Monatshefte für Chemie 128, 1051–1060 (1997)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

On the Reaction of 2-Amino-4-thiazoliniminium Salts with Active Methylene Compounds

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Summary. The easily available 2-amino-4-thiazoliniminium salts **6** react with different types of active methylene compounds. Whereas 2-amino-4-cyanomethylene-4,5-dihydrothiazoles **13** and **14** are formed with malononitrile (**11**) or ethyl cyanoacetate (**12**) in the presence of bases, acetyl acetone (**15**) and ethyl acetic acetate (**16**) afford 2-amino-thiazolo[4,5-*b*]pyridines **21** and **22**, resp. The structures of the new compounds **13**, **14**, **21** and **22** have been elucidated by means of analytical and spectroscopic methods and confirmed by some chemical reactions.

Keywords. Active methylene compounds; 2-Amino-4-cyanomethylene-4,5-dihydrothiazoles; 2-Amino-4-thiazoliniminium chlorides; 2-Amino-thiazolo[4,5-*b*]pyridines.

Reaktion von 2-Amino-4-thiazoliniminium-Salzen mit aktivierten Methylenverbindungen

Zusammenfassung. Durch Reaktion der einfach zugänglichen 2-Amino-4-thiazoliniminium-Salze **6** mit Malonsäuredinitril (**11**) oder Cyanessigsäureethylester (**12**) in Gegenwart von Basen werden die 2-Amino-4-cyanmethylen-4,5-dihydrothiazole **13** bzw. **14** gebildet, während mit Acetylaceton (**15**) und Acetessigsäureethylester (**16**) auf analoge Weise die 2-Aminothiazolo[4,5-*b*]pyridine **21** bzw. **22** entstehen. Die Strukturen der neu dargestellten Verbindungen des Typs **13**, **14**, **21** und **22** wurden spektroskopisch abgesichert und durch einige Folgereaktionen bestätigt.

Introduction

Although 2-amino-4-thiazolinones **3** are easily available *via* the reaction of thioureas **1** with chloroacetic acid derivatives, such as alkyl chloroacetates **2** [1], they have found hitherto little interest as synthones in organic chemistry. The main reason seems to be their low reactivity towards common nucleophilic or electrophilic reagents. 2-Amino-4-thiazolinones **3**, for example, are not able – unlike the isomeric 2-amino-5-thiazolinones [2] – to react with secondary amines to give 2,4-diaminothiazoles **4**, an interesting class of highly reactive thiazole derivatives [3].

Recently is has been found, however, that *N*(4)-unsubstituted 2-amino-4-thiazoliniminium chlorides **6**, easily available by the reaction of thioureas **1** with chloroacetonitrile (**5**) [4, 5] are by far more reactive towards nucleophilic reagents than their carbonyl analogs **3** [6]. Heating salts **6** with secondary amines results – under elimination of ammonia – in *N*(4)-disubstituted 2-amino-4-thiazoliniminium

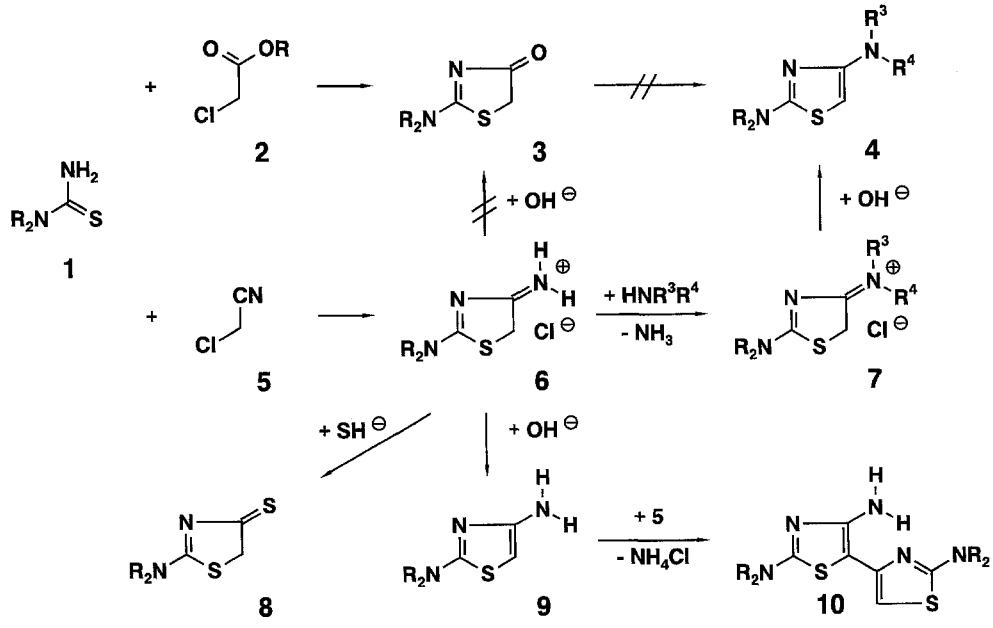
chlorides **7** which can be further transformed by reaction with suitable bases such as hydroxides or secondary amines to the corresponding 2,4-diamino-thiazoles **4**. Moreover, the 2-amino-4-thiazoliniminium chlorides **6** are able, in contrast to their corresponding carbonyl analogs **3**, to react with sulfur nucleophiles as *e.g.* sodium hydrogen sulfide in aqueous solution to 2-amino-4-thiazolinthiones **8**, a hitherto unknown class of 2-amino-thiazolidine derivatives [7].

A further peculiarity concerning the reactivity of the *N*(4)-unsubstituted 2-amino-4-thiazoliniminium chlorides **6** has been found in connection with aqueous bases or aliphatic tertiary amines. Instead of 2-amino-4-thiazolinones **3** as the hydrolysis products of the starting iminium salts **6** or *N*(4)-unsubstituted 2,4-diaminothiazoles **9** as their deprotonation products, the triamino substituted *bis*-thiazoles **10** are obtained [8]. Obviously, these products result from a condensation reaction of the intermediately formed *N*(4)-unsubstituted 2,4-diaminothiazoles **9** with the starting 2-amino-4-thiazoliniminium salts **6** under elimination of ammonium chloride.

Results and Discussion

The high reactivity of the iminium group in the easily available 2-amino-4-thiazoliniminium chlorides **6** towards *N*, *S*, and *O* nucleophiles stimulates to study their reactivity towards appropriate *C* nucleophiles, too. Representative examples for such reagents are nitriles **11** and **12** as well as acetoacetyl derivatives **15** and **16**.

Thus, by the reaction of malononitrile (**11**) or ethyl cyanoacetic acetate (**12**) with several *N*(2)-substituted 2-amino-4-thiazoliniminium chlorides (**6a–f**) in aqueous alkaline solution, a condensation reaction giving rise to the formation of 2-amino-4-cyanomethylene-4,5-dihydrothiazoles **13** and **14**, respectively, occurs. As



Scheme 1

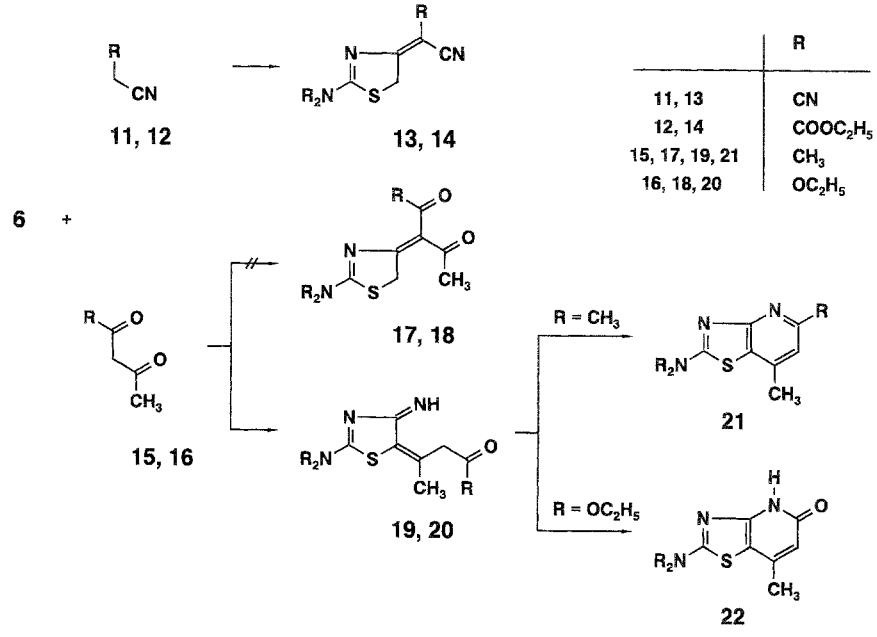
can be seen from Table 1, these compounds are obtained in fairly good yields as solids of rather high melting points.

The formation of **13** and **14** can be explained by a nucleophilic attack of a carbanion primarily formed from the starting acetonitrile derivatives **11** or **12** and the employed base at the iminium group in position 4 of the salts **6**, followed by elimination of ammonium chloride.

In contrast to the reaction of the acetonitrile derivatives **11** and **12**, the base mediated reaction of the ketomethylene derivatives **15** and **16** with **6** gives a different result. Instead of the 4-ketomethylene substituted 4,5-dihydrothiazoles **17** and **18**, the new thiazolo[4,5-*b*]pyridines **21** and thiazolo[4,5-*b*]pyridones **22**, respectively, were formed. These compounds could also be isolated in rather high yields.

The formation of **21** and **22** can be explained by a primary formation of the corresponding *N*(4)-unsubstituted 2,4-diamino-thiazoles **9** from their iminium salt precursors **6** by reaction with the base applied. Subsequently, **9** react with the ketomethylene compounds at their carbonyl group to give intermediates **19** and **20** which cyclize, in turn, at their terminal carbonyl group to the final products **21** and **22**.

The formation of different types of products in the course of the reaction of the 2-amino-4-thiazoliniminium chlorides **6** with the active methylene compounds **11**, **12**, **15**, and **16** can be understood taking into account the known differences in the CH acidities of the reagents used [9]. Whereas the acetonitrile derivatives **11** and **12** are relatively strong acids which can be deprotonated by the applied bases to a larger extent than the concurrent iminium salts **6**, the ketomethylene derivatives **15** and **16** are weaker acids which are deprotonated to a much lesser extent than **6**. Therefore, these salts are transformed *via* reaction with the ketomethylene compounds **15** and **16** to the highly nucleophilic 2,4-diamino-thiazoles **9** which are able to condense with the non-deprotonated ketomethylene reagents at their carbonyl groups.

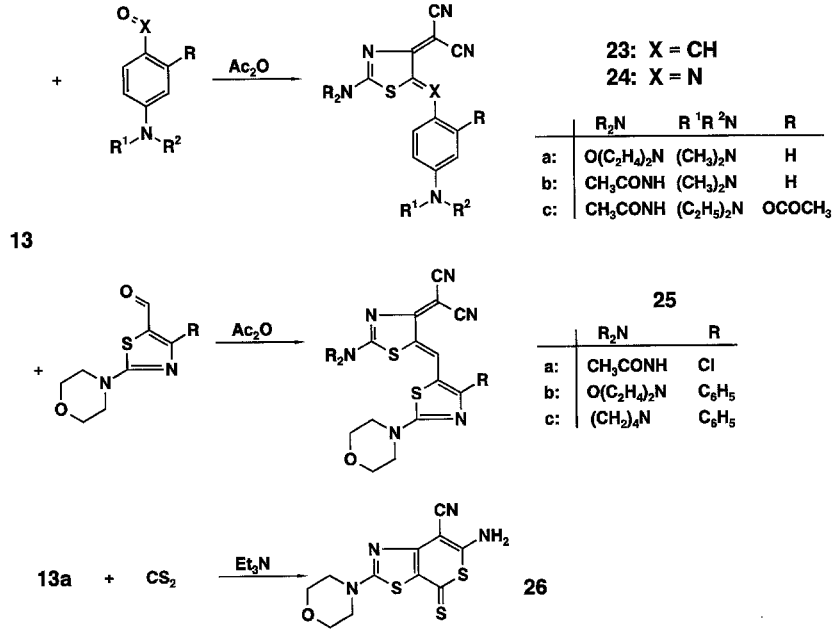


Scheme 2

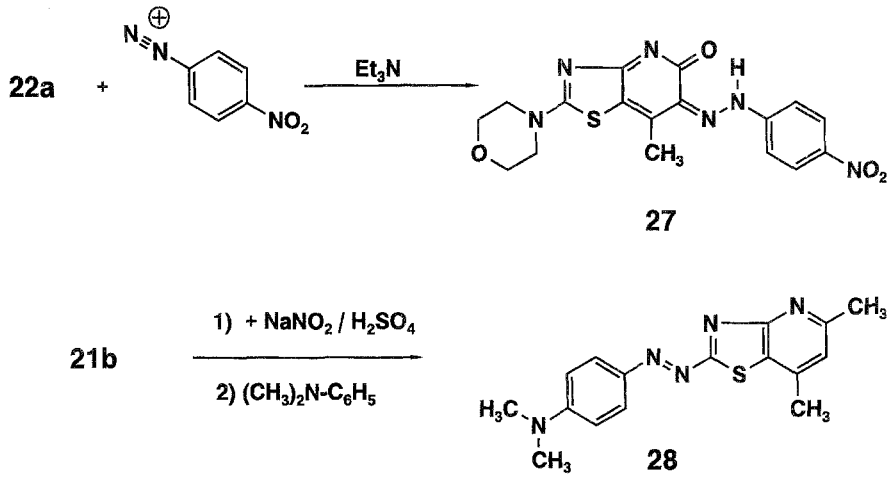
The structures of the new compounds **13**, **14**, **21**, and **22** follow unambiguously from their analytical and spectroscopic data. Thus, the cyanomethylene derivatives **13** and **14** exhibit characteristic signals at about 4.60 ppm in their ^{1}H NMR spectra which can be attributed to the protons at their heterocyclic methylene groups. In contrast, the thiazolo[4,4-*b*]pyridine derivatives **21** and the thiazolo[4,5-*b*]pyridone derivatives **22** show characteristic signals of the protons at their pyridine moieties (about 6.00 ppm) indicating a consecutive ring closure reaction of the reactants after the primary condensation. Due to these data, in no case an attack of the appropriate CH acidic compound at *C*(2) of the starting 2-amino-4-thiazolinminium chlorides **6** has been observed to give 2-methylene substituted 4-amino-2,3-dihydrothiazoles or their 4-imino tautomers.

The new compounds exhibit several interesting properties. The 2-amino-4-dicyanomethylene-4,5-dihydrothiazoles **13**, for example, are able to react at their heterocyclic methylene group with different types of electrophiles such as aromatic and heteroaromatic aldehydes, aromatic nitroso compounds, and heterocumulenes to give different types of condensation products. (cf. Scheme 3). Thus, heating of **13** in acetic anhydride with aromatic and heteroaromatic aldehydes affords condensation products **23** and **25**. With 4-nitroso-anilines, the deeply colored azomethines **24** have been obtained under analogous conditions. Carbon disulfide in *DMF* and triethylamine as base lead to the thiazolo[5,4-*c*]thiopyrane-2-thione derivative **26** in analogy to known reactions [10].

The thiazolo[4,5-*b*]pyridine derivatives **21** and **22** also react with several electrophilic reagents. Thus, the thiazolo[4,5-*b*]pyridone derivatives **22** is transformed, as shown with compound **22a**, to thiazolo[4,5-*b*]pyrid-2-one-3-hydrazone (**27**) upon reaction with an aryldiazonium salt. In contrast, the thiazolo[4,5-*b*]-pyridine derivative **21b** react, with sodium nitrite in strongly acidic solution to give



Scheme 3



Scheme 4

a corresponding diazonium salt which is able to couple with suitable nucleophiles (*e.g. N,N*-dimethylaniline) to give the azo compound **28**.

The structures of compounds **27** and **28** have been unambiguously assigned by means of their analytical and spectroscopic data (cf. Experimental).

Experimental

Melting points were determined using a Boetius heating-block microscope. The NMR spectra were recorded on a Gemini 300 MHz NMR spectrometer (Varian, Zurich, Switzerland) with *HMDS* as internal standard. The mass spectra were measured with a sector-field spectrometer AMD 402 (Intectra GmbH, Harpstedt, Germany). The elemental analytical data were obtained using a CHNS analyser 932 (LECO, USA). The UV/Vis spectra were recorded with a Lambda 2 spectrometer (Perkin Elmer, Ueberlingen, Germany).

The preparation of the 2-amino-4-thiazoliniminium chlorides **6** used as educts has been reported elsewhere [4, 5].

2-Amino-4-(dicyanomethylene)-4,5-dihydrothiazoles (**13**), *2-amino-4-(cyanethoxycarbonyl-methylene)-4,5-thiazoles* (**14**), *2-amino-5,7-dimethyl-thiazolo[4,5-b]pyridines* (**21**), *and 2-amino-7-methyl-5-keto-thiazolo[4,5-b]4,5-dihydropyridines* (**22**); *general procedure*

0.05 mol of 2-amino-4-thiazoliniminium chloride (**6**) and 0.05 mol of acetonitrile or ketomethylene derivative [**11**, **12**, **15**, **16**] are stirred in 100 ml 2*N* NaOH for 2 h at room temperature. The crystalline products formed during this procedure are isolated by suction and recrystallized for purification.

Condensation of 2-amino-substituted 4-dicyanomethylene-4,5-dihydro-thiazoles (**13**) *with electrophilic compounds; general procedure*

A mixture of 0.01 mol of 2-amino-4-dicyanomethylen-4,5-dihydro-thiazole (**13**) and 0.01 mol of electrophilic reagent in 20 ml of acetic anhydride is refluxed for 10 min. After cooling, the product formed is isolated by suction and recrystallized.

4-Dicyanomethylene-5-(4-dimethylaminophenyl-methylene)-2-morpholino-4,5-dihydrothiazole (**23a**)

From 4-dimethylamino benzaldehyde and **13a**; yield: 55%; m.p.: 268–269°C; λ_{max} (CH_2Cl_2): 514 nm; log ε: 4.48; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.05$ (s, 6H, CH_3), 3.64 (m, 2H, CH_2), 3.74 (m, 4H, CH_2), 3.92 (m, 2H, CH_2), 6.82 (d, 2H, CH), 7.42 (d, 2H, CH), 8.26 (s, 1H, CH) ppm; $C_{19}H_{19}N_5SO$ (365.0); calcd.: C 62.46, H 5.20, N 19.17, S 8.76; found; C 62.13, H 5.89, N 19.04, S 8.70.

2-Acetamido-4-dicyanomethylene-5-(4-dimethylaminophenyl-methylene)-4,5-dihydro-thiazole (**23b**)

From 4-dimethylamino benzaldehyde and **13f**; yield: 54%; m.p.: 297°C (dec.); λ_{max} (CH_2Cl_2): 582 nm; log ε: 4.66; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.23$ (s, 3H, $COCH_3$), 3.09 (s, 6H, NCH_3), 6.90–6.92 (d, 2H, CH), 7.41–7.51 (d, 2H, CH), 8.45 (s, 1H, CH), 13.07 (s, 1H, NH) $C_{17}H_{15}$-N_5SO (337.0); calcd.: C 60.53, H 4.42, N 20.77, S 9.49; found: C 60.30, H 4.81, N 20.78, S 9.22.

2-Acetamido-4-dicyanomethylene-5-(2-acetoxy-4-diethylaminophenyl-methylene)-4,5-dihydrothiazole (**23c**)

From 4-diethylamino salicyclic aldehyde and **13f**; yield: 31%; m.p.: 282–285°C; λ_{max} (CH_2Cl_2): 590 nm; log ε: 4.72; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.12$ (t, 6H, CH_3), 2.23 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.46 (q, 4H, CH_2), 6.64 (s, 1H, NH), 6.94 (d, 1H, CH), 7.66 (1H, CH), 8.54 (s, 1H, CH) ppm; $C_{21}H_{21}N_5SO_3$ (423.0); calcd.: C 59.57, H 4.96, N 16.54, S 7.56; found: C 59.66, H 5.68, N 16.78, S 7.67.

4-Dicyanomethylene-5-(4-dimethylaminophenylimino)-2-morpholino-4,5-dihydro-thiazole (**24a**)

From 4-nitroso-*N*,*N*-dimethylaniline and **13a**; yield: 61%; m.p.: 255–257°C; λ_{max} (CH_2Cl_2): 530; log ε: 4.19; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.02$ (s, 6H, CH_3), 3.74 (m, 6H, CH_2), 4.00 (m, 2H, CH_2), 6.84 (d, 2H, CH), 7.27 (d, 2H, CH) ppm; $C_{18}H_{18}N_6SO$ (366.0); calcd.: C 59.02, H 4.92, N 22.96, S 8.73; found: C 58.76, H 5.44, N 22.81, S 8.35.

2-Acetamido-4-dicyanomethylene-5-((4-chloro-2-morpholino-5-thiazolyl)-methylene)-4,5-dihydrothiazole (**25a**)

From 4-chloro-5-formyl-2-morpholino-thiazole [11] and **13f**; yield: 21%; m.p.: 311–313°C; λ_{max} (CH_2Cl_2): 552 nm; log ε: 4.76; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.20$ (s, 3H, CH_3), 3.62–3.73 (m, 8H, CH_2), 8.67 (s, 1H, CH) ppm; $C_{16}H_{13}N_6S_2ClO_2$ (420.5); calcd.: C 45.66, H 3.09, N 19.97, S 15.21; found: C 45.55, H 3.09, N 20.09, S 15.00.

4-Dicyanomethylene-2-morholino-5-((4-phenyl-2-morpholino-5-thiazolyl)-methylene)-4,5-dihydrothiazole (**25b**)

From 5-formyl-2-morpholino-4-phenyl-thiazole [12] and **13a**; yield: 65%; m.p.: 350–351°C; λ_{max} (CH_2Cl_2): 524 nm; log ε: 4.44; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.04$–3.74 (m, 16H, CH_2), 7.44–7.61 (m, 5H, H_{arom}), 8.52 (s, 1H, CH) ppm; $C_{24}H_{22}N_6O_2S_2$ (490.0); calcd.: C 58.78, H 4.49, N 17.14, S 13.06; found: C 58.62, H 4.59, N 17.20, S 12.50.

4-Dicyanomethylene-5-[(4-phenyl-2-morpholino-5-thiazolyl)-methylene]-2-pyrrolidino-4,5-dihydrothiazole (**25c**)

From 5-formyl-2-morpholino-4-phenyl-thiazole [12] and **13d**; yield: 21%; m.p.: 311–313°C; λ_{max} (CH_2Cl_2): 517 nm; log ε: 4.44; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.00$ (m, 4H, CH_2), 3.64–3.74 (m, 12H,

Table 1. Data of compounds **13** and **14**

	R_2N	Yield (%)	M.p. (°C)	Molecular fomula[a] (molecular weight)	MS	^{1}H NMR (ppm)	^{13}C NMR (ppm)
13a	Morpholino	60	220–222 (Chlorobenzene)	$C_{10}H_{10}N_4SO$ (234.0)	(260°C); 234 (100%, M^+), 219 (5%), 203 (5%), 189 (11%), 177 (40%), 163 (3%), 148 (7%), 122 (4%), 86 (5%)	(CD_3NO_2) 3.61 (t, 2H, CH_2), 3.78 (m, 4H, CH_2), 4.03 (t, 2H, CH_2), 4.57 (s, 2H, CH_2)	($C_2D_2Cl_4$) 42.8, 49.6, 51.5, 60.3, 66.1, 66.4, 114.8, 116.2, 180.9, 185.1
13b	Diethylamino	34	129 (EtOH)	$C_{10}H_{12}N_4S$ (220.0)	(140°C) 220 (100%, M^+), 205 (31%), 191 (46%), 177 (86%)	($CDCl_3$) 1.26–1.35 (m, 6H, CH_3), 3.46 (q, 2H, CH_2), 3.81 (q, 2H, CH_2), 4.47 (s, 2H, CH_2)	($CDCl_3$) 12.8, 42.5, 46.8, 48.2, 58.9, 114.4, 116.1, 180.1, 184.6
13c	Di-*n*-butylamino	60	112–113 (EtOH)	$C_{14}H_{20}N_4S$ (276.0)	(180°C) 276 (100%, M^+), 247 (17%), 234 (26%), 219 (19%), 192 (35%), 177 (69%)	($CDCl_3$) 0.92–0.98 (m, 6H, CH_3), 1.29–1.40 (m, 4H, CH_2), 1.59–1.72 (m, 4H, CH_2), 3.36 (t, 2H, CH_2), 3.74 (t, 2H, CH_2), 4.45 (s, 2H, CH_2)	($CDCl_3$) 13.5, 19.7, 19.8, 29.4, 29.5, 42.5, 51.7, 53.5, 58.8, 114.4, 116.1, 180.6, 184.5
13d	Pyrrolidino	46	191–192 (EtOH)	$C_{10}H_{10}N_4S$ (218.0)	(180°C) 218 (100%, M^+), 190 (32%), 163 (10%)	($CDCl_3$) 2.00–2.17 (m, 4H, CH_2), 3.56 (t, 2H, CH_2), 3.86 (t, 2H, CH_2), 4.48 (s, 2H, CH_2)	($CDCl_3$) 25.0, 25.3, 43.0, 50.9, 51.7, 58.5, 114.5, 116.2, 177.6, 184.6
13e	Piperidino	48	160–162 (EtOH)	$C_{11}H_{12}N_4S$ (232.0)	(200°C) 232 (100%, M^+), 217 (21%), 203 (28%), 177 (10%), 165 (11%)	($CDCl_3$) 1.65–180 (m, 6H, CH_2), 3.46–3.53 (m, 2H, CH_2), 3.97–4.04 (m, 2H, CH_2), 4.45 (s, 2H, CH_2)	($CDCl_3$) 25.5, 25.4, 25.9, 42.4, 50.4, 52.9, 58.7, 114.5, 116.1, 179.6, 184.8
13f	Amino	81	> 360	$C_6H_4N_4S$ (164.0)	(300°C) 164 (100%, M^+), 137 (22%), 122 (22%), 105 (44%), 95 (24%), 60 (18%)	(*DMSO*-d_6) 4.65 (s, 2H, CH_2), 9.81 (s, 2H, NH_2)	(*DMSO*-d_6) 43.2, 55.7, 115.8, 116.9, 184.5, 188.4
14a	Morpholino	64	194–195 (MeOH)	$C_{12}H_{15}N_3SO_3$ (281.0)	(190°C) 281 (100%, M^+), 235 (85%), 224 (20%), 208 (25%), 191 (7%), 178 (14%)	($CDCl_3$) 1.30 (t, 3H, CH_3), 3.54 (t, 2H, CH_2), 3.78 (m, 4H, CH_2), 4.07 (t, 2H, CH_2), 4.21 (q, 2H, CH_2), 4.77 (s, 2H, CH_2)	($CDCl_3$) 14.2, 43.5, 48.7, 50.9, 60.4, 65.8, 66.1, 82.9, 117.4, 165.6, 179.8, 183.1

[a] All compounds gave satisfactory elemental analyses (C, H, N, S)

Table 2. Data of compounds **21** and **22**

	R_2N	R	Yield (%)	M.p. (°C)	Molecular formula[a] (molecular weight)	MS (%)	^{1}H NMR (ppm)	^{13}C NMR (ppm)
21a	Morpholino	–	61	142–143	$C_{12}H_{15}N_3SO$ (249.0)	(30°C) 249 (99%), 218 (8%), 204 (10%), 192 (100%), 178 (9%), 164 (21%), 136 (9%)	($CDCl_3$) 2.37 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.77 (t, 4H, CH_2), 3.64 (t, 4H, CH_2), 6.64 (s, 1H, H_{arom})	($CDCl_3$) 20.8, 24.2, 48.3, 66.2 117.3, 121.5, 140.2, 155.9, 164.0, 169.6
21b	Amino	–	65	300–302	$C_8H_9N_3S$ (179.0)	(310°C) 179 (100%), 164 (8%), 152 (26%), 146 (22%), 136 (62%), 133 (16%)	(*DMSO*-d_6 2.28 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 6.68 (s, 1H, H_{arom}), 7.82 (s, 2H, NH_2)	(*DMSO*-d_6) 20.6, 23.8, 116.7, 121.8, 139.5, 154.4, 164.4, 168.0
22a	Morpholino	Me	65	308–310	$C_{11}H_{13}N_3SO_2$ (251.0)	(260°C) 251 (100%), 220 (7%), 206 (12%), 194 (51%), 180 (8%), 166 (10%), 138 (35%), 112 (7%)	($C_2D_2Cl_4$) 2.27 (s, 3H, CH_3), 3.79 (m, 4H, CH_2), 3.58 (m, 4H, CH_2), 4.00–4.50 (s, 1H, NH), 6.08 (s, 1H, H_{arom})	($C_2D_2Cl_4$) 21.5, 48.4, 66.2, 106.7, 110.3, 146.9, 151.9, 164.1, 171.7
22b	Pyrrolidino	Me	72	312–314	$C_{11}H_{13}N_3SO$ (235.0)	(240°C) 235 (100%), 207 (37%), 180 (45%)	($C_2D_2Cl_4$) 2.05 (t, 4H, CH_2), 2.26 (s, 3H, CH_3), 3.49–3.60 (m, 4H, CH_2), 6.03 (s, 1H, H_{arom}), 8.00–9.00 (s, 1H, NH)	($C_2D_2Cl_4$) 25.9, 50.1, 106.9, 108.9, 146.9, 152.6, 163.3, 168.2
22c	Piperidino	Me	84	265–266	$C_{12}H_{15}N_3SO$ (249.0)	(250°C) 249 (100%), 220 (63%), 193 (48%), 181 (20%), 166 (20%)	($C_2D_2Cl_4$) 1.61–1.72 (m, 6H, CH_2), 2.25 (s, 3H, CH_3), 3.50–3.60 (m, 4H, CH_2), 6.01 (s, 1H, H_{arom}), 9.50–10.50 (s, 1H, NH)	($C_2D_2Cl_4$) 24.2, 25.2, 49.8, 106.4, 109.4, 146.6, 152.6, 163.9, 171.4

[a] All compounds gave satisfactory elemental analyses (C, H, N, S)

CH_2), 7.44–7.60 (m, 5H, H_{arom}), 8.48 (s, 1H, CH) ppm; $C_{24}H_{22}N_6OS_2$ (474.0); calcd.: C 60.76, H 4.64, N 17.72, S 13.50; found: C 60.60, H 4.89, N 17.89, S 13.20.

5-Amino-4-cyano-2-morpholino-thiazolo[5,4-c]-7H-thiapyran-7-thione (**26**)

To a suspension of 23.4 g (0.1 mol) of 4-dicyanomethylene-2-morpholino-4,5-dihydrothiazole (**13a**) in 50 ml *DMF*, 11.5 g (0.15 mol) carbon disulfide and 25.3 g (0.25 mol) triethylamine are added dropwise under stirring. After a few minutes, a precipitate is formed. It is isolated by suction and washed with hot ethanol.

Yield: 13.4 g (43%); m.p.: 350°C (dec.); ^{1}H NMR (pyridine-d_6): $\delta = 3.57$ (m, 8H, CH_2), 10.14 (s, 2H, NH_2) ppm; MS (340°C): *m/z* (%) = 310 (100) [M^+], 266 (22), 253 (27), 224 (28), 86 (27); $C_{11}H_{10}N_6S_3O$ (310.0); calcd.: C 42.58, H 3.23, N 18.06, S 30.97; found: C 42.71, H 3.75, N 17.64, S 31.34.

5,6-Dihydro-7-methyl-2-methyl-2-morpholino-thiazolo[4,5-b]pyrid-5,6-dion-5-(4-nitrophenyl)-hydrazone (**27**)

To a solution of 2.5 g (0.01 mol) of 7-methyl-2-morpholino-thiazolo[4,5-*b*]-5-pyridone (**22a**) in 20 ml acetic acid, 0.01 mol of a solution of 4-nitrophenyldiazonium salt are added dropwise. After stirring at room temperature for 1 h, the solution is neutralized with 2*N* aqueous sodium hydroxide. The precipitate formed is isolated by suction, washed with water and dried.

Yield: 3.8 g (95%); m.p.: > 360°C; MS (340°C): *m/z* (%) = 400 (4) [M^+]); 265 (100); 208 (17); 138(41); 108 (11); 92 (15); $C_{17}H_{16}N_6SO_4$ (400.0); calcd.: C 51.00, H 4.00, N 21.00, S 8.00; found: C 49.91, H 4.27, N 21.18, S 7.28.

5,7-Dimethyl-2-(4-dimethylamino-(phenylazo))-thiazolo[4,5-b]pyridine (**28**)

To a solution of 3.6 g (0.02 mol) of 2-amino-5,7-dimethyl-thiazolo[4,5-*b*]pyridine (**21b**) in 20 ml acetic acid and 2 ml conc. sulfuric acid, a concentrated aqueous solution of 1.7 g 90.025 mol) sodium nitrite is added under ice cooling at 0°C. After stirring for 2 h and dropwise addition of 2.4 g (0.02 mol) *N,N*-dimethylaniline, the solution is neutralized with 2*N* aqueous sodium hydroxide. The precipitate formed is isolated by suction, washed with water, dried, and recrystallized from *DMF*.

Yield: 2.3 g (37%); m.p.: 276–278°C; ^{1}H NMR ($CDCl_3$): $\delta = 2.51$ (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.15 (s, 6H, CH_3), 6.73 (d, 2H, H_{arom}), 6.97 (s, 1H, CH), 7.98 (d, 2H, H_{arom}); MS (220°C): *m/z* (%) = 311 (27) [M^+]; 282 (67); 120 (100); 105 (21); 77 (21); $C_{16}H_{17}N_5S$ (311.0); calcd.: C 61.73, H 5.46, N 22.51, S 10.29; found: C 61.38, H 5.81, N 21.93, S 10.20.

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Received April 4, 1997. Accepted April 12, 1997