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

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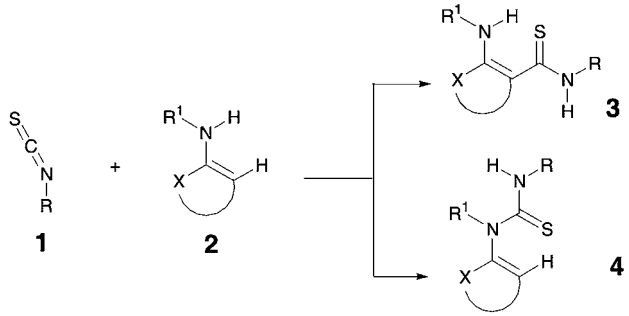
In the reaction of thiazole-2,4-diamines **8** with isothiocyanates **1**, 2,4-diaminothiazole-5-carbothioamides **9**, **10**, **18**, and **19** as well as thiazolo[4,5-*d*]pyrimidine-7(6*H*)-thiones **21** were formed. The carbothioamides **9**, **10**, and **18** were transformed by reaction with 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].

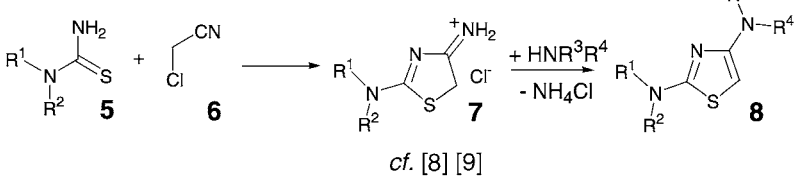
Scheme 1



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



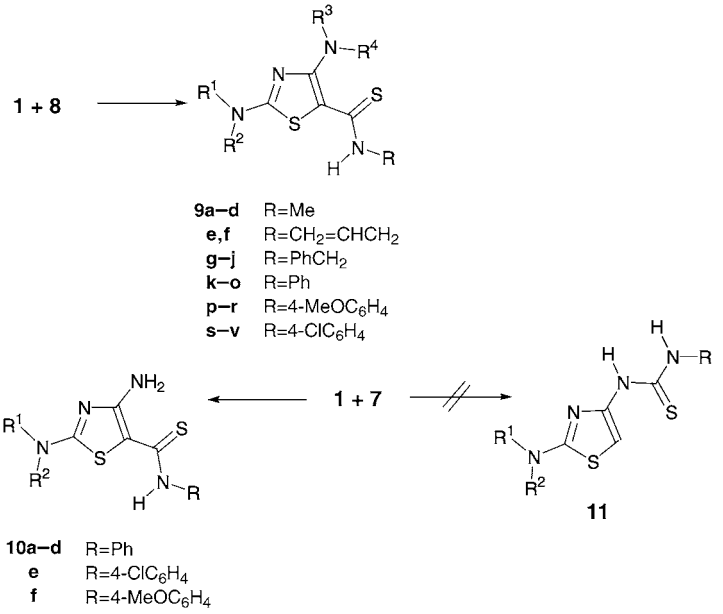
cf. [8] [9]

7, 8	R^1R^2N	R^3R^4N
a	mor	mor
b	pip	pip
c	pyr	pyr
d	pip	mor
e	pyr	mor
f	Pr_2N	mor
g	Ph_2N	mor

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 ^{1}H-decoupled ^{13}C-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])



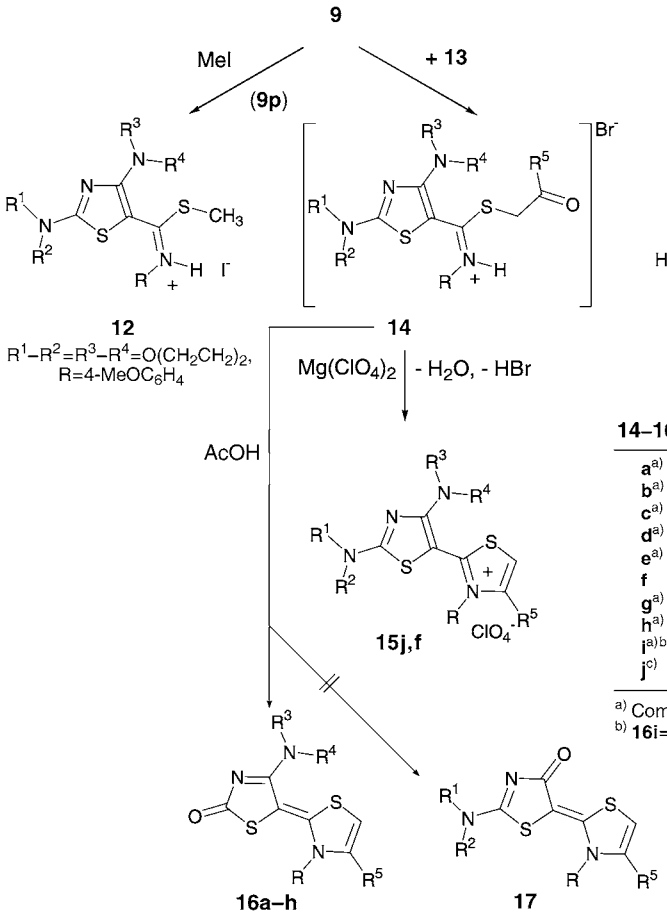
[a]) For R^1–R^4, see *Table 1*.

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 $Mg(ClO_4)_2$ in Ac_2O, 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 ^{1}H-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



13	Hal	R^5
a	Cl	Me
b	Cl	$ClCH_2$
c	Br	MeO
d	Br	Ph
e	Br	4-ClC_6H_4
f	Br	4-$NO_2C_6H_4$
g	Br	4-$(C_6H_4)C_6H_4$

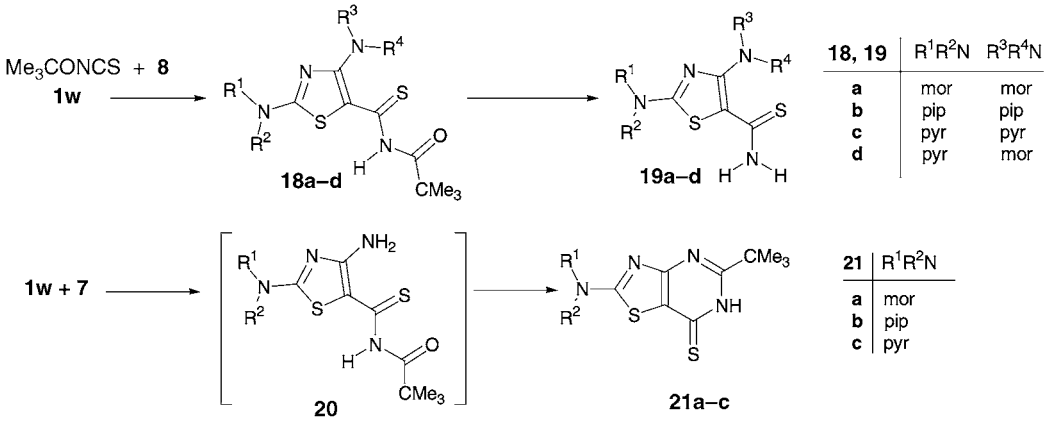
14–16	R^1R^2N	R^3R^4N	R	R^5
a[a]	mor	mor	4-$MeOC_6H_4$	4-$NO_2C_6H_4$
b[a]	mor	mor	4-ClC_6H_4	4-$NO_2C_6H_4$
c[a]	mor	mor	4-ClC_6H_4	4-ClC_6H_4
d[a]	mor	mor	4-$MeOC_6H_4$	4-ClC_6H_4
e[a]	pip	pip	4-ClC_6H_4	4-$NO_2C_6H_4$
f	pip	pip	4-$MeOC_6H_4$	4-$NO_2C_6H_4$
g[a]	pip	pip	Ph	4-ClC_6H_4
h[a]	pip	pip	4-ClC_6H_4	4-ClC_6H_4
i[a,b]	pip	mor	4-$MeOC_6H_4$	4-$NO_2C_6H_4$
j[c]	pip	pip	Ph	4-$NO_2C_6H_4$

[a] Compounds of type **15** were not formed. [b] **16i**=**16a**. [c] **16j** was not formed.

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



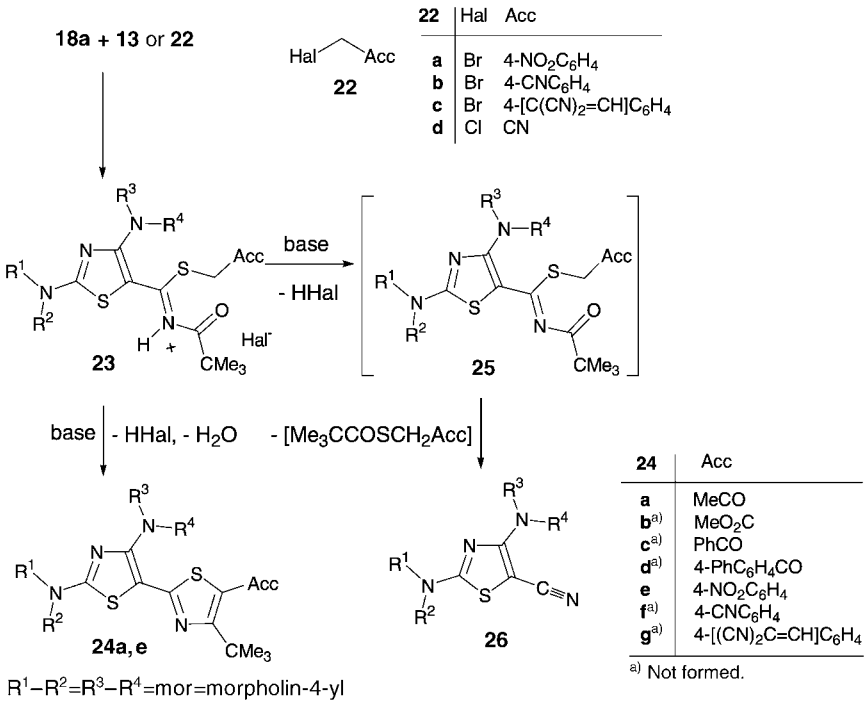
mor=morpholin-4-yl, pip=piperidin-1-yl, pyr=pyrrolidin-1-yl

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 Et_3N 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

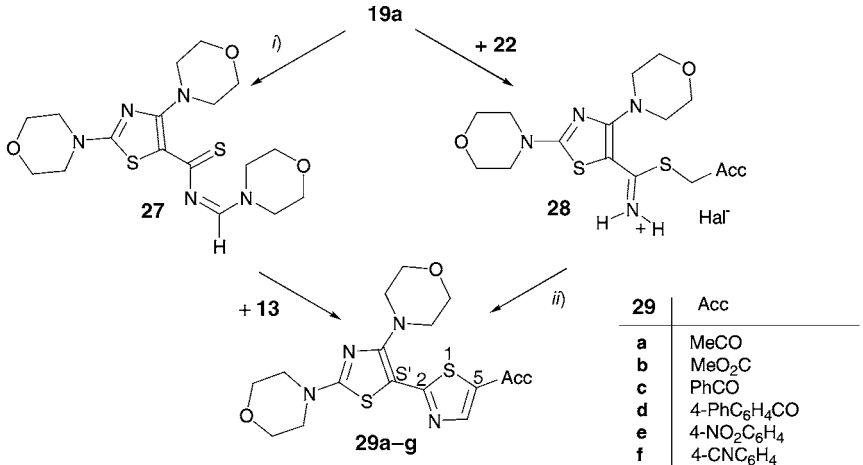


([2,5′-bithiazole]-2′,4′-diyl)bis[morpholines] **29** were available *via* the reaction with **13**. Alternatively, **29** could be prepared also by the reaction of **19a** with **22** to yield the intermediate carbothioamide hydrohalide **28** (not isolated), from which the products **29** were obtained, subsequently, by reaction with a formylating agent, *e.g.*, with the *Vilsmeier* reagent prepared from DMF and $POCl_3$ [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 H_3BO_3 and Ac_2O, 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



29	Acc
a	MeCO
b	MeO_2C
c	PhCO
d	4-PhC_6H_4CO
e	4-$NO_2C_6H_4$
f	4-CNC_6H_4
g	4-$[(CN)_2C{=}CH]C_6H_4$

i) $HC(OEt)_3$, morpholine. *ii*) 1. DMF, $POCl_3$, 2. H_2O/Et_3N.

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 CS_2. 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 Et_3N, 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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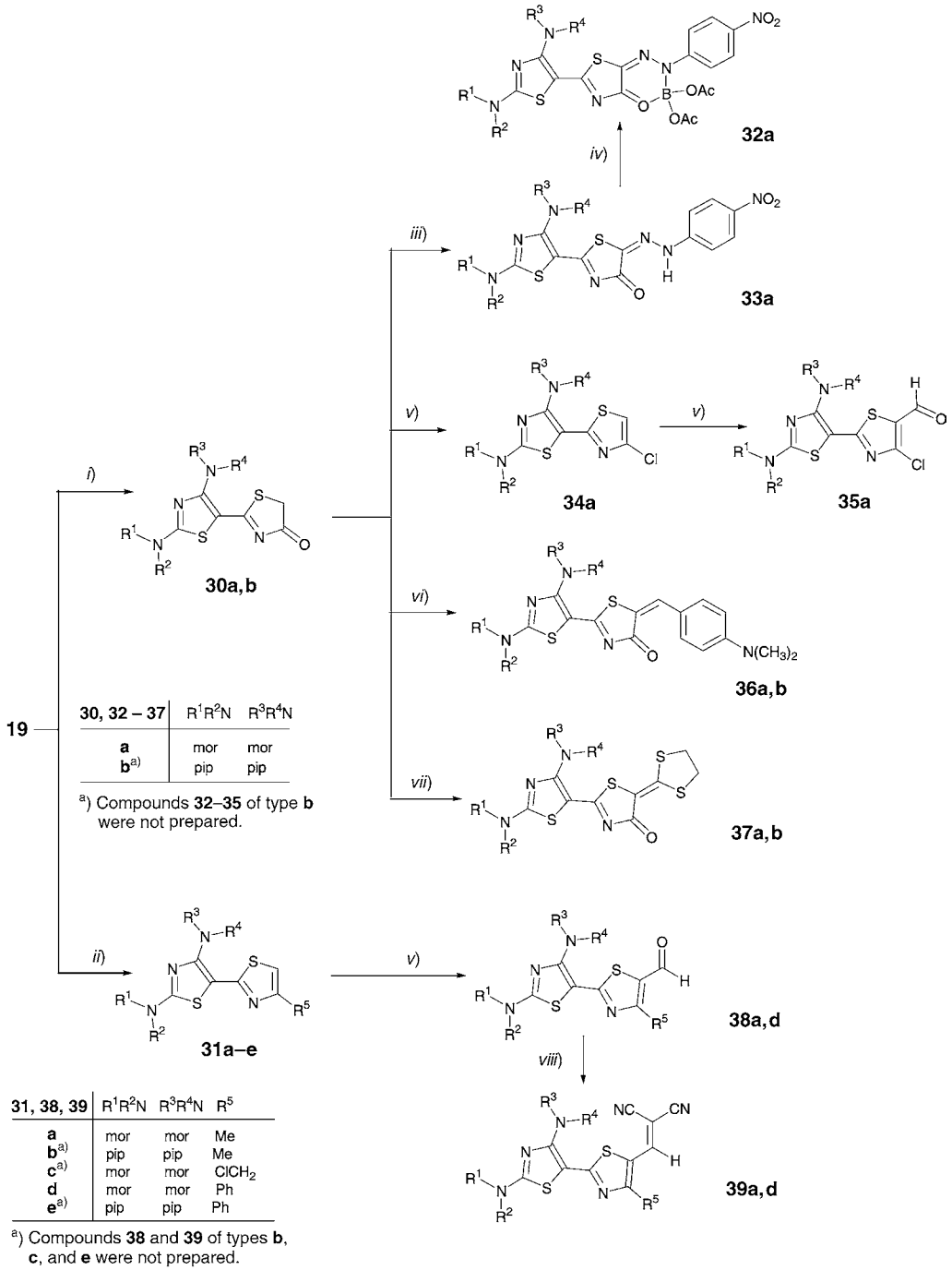
Scheme 8



i) **13c** Et_3N. *ii*) **13a**,**b**,**d** Et_3N. *iii*) 4-$NO_2C_6H_4N_2^+$. *iv*) H_3BO_3, Ac_2O. *v*) DMF, $POCl_3$. *vi*) 4-$Me_2NC_6H_4CHO$. *vii*) 1. CS_2, NaOH: 2. $(CH_2Br)_2$. *viii*) $CH_2(CN)_2$, Et_3N.

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 ε) in nm. NMR Spectra: *Varian Gemini-300* 300 MHz spectrometer; δ in ppm. Elemental analyses: *Leco CHNS-932* analyzer.

*2-(Dialkylamino)thiazol-4(5*H*)-iminium Chlorides* **7** *and* N^2,^{2},N^4,N^4*-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 Et_2O: **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(5*H*)-iminium chloride **7** (0.02 mol) in toluene (100 ml), Et_3N (28 ml, 0.02 mol) and isothiocyanate **1** (0.02 mol) were added. After refluxing the mixture for 1 h, the precipitated $Et_3N \cdot HCl$ was filtered off and washed with hot toluene. After cooling, the product crystallized from the filtrate. The crystals were washed with Et_2O: **10a**–**f**, see *Tables 1* and *2*.

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

	R^1R^2N[a])	R^3R^4N[a])	R	Yield [%]	M.p. [°]	Formula (M_r)	calc. found	C	H	N	S
9a	mor	mor	Me	34	172–173	$C_{13}H_{20}N_4O_2S_2$		47.54	6.14	17.06	19.53
						(328.46)		47.87	6.17	16.99	19.48
b	pip	pip	Me	84	191–193	$C_{15}H_{24}N_4S_2$		55.52	7.45	17.27	19.76
						(324.51)		55.53	7.47	17.19	19.44
c	pyr	pyr	Me	80	193–195	$C_{13}H_{20}N_4S_2$		52.67	6.80	18.90	21.63
						(296.46)		52.51	6.88	18.85	21.43
d	pip	mor	Me	25	127–129	$C_{14}H_{22}N_4OS_2$		51.50	6.79	17.16	19.64
						(326.48)		52.08	6.45	17.19	19.66
e	mor	mor	CH_2=$CHCH_2$	69	128–130	$C_{15}H_{22}N_4O_2S_2$		50.82	6.26	15.80	18.09
						(354.49)		50.49	6.18	15.93	18.05
f	pip	mor	CH_2=$CHCH_2$	71	84–85	$C_{16}H_{24}N_4OS_2$		54.51	6.86	15.89	18.19
						(358.52)		54.08	6.99	16.00	18.61
g	mor	mor	$PhCH_2$	83	171–173	$C_{19}H_{24}N_4O_2S_2$		56.41	5.98	13.85	15.85
						(404.55)		56.32	5.94	13.86	15.83
h	pip	pip	$PhCH_2$	88	170–172	$C_{21}H_{28}N_4S_2$		62.96	7.04	13.00	16.01
						(400.61)		63.37	6.80	13.82	16.06
i	mor	pyr	$PhCH_2$	69	117–119	$C_{19}H_{24}N_4OS_2$		58.73	6.23	14.42	16.51
						(388.55)		59.28	6.33	14.69	16.77
j	pip	mor	$PhCH_2$	87	191–192	$C_{20}H_{26}N_4OS_2$		59.67	6.51	13.92	15.93
						(402.58)		59.90	6.36	14.00	15.77
k	mor	mor	Ph	73	211	$C_{18}H_{22}N_4O_2S_2$		55.36	5.68	14.35	16.42
						(390.53)		55.73	5.32	14.23	16.31
l	pip	pip	Ph	74	168–170	$C_{20}H_{26}N_4S_2$		62.14	6.78	14.49	16.59
						(386.56)		62.01	6.83	14.80	16.45
m	pyr	pyr	Ph	72	164	$C_{18}H_{22}N_4S_2$		60.30	6.18	15.63	17.89
						(358.53)		60.52	6.34	15.58	17.65
n	mor	pyr	Ph	70	160–162	$C_{18}H_{22}N_4OS_2$		57.72	5.92	14.96	17.12
						(374.53)		58.01	5.83	14.80	17.45
o	pip	mor	Ph	87	207–210	$C_{19}H_{24}N_4OS_2$		58.73	6.23	14.42	16.51
						(388.55)		59.19	6.15	14.72	16.68
p	mor	mor	4-$MeOC_6H_4$	86	172	$C_{19}H_{24}N_4O_3S_2$		54.26	5.75	13.32	15.25
						(420.55)		54.65	5.84	13.38	15.26
q	pip	pip	4-$MeOC_6H_4$	74	178–180	$C_{21}H_{28}N_4OS_2$		60.54	6.77	13.45	15.39
						(416.61)		60.85	6.75	13.51	15.36

Table 1 (cont.)

r	pip	mor	4-$MeOC_6H_4$	88	184–185	$C_{20}H_{26}N_4O_2S_2$	57.39	6.26	13.39	15.32
						(418.58)	57.18	6.44	13.69	15.58
s	mor	mor	4-ClC_6H_4	74	216–218	$C_{18}H_{21}ClN_4O_2S_2$	50.87	4.98	13.18	15.09
						(424.97)	51.31	5.04	13.17	15.06
t	pip	pip	4-ClC_6H_4	67	183–185	$C_{20}H_{25}ClN_4S_2$	57.05	5.99	13.31	15.23
						(421.02)	57.26	6.08	13.31	15.30
u	mor	pyr	4-ClC_6H_4	61	169–171	$C_{18}H_{21}ClN_4OS_2$	52.86	5.18	13.70	15.68
						(408.97)	52.93	5.12	14.15	15.99
v	pip	mor	4-ClC_6H_4	93	180–182	$C_{19}H_{23}ClN_4OS_2$	53.95	5.48	13.25	15.16
						(423.00)	54.19	5.86	13.67	15.50
10a	mor	–	Ph	75	205–207	$C_{14}H_{16}N_4OS_2$	52.48	5.03	17.48	20.01
						(320.44)	52.24	4.82	17.01	19.79
b	pip	–	Ph	72	190–193	$C_{15}H_{18}N_4S_2$	56.57	5.70	17.59	20.14
						(318.46)	56.25	5.65	17.11	19.98
c	pyr	–	Ph	65	185–186	$C_{14}H_{16}N_4S_2$	55.23	5.30	18.40	21.07
						(304.44)	55.08	4.85	18.59	20.86
d	Pr_2N	–	Ph	63	138–139	$C_{16}H_{22}N_4S_2$	57.45	6.63	16.75	19.17
						(334.50)	57.71	6.74	16.39	18.78
e	mor	–	4-ClC_6H_4	79	204–206	$C_{14}H_{15}ClN_4OS_2$	47.38	4.26	15.79	18.07
						(354.88)	47.29	3.80	16.10	17.76
f	mor	–	4-$MeOC_6H_4$	81	217–218	$C_{15}H_{18}N_4O_2S_2$	51.41	5.18	15.99	18.30
						(350.46)	51.14	4.62	16.02	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 CH_2Cl_2 (50 ml), MeI (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°. ^{1}H-NMR ($CDCl_3$): 1.57 (*s*, MeS); 2.24 (*s*, MeN); 3.68 (*m*, 8 H, CH_2N); 3.78 (*m*, 8 H, CH_2O); 6.83 (*d*, 2 arom. H); 7.50 (*d*, 2 arom. H); 11.29 (*s*, NH). Anal. calc. for $C_{20}H_{27}IN_4O_3S_2$ (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), $Mg(ClO_4)_2$ (1.15 g, 5 mmol), and Ac_2O (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 (CH_2Cl_2): 467 (4.38). ^{1}H-NMR ((D_6)DMSO): 1.54 (*m*, 6 H, CH_2); 1.68 (*m*, 6 H, CH_2); 3.32 (*t*, 4 H, CH_2N); 3.46 (*t*, 4 H, CH_2N); 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 $C_{28}H_{30}ClN_5O_6S_2$ (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). ^{1}H-NMR ((D_6)DMSO): 1.57 (*m*, 6 H, CH_2); 1.69 (*m*, 6 H, CH_2); 3.28 (*t*, 4 H, CH_2N); 3.47 (*t*, 4 H, CH_2N); 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 $C_{29}H_{32}ClN_5O_7S_2$ (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(3*H*)-ylidene]-4-(dialkylamino)-thiazol-2(5*H*)-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. *^{1}H-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(3 H)-ylidene]-4-(morpholin-4-yl)thiazol-2-(5*H*)-one* (**16a**). From N^5-(4-methoxyphenyl)-2,4-dimorpholin-4-yl)thiazole-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). ^{1}H-NMR ((D$_6$)DMSO): 3.35 (*t*, 4 H, CH_2N); 3.61 (*t*, 4 H, CH_2O); 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 heteroarom. H). Anal. calc. for $C_{23}H_{20}N_4O_5S_2$ (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(3*H*)-ylidene]-4-(morpholin-4-yl)thiazol-2(5*H*)-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). ^{1}H-NMR ((D$_6$)DMSO): 3.20 (*t*, 4 H, CH_2N); 3.63 (*t*, 4 H, CH_2O); 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 heteroarom. H). Anal. calc. for $C_{22}H_{17}ClN_4O_4S_2$ (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-Bis(4-chlorophenyl)thiazol-2(3*H*)-ylidene]-4-(morpholin-4-yl)thiazol-2(5*H*)-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). ^{1}H-NMR ((D$_6$)DMSO): 3.43 (*t*, 4 H, CH_2N); 3.66 (*t*, 4 H, CH_2O); 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 heteroarom. H). Anal. calc. for $C_{22}H_{17}Cl_2N_3O_2S_2$ (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(3*H*)-ylidene]-4-(morpholin-4-yl)thiazol-2(5*H*)-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). ^{1}H-NMR ((D$_6$)DMSO): 3.40 (*t*, 4 H, CH_2N); 3.65 (*t*, 4 H, CH_2O); 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 heteroarom. H). Anal. calc. for $C_{23}H_{20}ClN_3O_3S_2$ (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(3*H *)-ylidene]-4-(piperidin-1-yl)thiazol-2(5*H*)-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). ^{1}H-NMR ((D$_6$)DMSO): 1.51 (*m*, 6 H, CH_2); 3.35 (*t*, 4 H, CH_2N); 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 heteroarom. H). Anal. calc. for $C_{23}H_{19}ClN_4O_3S_2$ (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(3*H*)-ylidene]-4-(piperidin-1-yl)thiazol-2(5*H*)-one* (**16f**). From N^5-(4-methoxyphenyl)-2,4-di(piperidin-1-yl)-5-carbothioamide (**9q**) and 4-nitrophenacyl bromide (**13f**). Yield 71%. M.p. 290–291°. UV/VIS: 427 (4.37). ^{1}H-NMR ((D$_6$)DMSO): 1.50 (*m*, 6 H, CH_2); 3.33 (*t*, 4 H, CH_2N); 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 heteroarom. H). Anal. calc. for $C_{24}H_{22}N_4O_4S_2$ (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-phenyl-thiazol-2(3*H*)-ylidene]-4-(piperidin-1-yl)thiazol-2(5*H*)-one* (**16g**). From N^5-(4-chlorophenyl)-2,4-di(piperidin-1-yl)thiazole-5-carbothioamide (**9l**) and 4-chlorophenacyl bromide (**13e**). Yield 54%. M.p. 218–220°. UV/VIS: 409 (4.28). ^{1}H-NMR ((D$_6$)DMSO): 1.56 (*m*, 6 H, CH_2); 3.40 (*t*, 4 H, CH_2N); 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 heteroarom. H). Anal. calc. for $C_{23}H_{20}ClN_3OS_2$ (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(3*H*)-ylidene]-4-(piperidin-1-yl)thiazol-2(5*H*)-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). ^{1}H-NMR ((D$_6$)DMSO): 1.60 (*m*, 6 H, CH_2); 3.44 (*t*, 4 H, CH_2N); 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 heteroarom. H). Anal. calc. for $C_{23}H_{19}Cl_2N_3OS_2$ (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). ^{1}H-NMR

($CDCl_3$): 1.26 (*s*, Me_3C); 3.59 (*m*, 8 H, CH_2N); 3.72 (*m*, 8 H, CH_2O); 8.82 (*s*, NH). Anal. calc. for $C_{17}H_{26}N_4O_3S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.21 (*s*, Me_3C); 1.95 (*m*, 4 H, CH_2); 3.24 (*t*, 4 H, CH_2N); 3.51 (*t*, 4 H, CH_2N); 3.67 (*t*, 4 H, CH_2O); 8.37 (*s*, NH). Anal. calc. for $C_{17}H_{26}N_4O_2S_2$ (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(6*H*)-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(5*H*)-iminium chloride **7** (0.1 mol) and Et_3N (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 H_2O (100 ml). The precipitated product was filtered off, washed with H_2O, and recrystallized from BuOH: **21a–c**.

*5-(*tert*-Butyl)-2-(morpholin-4-yl)thiazolo[4,5-*d*]pyrimidine-7(6*H*)-thione* (**21a**). From 2-(morpholin-4-yl)-thiazol-4(5*H*)-iminium chloride (**7a**) and **1w**. Yield 71%. Brown crystals. M.p. 175–176°. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, Me_3C); 3.72 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 10.00 (*s*, NH). Anal. calc. for $C_{13}H_{18}N_4OS_2$ (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(6*H*)-thione* (**21b**). From 2-(piperidin-1-yl)-thiazol-4(5*H*)-iminium chloride (**7b**) and **1w**. Yield 69%. Orange crystals. M.p. 250–252°. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, Me_3C); 1.69 (*m*, 6 H, CH_2); 3.69 (*t*, 4 H, CH_2N); 9.94 (*s*, NH). Anal. calc. for $C_{14}H_{20}N_4S_2$ (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(6*H*)-thione* (**21c**). From 2-(pyrrolidin-1-yl)thiazol-4(5*H*)-iminium chloride (**7c**) and **1w**. Yield 62%. Light green crystals. M.p. 295–297°. ^{1}H-NMR ($CDCl_3$): 1.42 (*s*, Me_3C); 2.09 (*m*, 4 H, CH_2); 3.41 (*m*, CH_2N); 3.81 (*m*, CH_2N); 9.91 (*s*, NH). Anal. calc. for $C_{13}H_{18}N_4S_2$ (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. NH_3 soln. The precipitated product was filtered off and washed with H_2O: **19a–d**.

2,4-Di(morpholin-4-yl)thiazole-5-carbothioamide (**19a**). From **18a**. Yield 81%. Brown crystals. M.p. 194–196° (BuOH). ^{1}H-NMR ($CDCl_3$): 3.09 (*t*, 4 H, CH_2N); 3.52 (*t*, 4 H, CH_2N); 3.76 (*m*, 8 H, CH_2O); 8.90 (br. *s*, NH_2). Anal. calc. for $C_{12}H_{18}N_4O_2S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.62 (*m*, 12 H, CH_2); 3.02 (*t*, 4 H, CH_2N); 3.48 (*t*, 4 H, CH_2N); 8.80 (br. *s*, NH_2). Anal. calc. for $C_{14}H_{22}N_4S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.85 (*m*, 4 H, CH_2); 1.97 (*m*, 4 H, CH_2); 3.37 (*m*, 8 H, CH_2N); 6.98 (*s*, NH_2). Anal. calc. for $C_{12}H_{18}N_4S_2$ (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). ^{1}H-NMR ($CDCl_3$): 2.00 (*m*, 4 H, CH_2N); 3.10 (*t*, 4 H, CH_2N); 3.41 (*t*, 4 H, CH_2N); 3.75 (*t*, 4 H, CH_2O); 8.70 (br. *s*, NH_2). Anal. calc. for $C_{12}H_{18}N_4OS_2$ (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′-diyl)bis[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 Et_3N (1.4 ml, 0.01 mol) was added at r.t., and the soln. was refluxed for 1 h. After cooling to r.t., H_2O (20 ml) was added, and the precipitated product was filtered off: **24a** and **24e**.

*1-[4-(*tert*-Butyl)-2′,4′-di(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). ^{1}H-NMR ($CDCl_3$): 1.40 (*s*, Me_3C); 2.53 (*s*, Me); 3.17 (*t*, 4 H, CH_2N); 3.53 (*t*, 4 H, CH_2N); 3.79 (*t*, 4 H, CH_2O); 3.88 (*t*, 4 H, CH_2O). Anal. calc. for $C_{20}H_{28}N_4O_3S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.20 (*s*, Me_3C); 3.07 (*t*, 4 H, CH_2N); 3.56 (*t*, 4 H, CH_2N); 3.80 (*m*, 8 H, CH_2O); 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. ^{1}H-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)-N^5*-[(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°. ^{1}H-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′-Bithiazole]-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). ^{1}H-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 heteroarom. 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′-bithiazole]-5-carboxylate (**29b**). From **27** and methyl bromoacetate (**13c**) by *Method A:* 2.14 g (54%) of **29b**. Colorless crystals. M.p. 179–181°. ^{1}H-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 heteroarom. 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). ^{1}H-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 heteroarom. 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). ^{1}H-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 heteroarom. 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′-bithiazole]-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). ^{1}H-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 heteroarom. 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). ^{1}H-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 heteroarom. 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). ^{1}H-NMR ($CDCl_3$): 3.15 (*t*, 4 H, CH_2N); 3.53 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H,

CH_2O); 3.92 (*t*, 4 H, CH_2O); 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 $C_{24}H_{22}N_6O_2S_2$ (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(5*H*)-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., Et_3N (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(5*H*)-one* (**30a**). From **19a**. Yield 74%. Colorless crystals. M.p. 209–211° (EtOH). ^{1}H-NMR ($CDCl_3$): 3.61 (*m*, 8 H, CH_2N); 3.79 (*m*, 8 H, CH_2O); 3.85 (*s*, 2 H, CH_2). Anal. calc. for $C_{14}H_{18}N_4O_3S_2$ (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(5*H*)-one* (**30b**). From **19b**. Yield 67%. Pale brown crystals. M.p. 125–126° (EtOH). ^{1}H-NMR ($CDCl_3$): 1.65 (*m*, 12 H, CH_2); 3.54 (*m*, 8 H, CH_2N); 3.82 (*m*, 2 H, CH_2). Anal. calc. for $C_{16}H_{22}N_4OS_2$ (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, Et_3N (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). ^{1}H-NMR ($CDCl_3$): 2.38 (*s*, Me); 3.07 (*t*, 4 H, CH_2N); 3.48 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 3.87 (*t*, 4 H, CH_2O); 6.68 (*s*, 1 heteroarom. H). Anal. calc. for $C_{15}H_{20}N_4O_2S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.57–1.76 (*m*, 12 H, CH_2); 2.38 (*s*, Me); 3.01 (*t*, 4 H, CH_2N); 3.47 (*t*, 4 H, CH_2N); 6.63 (*s*, 1 heteroarom. H). Anal. calc. for $C_{17}H_{24}N_4S_2$ (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). ^{1}H-NMR ($CDCl_3$): 3.09 (*t*, 4 H, CH_2N); 3.49 (*t*, 4 H, CH_2N); 3.77 (*t*, 4 H, CH_2O); 3.86 (*t*, 4 H, CH_2O); 4.63 (*s*, 2 H, CH_2); 7.09 (*s*, 1 heteroarom. H). Anal. calc. for $C_{15}H_{19}ClN_4O_2S_2$ (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). ^{1}H-NMR ($CDCl_3$): 3.13 (*t*, 4 H, CH_2N); 3.51 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H, CH_2O); 3.90 (*t*, 4 H, CH_2O); 7.28 (*s*, 1 heteroarom. H); 7.36 (*m*, 3 arom. H); 7.88 (*d*, 2 arom. H). Anal. calc. for $C_{20}H_{22}N_4O_2S_2$ (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). ^{1}H-NMR ($CDCl_3$): 1.65–1.76 (*m*, 12 H, CH_2); 3.05 (*t*, 4 H, CH_2N); 3.50 (*t*, 4 H, CH_2N); 7.28–7.40 (*m*, 4 arom. and heteroarom. H); 7.90 (*d*, 2 arom. H). Anal. calc. for $C_{22}H_{26}N_4S_2$ (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 H_2O (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). ^{1}H-NMR ($CDCl_3$): 3.62–3.85 (*m*, 12 H, CH_2N); 4.24 (*t*, 4 H, CH_2O); 7.28 (*s*, NH); 7.31 (*d*, 2 arom. H); 8.10 (*d*, 2 arom. H). Anal. calc. for $C_{20}H_{21}N_7O_5S_2$ (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 H_3BO_3 (0.04 g, 6 mmol) in Ac_2O (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 Et_2O: 2.5 g (66%) of **32a**. M.p. 297–300°. UV/VIS: 572 (4.78). ^{1}H-NMR ($CDCl_3$): 1.99 (*s*, 6 H, Me); 3.51 (*t*, 2 H, CH_2N); 3.63 (*t*, 2 H, CH_2N); 3.85 (*m*, 8 H, CH_2); 3.91 (*t*, 4 H, CH_2O); 7.68 (*d*, 2 arom. H); 8.05 (*d*, 2 arom. H). Anal. calc. for $C_{24}H_{26}BN_7O_9S_2$ (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), $POCl_3$ (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 H_2O, and recrystallized from EtOH: 5.3 g (71%) of **34a**. M.p. 150°. ^{1}H-NMR ($CDCl_3$): 3.08 (*t*, 4 H, CH_2N); 3.50 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 3.86 (*t*, 4 H, CH_2O); 6.84 (*s*, 1 heteroarom. H). Anal. calc. for $C_{14}H_{17}ClN_4O_2S_2$ (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 $POCl_3$ (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 H_2O (50 ml), and recrystallized from EtOH: 2.8 g (35%) of **35a**. M.p. 147–148°. ^{1}H-NMR ($CDCl_3$): 3.23 (*t*, 4 H, CH_2N); 3.59 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 3.86 (*t*, 4 H, CH_2O); 9.86 (*s*, CHO). Anal. calc. for $C_{15}H_{17}ClN_4O_3S_2$ (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(5*H*)-ones* **36**: *General Procedure.* A mixture of a 2′,4′-bis(dialkylamino)[2,5′-bithiazol]-4(5*H*)-one **30** (0.01 mol), 4-(dimethylamino)-benzaldehyde (1.5 g, 0.01 mol), and Et_3N (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(5*H*)-one* (**36a**). From **30a**. Yield 76%. Orange crystals. M.p. 279–281° (DMF). UV/VIS: 497 (4.32). ^{1}H-NMR ($CDCl_3$): 2.97 (*s*, 6 H, MeN); 3.56 (*m*, 8 H, CH_2N); 3.74 (*t*, 4 H, CH_2O); 3.83 (*t*, 4 H, CH_2O); 6.64 (*d*, 2 arom. H); 7.38 (*d*, 2 arom. H); 7.66 (*s*, CH). Anal. calc. for $C_{23}H_{27}N_5O_3S_2$ (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(5*H*)-one* (**36b**). From **30b**. Yield 68%. Orange crystals. M.p. 220–222° (DMF). UV/VIS: 492 (4.40). ^{1}H-NMR ($CDCl_3$): 1.66 (*m*, 12 H, CH_2); 2.99 (*s*, 6 H, MeN); 3.56 (*m*, 8 H, CH_2N); 6.68 (*d*, 2 arom. H); 7.44 (*d*, 2 arom. H); 7.67 (*s*, CH). Anal. calc. for $C_{25}H_{31}N_5OS_2$ (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(5*H*)-ones* **37**: *General Procedure.* To a suspension of a 2′,4′-bis(dialkylamino)[2,5′-bithiazol]-4(5*H*)-one **30** (0.01 mol) in DMF (30 ml), KOH (1.1 g, 0.02 mol) in H_2O (2 ml), followed by CS_2 (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 H_2O (250 ml). The precipitated product was filtered off, washed with H_2O, and recrystallized from DMF: **37a** or **37b**.

*2′,4′-Di(morpholin-4-yl)-5-(1,3-dithiolan-2-ylidene)[2,5′-bithiazol]-4(5*H*)-one* (**37a**). From **30a**. Yield 73%. Orange crystals. M.p. 265–267° (DMF). UV/VIS: 464 (4.69). ^{1}H-NMR ($CDCl_3$): 3.42 (*t*, 4 H, CH_2N); 3.46 (*t*, 2 H, CH_2); 3.51 (*t*, 2 H, CH_2); 3.55 (*t*, 4 H, CH_2N); 3.75 (*t*, 4 H, CH_2O); 3.82 (*t*, 4 H, CH_2O). Anal. calc. for $C_{16}H_{20}N_4O_3S_4$ (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(5*H*)-one* (**37b**). From **30b**. Orange crystals. Yield 64%. M.p. 221–223° (DMF). UV/VIS: 469 (4.65). ^{1}H-NMR ($CDCl_3$): 1.67 (*m*, 12 H, CH_2); 3.39 (*t*, 4 H, CH_2N); 3.43 (*t*, 2 H, CH_2); 3.47 (*t*, 2 H, CH_2); 3.50 (*t*, 4 H, CH_2N). Anal. calc. for $C_{19}H_{24}N_4OS_4$ (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), $POCl_3$ (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 H_2O (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. ^{1}H-NMR ($CDCl_3$): 2.61 (*s*, Me); 3.16 (*t*, 4 H, CH_2N); 3.53 (*t*, 4 H, CH_2N); 3.78 (*t*, 4 H, CH_2O); 3.89 (*t*, 4 H, CH_2O); 9.94 (*s*, CHO). 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 50.61, 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. ^{1}H-NMR ($CDCl_3$): 3.22 (*t*, 4 H, CH_2N); 3.56 (*t*, 4 H, CH_2N); 3.80 (*t*, 4 H, CH_2O); 3.91 (*t*, 4 H, CH_2O); 7.46 (*m*, 3 arom. H); 7.69 (*d*, 2 arom. H); 9.88 (*s*, CHO). 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 57.09, 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), Ac_2O (10 ml), and 3 drops of Et_3N 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). ^{1}H-NMR ($CDCl_3$): 2.49 (*s*, Me); 3.24 (*t*, 4 H,

CH_2N); 3.59 (*t*, 4 H, CH_2N); 3.79 (*t*, 4 H, CH_2O); 3.90 (*t*, 4 H, CH_2O); 7.69 (*s*, CH). Anal. calc. for $C_{19}H_{20}N_6O_2S_2$ (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). ^{1}H-NMR ($CDCl_3$): 3.34 (*t*, 4 H, CH_2N); 3.61 (*t*, 4 H, CH_2N); 7.39 (*t*, 4 H, CH_2O); 3.93 (*t*, 4 H, CH_2O); 7.55 (*m*, 5 arom. H); 7.70 (*s*, CH). Anal. calc. for $C_{24}H_{22}N_6O_2S_2$ (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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