SYNTHESIS OF *N*-SUBSTITUTED 2,4-DIAMINOTHIAZOLES AND THEIR SALTS

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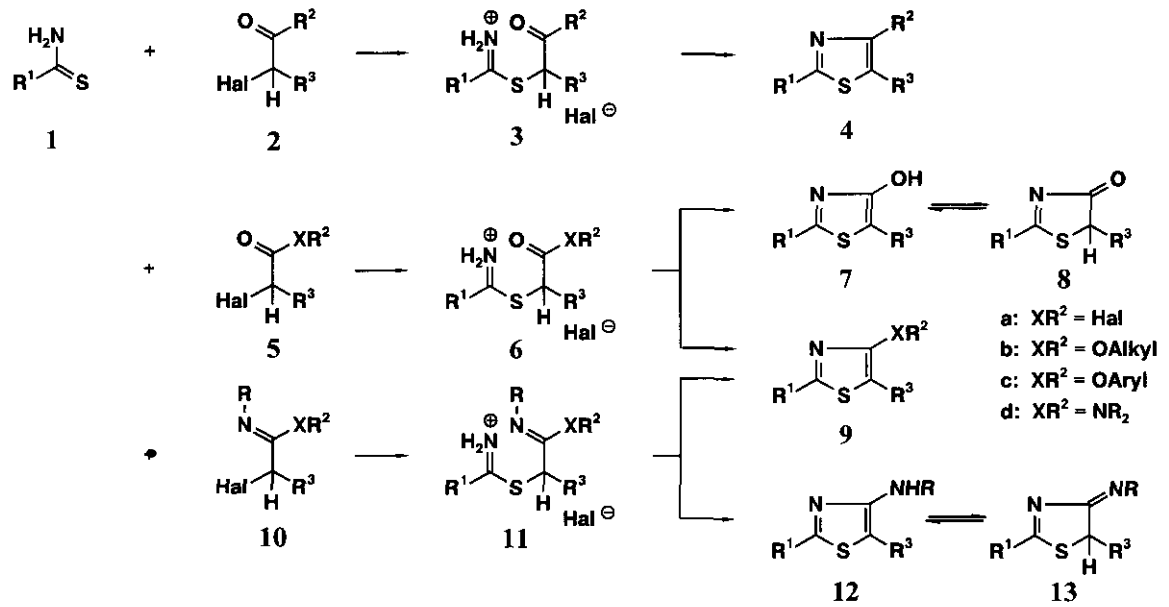
Abstract- A series of *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22)** and their corresponding mineral acid salts **(22·HX)** and **(22·2HX)** have been prepared by the reaction of $POCl_3$ with *N*-substituted *S*-(dialkylaminocarbonylmethylene)-isothiouronium salts **(20)** available from corresponding substituted thioureas **(18)** and *N,N*-disubstituted chloroacetamides **(19)** or by the reaction of primary or secondary amines **(25)** in excess with *N*(2)-unsubstituted or *N*(2)-disubstituted 2-amino-4-thiazolinimine hydrochlorides **(24)** available by the reaction of corresponding *N*-substituted thioureas **(18)** with chloroacetonitrile **(23)**.

The Hantzsch method is one of the simplest route for preparing thiazoles. By starting with *N*-unsubstituted thioamides **(1)** and α-halogeno carbonyl compounds **(2)** it allows the preparation of a large variety of differently substituted thiazoles of the general structure **(4)**. The reaction runs very regioselectively by intermediate iminium salts **(3)** which cyclisize subsequently by elimination of water to yield the corresponding heterocycles **(4)**.[1,2]

Whereas the Hantzsch thiazole route has nearly no complications in respect of the type of substituent R^1 attached at the thioamide educt **(1)**, it has, however, some complications concerning the substituentes R^2 in the α-halogeno carbonyl compound **(2)**. Thus, by starting with α-halogenoacetic acid derivatives of the general formula **(5)** instead of the simple α-halogeno carbonyl compounds **(2)** with R^2 = H, alkyl, or aryl, different types of products can be formed depending on the kind of substituents XR^2 and R^3 in the educts **(5)** used and the conditions applied. Usually, by starting with the α-halogenoacetic acid derivatives **(5a-5c)** 4-thiazolinones **(8)** or their tautomeric 4-hydroxythiazoles **(7)** are obtained *via* the intermediate iminium salts **(6)**.[3-6] Hence, neither 4-halothiazoles **(9a)** nor 4-alkoxy- **(9b)** or 4-aryloxythiazoles **(9c)**,

could be prepared by the Hantzsch route starting from α-halogeno carbonyl halides or esters **(5a-5c)**, respectively.



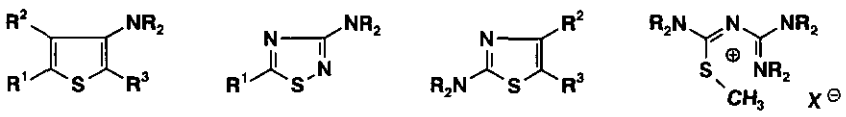
Scheme 1

The same has been found by using α-halogenoacetamides **(5d)** ($XR^2 = NR_2$) or α-halogenoacetamidines **(10d)** ($XR^2 = NH_2$) as thiazole educts. By their reaction, e.g., with simple thioureas **(1)** ($R^1 = NH_2$) 2-aminothiazoline-4-ones **(8)** ($R^1 = NH_2$) or 2-aminothazoline-4-imines **(13)** ($R^1 = NH_2$) instead of the corresponding 4-dialkylaminothiazoles **(9d)** are formed from the intermediate iminium salts **(11)**.[7,8]

Such 4-dialkylaminothiazoles **(9d)** should receive, however, some interest due to their structural resemblance to 3-dialkylaminothiophenes **(14)**, which are highly reactive synthons for different synthetic applications,[9-13] e.g., for preparing methine dyes,[14] or to 3-dialkylamino-1,2,4-thiadiazoles **(15)** which exhibit, in some cases, besides their use in dyestuff chemistry[15,16] pharmacological or biological activities.[17,18] Moreover, the 4-dialkylaminothiazoles **(9d)** are isomers of the well-known 2-dialkylaminothiazoles **(16)** which also exhibit, *inter alia*, a lot of interest as dyestuff precursors. Thus, they can be transformed, in dependence of their substitution pattern at C(4) and C(5), into deeply coloured 2-aminothiazolylazo[19-24] or methine dyes.[25-28]

In respect to the usefulness of the aminothiazoles **(16)**, 1,2,4-thiadiazoles **(15)**, and thiophenes **(14)** as dyestuff educts, the 2,4-diaminothiazoles of the general structure **(22)** seem also to be of similar interest. Such compounds, especially if they are disubstituted at both their amino groups and unsubstituted at their

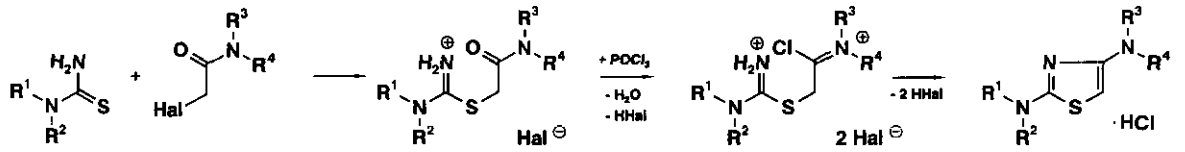
C(5), are nearly unknown at yet. The few compounds known of this type have been prepared by a base-mediated ring closure reaction of alkylmercaptoazavinamidinium salts **(17)**.[29-31]



14 **15** **16** **17**

Scheme 2

Due to the rather inconvenient availability of these precursors required and the peculiar conditions applied for their transformation into the 2,4-diaminothiazoles **(22)**, this route failed hitherto to prepare a larger variety of such interesting compounds, obviously.



18 **19** **20** **21** **22·HCl**

Scheme 3

For a simple route to preparing *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** we tried to modify the usual Hantzsch method by starting with *N*-disubstituted thioureas **(18)** and *N*-disubstituted α-chloroacetamides **(19)** as educts, by using an aprotic solvent, like dichloromethane, and by using $POCl_3$ as an efficient water-splitting reagent for preventing the amine elimination from the isothiouronium salts **(20)** primarily formed.

Under these conditions, *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazole hydrochlorides **(22·HCl)** are obtained. Obviously, the reaction runs via intermediate bis-iminium salts **(21)** which give rise to the formation of the desired products **(22·HCl)**.

Because the 2,4-diaminothiazole hydrochlorides **(22·HCl)** do not crystallise easily, in common, they have been transformed either into their corresponding free bases **(22)** by adding aqueous sodium hydroxide or ammonia to the primary reaction mixture or into their hydroperchlorates **(22·$HClO_4$)**, hydrotetrafluoroborates **(22·HBF_4)** or hydrotetraphenylborates **(22·$HB(C_6H_5)_4$)** by adding of aqueous perchloric acid, tetrafluoroboric acid or sodium tetrafluoroborate, resp., to their reaction mixture.

Surprisingly, in some cases 2,4-diaminothiazolium salts of the general structure **(22·2HX)** also could be obtained by this procedure.

Table 1 *N*(2),*N*(4)-Substituted 2,4-diaminothiazoles **(22)** and their mineral acid salts **(22·HX)** and **(22·2HX)**

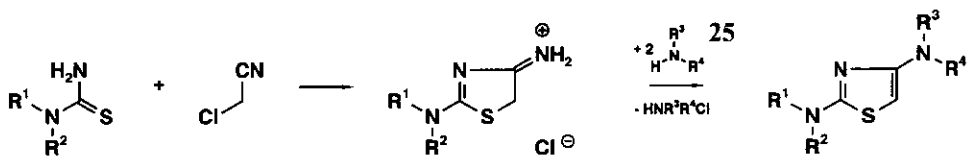
Compound	R^1R^2N	R^3R^4N	Method	Yield (%)	mp (°C)
22a	Morpholino	Morpholino	B	86	98[a]
			C	70	99[a]
22a·HClO$_4$			A	67	265[b]
			B	73	267[b]
			C	72	266[b]
22a·HBF$_4$			A	41	263[b]
			C	47	262-265[b]
22b·HClO$_4$	Morpholino	Pyrrolidino	B	65	146[a]
22c	Morpholino	Piperidino	B	70	88[c]
22c·HClO$_4$			B	60	171[e]
22d·2HClO$_4$	Morpholino	Piperazyl	B	36	270[d]
22e	Pyrrolidino	Pyrrolidino	C	88	123-126[e]
22e·HClO$_4$			A	43	137-139[a]
			C	80	138-139[a]
22e·2HClO$_4$			A	61	230-232[b]
			B	57	231[b]
22e·HBPh$_4$			C	70	196-198[f]
22f	Pyrrolidino	Morpholino	B	74	83[c]
22f·HClO$_4$			A	60	165-166[b]
			B	69	166[b]
22g·HClO$_4$	Pyrrolidino	Piperidino	A	42	121-123[g]
			B	72	126[a]
22h·HClO$_4$	Pyrrolidino	Diphenylamino	A	32	171-172[a]
22i·2HClO$_4$	Pyrrolidino	Diethylamino	A	35	215-216[b]
22j·HClO$_4$	Piperidino	Piperidino	B	81	131[g]
22k	Piperidino	Morpholino	B	56	63-64[e]
22k·HClO$_4$			A	45	188-189[b]
			B	81	191[b]
22l·HClO$_4$	Piperidino	Pyrrolidino	B	75	103[g]
22m·HClO$_4$	Diethylamino	Morpholino	B	73	130[g]
22n·2HClO$_4$	Diethylamino	Piperidino	B	32	223[b]
22o·2HClO$_4$	Diethylamino	Pyrrolidino	B	70	237[b]
22p·HClO$_4$	Di-n-propylamino	Morpholino	A	21	118-120[h]
22q·2HClO$_4$	Di-n-propylamino	Pyrrolidino	A	29	205-207[b]
22r·HClO$_4$	Phenylamino	Morpholino	A	10	173-174[d]
22s·HClO$_4$	Amino	Morpholino	A	30	211-212[e]
22t·HClO$_4$	Amino	Pyrrolidino	A	31	273-275[b]
22u·HClO$_4$	n-Butylamino	n-Butylamino	C	23	82-84[i]

[a] from ethanol; [b] from glacial acetic acid; [c] from petroleum ether; [d] from acetonitrile by slow addition of ether; [e] from methanol; [f] from acetonitrile; [g] from glacial acid by slow addition of ethyl acetate; [h] from ethyl acetate; [i] from chloroform by slow addition of ether

The educts **(18)** and **(19)** required for this synthesis, designed as method A, were prepared according to known routes. Whereas the *N,N*-disubstituted thioureas **(18)** have been prepared by the hydrolysis of *N,N*-disubstituted *N'*-acylthioureas,[32] the *N,N*-disubstituted chloroacetamides **(19)** were available by the reaction of chloroacetyl chloride with an appropriated secondary amine.[33]

As seen from Table 1, a variety of *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** and their mineral acid salts **(22·nHX)** have been prepared by means of the method A.

Furthermore, a more efficient method B for preparing *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** or their mineral acid salts **(22·nHX)** has been found. It starts from *N*-disubstituted 2-amino-4-thiazolinimine hydrochlorides **(24)** and transforms these salts into the desired products **(22)** by their reaction with an appropriate secondary amine **(25)**. This transformation can be performed, very simply, by heating the salts **(24)** with the amine **(25)** in ethereal solution until the evolution of ammonia is complete. The separation of the *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** formed from the reaction mixture is achieved by their transformation into the corresponding mineralic acid salts **(22·nHX)** by addition of perchloric acid or tetrafluoric acid as mentioned before.



18 **23** **24** **22**

Scheme 4

The *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** and their mineral acid salts **(22·nHX)** prepared by this method B are compiled in Table 1 also.

The necessary *N,N*-disubstituted 2-amino-4-thiazolinimine hydrochlorides **(24)** are available by the reaction of a *N,N*-disubstituted thiourea **(18)** with chloroacetonitrile **(23)** in ethanolic solution according to a route described in the literature.[34-38] Because this route has been applied until now mainly for the synthesis of *N*(2)-unsubstituted 2-amino-4-thiazolinimine hydrochlorides **(24)**, the hitherto unknown *N*(2)-disubstituted 2-amino-4-thiazolinimine hydrochlorides **(24)** ($R^1 = R^2 \neq H$) are listed for their characterisation in Table 2.

Finally, a third method C for preparing *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** was elaborated. It starts from the *N*(2)-unsubstituted 2-amino-4-thiazolimine hydrochloride **(24a)** which is simple available from the reaction of the unsubstituted thiourea **(18a)** ($R^1 = R^2 = H$) with chloroacetonitrile **(23)**.[34] This compound **(24a)** is able to react by heating in ethereal solution with

secondary amines **(25)** under elimination of ammonia. As long as the secondary amines **(25)** are used in at least three equivalents, corresponding *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** containing two identically substituted amino groups at their C(2) and C(4) position are formed in course of this method C.

Table 2 *N*(2)-Substituted 2-amino-4-thiazolinimine hydrochlorides **(24)**

Compd.	NR^1R^2	Yield (%)	mp (°C)	^{1}H-NMR in DMSO-d_6 N-H	H(5)	Other signals
24a Ref.[34-37]	Amino	98	>360[a]	10.00 (s, 1H) 10.03 (s, 1H) 10.29 (s, 1H) 10.38 (s, 1H)	4.60 (s, 2H)	
24b	Diethylamino	92	199-201	10.17 (s, 1H) 10.48 (s, 1H)	4.73 (s, 2H)	1.20 (t, J = 10 Hz, 3H, CH_3CH_2); 1.25 (t, J = 10 Hz, 3H, CH_3CH_2); 3.56 (q, J = 10 Hz, 2H, CH_2CH_3); 3.75 (q, J = 10 Hz, 2H, CH_2CH_3)
24c	Dipropylamino	29	143-145	10.12 (s, 1H) 10.38 (s, 1H)	4.71 (s, 2H)	0.85 (t, J = 7 Hz, 3H, CH_3CH_2); 0.90 (t, J = 7 Hz, 3H, CH_3CH_2); 1.60-1.72 (m, J = 7 Hz, 4H, $CH_2CH_2CH_3$); 3.46 (t, J = 7 Hz, 2H, CH_2CH_2); 3.66 (t, J = 7 Hz, 2H, CH_2CH_2)
24d	Di-n-buthylamino	91	134-135	10.07 (s, 1H) 10.17 (s, 1H)	4,69 (s, 2H)	0.90 (q, J = 7 Hz, 6H, CH_3CH_2); 1.20-1.39 (m, 4H, $CH_2CH_2CH_3$); 1.54-1.70 [m, 4H, $CH_2(CH_2)_2$]; 3.48 (t, J = 7 Hz, 2H, CH_2CH_2); 3.69 (t, J = 7 Hz, 2H, CH_2CH_2)
24e	Pyrrolidino	93	230-232	10.16 (s, 1H) 10.54 (s, 1H)	4.74 (s,1H)	1.93-2.05 [m, 4H, $CH_2(CH_2)_2$]; 3.57 (t, J = 6 Hz, 2H, CH_2CH_2); 3.73 (t, J = 6 Hz, 2H, CH_2CH_2)
24f	Piperidino	42	238-240	10.05 (s, 1H) 10.20 (s, 1H)	4.69 (s, 2H)	1.55-1.72 [m, 6H, $CH_2(CH_2)_2$]; 3.55-3.62 (m, 2H, CH_2CH_2)[b]; 3.88-3.95 (m, 2H, CH_2CH_2)[b]
24g	Morpholino	92	200-202	10.16 (s, 1H) 10.26 (s, 1H)	4.72 (s, 2H)	3.64 (t, J = 4 Hz, 2H, CH_2CH_2); 3.70-3.76 (m, 4H, CH_2CH_2)[c]; 3.92 (t, J = 4 Hz, 2H, CH_2CH_2)
24h	Diphenylamino	59	162-165	10.54 (s, 1H) 10.87 (s, 1H)	4,75 (s, 2H)	7.38-7.75 (m, 10H, aromatic H)
24i	Methylphenylamino	62	246-248	isomer A: 10.17 (s, 1H) 10.33 (s, 1H) isomer B: 10.44 (s, 1H) 10.54 (s, 1H)	isomer A: 4.80 (s, 2H) isomer B: 4.67 (s, 2H)	isomer A: 3.61 (s, 3H, CH_3) 7.37-7.53 (m, 5H, aromatic H) isomer B: 3.66 (s, 3H, CH_3) 7.58 (s, 5H, aromatic H)

[a] crystals darkened about 250°C; [b] broad signal without detectable coupling; [c] two superimposed triplets

By application of two equivalents of secondary amine **(25)** only one amino group of the 2-amino-4-thiazolinimine hydrochloride educt **(24a)** is split off giving rise to the formation of 2,4-diaminothiazoles **(22)** unsubstituted at their 2-amino and disubstituted at their 4-amino group. Usually, the *N*(4)-disubstituted 2,4-diaminothiazoles **(22)** ($R^3 = R^4 \neq H$) so received are, unfortunately, accompanied by some *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)**. They result from a twofold exchange of both the amino and imino group in the educt **(24a)** and have to be separated from the reaction mixture to isolate pure *N*(4)-disubstituted 2,4-diaminothiazoles **(22)** ($R^3 = R^4 \neq H$). Therefore, the method C has been

advantageously applied, as seen from Table 1, for the preparation of symmetrically *N*(2)- and *N*(4)-substituted 2,4-diaminothiazoles **(22)** or their salts **(22·nHX)** only.

The method C can be applied, as exemplified by the synthesis of the 2,4-dibutylaminothiazole **(22u·HClO$_4$)** from **(24a)** and n-butylamine **(25)** (R^3 = n-C_4H_9, R^4 = H), for the preparation of 2,4-bis(monoalkylamino)thiazoles **(22)** or their salts **(22·nHX)** also.

In contrast to the *N*(4)-unsubstituted and *N*(4)-monosubstituted 2,4-diaminothiazoles **(22)** which are rather unstable in the form of their free bases and isolable, therefore, as mineral acid salts **(22·HX)** only, the *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** described in Table 1 are more stable and can be generated, if required, from their corresponding mineral acid salts **(22·HX)** by addition of suited bases, like ammonia or aqueous sodium hydroxide, to their ethanolic solution in sufficiently high yields.

The free *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** can be stored under nitrogen at room temperature without decomposition.

All the *N*(2) and *N*(4) substituted 2,4-diaminothiazoles **(22)** and their corresponding mineralic acid salts **(22·nHX)** summarised in Table 1 are new compounds. Their constitution follow from their preparation routes as well as from their elemental analytical and spectroscopic data unambiguously. Whereas the constitution of the free 2,4-diaminothiazoles **(22)** requires no further manifestation, the constitution of the salts **(22·nHX)** requires a more detailed analysis. In this respect, the NMR spectra of these salts are of special interest. Some of these data are summarised in the Tables 3 and 4.

The free *N*(2),*N*(4)-tetrasubstituted 2,4-diaminothiazoles **(22)** exhibit in their ^{1}H-NMR spectra sharp signals at about 5.1 ppm and several signals at about 0.9 ppm and 4.2 ppm which can be attributed to their H-atoms at C(5) and at their alkylamino groups, respectively.

In contrast, the salts **(22·HX)** and **(22·2HX)** exhibit caracteristic signals at about 4.5-4.9 ppm and 1.0-4.2 ppm. Whereas the first signals which appear as singlet can be attributed, in accordance with their intensity and multiplicity, to two protons bonded at C(5) of the heterocyclic moieties, the second signal has to be attributed to the protons at their alkylamino groups. Additional signals at about 7.1-10.4 ppm occur in the ^{1}H-NMR spectra of the salts **(22·2HX)**. They can be attributed to a *N*(3)-bounded protons. These facts reveal that the first protonation occurs at C(5) of the corresponding *N*(2),*N*(4)-substituted 2,4-diaminothiazole **(22)** giving rise to the formation of a species its constitution can be represented by the formula **(22D·HX)** and not by the formulae **(22A·HX - 22C·HX)** (see Scheme 5). The second protonation occurs at *N*(3) of the thiazole moiety giving rise to a species its constitution can be represented by the formula **(22·2HX)** depicted in Scheme 5. It is worth mentioning that the chemical shift as well as the intensity of the NH signals in the salts **(22·2HX)** depends on the water content of the

solvent used. By raising the water content of the solution the intensities of the signals increase and their positions are shifted at higher field.

Table 3 ^{1}H-NMR-data of *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22)** and their mineral acid salts **(22·HX)** and **(22·2HX)**

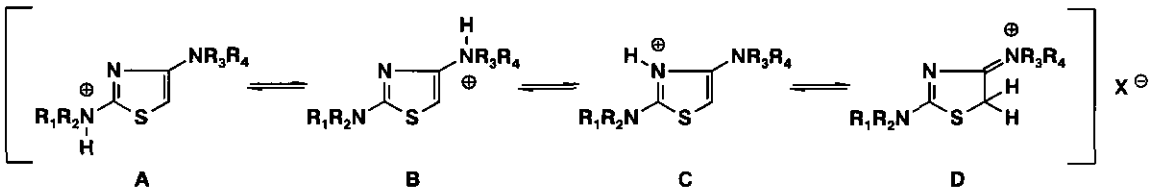
Compound	Solvent	H(5)	Other signals	N(3)-H
22a	$CDCl_3$	5.18 (s, 1H)	3.14 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.38 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.72-3.79 (m, 8H, $C\underline{H}_2CH_2$)[a]	
22a·HClO$_4$	DMSO-d_6	4.90 (s, 2H)	3.60-3.67 (m, 4H, $C\underline{H}_2CH_2$)[a]; 3.70-3.79 (m, 8H, $C\underline{H}_2CH_2$)[b]; 3.93 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 4.00 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$);	
22a·HBF$_4$	DMSO-d_6	4.89 (s, 2H)	3.60-3.66 (m, 4H, $C\underline{H}_2CH_2$)[a]; 3.70-3.79 (m, 8H, $C\underline{H}_2CH_2$)[b] 3.93 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 4.00 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22b·HClO$_4$	$CDCl_3$	4.64 (s, 2H)	2.04 [quint, J = 5 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 2.13 [quint, J = 5 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 3.62 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.71-3.85 (m, 8H, $C\underline{H}_2CH_2$)[b]; 4.04 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22c	$CDCl_3$	5.14 (s, 1H)	1.47-1.57 [m, 2H, $C\underline{H}_2(CH_2)_2$]; 1.64 [quint, J = 5 Hz, 4H, $C\underline{H}_2(CH_2)_2$]; 3.12 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.38 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.75 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$)	
22c·HClO$_4$	$CDCl_3$	4.73 (s, 2H)	1.69-1.76 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 1.76-1.85 [m, 2H, $C\underline{H}_2(CH_2)_2$]; 3.62 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.67 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.80 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.84 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.91-3.98 (m, 2H, $C\underline{H}_2CH_2$)[c]; 4.03 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22d·2HClO$_4$	CD_3CN	4.65 (s, 2H)	3.39 (quint, J = 5 Hz, 2H, $CH_2C\underline{H}_2NH_2$); 3.45 (quint, J = 5 Hz, 2H, $CH_2C\underline{H}_2NH_2$); 3.61 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.74 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.78 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.88 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 4.02 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 4.21 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	7.16 (s, 2H)
22e	$CDCl_3$	4.71 (s, 1H)	1.88 [quint, J = 3 Hz, 4H, $C\underline{H}_2(CH_2)_2$]; 1.96 [quint, J = 3 Hz, 4H, $C\underline{H}_2(CH_2)_2$]; 3.26 (t, J = 6 Hz, 4H, $C\underline{H}_2CH_2$); 3.39 (t, J = 6 Hz, 4H, $C\underline{H}_2CH_2$)	
22e·HClO$_4$	$CDCl_3$	4.62 (s, 2H)	2.00-2.20 [m, 8H, $C\underline{H}_2(CH_2)_2$]; 3.56 (t, J = 7 Hz, 2H, $C\underline{H}_2CH_2$); 3.70-3.85 (m, 6H, $C\underline{H}_2CH_2$)[d]	
22e·2HClO$_4$	CD_3NO_2	4.69 (s, 2H)	2.00-2.15 [m, 8H, $C\underline{H}_2(CH_2)_2$]; 3.67 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$); 3.77 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$); 3.83-3.96 (m, 4H, $C\underline{H}_2CH_2$)[a];	7.46 (s, 1H)
22e·BPh$_4$	DMSO-d_6	4.66 (s, 2H)	1.86-1.99 [m, 8H, $C\underline{H}_2(CH_2)_2$]; 3.48-3.55 (m, 4H, $C\underline{H}_2CH_2$)[a]; 3.61 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$); 3.69 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$); 6.77 (t, J = 7 Hz, 4H, aromatic H)[e]; 6.90 (t, J = 7 Hz, 8H, aromatic H)[e]; 7.13-7.21 (m, 8H, aromatic H)[e]	
22f	$CDCl_3$	5.06 (s, 1H)	1.94-1.98 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 3.15 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.35-3.39 (m, 4H, $C\underline{H}_2CH_2$); 3.78 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$)	
22f·HClO$_4$	$CDCl_3$	4.77 (s, 2H)	2.08 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 2.15 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 3.58 (t, J = 7 Hz, 2H, $C\underline{H}_2CH_2$); 3.75 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.80-3.84 (m, 4H, $C\underline{H}_2CH_2$)[a]; 3.88 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.99 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22g·HClO$_4$	$CDCl_3$	4.71 (s, 2H)	1.67-1.76 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 1.76-1.85 [m, 2H, $C\underline{H}_2(CH_2)_2$]; 2.08 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 2.15 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 3.57 (t, J = 7 Hz, 2H, $C\underline{H}_2CH_2$); 3.67 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.82 (t, J = 7 Hz, 2H, $C\underline{H}_2CH_2$); 3.91-3.98 (m, 2H, $C\underline{H}_2CH_2$)[c]	
22h·HClO$_4$	DMSO-d_6	4.62 (s, 2H)	1.92 [quint, J = 6 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 2.03 [quint, J = 6 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 3.58-3.64 (m, 4H, $C\underline{H}_2CH_2$)[a]; 7.35-7.72 (m, 10H, aromatic H)	
22i·2HClO$_4$	CD_3NO_2	4.84 (s, 2H)	1.35 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 1.38 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 2.14-2.23 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 3.72-3.79 (m, 4H)[f]; 3.92 (q, J = 7 Hz, 2H, $C\underline{H}_2CH_3$); 4.01 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$)	8.34 (s, 1H)
22j·HClO$_4$	$CDCl_3$	4.70 (s,2H)	1.67-1.85 [m, 12H, $C\underline{H}_2(CH_2)_2$]; 3.51-3.58 (m, 2H, $C\underline{H}_2CH_2$)[c]; 3.67 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.90-4.00 (m, 4H, $C\underline{H}_2CH_2$)[a]	

Compound	Solvent	H(5)	Other signals	N(3)-H
22k	$CDCl_3$	5.11 (s, 1H)	1.56-1.67 [m, 6H, $C\underline{H}_2(CH_2)_2$]; 3.13 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$); 3.35-3.39 (m, 4H, $C\underline{H}_2CH_2$)[c]; 3.78 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$)	
22k·HClO$_4$	$CDCl_3$	4.79 (s, 2H)	1.69-1.83 [m, 6H, $C\underline{H}_2(CH_2)_2$]; 3.55 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.76 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.82 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.90 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.98 (t, J = 5 Hz, 4H, $C\underline{H}_2CH_2$)	
22l·HClO$_4$	$CDCl_3$	4.60 (s, 2H)	1.63-1.80 [m, 6H, $C\underline{H}_2(CH_2)_2$]; 2.01 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 2.11 [quint, J = 7 Hz, 2H, $C\underline{H}_2(CH_2)_2$]; 3.47-3.53 (m, 2H, $C\underline{H}_2CH_2$)[c]; 3.69-3.76 (m, 4H, $C\underline{H}_2CH_2$)[a]; 3.91-3.97 (m, 2H, $C\underline{H}_2CH_2$)[c]	
22m·HClO$_4$	$CDCl_3$	4.75 (s, 2H)	1.26 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 1.32 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 3.50 (q, J = 7 Hz, 2H, $C\underline{H}_2CH_3$); 3.71-3.82 (m, 6H)[g]; 3.87 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.97 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22n·2HClO$_4$	CD_3NO_2	4.98 (s, 2H)	1.43 (t, 3H, $C\underline{H}_3CH_2$); 1.46 (t, 3H, $C\underline{H}_3CH_2$); 1.78-1.88 [m, 2H, $C\underline{H}_2(CH_2)_2$]; 1.90-2.00 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 3.86 (q, J = 7 Hz, 2H, $C\underline{H}_2CH_3$); 3.93 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 4.05 (q, J = 7 Hz, 2H, $C\underline{H}_2CH_3$); 4.11 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	10.44 (s, 1H)
22o·2HClO$_4$	CD_3NO_2	4.75 (s, 2H)	1.35 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 1.39 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 2.13-2.22 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 3.74 (q, J = 7 Hz, 2H, $C\underline{H}_2CH_3$); 3.85 (t, J = 6 Hz, 2H, $C\underline{H}_2CH_2$); 3.92-3.99 (m, 4H)[f]	8.33 (s, 1H)
22p·HClO$_4$	$CDCl_3$	4.79 (s, 2H)	0.92 (t, J = 8 Hz, 3H, $C\underline{H}_3CH_2$); 0.97 (t, J = 8 Hz, 3H, $C\underline{H}_3CH_2$); 1.64-1.82 (m, 4H, $CH_2C\underline{H}_2CH_3$); 3.38 (t, J = 8 Hz, 2H, $C\underline{H}_2CH_2$); 3.67 (t, J = 8 Hz, 2H, $C\underline{H}_2CH_2$); 3.77 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.81 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.90 (t, J = 5 Hz, 2H, CH_2CH_2); 3.97 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	
22q·2HClO$_4$	CD_3NO_2	4.87 (s, 2H)	0.97 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 1.00 (t, J = 7 Hz, 3H, $C\underline{H}_3CH_2$); 1.79-1.93 (m, 4H, $CH_2C\underline{H}_2CH_3$); 2.16-2.28 [m, 4H, $CH_2(CH_2)_2$]; 3.74 (t, J = 8 Hz, 2H, $C\underline{H}_2CH_2$); 3.88-3.98 (m, 4H, $C\underline{H}_2CH_2$)[a]; 4.03-4.12 (m, 2H, $C\underline{H}_2CH_2$)[c]	9.97 (s, 1H)
22r·HClO$_4$	CD_3CN	isomer A: 4.57 (s, 2H)	isomer A: 3.61-3.69 (m, 2H, $C\underline{H}_2CH_2$); 3.76-3.84 (m, 4H, CH_2CH_2); 3.95-4.02 (m, 2H, $C\underline{H}_2CH_2$); 7.26-7.65 (m, 5H, aromatic H)	isomer A: 10.28 (s, 1H)
		isomer B: 4.60 (s, 2H)	isomer B: 3.61-3.69 (m, 2H, $C\underline{H}_2CH_2$); 3.76-3.84 (m, 4H, $C\underline{H}_2CH_2$); 3.95-4.02 (m, 2H, $C\underline{H}_2CH_2$); 7.26-7.65 (m, 5H, aromatic H)	isomer B: 10.03 (s, 1H)
22s·HClO$_4$	DMSO-d_6	4.76 (s, 2H)	3.61 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.72 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.76 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$); 3.86 (t, J = 5 Hz, 2H, $C\underline{H}_2CH_2$)	10.00 (s, 1H) 10.24 (s, 1H)
22t·HClO$_4$	DMSO-d_6	4.67 (s, 2H)	1.92-2.02 [m, 4H, $C\underline{H}_2(CH_2)_2$]; 3.59-3.68 (m, 4H, $C\underline{H}_2CH_2$)[a]	9.90 (s, 1H) 10.23 (s, 1H)
22u·HClO$_4$	$CDCl_3$	isomer A: 4.58 (s, 2H)	isomer A: 0.86-0.96 (m, 6H, $C\underline{H}_3CH_2$); 1.29-1.46 (m, 4H, $C\underline{H}_2CH_2$); 1.56-1.76 (m, 4H, $C\underline{H}_2CH_2$); 3.41 (q, J = 7 Hz, 2H, $CH_2C\underline{H}_2NH$); 3.53 (q, J = 7 Hz, 2H, $CH_2C\underline{H}_2NH$)	isomer A: 8.38 (t, 1H) 8,51 (m, 1H)[c]
		isomer B: 4.52 (s, 2H)	isomer B: 0.86-0.96 (m, 6H, $C\underline{H}_3CH_2$); 1.29-1.46 (m, 4H, $C\underline{H}_2CH_2$); 1.56-1.76 (m, 4H, $C\underline{H}_2CH_2$); 3.57 (q, J = 6 Hz, 2H, $CH_2C\underline{H}_2NH$); 3.66 (q, J = 6 Hz, 2H, $CH_2C\underline{H}_2NH$)	isomer B: 8.57 (m, 2H)

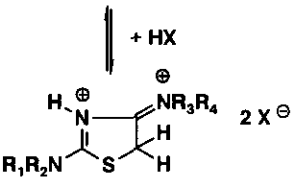
[a] two superimposed triplets; [b] four superimposed triplets; [c] broad signals without detectable coupling; [d] three superimposed triplets; [e] signal of the anion; [f] superimposed triplet and quartet; [g] quartet and two triplets superimposed

The given protonation Scheme 5 can be manifested, furthermore, by analysing the ^{13}C-NMR spectra of the unprotonated and protonated species **(22)**, **(22·HX)** and **(22·2HX)**, respectively. As exemplified in Table 5, in which the measured ^{13}C-NMR signals of the compound **(22e)** and its protonated species **(22e·HClO$_4$)** and **(22e·2HClO$_4$)** are depicted, their signals can be attributed, unambiguously, to the corresponding C-atoms of the free bases **(22e)** as well as their monoprotonated and diprotonated species **(22e·HClO$_4$)** and **(22e·2HClO$_4$)**, respectively. Whereas the C(5)-signal in the free base **(22e)** occurs at

about 70 ppm, the signals of the same C(5) in the protonated species (**22e·HClO$_4$**) and (**22e·2HClO$_4$**) occur at about 40 ppm. This fact supports the findings derived from ^{1}H-NMR experiments, that mineral acid salts (**22·HX**) of the new 2,4-diaminothiazoles (**22**) exist in an azavinamidinium salt structure (**22D·HX**) and not, as conceivable, in a heteroaromatic ammonium-substituted aminothiazole structure (**22A·HX**) or (**22B·HX**), or, alternatively, in a diamino-substituted thiazolium structure (**22C·HX**).



22·HX



22·2HX

Scheme 5

Table 4 ^{13}C-NMR-data of 2,4-bis(pyrrolidino)thiazole (**22e**) and its mono- and dihydroperchlorate (**22e·HClO$_4$**) and (**22e·2HClO$_4$**)

Compound	^{13}C-NMR-signals (ppm)		
	22e[a]	**22e·HClO$_4$**[b]	**22e·2HClO$_4$**[b]
C(5)	71.7	41.2	38.0
C(2) and C(4)	157.1; 166.2	176.1; 179.6	166.9; 172.1
Carbon atoms at the pyrrolidino moieties	25.2; 25.6; 48.6; 49.0	25.5; 25.9; 26.1; 26.2; 50.6; 52.1; 52.4; 53.0	26.1; 26.3; 26.3; 26.8; 55.0; 55.1; 55.6; 56.2

[a] in $CDCl_3$; [b] in CD_3NO_2

A further peculiarity in the NMR spectra can be observed for the salts (**22·HX**), their amino groups are, as given for the compounds (**22r·HClO$_4$**), (**22u·HClO$_4$**) and (**24i**), mono-substituted. In the ^{1}H-NMR spectra of each of these compounds two sets of signals occur. They can be attributed to different conformers their ratio is shown in Table 5 and estimated by integrating the corresponding ^{1}H-NMR signals. The isomers results, obviously, from a different orientation of the mono substituted amino groups in respect to their parent thiazole moieties.

Table 5 Isomers of the mineral acid salts of the *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22r·HClO$_4$)**, **(22u·HClO$_4$)** and **(24i)**

Compound	Number of isomers formed	Ratio isomer A : isomer B
22r·HClO$_4$	2	1 : 1.5...1.6
22u·HClO$_4$	2	1 : 2.8...2.9
24i	2	1 : 4.0...5.0

Table 6 Elementary analysis of *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22)**, their mineral acid salts **(22·HX)** and **(22·2HX)** and of *N*(2)-substituted 2-amino-4-thiazolinimine hydrochlorides **(24)**

Compound	Formula	Requires / Found C (%) / C (%)	H (%) / H (%)	N (%) / N (%)	S (%) / S (%)
22a	$C_{11}H_{17}N_3O_2S$	51.76 / 51.63	6.66 / 7.07	16.47 / 16.46	12.55 / 12.53
22a·HClO$_4$	$C_{11}H_{18}N_3O_6ClS$	37.13 / 37.08	5.06 / 5.72	11.81 / 11.55	9.00 / 8.94
22a·HBF$_4$	$C_{11}H_{18}N_3O_2BF_4S$	38.50 / 38.20	5.25 / 5.27	12.25 / 12.49	9.33 / 9.39
22b·HClO$_4$	$C_{11}H_{18}N_3O_5ClS$	38.88 / 38.85	5.30 / 5.79	12.37 / 12.41	9.42 / 9.46
22c	$C_{12}H_{19}N_3OS$	56.91 / 57.51	7.51 / 7.71	16.60 / 16.60	12.65 / 12.82
22c·HClO$_4$	$C_{12}H_{20}N_3O_5ClS$	40.73 / 40.70	5.65 / 5.95	11.88 / 11.83	9.05 / 9.09
22d·2HClO$_4$	$C_{11}H_{20}N_4O_9Cl_2S$	29.01 / 29.06	4.40 / 4.40	12.31 / 12.31	7.00 / 6.46
22e	$C_{11}H_{17}N_3S$	59.19 / 58.92	7.62 / 7.97	18.83 / 18.73	14.35 / 14.32
22e·HClO$_4$	$C_{11}H_{18}N_3O_4ClS$	40.80 / 40.76	5.56 / 6.04	12.98 / 12.59	9.89 / 9.96
22e·2HClO$_4$	$C_{11}H_{19}N_3O_8Cl_2S$	31.13 / 31.00	4.48 / 4.68	9.91 / 9.67	7.54 / 7.64
22e·HBPh$_4$	$C_{35}H_{38}N_3BS$	77.34 / 77.43	6.99 / 7.09	7.73 / 7.62	5.89 / 5.80
22f	$C_{11}H_{17}N_3OS$	55.23 / 55.36	7.11 / 7.53	17.57 / 17.37	13.39 / 13.44
22f·HClO$_4$	$C_{11}H_{19}N_3O_5ClS$	38.88 / 39.21	5.30 / 5.22	12.37 / 12.36	9.42 / 9.50
22g·HClO$_4$	$C_{12}H_{20}N_3O_4ClS$	42.66 / 42.46	5.92 / 5.81	12.44 / 12.59	9.48 / 9.49
22h·HClO$_4$	$C_{19}H_{20}N_3O_4ClS$	54.09 / 54.11	4.74 / 4.78	9.96 / 9.82	7.59 / 7.69
22i·2HClO$_4$	$C_{11}H_{21}N_3O_8ClS$	30.98 / 31.31	4.93 / 4.94	9.86 / 10.21	7.51 / 7.91
22j·HClO$_4$	$C_{13}H_{22}N_3O_4ClS$	44.38 / 44.03	6.26 / 6.65	11.95 / 11.51	9.10 / 9.05
22k	$C_{12}H_{19}N_3OS$	56.91 / 57.01	7.51 / 7.37	16.60 / 16.47	12.65 / 12.96
22k·HClO$_4$	$C_{12}H_{20}N_3O_5ClS$	40.74 / 40.85	5.66 / 6.11	11.88 / 11.52	9.05 / 9.03
22l·HClO$_4$	$C_{12}H_{20}N_3O_4ClS$	42.65 / 42.87	5.93 / 6.27	12.44 / 12.19	9.48 / 9.54
22m·HClO$_4$	$C_{11}H_{20}N_3O_5ClS$	38.65 / 38.31	5.86 / 6.37	12.30 / 11.93	9.37 / 9.33
22n·2HClO$_4$	$C_{12}H_{23}N_3O_8Cl_2S$	32.65 / 32.38	5.22 / 5.91	9.52 / 9.48	7.26 / 7.41
22o·2HClO$_4$	$C_{11}H_{21}N_3O_8ClS$	30.98 / 30.96	4.93 / 5.59	9.86 / 9.68	7.51 / 7.58
22p·HClO$_4$	$C_{13}H_{24}N_3O_5ClS$	42.22 / 41.34	6.49 / 6.26	11.36 / 10.89	8.66 / 8.15
22q·2HClO$_4$	$C_{13}H_{25}N_3O_8Cl_2S$	34.36 / 34.42	5.51 / 5.31	9.25 / 9.01	7.05 / 7.24
22r·HClO$_4$	$C_{13}H_{16}N_3O_5ClS$	43.15 / 43.02	4.43 / 4.56	11.62 / 11.88	8.85 / 8.76
22s·HClO$_4$	$C_7H_{12}N_3O_5ClS$	29.42 / 30.08	4.20 / 4.35	14.71 / 14.75	11.21 / 10.96
22t·HClO$_4$	$C_7H_{12}N_3O_4ClS$	31.16 / 31.63	4.45 / 4.45	15.58 / 15.57	11.87 / 12.36
22u·HClO$_4$	$C_{11}H_{22}N_3O_4ClS$	40.30 / 40.34	6.72 / 6.70	12.82 / 12.81	9.77 / 9.23
24a	$C_3H_6N_3ClS$	23.76 / 23.67	3.96 / 4.09	27.70 / 27.74	21.12 / 21.16
24b	$C_7H_{14}N_3ClS$	40.48 / 40.58	6.75 / 7.62	20.24 / 19.87	15.42 / 15.45
24c	$C_9H_{18}N_3ClS$	45.85 / 45.55	7.65 / 7.80	17.83 / 17.44	13.59 / 13.42
24d	$C_{11}H_{22}N_3ClS$	50.00 / 50.23	8.30 / 7.91	15.93 / 15.89	12.14 / 12.29
24e	$C_7H_{12}N_3ClS$	40.87 / 40.56	5.84 / 6.89	20.43 / 20.37	15.57 / 15.95
24f	$C_8H_{14}N_3ClS$	43.73 / 44.07	6.36 / 6.66	19.13 / 18.77	14.58 / 14.63
24g	$C_7H_{12}N_3OClS$	37.92 / 38.08	5.42 / 5.58	18.96 / 18.79	14.45 / 14.29
24h	$C_{15}H_{14}N_3ClS$	59.31 / 59.43	4.61 / 5.01	13.83 / 12.82	10.54 / 10.00
24i	$C_{10}H_{12}N_3ClS$	49.68 / 49.87	4.79 / 5.13	17.39 / 17.05	13.25 / 12.80

EXPERIMENTAL

Melting points of the compounds prepared were determined by means of a heating-table-microscope. The NMR spectra were recorded by using a GEMINI 300 MHz NMR spectrometer (VARIAN, Zurich, Switzerland). The elemental analytical data were estimated by means of a CHNS analyser 932 (LECO, St. Joseph, Michigan, U.S.A.).

Preparation of *N*(2)-disubstituted 2-amino-4-thiazolinimine hydrochlorides (24)

A mixture of 0.2 mol of the appropriate *N,N*-disubstituted thiourea[32] **(18)** and 17.5 g (0.22 mol) of chloroactonitrile **(23)** (ALDRICH) in 150 mL of ethanol is refluxed for 1 h. After cooling, the product formed is precipitated by slowly adding of 200 mL of ether to the reaction mixture and isolated by suction.

Preparation of differently *N*(2),*N*(4)-substituted 2,4-diaminothiazoles (22) or their hydroperchlorates (22·$HClO_4$) and hydrotetrafluoroborates (22·HBF_4)

Method A:

To a suspension of 0.06 mol of the appropriate *N,N*-disubstituted thiourea[32] **(18)** in 80 mL of dichloromethane 0.06 mol of a *N,N*-disubstituted chloroacetamide[33] **(19)** and 15 g (0.1 mol) $POCl_3$ are subsequently added. After stirring the mixture for 20 h at room temperature, 100 mL of ethyl acetate and 0.06 mol of aqueous $HClO_4$ (70 %) or 0.06 mol of aqueous HBF_4 (40 %) are added, followed by the addition of 30 mL acetic anhydride and 50 mL of ether. The product crystallised can be isolated by suction and purified by recrystallisation.

Method B:

After addition of 0.1 mol of a primary or secondary amine **(25)** to a suspension of 0.05 mol of the a *N*(2)-substituted 2-amino-4-thiazolinimine hydrochloride **(24)** in 100 mL of ether, the resulting mixture is refluxed for several hours until the evolution of ammonia is complete. For isolation of the free *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22),** the hot mixture is filtered off and the residue is extracted several times with hot ether. Both the filtrate and extracts are unified and evaporated to precipitate the products formed.

In order to isolate the mineral acid salts **(22·HX)** of the *N*(2),*N*(4)-substituted 2,4-diaminothiazoles **(22)** 0.05 mol of aqueous $HClO_4$ (70 %) or 0.05 mol of aqueous HBF_4 (40 %) is added to the unified extracts received as before containing some acetic anhydride. The crystalline product **(22·HX)** can be isolated by suction and purified by recrystallisation.

Method C:

This method differs from method B insofar as the *N*(2),*N*(4)-unsubstituted 2-aminothiazoline-4-iminium hydrochloride **(24a)** is used as educt and instead of two equivalents three equivalents of an amine **(25)** are applied.

2,4-Bis(pyrrolidino)thiazoline-4-iminium tetraphenyloborate (22e·HB(C_6H_5)$_4$)

To a saturated solution of 2,4-bis(pyrrolidino)-thiazoline-4-iminium perchlorate **(22e·HClO$_4$)** in water an equivalent amount of NaB(C_6H_5)$_4$ in water at 80 °C is added. The crystalline precipitate immediately formed is filtered off after cooling from the reaction mixture, washed with water, and dried.

Preparation of *N*(2),*N*(4)-disubstituted 2,4-diaminothiazole dihydroperchlorates (22·2HClO$_4$)

To a solution of 0.02 mol of the appropriate 2,4-diaminothiazole **(22)** or its hydroperchlorate **(22·HClO$_4$)** in 100 mL chloroform an eccess of $HClO_4$ (about 0,04 mol) is added. The product precipitated is filtered off, washed with ethyl acetate, dried, and recrystallised.

ACKNOWLEDGEMENT

The authors thank the Bundesministerium für Forschung und Technik, Germany, for financial support and the BASF AG for a kind gift of chemicals. They thank also Dr. J. Scholz, Fachbereich Chemie, Martin-Luther-Universität Halle, Standort Merseburg, and his staff for recording the NMR spectra.

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Received, 22nd October, 1996