5-carbothioamides **19** in the presence of strong mineral acid at room temperature. With the unsubstituted carbothioamide moiety, compounds **19** are interesting starting materials for preparing the unknown acceptor-substituted 4,4'-([2,5'-bithiazole]-2',4'-diyl)bis[morpholines] **29** (Scheme 7). For example, **19a** was transformed by reaction with triethyl orthoformate and morpholine according to a recently published procedure [15] into 2,4-di(morpholin-4-yl)-*N*⁵-[(morpholin-4-yl)-methylene]thiazole-5-carbothioamide (**27**), from which the 5-acceptor-substituted 4,4'-

Scheme 6

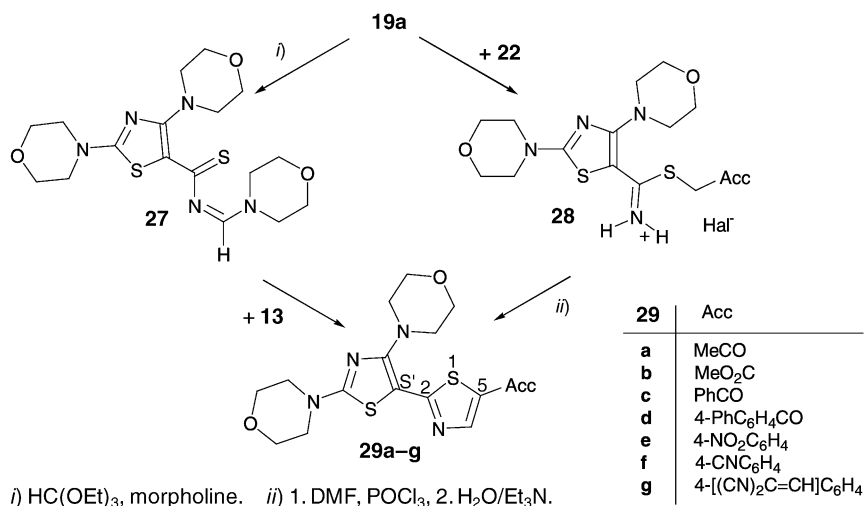


([2,5'-bithiazole]-2',4'-diyl)bis[morpholines] **29** were available *via* the reaction with **13**. Alternatively, **29** could be prepared also by the reaction of **19a** with **22** to yield the intermediate carbothioamide hydrohalide **28** (not isolated), from which the products **29** were obtained, subsequently, by reaction with a formylating agent, *e.g.*, with the *Vilsmeier* reagent prepared from DMF and POCl₃ [16].

Furthermore, the 2,4-diaminothiazole-5-carbothioamides **19** were transformed into 2',4'-diamino[2,5'-bithiazol]-4(5*H*)-ones **30** by reaction with methyl bromoacetate (**13c**) or into 4-substituted 2',4'-diamino-2,5'-bithiazoles **31** by reaction with halomethyl ketones **13a**, **13b**, or **13d**. Satisfactory yields of products were obtained by heating the appropriate components in EtOH solution (see Scheme 8).

To study the reactivity of **30** and **31** towards electrophiles, they were allowed to react with arenediazonium salts and with the *Vilsmeier* reagent. As reported earlier [17][18], such reagents are able to react with 2-amino-substituted thiazol-4(5*H*)-ones or thiazole-2-amines unsubstituted at C(5). Thus, the reaction of **30a** with 4-nitrobenzenediazonium salt gave the 2',4'-di(morpholin-4-yl)[2,5'-bithiazole]-4,5-dione 5-[4-nitrophenyl]hydrazone] (**33a**), which, by subsequent reaction with H₃BO₃ and Ac₂O, was converted to the fused thiazolo[5,4-*e*]-1,3,4,2-oxadiazaborine derivative **32**, in analogy to the reaction of other 1,2-dione monohydrazones [19]. With the *Vilsmeier* reagent, **30a** yielded, depending on the reaction conditions, the chloro-substituted 4,4'-([2,5'-bithiazol]-2',4'-diyl)bis[morpholine] **34a** or 2',4'-di(morpholin-4-yl)[2,5'-bithiazole]-5-carboxaldehyde **35a**. Obviously, **34a** is the precursor of **35a**.

Scheme 7



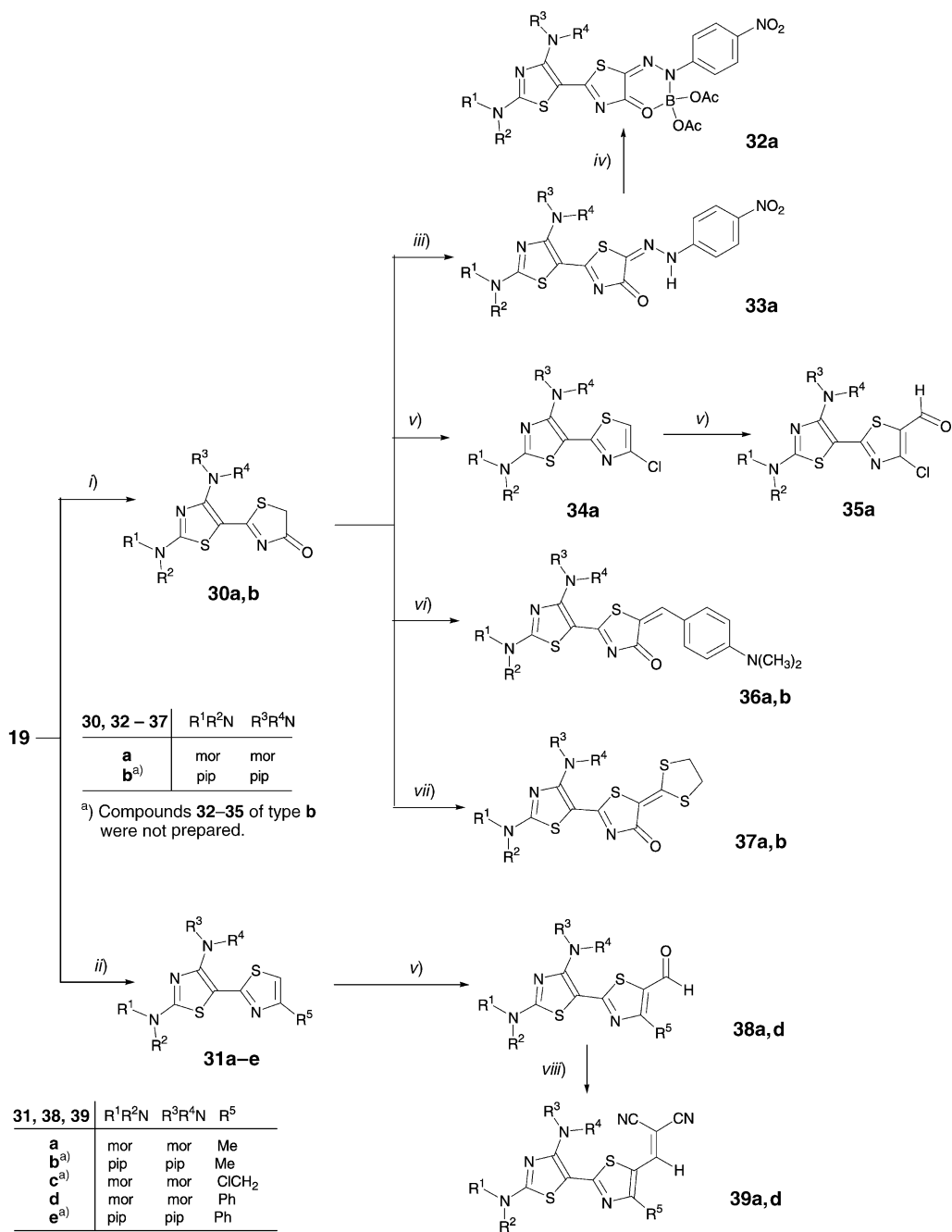
Owing to their thiazol-4(5*H*)-one structure, compounds **30** undergo also base-catalyzed reactions with less-reactive electrophiles, *e.g.*, with 4-(dimethylamino)benzaldehyde or CS₂. Whereas, in the former case, deeply colored 5-[(4-dimethylamino)-benzylidene][2,5'-bithiazol]-4(5*H*)-ones **36** were formed, in the latter case, unstable 4,5-dihydro-4-oxo[2,5'-bithiazole]carbodithioic acids were generated. These compounds could be transformed into stable 5-(1,3-dithiolan-2-ylidene)[2,5'-bithiazol]-4(5*H*)-ones **37** by reaction with 1,2-dibromoethane.

In contrast to **30**, the 2,5'-bithiazole derivatives **31** were unable to react with less-reactive electrophilic reagents such as arenediazonium salts. With the *Vilsmeier* reagent at elevated temperatures, however, they were transformed into 4-substituted [2,5'-bithiazole]-5-carboxaldehydes **38**. These compounds can be subsequently transformed, *e.g.*, by treatment with malononitrile in the presence of catalytic amounts of Et₃N, into deeply colored 2-[(2,5'-bithiazol]-5-yl)methylene]propanedinitriles **39**.

Because thiazole-2-amines are frequently biologically active, *e.g.*, as active compounds for treatment of allergies [20], hypertension [21], inflammation [22], tumors [23], schizophrenia [24], HIV infection [25], as antibiotics [26], or as inhibitors for cyclin-dependent kinases [27], several of the compounds described in this paper, especially carbothioamide derivatives **9** and **10**, were tested for some of these activities. Other compounds, such as the 2-methylenepropanedinitriles **39** or the [2,5'-bithiazole]-5-carboxaldehydes **35a** and **38**, were tested accordingly to their nonlinear optical properties [28] or used as precursors for preparing compounds with such properties [29]. The results of these studies will be reported elsewhere.

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Scheme 8



i) **13c** Et₃N. *ii)* **13a,b,d** Et₃N. *iii)* 4-NO₂C₆H₄N₂⁺. *iv)* H₃BO₃, Ac₂O. *v)* DMF, POCl₃. *vi)* 4-Me₂NC₆H₄CHO.

vii) 1. CS₂, NaOH; 2. (CH₂Br)₂. *viii)* CH₂(CN)₂, Et₃N.

Experimental Part

General. M.p.: Boetius heating-table microscope; uncorrected. IR Spectra: KBr pellets; *Philips FTIR-PU-9624* spectrometer; in cm^{-1} . UV/VIS Spectra: *Zeiss MC-400* spectrometer; λ_{max} ($\log \epsilon$) in nm. NMR Spectra: *Varian Gemini-300* 300 MHz spectrometer; δ in ppm. Elemental analyses: *Leco CHNS-932* analyzer.

2-(Dialkylamino)thiazol-4(5H)-iminium Chlorides 7 and N^{2,2},N⁴,N⁴-Tetraalkyl-Substituted Thiazole-2,4-diamines 8. These starting materials were prepared according to [8][9].

2,4-Bis(dialkylamino)thiazole-5-carbothioamides 9: General Procedure. A mixture of a thiazole-2,4-diamine **8** (0.01 mol), prepared from the corresponding mineral-acid adduct **8**·HX [8] by treatment with aq. NaOH soln., and an isothiocyanate **1** (0.01 mol) in MeOH (50 ml) was heated to reflux for 15 min. The precipitated product was filtered off after cooling to r.t. and then washed with EtOH and Et₂O: **9a–v**, see *Tables 1* and *2*.

4-Amino-2-(dialkylamino)thiazole-5-carbothioamides 10: General Procedure. To a suspension of a 2-(dialkylamino)thiazol-5(5H)-iminium chloride **7** (0.02 mol) in toluene (100 ml), Et₃N (28 ml, 0.02 mol) and isothiocyanate **1** (0.02 mol) were added. After refluxing the mixture for 1 h, the precipitated Et₃N·HCl was filtered off and washed with hot toluene. After cooling, the product crystallized from the filtrate. The crystals were washed with Et₂O: **10a–f**, see *Tables 1* and *2*.

Table 1. Characteristic Data of Compounds **9** and **10**

	R ¹ R ² N ^a)	R ³ R ⁴ N ^a)	R	Yield [%]	M.p. [°]	Formula (<i>M_r</i>)	calc. found	C	H	N	S
9a	mor	mor	Me	34	172–173	C ₁₃ H ₂₀ N ₄ O ₂ S ₂ (328.46)	47.54 47.87	6.14 6.17	17.06 16.99	19.53 19.48	
b	pip	pip	Me	84	191–193	C ₁₅ H ₂₄ N ₄ S ₂ (324.51)	55.52 55.53	7.45 7.47	17.27 17.19	19.76 19.44	
c	pyr	pyr	Me	80	193–195	C ₁₃ H ₂₀ N ₄ S ₂ (296.46)	52.67 52.51	6.80 6.88	18.90 18.85	21.63 21.43	
d	pip	mor	Me	25	127–129	C ₁₄ H ₂₂ N ₄ OS ₂ (326.48)	51.50 52.08	6.79 6.45	17.16 17.19	19.64 19.66	
e	mor	mor	CH ₂ =CHCH ₂	69	128–130	C ₁₅ H ₂₂ N ₄ O ₂ S ₂ (354.49)	50.82 50.49	6.26 6.18	15.80 15.93	18.09 18.05	
f	pip	mor	CH ₂ =CHCH ₂	71	84–85	C ₁₆ H ₂₄ N ₄ OS ₂ (358.52)	54.51 54.08	6.86 6.99	15.89 16.00	18.19 18.61	
g	mor	mor	PhCH ₂	83	171–173	C ₁₉ H ₂₄ N ₄ O ₂ S ₂ (404.55)	56.41 56.32	5.98 5.94	13.85 13.86	15.85 15.83	
h	pip	pip	PhCH ₂	88	170–172	C ₂₁ H ₂₈ N ₄ S ₂ (400.61)	62.96 63.37	7.04 6.80	13.00 13.82	16.01 16.06	
i	mor	pyr	PhCH ₂	69	117–119	C ₁₉ H ₂₄ N ₄ OS ₂ (388.55)	58.73 59.28	6.23 6.33	14.42 14.69	16.51 16.77	
j	pip	mor	PhCH ₂	87	191–192	C ₂₀ H ₂₆ N ₄ OS ₂ (402.58)	59.67 59.90	6.51 6.36	13.92 14.00	15.93 15.77	
k	mor	mor	Ph	73	211	C ₁₈ H ₂₂ N ₄ O ₂ S ₂ (390.53)	55.36 55.73	5.68 5.32	14.35 14.23	16.42 16.31	
l	pip	pip	Ph	74	168–170	C ₂₀ H ₂₆ N ₄ S ₂ (386.56)	62.14 62.01	6.78 6.83	14.49 14.80	16.59 16.45	
m	pyr	pyr	Ph	72	164	C ₁₈ H ₂₂ N ₄ S ₂ (358.53)	60.30 60.52	6.18 6.34	15.63 15.58	17.89 17.65	
n	mor	pyr	Ph	70	160–162	C ₁₈ H ₂₂ N ₄ OS ₂ (374.53)	57.72 58.01	5.92 5.83	14.96 14.80	17.12 17.45	
o	pip	mor	Ph	87	207–210	C ₁₉ H ₂₄ N ₄ OS ₂ (388.55)	58.73 59.19	6.23 6.15	14.42 14.72	16.51 16.68	
p	mor	mor	4-MeOC ₆ H ₄	86	172	C ₁₉ H ₂₄ N ₄ O ₃ S ₂ (420.55)	54.26 54.65	5.75 5.84	13.32 13.38	15.25 15.26	
q	pip	pip	4-MeOC ₆ H ₄	74	178–180	C ₂₁ H ₂₈ N ₄ OS ₂ (416.61)	60.54 60.85	6.77 6.75	13.45 13.51	15.39 15.36	

Table 1 (cont.)

r	pip	mor	4-MeOC ₆ H ₄	88	184–185	C ₂₀ H ₂₆ N ₄ O ₂ S ₂ (418.58)	57.39 57.18	6.26 6.44	13.39 13.69	15.32 15.58
s	mor	mor	4-ClC ₆ H ₄	74	216–218	C ₁₈ H ₂₁ ClN ₄ O ₂ S ₂ (424.97)	50.87 51.31	4.98 5.04	13.18 13.17	15.09 15.06
t	pip	pip	4-ClC ₆ H ₄	67	183–185	C ₂₀ H ₂₅ ClN ₄ S ₂ (421.02)	57.05 57.26	5.99 6.08	13.31 13.31	15.23 15.30
u	mor	pyr	4-ClC ₆ H ₄	61	169–171	C ₁₈ H ₂₁ ClN ₄ OS ₂ (408.97)	52.86 52.93	5.18 5.12	13.70 14.15	15.68 15.99
v	pip	mor	4-ClC ₆ H ₄	93	180–182	C ₁₉ H ₂₃ ClN ₄ OS ₂ (423.00)	53.95 54.19	5.48 5.86	13.25 13.67	15.16 15.50
10a	mor	–	Ph	75	205–207	C ₁₄ H ₁₆ N ₄ OS ₂ (320.44)	52.48 52.24	5.03 4.82	17.48 17.01	20.01 19.79
b	pip	–	Ph	72	190–193	C ₁₅ H ₁₈ N ₄ S ₂ (318.46)	56.57 56.25	5.70 5.65	17.59 17.11	20.14 19.98
c	pyr	–	Ph	65	185–186	C ₁₄ H ₁₆ N ₄ S ₂ (304.44)	55.23 55.08	5.30 4.85	18.40 18.59	21.07 20.86
d	Pr ₂ N	–	Ph	63	138–139	C ₁₆ H ₂₂ N ₄ S ₂ (334.50)	57.45 57.71	6.63 6.74	16.75 16.39	19.17 18.78
e	mor	–	4-ClC ₆ H ₄	79	204–206	C ₁₄ H ₁₅ ClN ₄ OS ₂ (354.88)	47.38 47.29	4.26 3.80	15.79 16.10	18.07 17.76
f	mor	–	4-MeOC ₆ H ₄	81	217–218	C ₁₅ H ₁₈ N ₄ O ₂ S ₂ (350.46)	51.41 51.14	5.18 4.62	15.99 16.02	18.30 18.23

^a) mor = morpholin-4-yl, pip = piperidin-1-yl, pyr = pyrrolidin-1-yl.

N-[2,4-Di(morpholin-4-yl)thiazol-5-yl](methylthio)methylene-4-methoxybenzenaminium Iodide (**12**). To a soln. of *N*⁵-(4-methoxyphenyl)-2,4-di(morpholin-4-yl)thiazole-5-carbothioamide (**9p**; 4.2 g, 10 mmol) in CH₂Cl₂ (50 ml), Mel (1.4 g, 10 mmol) was added. After keeping the mixture overnight, the precipitate was filtered off: 4.3 g (77%) of **12**. Yellow crystals. M.p. 207–210°. ¹H-NMR (CDCl₃): 1.57 (s, MeS); 2.24 (s, MeN); 3.68 (m, 8 H, CH₂N); 3.78 (m, 8 H, CH₂O); 6.83 (d, 2 arom. H); 7.50 (d, 2 arom. H); 11.29 (s, NH). Anal. calc. for C₂₀H₂₇IN₄O₃S₂ (562.49): C 42.71, H 4.84, N 9.96, S 11.40; found: C 42.57, H 4.99, N 10.04, S 11.25.

2',4'-Bis(dialkylamino)-3,4-diaryl[2,5'-bithiazol]-3-ium Perchlorates **15**: General Procedure. A mixture of 2,4-bis(dialkylamino)thiazole-5-carbothioamide **9l** or **9q** (0.01 mol), phenacyl bromide **13f** (0.01 mol), Mg(ClO₄)₂ (1.15 g, 5 mmol), and Ac₂O (15 ml) was refluxed for 25 min. After cooling, the mixture was diluted with aq. EtOH soln. (50 ml). The precipitated product was filtered off and recrystallized from AcOH: **15a'** or **15f**, resp.

4-(4-Nitrophenyl)-3-phenyl-2',4'-dipiperidin-1-yl[2,5'-bithiazol]-3-ium Perchlorate (**15j**) from *N*⁵-phenyl-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9o**) and 4-nitrophenacyl bromide (**13f**). Yield 19%. M.p. 303–305°. UV/VIS (CH₂Cl₂): 467 (4.38). ¹H-NMR ((D₆)DMSO): 1.54 (m, 6 H, CH₂); 1.68 (m, 6 H, CH₂); 3.32 (t, 4 H, CH₂N); 3.46 (t, 4 H, CH₂N); 7.75 (m, 5 arom. H); 8.10 (d, 2 arom. H); 8.40 (d, 2 arom. H); 10.82 (s, 1 heteroarom. H). Anal. calc. for C₂₈H₃₀ClN₅O₆S₂ (632.15): C 53.20, H 4.78, N 11.08, S 10.15; found: C 53.41, H 4.91, N 10.88, S 9.99.

3-(4-Methoxyphenyl)-4-(4-nitrophenyl)-2',4'-di(piperidin-1-yl)[2,5'-bithiazol]-3-ium Perchlorate (**15f**). From *N*⁵-(4-methoxyphenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9q**) and 4-nitrophenacyl bromide (**13f**). Yield 23%. M.p. 268–269°. UV/VIS: 470 (4.43). ¹H-NMR ((D₆)DMSO): 1.57 (m, 6 H, CH₂); 1.69 (m, 6 H, CH₂); 3.28 (t, 4 H, CH₂N); 3.47 (t, 4 H, CH₂N); 3.89 (s, MeO); 7.24 (d, 2 arom. H); 7.65 (d, 2 arom. H); 8.09 (d, 2 arom. H); 8.41 (d, 2 arom. H); 10.69 (s, 1 heteroarom. H). Anal. calc. for C₂₉H₃₂ClN₅O₇S₂ (662.14): C 52.60, H 4.87, N 10.58, S 9.69; found: C 52.32, H 5.01, N 10.38, S 9.97.

5-[3-Aryl-4-aryl'-thiazol-2(3H)-ylidene]-4-(dialkylamino)-thiazol-2(5H)-ones **16**: General Procedure. A mixture of a 2,4-bis(dialkylamino)thiazole-5-carbothioamide **9** (0.01 mol) and a phenacyl bromide **13f** or **13e** (0.01 mol) in AcOH (15 ml) was refluxed for 20 min. The products precipitated during heating were isolated by filtration after cooling to r.t.: **16a–h**.

Table 2. ^1H -NMR Data of Compounds **9** and **10**. In CDCl_3

9a	3.03 (t, 4 H, CH_2N); 3.24 (t, 4 H, CH_2N); 3.48 (t, 4 H, CH_2O); 3.76 (m, 7 H, CH_2O , Me); 9.99 (s, NH)
b	1.61 (m, 12 H, CH_2); 2.95 (t, 4 H, CH_2N); 3.23 (d, 3 H, Me); 3.45 (t, 4 H, CH_2N); 10.70 (s, NH)
c	1.87 (m, 4 H, CH_2); 1.98 (m, 4 H, CH_2); 3.26 (t, 7 H, CH_2N , Me); 3.40 (t, 4 H, CH_2N); 8.75 (s, NH)
d	1.63 (m, 6 H, CH_2); 3.05 (t, 4 H, CH_2N); 3.24 (d, 3 H, Me); 3.46 (t, 4 H, CH_2N); 3.82 (t, 4 H, CH_2N); 9.88 (s, NH)
e	3.02 (t, 4 H, CH_2N); 3.48 (t, 4 H, CH_2N); 3.75 (m, 8 H, CH_2O); 4.35 (t, 2 H, CH_2); 5.24–5.35 (m, 2 H, CH_2); 5.96 (m, CH); 10.09 (s, NH)
f	1.62 (m, 6 H, CH_2); 3.01 (t, 4 H, CH_2N); 3.46 (t, 4 H, CH_2N); 3.73 (t, 4 H, CH_2O); 4.37 (t, 2 H, CH_2); 5.22–5.35 (m, 2 H, CH_2); 5.98 (m, CH); 9.99 (s, NH)
g	2.88 (t, 4 H, CH_2N); 3.30 (t, 4 H, CH_2N); 3.48 (t, 4 H, CH_2O); 3.75 (t, 4 H, CH_2O); 4.84 (d, 2 H, CH_2); 7.34 (m, 5 arom. H); 10.26 (s, NH)
h	1.62 (m, 12 H, CH_2); 2.85 (t, 4 H, CH_2N); 3.46 (t, 4 H, CH_2N); 4.87 (d, 2 H, CH_2); 7.36 (m, 5 arom. H); 10.45 (s, NH)
i	1.64 (m, 4 H, CH_2); 1.98 (t, 4 H, CH_2N); 3.11 (t, 4 H, CH_2N); 3.41 (t, 4 H, CH_2O); 4.91 (d, 2 H, CH_2); 7.33 (m, 5 arom. H); 9.35 (s, NH)
j	1.62 (m, 6 H, CH_2); 2.89 (t, 4 H, CH_2N); 3.29 (t, 4 H, CH_2N); 3.47 (t, 4 H, CH_2O); 4.85 (d, 2 H, CH_2); 7.35 (m, 5 arom. H); 10.16 (s, NH)
k	3.12 (t, 4 H, CH_2N); 3.53 (t, 4 H, CH_2N); 3.78 (t, 4 H, CH_2O); 3.82 (t, H, CH_2O); 7.19 (m, 1 arom. H); 7.38 (m, 2 arom. H); 7.81 (d, 2 arom. H); 12.11 (s, NH)
l	1.64 (m, 12 H, CH_2); 3.05 (t, 4 H, CH_2N); 3.50 (t, 4 H, CH_2N); 7.15 (m, 1 arom. H); 7.36 (m, 2 arom. H); 7.81 (d, 2 arom. H); 12.28 (s, NH)
m	1.90 (m, 4 H, CH_2); 2.01 (m, 4 H, CH_2); 3.34 (t, 4 H, CH_2N); 3.44 (t, 4 H, CH_2N); 7.12 (m, 1 arom. H); 7.30 (m, 2 arom. H); 7.67 (d, 2 arom. H); 10.64 (s, NH)
n	1.90 (t, 4 H, CH_2); 2.02 (t, 4 H, CH_2N); 3.34 (t, 4 H, CH_2N); 3.45 (t, 4 H, CH_2O); 7.13 (m, 1 arom. H); 7.33 (m, 2 arom. H); 7.67 (d, 2 arom. H); 10.64 (s, NH)
o	1.65 (m, 6 H, CH_2); 3.13 (t, 4 H, CH_2N); 3.51 (t, 4 H, CH_2N); 3.83 (t, 4 H, CH_2O); 7.19 (m, 1 arom. H); 7.34 (m, 2 arom. H); 7.80 (d, 2 arom. H); 12.00 (s, NH)
p	3.11 (t, 4 H, CH_2N); 3.52 (t, 4 H, CH_2N); 3.80 (m, 11 H, CH_2O , MeO); 6.90 (d, 2 arom. H); 7.66 (d, 2 arom. H); 11.96 (s, NH)
r	1.65 (m, 6 H, CH_2); 3.12 (t, 4 H, CH_2N); 3.50 (t, 4 H, CH_2N); 3.80 (m, 7 H, CH_2O , MeO); 6.90 (d, 2 arom. H); 7.65 (d, 2 arom. H); 11.85 (s, 1 H, NH)
q	1.64 (m, 12 H, CH_2); 3.04 (t, 4 H, CH_2N); 3.50 (t, 4 H, CH_2N); 3.80 (s, 3 H, MeO); 6.90 (d, 2 arom. H); 7.66 (d, 2 arom. H); 12.11 (s, NH)
s	3.11 (t, 4 H, CH_2N); 3.53 (t, 4 H, CH_2N); 3.78 (t, 4 H, CH_2O); 3.83 (t, 4 H, CH_2O); 7.32 (d, 2 arom. H); 7.76 (d, 2 arom. H); 12.11 (s, 1 H, NH)
t	1.64 (m, 12 H, CH_2); 3.04 (t, 4 H, CH_2N); 3.51 (t, 4 H, CH_2N); 7.30 (d, 2 arom. H); 7.76 (d, 2 arom. H); 12.29 (s, NH)
u	1.92 (m, 4 H, CH_2); 2.02 (m, 4 H, CH_2N); 3.33 (t, H, CH_2N); 3.44 (t, 4 H, CH_2O); 7.26 (d, 2 arom. H); 7.63 (d, 2 arom. H); 10.61 (s, 1 H, NH)
v	1.65 (m, 6 H, CH_2); 3.12 (t, 4 H, CH_2N); 3.51 (t, 4 H, CH_2N); 3.82 (t, 4 H, CH_2O); 7.31 (d, 2 arom. H); 7.76 (d, 2 arom. H); 12.00 (s, NH)
10a	3.51 (t, 4 H, CH_2N); 3.75 (t, 4 H, CH_2O); 7.36 (m, 5 arom. H); 7.40–8.24 (br., 3 H, NH)
b	1.65 (m, 6 H, CH_2); 3.45 (t, 4 H, CH_2N); 7.18 (m, 1 arom. H); 7.35 (m, 4 arom. H); 7.50–8.20 (br., 3 H, NH)
c	2.03 (m, 4 H, CH_2); 3.44 (t, 4 H, CH_2N); 7.17–7.40 (m, 5 arom. H); 7.50–8.10 (br., 3 H, NH)
d	0.91 (t, 6 H, Me); 1.64 (m, 4 H, CH_2); 3.33 (t, 4 H, CH_2N); 7.14 (m, 1 arom. H); 7.29–7.40 (m, 4 arom. H); 7.50–8.00 (br., 3 H, NH)
e	3.53 (t, 4 H, CH_2N); 3.76 (t, 4 H, CH_2O); 7.22 (d, 2 arom. H); 7.29 (d, 2 arom. H); 7.40–8.20 (br., 3 H, NH)
f	3.50 (t, 4 H, CH_2N); 3.76 (m, 7 H, CH_2O , MeO); 6.86 (d, 2 arom. H); 7.26 (d, 2 arom. H); 7.50–8.10 (br., 3 H, NH)

5-[3-(4-Methoxyphenyl)-4-(4-nitrophenyl)thiazol-2(3H)-ylidene]-4-(morpholin-4-yl)thiazol-2(5H)-one (**16a**). From *N*⁵-(4-methoxyphenyl)-2,4-dimorpholin-4-ylthiazole-5-carbothioamide (**9p**) or *N*⁵-(4-methoxyphenyl)4-(morpholin-4-yl)-2-(piperidin-1-yl)thiazole-5-carbothioamide (**9r**) and 4-nitrophenacyl bromide (**13f**). Yield 79 and 56%, resp. M.p. 303–305°. UV/VIS: 431 (4.24). ¹H-NMR ((D₆)DMSO): 3.35 (*t*, 4 H, CH₂N); 3.61 (*t*, 4 H, CH₂O); 6.97 (*d*, 2 arom. H); 7.19 (*d*, 2 arom. H); 7.98 (*d*, 2 arom. H); 8.22 (*d*, 2 arom. H); 10.02 (*s*, 1 heteroatom. H). Anal. calc. for C₂₃H₂₀N₄O₅S₂ (496.56): C 55.63, H 4.06, N 11.28, S 12.92; found: C 55.79, H 4.28, N 11.29, S 13.11.

5-[3,4-Chlorophenyl]-4-(4-nitrophenyl)thiazol-2(3H)-ylidene]-4-(morpholin-4-yl)thiazol-2(5H)-one (**16b**). From *N*⁵-(4-chlorophenyl)-4-(morpholin-4-yl)-2-(piperidin-1-yl)thiazole-5-carbothioamide (**9v**) and 4-nitrophenacyl bromide (**13f**). Yield 80%. M.p. 248–250°. UV/VIS: 422 (4.29). ¹H-NMR ((D₆)DMSO): 3.20 (*t*, 4 H, CH₂N); 3.63 (*t*, 4 H, CH₂O); 7.22 (*d*, 2 arom. H); 7.41 (*d*, 2 arom. H); 8.01 (*d*, 2 arom. H); 8.22 (*d*, 2 arom. H); 10.06 (*s*, 1 heteroatom. H). Anal. calc. for C₂₂H₁₇ClN₄O₄S₂ (500.98): C 52.74, H 3.42, N 11.18, S 12.80; found: C 52.36, H 3.96, N 11.08, S 12.65.

5-[3,4-Chlorophenyl]-3-(4-methoxyphenyl)thiazol-2(3H)-ylidene]-4-(morpholin-4-yl)thiazol-2(5H)-one (**16c**). From *N*⁵-(4-chlorophenyl)-2,4-di(morpholin-4-yl)thiazole-5-carbothioamide (**9s**) and 4-chlorophenacyl bromide (**13e**). Yield 62%. M.p. 285–287°. UV/VIS: 409 (4.32). ¹H-NMR ((D₆)DMSO): 3.43 (*t*, 4 H, CH₂N); 3.66 (*t*, 4 H, CH₂O); 7.19 (*d*, 2 arom. H); 7.41 (*d*, 2 arom. H); 7.47 (*d*, 2 arom. H); 7.87 (*d*, 2 arom. H); 10.11 (*s*, 1 heteroatom. H). Anal. calc. for C₂₂H₁₇Cl₂N₃O₅S₂ (489.01): C 53.88, H 3.49, N 8.57, S 13.08; found: C 53.81, H 3.71, N 8.96, S 13.42.

5-[4-(4-Chlorophenyl)-3-(4-methoxyphenyl)thiazol-2(3H)-ylidene]-4-(morpholin-4-yl)thiazol-2(5H)-one (**16d**). From *N*⁵-(4-methoxyphenyl)-2,4-di(morpholin-4-yl)thiazole-5-carbothioamide (**9p**) and 4-chlorophenacyl bromide (**13e**). Yield 65%. M.p. 280–282°. UV/VIS: 415 (4.35). ¹H-NMR ((D₆)DMSO): 3.40 (*t*, 4 H, CH₂N); 3.65 (*t*, 4 H, CH₂O); 3.75 (*s*, MeO); 6.96 (*d*, 2 arom. H); 7.18 (*d*, 2 arom. H); 7.45 (*d*, 2 arom. H); 7.85 (*d*, 2 arom. H); 9.88 (*s*, 1 heteroatom. H). Anal. calc. for C₂₃H₂₀ClN₃O₅S₂ (485.06): C 56.84, H 4.15, N 8.65, S 13.20; found: C 57.04, H 4.47, N 8.40, S 13.36.

5-[3-(4-Chlorophenyl)-4-(4-nitrophenyl)thiazol-2(3H)-ylidene]-4-(piperidin-1-yl)thiazol-2(5H)-one (**16e**). From *N*⁵-(4-chlorophenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9t**) and 4-nitrophenacyl bromide (**13f**). Yield 76%. M.p. 293–294°. UV/VIS: 417 (4.32). ¹H-NMR ((D₆)DMSO): 1.51 (*m*, 6 H, CH₂); 3.35 (*t*, 4 H, CH₂N); 7.20 (*d*, 2 arom. H); 7.41 (*d*, 2 arom. H); 7.97 (*d*, 2 arom. H); 8.22 (*d*, 2 arom. H); 10.17 (*s*, 1 heteroatom. H). Anal. calc. for C₂₃H₁₉ClN₄O₃S₂ (498.06): C 55.36, H 3.84, N 11.23, S 12.85; found: C 55.54, H 4.13, N 11.18, S 12.98.

5-[3-(4-Methoxyphenyl)-4-(4-nitrophenyl)thiazol-2(3H)-ylidene]-4-(piperidin-1-yl)thiazol-2(5H)-one (**16f**). From *N*⁵-(4-methoxyphenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9q**) and 4-nitrophenacyl bromide (**13f**). Yield 71%. M.p. 290–291°. UV/VIS: 427 (4.37). ¹H-NMR ((D₆)DMSO): 1.50 (*m*, 6 H, CH₂); 3.33 (*t*, 4 H, CH₂N); 3.76 (*s*, MeO); 6.97 (*d*, 2 arom. H); 7.18 (*d*, 2 arom. H); 7.95 (*d*, 2 arom. H); 8.21 (*d*, 2 arom. H); 9.96 (*s*, 1 heteroatom. H). Anal. calc. for C₂₄H₂₂N₄O₄S₂ (494.59): C 58.28, H 4.48, N 11.33, S 12.97; found: C 58.18, H 4.79, N 11.07, S 13.00.

5-[4-(4-Chlorophenyl)-3-phenylthiazol-2(3H)-ylidene]-4-(piperidin-1-yl)thiazol-2(5H)-one (**16g**). From *N*⁵-(4-chlorophenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9t**) and 4-chlorophenacyl bromide (**13e**). Yield 54%. M.p. 218–220°. UV/VIS: 409 (4.28). ¹H-NMR ((D₆)DMSO): 1.56 (*m*, 6 H, CH₂); 3.40 (*t*, 4 H, CH₂N); 7.07 (*t*, 1 arom. H); 7.20 (*d*, 2 arom. H); 7.36 (*t*, 2 arom. H); 7.44 (*d*, 2 arom. H); 7.84 (*d*, 2 arom. H); 10.00 (*s*, 1 heteroatom. H). Anal. calc. for C₂₃H₂₀ClN₃O₃S₂ (453.07): C 60.85, H 4.44, N 9.26, S 14.13; found: C 60.51, H 4.60, N 9.48, S 13.98.

5-[3,4-Bis(4-chlorophenyl)thiazol-2(3H)-ylidene]-4-(piperidin-1-yl)thiazol-2(5H)-one (**16h**). From *N*⁵-(4-chlorophenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9t**) and 4-chlorophenacyl bromide (**13e**). Yield 59%. M.p. 284–285°. UV/VIS: 409 (4.33). ¹H-NMR ((D₆)DMSO): 1.60 (*m*, 6 H, CH₂); 3.44 (*t*, 4 H, CH₂N); 7.19 (*d*, 2 arom. H); 7.41 (*d*, 2 arom. H); 7.46 (*d*, 2 arom. H); 7.87 (*d*, 2 arom. H); 9.90 (*s*, 1 heteroatom. H). Anal. calc. for C₂₃H₁₉Cl₂N₃O₃S₂ (487.03): C 56.56, H 3.92, N 8.60, S 13.13; found: C 56.35, H 4.35, N 8.24, S 13.11.

N-[(2,4-Diaminothiazol-5-yl)thioxomethyl]-2,2-dimethylpropanamides **18**: General Procedure. To a soln. of pivaloyl isothiocyanate (=2,2-dimethylpropanoyl isothiocyanate; **1w**), prepared from KSCN (63.6 g, 0.6 mol) and pivaloyl chloride (66.4 ml, 0.54 mol) in MeCN (300 ml), a thiazole-2,4-diamine **8** (0.5 mol) was added, and the mixture was refluxed for 30 min. After concentration to half of the volume, the precipitated product was filtered off: **18a** or **18d**.

N-[[2,4-Di(morpholin-4-yl)thiazol-5-yl]thioxomethyl]-2,2-dimethylpropanamide (**18a**). From 4,4'-(thiazol-2,4-diyl)bis[morpholine] (**8a**) and **1w**. Yield 73%. Red-brown crystals. M.p. 163–164° (BuOH). ¹H-NMR

(CDCl₃): 1.26 (s, Me₃C); 3.59 (m, 8 H, CH₂N); 3.72 (m, 8 H, CH₂O); 8.82 (s, NH). Anal. calc. for C₁₇H₂₆N₄O₃S₂ (398.55): C 51.23, H 6.58, N 14.06, S 16.09; found: C 51.34, H 5.98, N 13.92, S 16.08.

Similarly, **18b** and **18c** were obtained and used as raw materials.

N-[4-(Morpholin-4-yl)-2-(pyrrolidin-1-yl)thiazol-5-yl]thioxomethyl]-2,2-dimethylpropanamide (**18d**). From 4-[2-(pyrrolidin-1-yl)thiazol-4-yl]morpholine (**8e**) and **1w**. Yield 65%. Red-brown crystals. M.p. 156–157° (EtOH). ¹H-NMR (CDCl₃): 1.21 (s, Me₃C); 1.95 (m, 4 H, CH₂); 3.24 (t, 4 H, CH₂N); 3.51 (t, 4 H, CH₂N); 3.67 (t, 4 H, CH₂O); 8.37 (s, NH). Anal. calc. for C₁₇H₂₆N₄O₂S₂ (382.55): C 53.37, H 6.85, N 14.65, S 16.76; found: C 53.44, H 7.28, N 14.46, S 16.94.

Thiazolo[4,5-*d*]pyrimidine-7(6H)-thiones **21**: *General Procedure*. To a soln. of **1w**, prepared from KSCN (11.7 g, 0.12 mol) and pivaloyl chloride (13.3 ml, 0.11 mol) in MeCN (60 ml), 2-(dialkylamino)thiazol-4(5H)-iminium chloride **7** (0.1 mol) and Et₃N (14 ml, 0.1 mol) were added successively, and the resulting mixture was refluxed for 30 min. After cooling to r.t., the mixture was diluted with H₂O (100 ml). The precipitated product was filtered off, washed with H₂O, and recrystallized from BuOH: **21a–c**.

5-(tert-Butyl)-2-(morpholin-4-yl)thiazolo[4,5-*d*]pyrimidine-7(6H)-thione (**21a**). From 2-(morpholin-4-yl)thiazol-4(5H)-iminium chloride (**7a**) and **1w**. Yield 71%. Brown crystals. M.p. 175–176°. ¹H-NMR (CDCl₃): 1.42 (s, Me₃C); 3.72 (t, 4 H, CH₂N); 3.78 (t, 4 H, CH₂O); 10.00 (s, NH). Anal. calc. for C₁₃H₁₈N₄OS₂ (310.44): C 50.30, H 5.84, N 18.05, S 20.66; found: C 50.62, H 6.44, N 17.65, S 20.58.

5-(tert-Butyl)-2-(piperidin-1-yl)thiazolo[4,5-*d*]pyrimidine-7(6H)-thione (**21b**). From 2-(piperidin-1-yl)thiazol-4(5H)-iminium chloride (**7b**) and **1w**. Yield 69%. Orange crystals. M.p. 250–252°. ¹H-NMR (CDCl₃): 1.41 (s, Me₃C); 1.69 (m, 6 H, CH₂); 3.69 (t, 4 H, CH₂N); 9.94 (s, NH). Anal. calc. for C₁₄H₂₀N₄S₂ (308.47): C 54.51, H 6.54, N 18.16, S 20.79; found: C 54.71, H 6.56, N 17.97, S 21.03.

5-(tert-Butyl)-2-(pyrrolidin-1-yl)thiazolo[4,5-*d*]pyrimidine-7(6H)-thione (**21c**). From 2-(pyrrolidin-1-yl)thiazol-4(5H)-iminium chloride (**7c**) and **1w**. Yield 62%. Light green crystals. M.p. 295–297°. ¹H-NMR (CDCl₃): 1.42 (s, Me₃C); 2.09 (m, 4 H, CH₂); 3.41 (m, CH₂N); 3.81 (m, CH₂N); 9.91 (s, NH). Anal. calc. for C₁₃H₁₈N₄S₂ (294.44): C 53.03, H 6.16, N 19.03, S 21.78; found: C 53.34, H 6.45, N 18.94, S 21.81.

2,4-Bis(dialkylamino)thiazole-5-carbothioamides **19**: *General Procedure*. A suspension of propanamide **18** (0.5 mol) in conc. HCl soln. (300 ml) was stirred at r.t. for 24 h while it separated into two phases. The aq. soln. was neutralized with aq. NH₃ soln. The precipitated product was filtered off and washed with H₂O: **19a–d**.

2,4-Di(morpholin-4-yl)thiazole-5-carbothioamide (**19a**). From **18a**. Yield 81%. Brown crystals. M.p. 194–196° (BuOH). ¹H-NMR (CDCl₃): 3.09 (t, 4 H, CH₂N); 3.52 (t, 4 H, CH₂N); 3.76 (m, 8 H, CH₂O); 8.90 (br. s, NH₂). Anal. calc. for C₁₂H₁₈N₄O₂S₂ (314.43): C 45.84, H 5.77, N 17.82, S 20.40; found: C 46.02, H 5.78, N 18.01, S 20.33.

2,4-Di(piperidin-1-yl)thiazole-5-carbothioamide (**19b**). From 1,1'-(thiazol-2,4-diyl)bis[piperidine] (**8b**) via *N*-[2,4-di(piperidin-1-yl)thiazol-5-yl]thioxomethyl]-2,2-dimethylpropanamide (**18b**). Yield 74%. Brown crystals. M.p. 171–173° (EtOH). ¹H-NMR (CDCl₃): 1.62 (m, 12 H, CH₂); 3.02 (t, 4 H, CH₂N); 3.48 (t, 4 H, CH₂N); 8.80 (br. s, NH₂). Anal. calc. for C₁₄H₂₂N₄S₂ (310.48): C 54.16, H 7.14, N 18.05, S 20.66; found: C 54.60, H 7.04, N 17.80, S 21.05.

2,4-Di(pyrrolidin-1-yl)thiazole-5-carbothioamide (**19c**). From *N*-[2,4-di(pyrrolidin-1-yl)thiazol-5-yl]thioxomethyl]-2,2-dimethylpropanamide (**18c**). Yield 83%. Brown crystals. M.p. 181–183° (EtOH). ¹H-NMR (CDCl₃): 1.85 (m, 4 H, CH₂); 1.97 (m, 4 H, CH₂); 3.37 (m, 8 H, CH₂N); 6.98 (s, NH₂). Anal. calc. for C₁₂H₁₈N₄S₂ (282.43): C 51.03, H 6.42, N 19.84, S 22.71; found: C 51.21, H 6.07, N 19.64, S 22.35.

4-(Morpholin-4-yl)-2-(pyrrolidin-1-yl)thiazole-5-carbothioamide (**19d**). From **18d**. Yield 85%. Brown crystals. M.p. 193–195° (EtOH). ¹H-NMR (CDCl₃): 2.00 (m, 4 H, CH₂N); 3.10 (t, 4 H, CH₂N); 3.41 (t, 4 H, CH₂N); 3.75 (t, 4 H, CH₂O); 8.70 (br. s, NH₂). Anal. calc. for C₁₂H₁₈N₄OS₂ (298.43): C 48.30, H 6.08, N 18.77, S 21.49; found: C 48.12, H 6.23, N 18.61, S 21.65.

Acceptor-Substituted 4,4'-(2,5'-Bithiazole)-2,4'-diylbis[morpholines] 24: *General Procedure*. A mixture **18a** (0.01 mol) and a α -halomethyl compound **13** or **22** (0.01 mol) was heated in MeCN (50 ml) for 3 h. Then Et₃N (1.4 ml, 0.01 mol) was added at r.t., and the soln. was refluxed for 1 h. After cooling to r.t., H₂O (20 ml) was added, and the precipitated product was filtered off: **24a** and **24e**.

1-[4-(tert-Butyl)-2'-(morpholin-4-yl)[2,5'-bithiazol]-5-yl]ethanone (**24a**). From **18a** and 1-chloropropan-2-one (**13b**). Yield 63%. Yellow crystals. M.p. 149–150° (EtOH). UV/VIS: 413 (4.30). ¹H-NMR (CDCl₃): 1.40 (s, Me₃C); 2.53 (s, Me); 3.17 (t, 4 H, CH₂N); 3.53 (t, 4 H, CH₂N); 3.79 (t, 4 H, CH₂O); 3.88 (t, 4 H, CH₂O). Anal. calc. for C₂₀H₂₈N₄O₃S₂ (436.59): C 55.02, H 6.46, N 12.83, S 14.69; found: C 55.08, H 6.87, N 12.57, S 14.59.

4,4'-[4-(tert-Butyl)-5-(4-nitrophenyl)-[2,5'-bithiazole]-2,4'-diyl]bis[morpholine] (**24e**). From **18a** and 4-nitrobenzyl bromide (**22a**). Yield 75%. Yellow crystals. M.p. 255–256° (EtOH/MeCN 1:1). UV/VIS: 363 (4.44). ¹H-NMR (CDCl₃): 1.20 (s, Me₃C); 3.07 (t, 4 H, CH₂N); 3.56 (t, 4 H, CH₂N); 3.80 (m, 8 H, CH₂O); 7.54

(*d*, 2 arom. H); 8.20 (*d*, 2 arom. H). Anal. calc. for $C_{24}H_{29}N_5O_4S_2$ (515.65): C 55.90, H 5.67, N 13.58, S 12.44; found: C 55.94, H 5.33, N 13.10, S 12.23.

2,4-Di(morpholin-4-yl)thiazole-5-carbonitrile (26). As described in the *General Procedure* for **24**; with **18a** (0.01 mol, 4.0 g) and chloroacetonitrile (**22d**; 125 mmol, 1.0 g), MeCN (100 ml), and Et_3N (0.01 mol, 1.4 ml). Precipitation with H_2O (50 ml) gave **26** (75%). Pale yellow crystals. M.p. 255–256°. IR (KBr): 2177. 1H -NMR ($CDCl_3$): 3.45 (*t*, 4 H, CH_2N); 3.67 (*t*, 4 H, CH_2N); 3.73 (*m*, 8 H, CH_2O). Anal. calc. for $C_{12}H_{16}N_4O_2S$ (280.35): C 51.41, H 5.75, N 19.98, S 11.44; found: C 51.60, H 6.12, N 19.52, S 11.49.

2,4-Di(morpholin-4-yl)-N⁵-[(morpholin-4-yl)methylene]thiazole-5-carbothioamide (27). A mixture of **19a** (6.3 g, 20 mmol), triethyl orthoformate (4.5 g, 30 mmol), and morpholine (2.6 g, 30 mmol) was heated at 120° under removal of the formed EtOH. After cooling to r.t., the solid product was filtered off and recrystallized from BuOH. Yield 6.0 g (73%). Orange crystals. M.p. 185–187°. 1H -NMR ($CDCl_3$): 3.08 (*t*, CH_2N); 3.52 (*m*, 6 H, CH_2N); 3.66–3.74 (*m*, 16 H, CH_2N , CH_2O); 8.75 (*s*, CH). Anal. calc. for $C_{17}H_{25}N_5O_3S_2$ (411.54): C 49.61, H 6.12, N 17.02, S 15.58; found: C 49.99, H 6.54, N 17.16, S 15.97.

Acceptor-Substituted 4,4'-(2,5'-Bithiazol-2',4'-diyl)bis[morpholines] 29: General Procedures. Method A. A mixture of **27** (4.1 g, 10 mmol) and an α -halomethyl compound **13** (10 mmol) in MeCN (50 ml) was refluxed for 3 h. After cooling to r.t., Et_3N (1.4 ml, 10 mmol) was added to the mixture, which was heated again for 1 h. The product, crystallized after cooling, was filtered off, washed with EtOH, and purified by recrystallization: **29a–d**.

Method B: A mixture of **19a** (3.15 g, 10 mmol) and an α -halomethyl compound **22** (10 mmol) in DMF (25 ml) was heated at 100° for 5 min. After cooling to r.t., $POCl_3$ (3.1 g, 20 mmol), followed by Et_3N (20 ml), was added to the mixture. The formed product was precipitated by addition of H_2O , filtered off, washed with H_2O , and recrystallized: **29e–g**.

1-[2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]ethanone (29a). From **27** and 1-chloropropan-2-one (**13a**) by *Method A*: 3.0 g (79%) of **29a**. Yellow crystals. M.p. 218–219°. UV/VIS: 420 (4.31). 1H -NMR ($CDCl_3$): 2.50 (*s*, Me); 3.13 (*t*, 4 H, CH_2N); 3.52 (*t*, 4 H, CH_2N); 3.77 (*t*, 4 H, CH_2O); 3.87 (*t*, 4 H, CH_2O); 8.07 (*s*, 1 hetero-arom. H). Anal. calc. for $C_{16}H_{20}N_4O_3S_2$ (380.49): C 50.51, H 5.30, N 14.73, S 16.86; found: C 50.49, H 5.56, N 14.03, S 17.01.

Methyl 2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-5-carboxylate (29b). From **27** and methyl bromoacetate (**13c**) by *Method A*: 2.14 g (54%) of **29b**. Colorless crystals. M.p. 179–181°. 1H -NMR ($CDCl_3$): 3.12 (*t*, 4 H, CH_2N); 3.52 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 3.86 (*s*, MeO); 3.89 (*t*, 4 H, CH_2O); 8.18 (*s*, 1 hetero-arom. H). Anal. calc. for $C_{16}H_{20}N_4O_4S_2$ (396.49): C 48.47, H 5.08, N 14.13, S 16.18; found: C 48.80, H 5.23, N 13.96, S 16.32.

[2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]phenylmethanone (29c). From **27** and phenacyl bromide (**13d**) by *Method A*: 3.23 g (73%) **29c**. Yellow crystals. M.p. 174–175°. UV/VIS: 439 (4.38). 1H -NMR ($CDCl_3$): 3.17 (*t*, 4 H, CH_2N); 3.53 (*t*, 4 H, CH_2N); 3.76 (*t*, 4 H, CH_2O); 3.90 (*t*, 4 H, CH_2O); 7.46–7.58 (*m*, 3 arom. H); 7.79 (*d*, 2 arom. H); 8.00 (*s*, 1 hetero-arom. H). Anal. calc. for $C_{21}H_{22}N_4O_3S_2$ (442.56): C 56.99, H 5.01, N 12.66, S 14.49; found: C 57.52, H 4.85, N 12.41, S 14.49.

[(1,1'-Biphenyl)-4-yl][2',4'-di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]methanone (29d). From **27** and 2-bromo-1-[(1,1'-biphenyl)-4-yl]ethanone (**13g**) by *Method A*: 3.37 g (65%) **29d**. Yellow crystals. M.p. 186–188°. UV/VIS: 441 (4.45). 1H -NMR ($CDCl_3$): 3.20 (*t*, 4 H, CH_2N); 3.55 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H, CH_2O); 3.92 (*t*, 4 H, CH_2O); 7.36–7.49 (*m*, 3 arom. H); 7.62 (*d*, 2 arom. H); 7.69 (*d*, 2 arom. H); 7.90 (*d*, 2 arom. H); 8.08 (*s*, 1 hetero-arom. H). Anal. calc. for $C_{27}H_{26}N_4O_3S_2$ (518.65): C 62.53, H 5.05, N 10.80, S 12.37; found: C 62.49, H 4.67, N 10.80, S 12.45.

4,4'-[5-(4-Nitrophenyl)[2,5'-bithiazol]-2,4-diyl]bis[morpholine] (29e). From **19a** and 4-nitrobenzyl bromide (**22a**) by *Method B*: 3.77 g (82%) of **29e**. Red crystals. M.p. 284–285°. UV/VIS: 446 (4.40). 1H -NMR ($CDCl_3$): 3.22 (*t*, 4 H, CH_2N); 3.57 (*t*, 4 H, CH_2N); 3.81 (*t*, 4 H, CH_2O); 3.90 (*t*, 4 H, CH_2O); 7.66 (*d*, 2 arom. H); 7.97 (*s*, 1 hetero-arom. H); 8.22 (*d*, 2 arom. H). Anal. calc. for $C_{20}H_{21}N_5O_4S_2$ (459.54): C 52.27, H 4.61, N 15.24, S 13.96; found: C 52.14, H 4.62, N 14.61, S 13.94.

4-[2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]benzonitrile (29f). From **19a** and 4-(bromomethyl)benzonitrile (**22b**) by *Method B*: 3.12 g (71%) of **29f**. Yellow crystals. M.p. 254–255°. UV/VIS: 414 (4.41). 1H -NMR ($CDCl_3$): 3.14 (*t*, 4 H, CH_2N); 3.52 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H, CH_2O); 3.92 (*t*, 4 H, CH_2O); 7.59 (*d*, 2 arom. H); 7.64 (*d*, 2 arom. H); 7.88 (*s*, 1 hetero-arom. H). Anal. calc. for $C_{21}H_{21}N_5O_2S_2$ (439.56): C 57.38, H 4.82, N 15.93, S 14.59; found: C 57.64, H 5.08, N 15.65, S 14.70.

2-[[4-[2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]phenyl]methylene]propanedinitrile (29g). From **19a** and 2-[[4-(bromomethyl)phenyl]methylene]propanedinitrile (**22c**) by *Method B*: 3.34 g (68%) of **29g**. Red crystals. M.p. 253–255°. UV/VIS: 487 (4.46). 1H -NMR ($CDCl_3$): 3.15 (*t*, 4 H, CH_2N); 3.53 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H,

CH₂O); 3.92 (t, 4 H, CH₂O); 7.34 (s, CH); 7.67 (d, 2 arom. H); 7.89 (d, 2 arom. H); 7.96 (s, 1 heteroarom. H). Anal. calc. for C₂₄H₂₂N₆O₂S₂ (490.60): C 58.76, H 4.52, N 17.13, S 13.07; found: C 59.17, H 4.74, N 16.88, S 13.16.

2',4'-Bis(dialkylamino)[2,5'-bithiazol]-4(5H)-ones 30: General Procedure. A mixture of a 2,4-bis(dialkylamino)thiazole-5-carbothioamide **19** (0.1 mol) and methyl bromoacetate (**13c**; 15.3 g, 0.1 mol) in EtOH (200 ml) was refluxed for 2 h. After cooling to r.t., Et₃N (14 ml, 0.1 mol) was added and the soln. refluxed for 30 min. The mixture was concentrated to half its volume, and the product, precipitated by cooling, was filtered off: **30a** and **30b**.

2',4'-Di(morpholin-4-yl)[2,5'-bithiazol]-4(5H)-one (30a). From **19a**. Yield 74%. Colorless crystals. M.p. 209–211° (EtOH). ¹H-NMR (CDCl₃): 3.61 (m, 8 H, CH₂N); 3.79 (m, 8 H, CH₂O); 3.85 (s, 2 H, CH₂). Anal. calc. for C₁₄H₁₈N₄O₃S₂ (354.45): C 47.44, H 5.12, N 15.81, S 18.09; found: C 47.33, H 5.13, N 15.24, S 18.28.

2',4'-Di(piperidin-1-yl)[2,5'-bithiazol]-4(5H)-one (30b). From **19b**. Yield 67%. Pale brown crystals. M.p. 125–126° (EtOH). ¹H-NMR (CDCl₃): 1.65 (m, 12 H, CH₂); 3.54 (m, 8 H, CH₂N); 3.82 (m, 2 H, CH₂). Anal. calc. for C₁₆H₂₂N₄O₂S₂ (350.50): C 54.83, H 6.33, N 15.98, S 18.30; found: C 54.73, H 6.53, N 15.74, S 18.68.

4-Substituted 2',4'-Bis(dialkylamino)-2,5'-bithiazoles 31: General Procedure. A mixture of a 2,4-bis(dialkylamino)thiazole-5-carbothioamide **19** (0.1 mol) and an α-halomethyl ketone **13** (0.1 mol) in EtOH (250 ml) was refluxed for 2 h. After cooling, Et₃N (14 ml, 0.1 mol) was added and the mixture refluxed for 30 min. The product, precipitated after cooling to r.t., was filtered off: **31a–e**.

4,4'-(4-Methyl[2,5'-bithiazole]-2',4'-diyl)bis[morpholine] (31a). From **19a** and 1-chloropropan-2-one (**13a**). Yield 70%. Colorless crystals. M.p. 155–156° (EtOH). ¹H-NMR (CDCl₃): 2.38 (s, Me); 3.07 (t, 4 H, CH₂N); 3.48 (t, 4 H, CH₂N); 3.78 (t, 4 H, CH₂O); 3.87 (t, 4 H, CH₂O); 6.68 (s, 1 heteroarom. H). Anal. calc. for C₁₅H₂₀N₄O₂S₂ (352.48): C 51.11, H 5.72, N 15.90, S 18.19; found: C 51.48, H 5.60, N 15.94, S 18.38.

1,1'-(4-Methyl[2,5'-bithiazole]-2',4'-diyl)bis[piperidine] (31b). From **19b** and 1-chloropropan-2-one (**13a**). Yield 59%. Colorless crystals. M.p. 142–144° (EtOH). ¹H-NMR (CDCl₃): 1.57–1.76 (m, 12 H, CH₂); 2.38 (s, Me); 3.01 (t, 4 H, CH₂N); 3.47 (t, 4 H, CH₂N); 6.63 (s, 1 heteroarom. H). Anal. calc. for C₁₇H₂₄N₄S₂ (348.53): C 58.58, H 6.94, N 16.08, S 18.40; found: C 58.42, H 6.72, N 16.25, S 18.96.

4,4'-(4-(Chloromethyl)[2,5'-bithiazole]-2',4'-diyl)bis[morpholine] (31c). From **19a** and 1,3-dichloropropan-2-one (**13b**). Yield 62%. Colorless crystals. M.p. 154–155° (EtOH). ¹H-NMR (CDCl₃): 3.09 (t, 4 H, CH₂N); 3.49 (t, 4 H, CH₂N); 3.77 (t, 4 H, CH₂O); 3.86 (t, 4 H, CH₂O); 4.63 (s, 2 H, CH₂); 7.09 (s, 1 heteroarom. H). Anal. calc. for C₁₅H₁₉ClN₄O₂S₂ (386.92): C 46.56, H 4.95, N 14.48, S 16.57; found: C 46.72, H 4.90, N 14.30, S 16.86.

4,4'-(4-Phenyl[2,5'-bithiazole]-2',4'-diyl)bis[morpholine] (31d). From **19a** and phenacyl bromide (**13d**). Yield 67%. Colorless crystals. M.p. 168–170° (EtOH). ¹H-NMR (CDCl₃): 3.13 (t, 4 H, CH₂N); 3.51 (t, 4 H, CH₂N); 3.80 (t, 4 H, CH₂O); 3.90 (t, 4 H, CH₂O); 7.28 (s, 1 heteroarom. H); 7.36 (m, 3 arom. H); 7.88 (d, 2 arom. H). Anal. calc. for C₂₀H₂₂N₄O₂S₂ (414.55): C 57.95, H 5.35, N 13.52, S 15.47; found: C 58.00, H 5.46, N 13.34, S 15.38.

1,1'-(4-Phenyl[2,5'-bithiazole]-2',4'-diyl)bis[piperidine] (31e). From **19b** and phenacyl bromide (**13d**). Yield 63%. Colorless crystals. M.p. 119–121° (EtOH). ¹H-NMR (CDCl₃): 1.65–1.76 (m, 12 H, CH₂); 3.05 (t, 4 H, CH₂N); 3.50 (t, 4 H, CH₂N); 7.28–7.40 (m, 4 arom. and heteroarom. H); 7.90 (d, 2 arom. H). Anal. calc. for C₂₂H₂₆N₄S₂ (410.60): C 64.35, H 6.38, N 13.65, S 15.62; found: C 63.75, H 5.96, N 13.88, S 16.06.

2',4'-Di(morpholin-4-yl)[2,5'-bithiazole]-4,5-dione 5-[(4-Nitrophenyl)hydrazone] (33a). A freshly prepared aq. 4-nitrobenzenediazonium hydrogen sulfate soln. (10 mM) was added under stirring to a mixture of **30a** (3.5 g, 0.01 mol) and DMF (35 ml). After standing for 1 h at r.t., the mixture was poured into H₂O (200 ml) and neutralized by addition of aq. NaOH soln. The crystallized product was filtered off and recrystallized from BuOH: 3.4 g (68%) of **33a**. M.p. 285–287°. UV/VIS: 514 (4.62). ¹H-NMR (CDCl₃): 3.62–3.85 (m, 12 H, CH₂N); 4.24 (t, 4 H, CH₂O); 7.28 (s, NH); 7.31 (d, 2 arom. H); 8.10 (d, 2 arom. H). Anal. calc. for C₂₀H₂₁N₇O₅S₂ (503.56): C 47.70, H 4.20, N 19.47, S 12.74; found: C 48.52, H 4.03, N 19.65, S 13.01.

6-[2,4-Di(morpholin-4-yl)thiazol-5-yl]-3-(4-nitrophenyl)thiazolo[5,4-e]-1,3,4,2-oxadiazaborine-2,2-diol Diacetate (32a). A suspension of **33a** (3.0 g, 6 mmol) and H₃BO₃ (0.04 g, 6 mmol) in Ac₂O (15 ml) was refluxed for 30 min. After cooling to r.t., the product precipitated from the deeply colored soln. It was filtered off and washed with AcOEt and Et₂O: 2.5 g (66%) of **32a**. M.p. 297–300°. UV/VIS: 572 (4.78). ¹H-NMR (CDCl₃): 1.99 (s, 6 H, Me); 3.51 (t, 2 H, CH₂N); 3.63 (t, 2 H, CH₂N); 3.85 (m, 8 H, CH₂); 3.91 (t, 4 H, CH₂O); 7.68 (d, 2 arom. H); 8.05 (d, 2 arom. H). Anal. calc. for C₂₄H₂₆BN₇O₉S₂ (631.45): C 45.65, H 4.15, N 15.53, S 10.16; found: C 46.02, H 4.40, N 15.67, S 9.98.

4,4'-(4-Chloro[2,5'-bithiazole]-2',4'-diyl)bis[morpholine] (34a). To a soln. of **30a** (7.1 g, 0.02 mol) in DMF (50 ml), POCl₃ (61 g, 0.04 mol) was slowly added at r.t. After stirring for 2 h, the red mixture was poured into ice water (300 ml). After neutralization of the mixture with aq. NaOH soln., the crystallized product was filtered

off, washed with H₂O, and recrystallized from EtOH: 5.3 g (71%) of **34a**. M.p. 150°. ¹H-NMR (CDCl₃): 3.08 (t, 4 H, CH₂N); 3.50 (t, 4 H, CH₂N); 3.78 (t, 4 H, CH₂O); 3.86 (t, 4 H, CH₂O); 6.84 (s, 1 heteroarom. H). Anal. calc. for C₁₄H₁₇ClN₄O₂S₂ (372.90): C 45.09, H 4.60, N 15.02, S 17.20; found: C 45.43, H 4.71, N 14.59, S 17.55.

4-Chloro-2',4'-di(morpholin-4-yl)[2,5'-bithiazole]-5-carboxaldehyde (35a). To a mixture of *N*-methylformanilide (5.4 g, 0.04 mol) and POCl₃ (9.2 g, 0.06 mol), **34a** (0.02 mol) in DMF (20 ml) was added dropwise. After stirring the mixture at r.t. overnight, it was heated at 65–70° for 7 h and then, after cooling, poured into ice water (400 ml). The mixture was neutralized by addition of aq. NaOH soln. and the precipitated product filtered off, washed with H₂O (50 ml), and recrystallized from EtOH: 2.8 g (35%) of **35a**. M.p. 147–148°. ¹H-NMR (CDCl₃): 3.23 (t, 4 H, CH₂N); 3.59 (t, 4 H, CH₂N); 3.78 (t, 4 H, CH₂O); 3.86 (t, 4 H, CH₂O); 9.86 (s, CHO). Anal. calc. for C₁₅H₁₇ClN₄O₃S₂ (400.91): C 44.94, H 4.27, N 13.98, S 16.00; found: C 44.45, H 4.48, N 14.54, S 16.09.

2',4'-Bis(dialkylamino)-5-[[4-(dimethylamino)phenyl]methylene][2,5'-bithiazole]-4(5H)-ones 36: *General Procedure*. A mixture of a 2',4'-bis(dialkylamino)[2,5'-bithiazol]-4(5H)-one **30** (0.01 mol), 4-(dimethylamino)-benzaldehyde (1.5 g, 0.01 mol), and Et₃N (5 drops) in DMF (100 ml) was refluxed for 2 h. The orange product that precipitated after cooling was filtered off and recrystallized from DMF: **36a** or **36b**.

5-[[4-(Dimethylamino)phenyl]methylene]-2',4'-di(morpholin-4-yl)[2,5'-bithiazol]-4(5H)-one (36a). From **30a**. Yield 76%. Orange crystals. M.p. 279–281° (DMF). UV/VIS: 497 (4.32). ¹H-NMR (CDCl₃): 2.97 (s, 6 H, MeN); 3.56 (m, 8 H, CH₂N); 3.74 (t, 4 H, CH₂O); 3.83 (t, 4 H, CH₂O); 6.64 (d, 2 arom. H); 7.38 (d, 2 arom. H); 7.66 (s, CH). Anal. calc. for C₂₃H₂₇N₅O₃S₂ (485.62): C 56.88, H 5.60, N 14.42, S 13.21; found: C 56.82, H 5.36, N 14.56, S 13.57.

5-[[4-(Dimethylamino)phenyl]methylene]-2',4'-di(piperidin-1-yl)[2,5'-bithiazol]-4(5H)-one (36b). From **30b**. Yield 68%. Orange crystals. M.p. 220–222° (DMF). UV/VIS: 492 (4.40). ¹H-NMR (CDCl₃): 1.66 (m, 12 H, CH₂); 2.99 (s, 6 H, MeN); 3.56 (m, 8 H, CH₂N); 6.68 (d, 2 arom. H); 7.44 (d, 2 arom. H); 7.67 (s, CH). Anal. calc. for C₂₅H₃₁N₅O₃S₂ (481.68): C 62.34, H 6.49, N 14.54, S 13.31; found: C 62.80, H 6.38, N 14.61, S 13.70.

2',4'-Bis(dialkylamino)-5-(1,3-dithiolan-2-ylidene)[2,5'-bithiazol]-4(5H)-ones 37: *General Procedure*. To a suspension of a 2',4'-bis(dialkylamino)[2,5'-bithiazol]-4(5H)-one **30** (0.01 mol) in DMF (30 ml), KOH (1.1 g, 0.02 mol) in H₂O (2 ml), followed by CS₂ (0.8 g, 0.01 mol), was added. After stirring the red mixture at r.t. for 1 h, 1,2-dibromoethane (2.0 g, 0.01 mol) was added. The mixture was stirred for 1 h at r.t. and then diluted with H₂O (250 ml). The precipitated product was filtered off, washed with H₂O, and recrystallized from DMF: **37a** or **37b**.

2',4'-Di(morpholin-4-yl)-5-(1,3-dithiolan-2-ylidene)[2,5'-bithiazol]-4(5H)-one (37a). From **30a**. Yield 73%. Orange crystals. M.p. 265–267° (DMF). UV/VIS: 464 (4.69). ¹H-NMR (CDCl₃): 3.42 (t, 4 H, CH₂N); 3.46 (t, 2 H, CH₂); 3.51 (t, 2 H, CH₂); 3.55 (t, 4 H, CH₂N); 3.75 (t, 4 H, CH₂O); 3.82 (t, 4 H, CH₂O). Anal. calc. for C₁₆H₂₀N₄O₃S₄ (456.63): C 44.71, H 4.41, N 12.27, S 28.09; found: C 45.00, H 4.64, N 12.36, S 28.01.

2',4'-Di(piperidin-1-yl)-5-(1,3-dithiolan-2-ylidene)[2,5'-bithiazol]-4(5H)-one (37b). From **30b**. Orange crystals. Yield 64%. M.p. 221–223° (DMF). UV/VIS: 469 (4.65). ¹H-NMR (CDCl₃): 1.67 (m, 12 H, CH₂); 3.39 (t, 4 H, CH₂N); 3.43 (t, 2 H, CH₂); 3.47 (t, 2 H, CH₂); 3.50 (t, 4 H, CH₂N). Anal. calc. for C₁₉H₂₄N₄OS₄ (452.68): C 50.41, H 5.34, N 12.38, S 28.33; found: C 50.82, H 5.36, N 12.86, S 28.95.

2',4'-Bis(dialkylamino)[2,5'-bithiazole]-5-carboxaldehyde 38: *General Procedure*. A mixture of DMF (35 ml), POCl₃ (9.2 g, 0.06 mol), and a 4-substituted 2',4'-bis(dialkylamino)-2,5'-bithiazole **31** (0.02 mol) was stirred at r.t. for 24 h and then heated at 75° for 7 h. The mixture was diluted with H₂O (50 ml) and neutralized by addition of aq. NaOH soln. The crystallized product was filtered off: **38a** or **38b**.

4-Methyl-2',4'-di(morpholin-4-yl)[2,5'-bithiazole]-5-carboxaldehyde (38a). From **31a**. Yield 42%. Yellow crystals. M.p. 215–216° (DMF). IR (KBr): 1647. ¹H-NMR (CDCl₃): 2.61 (s, Me); 3.16 (t, 4 H, CH₂N); 3.53 (t, 4 H, CH₂N); 3.78 (t, 4 H, CH₂O); 3.89 (t, 4 H, CH₂O); 9.94 (s, CHO). Anal. calc. for C₁₆H₂₀N₄O₃S₂ (380.49): C 50.51, H 5.30, N 14.73, S 16.86; found: C 50.61, H 5.69, N 14.88, S 16.90.

2',4'-Di(morpholin-4-yl)-4-phenyl[2,5'-bithiazole]-5-carboxaldehyde (38d). From **31d**. Yellow crystals. Yield 33%. M.p. 246–248° (DMF). IR (KBr): 1637. ¹H-NMR (CDCl₃): 3.22 (t, 4 H, CH₂N); 3.56 (t, 4 H, CH₂N); 3.80 (t, 4 H, CH₂O); 3.91 (t, 4 H, CH₂O); 7.46 (m, 3 arom. H); 7.69 (d, 2 arom. H); 9.88 (s, CHO). Anal. calc. for C₂₁H₂₂N₄O₃S₂ (442.56): C 56.99, H 5.01, N 12.66, S 14.49; found: C 57.09, H 5.04, N 12.68, S 14.45.

2-[[2',4'-Bis(dialkylamino)[2,5'-bithiazol]-5-yl]methylene]propanedinitrile 39: *General Procedure*. A mixture of a 2',4'-bis(dialkylamino)[2,5'-bithiazole]-5-carboxaldehyde **38** (0.01 mol), malononitrile (0.8 g, 0.012 mol), Ac₂O (10 ml), and 3 drops of Et₃N was refluxed for 1 h. The product, precipitated after cooling of the mixture, was filtered off and recrystallized: **39a** or **39b**.

2-[[4-Methyl-2',4'-di(morpholin-4-yl)[2,5'-bithiazol]-5-yl]methylene]propanedinitrile (39a). From **38a**. Red crystals. Yield 60%. M.p. 233–235° (DMF). UV/VIS: 536 (4.58). ¹H-NMR (CDCl₃): 2.49 (s, Me); 3.24 (t, 4 H,

CH₂N); 3.59 (t, 4 H, CH₂N); 3.79 (t, 4 H, CH₂O); 3.90 (t, 4 H, CH₂O); 7.69 (s, CH). Anal. calc. for C₁₉H₂₀N₆O₂S₂ (428.53): C 53.25, H 4.70, N 19.61, S 14.97; found: C 53.16, H 4.79, N 19.49, S 15.09.

2-/[2',4'-Di(morpholin-4-yl)-4-phenyl[2,5'-bithiazol]-5-yl]methylene]propanedinitrile (**39d**). From **38d**. Yield 53%. Red crystals. M.p. 170–171° (DMF). UV/VIS: 538 (4.46). ¹H-NMR (CDCl₃): 3.34 (t, 4 H, CH₂N); 3.61 (t, 4 H, CH₂N); 7.39 (t, 4 H, CH₂O); 3.93 (t, 4 H, CH₂O); 7.55 (m, 5 arom. H); 7.70 (s, CH). Anal. calc. for C₂₄H₂₂N₆O₂S₂ (490.60): C 58.76, H 4.52, N 17.13, S 13.07; found: C 58.61, H 4.51, N 17.19, S 13.09.

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