

213. Rearrangement of Derivatives of 1,3-Dithian-5-amine into Bicyclic 2-Thiazolidines. Crystal Structures of *cis*- and *trans*-1-(2-Aryl-1,3-dithian-5-yl)-2-thioureas and *cis*- and *trans*-5-Aryl-3-imino-7,7a-dihydro-1*H*,3*H*,5*H*-thiazolo[3,4-*c*]thiazoles

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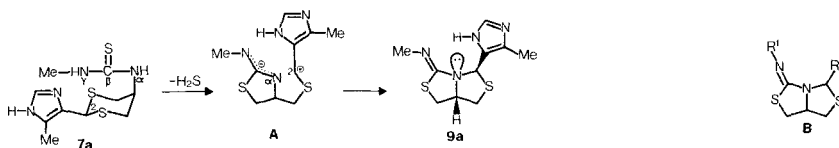
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Summary

Under conditions normally applied to transform thioureas into the corresponding carbodiimides, *cis*- and *trans*-1-(2-aryl-1,3-dithian-5-yl)-2-thioureas **7** and **8** undergo a rearrangement to 5-aryl-3-imino-7,7a-dihydro-1*H*,3*H*,5*H*-thiazolo[3,4-*c*]thiazoles **9/10** with *cis*- and *trans*-fused rings, respectively. The structures of these novel heterocycles were established by X-ray analysis of compounds **9a**, **9d**, and **10d**. The *cis*-fused compounds **9** are the thermodynamically more stable ones. The stereochemical outcome of the rearrangement depends on the carbenium ion stabilizing capability of the aryl moiety and on the reagent system applied. With Ar = Ph, *p*-Cl-Ph, *p*-O₂N-Ph, the reaction can be directed to deliver mainly either the *cis*-thiazolothiazoles **9** or the *trans*-thiazolothiazoles **10**. With Ar = 5-methyl-4-imidazolyl or *p*-Me₂N-Ph, formation of the *cis*-thiazolothiazoles (**9a** and **9b**, resp.) is strongly favored independently of the reaction conditions. In contrast to its 2-aryl analogs, (1,3-dithian-5-yl)-2-thiourea **7g** can be transformed into the carbodiimide **11**. Under rigorous conditions, **11** also undergoes rearrangement to the corresponding thiazolothiazole **9g**. Mechanisms explaining the above findings are discussed. Reaction of *trans*-2-phenyl-1,3-dithian-5-amine **6d** with phosgene or trichloromethyl chloroformate gives the 5-phenyl-7,7a-dihydro-1*H*,3*H*,5*H*-thiazolo[3,4-*c*]thiazol-3-ones **12** and **13**, whereas the amine **5g** lacking an aryl substituent forms the stable isocyanate **14**. Compound **14** is transformed into the corresponding thiazolothiazolone **15** by refluxing in diglyme. Syntheses are described for the 1,3-dithian-5-amines **5/6** and the thioureas **7/8** derived therefrom. The relative configuration of **7d** and **8d** was determined by X-ray analysis. NMR data then allowed to assign the configurations of all compounds of types **7** and **8**.

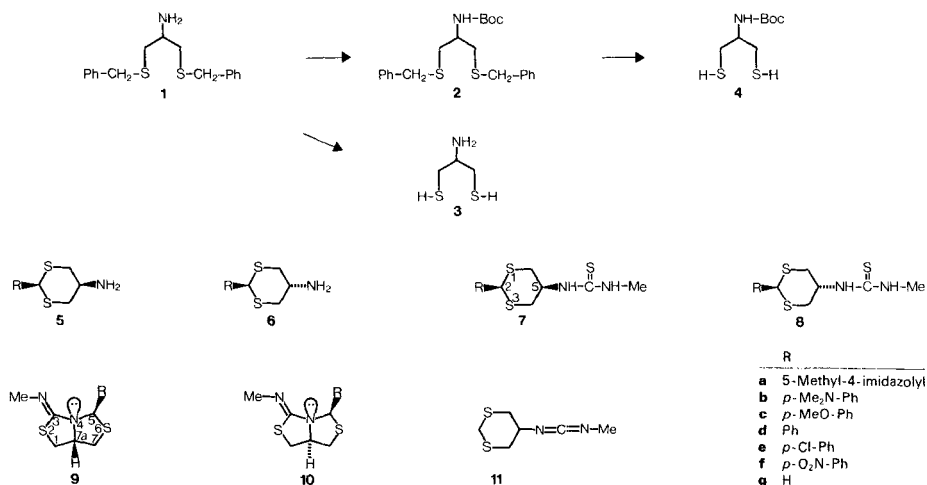
1. Introduction. – In the course of a synthetic programme aiming at histamine H₂ receptor blockers, we prepared the thiourea **7a** with the intention to transform it into the corresponding diimide. Upon treatment of **7a** with lead oxide a compound **9a** of the expected empirical formula was obtained, but it was immediately evident from its IR spectrum that a diimide grouping was not present in the product. The ¹H-NMR

spectrum showed that the 1,3-dithiane symmetry was lost and pointed to a structure of type **B** (see *Scheme 1*). This hypothetical structure was confirmed by an X-ray analysis (*cf. Section 7*), which at the same time established the configuration of **9a**, *i.e.* *cis*-fused rings, '*exo*'-position of the imidazo substituent and (*Z*)-arrangement at the (C=N)-bond. Apparently, **9a** is formed by a rearrangement in which one of the S-atoms of the 1,3-dithiane ring is captured by the strongly electrophilic β -C-atom of the side chain (either in a carbodiimide grouping or an equivalent precursor thereof), leading to the zwitterionic species **A**. Ring closure, connecting N(α) and C(2), affords the thiazolo[3,4-*c*]thiazole skeleton (*Scheme 1*).

Scheme 1

Starting from these preliminary results and ideas, we embarked on a more detailed investigation mainly concerned with scope, mechanism, and stereochemistry of this novel type of rearrangement reaction. Variation of the substituent **R** in position 2 of the educts **7** and **8** (*Scheme 2*), especially with respect to its electron-donating power, appeared to be of greatest importance. Although the electron-withdrawing power of C(β) could also be an objective for more thorough investigations, we restricted our experimental work to simple 1,3-dithiane-5-carbamic acid derivatives: the diimides, the isocyanates, and their respective precursors.

2. Synthesis and Relative Configuration of 1,3-Dithian-5-amines and 1-(1,3-Dithian-5-yl)-2-thioureas. – The 1,3-dithian-5-amines of types **5/6** can be synthesized by condensation of aldehydes with 2-amino-1,3-propanedithiol (**3**; see *Scheme 2*). Since **3**

Scheme 2

is very quickly dehydrogenated to 1,2-dithiolan-4-amine, it cannot be isolated in a pure form. It can, however, be generated from its *S,S'*-dibenzyl derivative **1** and further reacted as a crude product. This methodology turned out to be unsatisfactory in experiments on a larger scale.

The *N*-Boc-derivative **4** of **3** is a stable compound, easily available, and gives with aldehydes under acid or *Lewis*-acid catalysis directly the 1,3-dithian-5-amines **5/6**¹⁾. Compounds **5** and **6** were isolated partly as pure stereoisomers, partly as mixtures **5/6** of *cis*- and *trans*-compounds (*Scheme 2*). The 1,3-dithian-5-amine (**5g**) is described in [1]. The amines **5/6** were transformed into *N*-methylthioureas **7/8** by reaction with methyl isothiocyanate. If necessary, mixtures of stereoisomeric thioureas **7/8** can be separated by chromatography. The relative configuration of compounds **7d** and **8d** has been established by X-ray analysis (*cf. Section 7*). Based on those relay structures, the relative configurations of all other 1,3-dithianes **7** and **8** were derived from ¹H-NMR data (*Table 1*), especially from the pattern and chemical shift of the H–C(5) signal.

Table 1. ¹H-NMR-Data ((*D*₆)DMSO) of the Thioureas **7** and **8**

R	Compound	H–C(2)	H–C(5)	<i>W</i> _{1/2} ^{b)} [Hz]
5-Methyl-4-imidazolyl	7a	5.39	4.59	15
	8a	5.38	4.45	24
<i>p</i> -Me ₂ N-Ph	7b	5.25	4.63	16
	8b	5.30	4.43	24
<i>p</i> -MeO-Ph	7c	5.36	4.69	13
	8c	5.38	4.47	23
Ph	7d ^{a)}	5.48	4.73	13
	8d ^{a)}	5.48	4.56	24
<i>p</i> Cl-Ph	7e	5.50	4.74	17
	8e	5.48	4.48	26
<i>p</i> -O ₂ N-Ph	7f	5.69	4.78	17
	8f	5.68	4.56	24
H	7g		4.5	24

^{a)} Structure elucidated by X-ray analysis.

^{b)} For H–C(5).

3. Transformation of 1-(1,3-Dithian-5-yl)-2-thioureas into 3-Imino-7,7a-dihydro-1*H*,3*H*,5*H*-thiazolo[3,4-*c*]thiazoles. – The first observed rearrangement of this type (**7a**→**9a**) was induced by lead oxide in boiling CHCl₃ [2] (*Method a*). Since that method turned out not to be generally applicable, we tried other reagents which have been described in the literature to transform thioureas into the corresponding carbodiimides (*cf. [2]*). Three systems were found to be useful: PPh₃/CCl₄/Et₃N/CH₂Cl₂ [3] (*Method b*), COCl₂/THF-toluene followed by Et₃N [4] (*Method c*) and 2-chloro-1-methylpyridinium halogenides/Et₃N/MeCN [5] (*Method d*). All 2-aryl compounds gave directly the 3-imino-7,7a-dihydro-1*H*,3*H*,5*H*-thiazolo[3,4-*c*]thiazoles; intermediates, *e.g.* carbodiimides, could not be observed by TLC. The simple 1-(1,3-dithian-5-yl)-2-thiourea **7g**, however, forms the stable carbodiimide **11**, but that compound also rearranges to a thiazolothiazole (**9g**), though under more rigorous conditions (120° in DMF).

¹⁾ In some cases, *N*-(*tert*-butyl)-1,3-dithian-5-amines are formed as sideproducts.

Table 2. Rearrangement of *cis*- and *trans*-1-(2-Aryl-1,3-dithian-5-yl)-2-thioureas **7** and **8** into *cis*- and *trans*-Fused 3-Imino-7,7a-dihydro-1H,3H,5H-thiazolo[3,4-c]thiazoles **9** and **10**, respectively

Entry	R	Educt	Method ^{a)}	Products			
				Isolated yield [%]	Crude yield [%]	Composition of crude product [%] ^{b)}	
				9	10	9	10
1	5-Methyl-4-imidazolyl	7a	<i>a</i>	65.8			
		7a^{c)}	<i>d</i>			36	ca. 100
2		8a	<i>a</i>	69.6		94	
3	<i>p</i> -Me ₂ N-Ph	8a	<i>d</i>			72	ca. 100
4		7b	<i>b</i>			84.5	ca. 100
5		7b	<i>d</i>	90.1		ca. 100	ca. 100
6		7b	<i>d</i>			98	ca. 100
7		8b	<i>b</i>			81	ca. 100
8		8b	<i>d</i>	91		ca. 100	ca. 100
9		8b	<i>d</i>			97	ca. 100
10	<i>p</i> -MeO-Ph	7c	<i>d</i>			98	95
11		8c	<i>d</i>	51.5	37.6		
12		8c	<i>d</i>			74	40
13	Ph	7d	<i>b</i>	61.7	12.6		
14		7d	<i>b</i>			ca. 100	75
15		7d	<i>d</i>			ca. 100	34
16		8d	<i>b</i>	7.6	72.2		
17		8d	<i>b</i>			ca. 100	10
18		8d	<i>d</i>			74	10
19		8d	<i>d</i>				90 ^{d)}
19	<i>p</i> -Cl-Ph	7e	<i>c</i>	74.7			
20		8e	<i>d</i>	5.1	76.3	94	
21		8e	<i>d</i>			72	10
22	<i>p</i> -O ₂ N-Ph	7f	<i>d</i>	23.7	56.5		
23		7f	<i>d</i>			96.2	28
24		8f	<i>d</i>			78.9	5

^{a)} Cf. Section 3.^{b)} Estimated by ¹H-NMR.^{c)} Method *d* transforms **7a** into a mixture of **9a** and an analog bearing a 2-pyridyl substituent at one of the imidazole N-atoms.^{d)} Estimated by TLC.

The results of the transformation **7/8**→**9/10** are compiled in Table 2. It is obvious that the stereochemical outcome of the rearrangement depends on the substituent R and the technique applied (cf. Section 5). Structures **9a**, **9d**, and **10d**²⁾ were elucidated by X-ray analysis (Section 7). The structure of the other compounds could then be deduced by ¹H-NMR comparison with the mentioned relay compounds. Typically, the signal of H–C(5) is found at 6.5 ppm for *cis*-fused compounds and at 5.5 ppm for *trans*-fused compounds (Table 3).

²⁾ In **10d** the two rings are *trans*-fused. In the corresponding structure with *cis*-fused rings, the substituent R would be in an 'endo'-position and give rise to severe steric interference (collision with the imino group).

Table 3. $\delta_{H-C(5)}$ Values ($CDCl_3$) of *cis*- and *trans*-Fused 5-Aryl-7,7a-dihydro-3-(methylimino)-1H,3H,5H-thiazolo[3,4-c]thiazoles

	a	b	c	d	e	f
9 (<i>cis</i>)	6.44 ^{a)}	6.50	6.62	6.51 ^{a)}	6.67	6.68
10 (<i>trans</i>)		5.57		5.51 ^{a)}	5.57	5.64

^{a)} Configuration established by X-ray analysis (*cf.* Section 7).

4. Isomerization of the 1-(2-Aryl-1,3-dithian-5-yl)-2-thioureas and of the 5-Aryl-7,7a-dihydro-1H,3H,5H-thiazolo[3,4-c]thiazoles. – To create the prerequisites for a better understanding of the steric course and the mechanism of the rearrangement reaction $7/8 \rightarrow 9/10$ we studied the equilibrations $7 \rightleftharpoons 8$ and $9 \rightleftharpoons 10$ under base and acid/base catalysis. Et_3N , the base involved in the rearrangement according to *Methods b, c*, and *d*, is not strong enough to equilibrate the compounds **7** and **8**³⁾, with the exception of the nitrophenyl compounds **7f** and **8f** (*Method d* can be modified by using Na_2CO_3 instead of Et_3N to avoid equilibration also in this case). A 7:3 ratio of **7f** and **8f** results after equilibration with $Et_3N/MeCN$ starting from the one or the other side. $NaOMe$ in boiling THF is needed to equilibrate the phenyl compounds **7d** and **8d**; again a ratio of *ca.* 7:3 is observed, *i.e.* in both cases the *cis*-compound is the thermodynamically more stable one.

The equilibration $9 \rightleftharpoons 10$ also needs a strong base. It can be carried out with $NaOMe$ in DMSO. With **9d/10d** and **9e/10e**, the equilibration could be clearly shown to be, as expected, far on the side of the *cis*-fused compounds **9**. Compound **9f** forms with that base/solvent system only traces of **10f**, even if kept at 80° for 4 days. Under the same conditions, the *trans*-fused **10f** was isomerized to give a ratio 6.5:3.5 of **10f/9f**⁴⁾. Similar results were obtained with sodium 2-methyl-2-butoxide as base. $Et_3N \cdot HCl$ does not equilibrate compounds **9** and **10**.

5. Steric Course and Mechanism of the Rearrangement. – The results of *Section 4* show that under conditions, which correspond, with respect to possible base or acid/base catalysis, to those of the rearrangement, isomerization of educts ($7 \rightleftharpoons 8$) and products ($9 \rightleftharpoons 10$) can be excluded. Under this premise, from the data of *Table 2* the following can be deduced: *A.* If R is a substituent which stabilizes carbenium ions only poorly, the rearrangement is stereoselective with *Methods b* or *c*. That is, *cis*-educts **7** give mainly products **9** with *cis*-fused rings; *trans*-educts **8** give mainly products **10** with *trans*-fused rings (*Entries 13,14,16,17,19–21*). These results are equivalent to preferential retention of the configuration at C(2), as will become evident below.

B. If R stabilizes carbenium ions well, formation of the *cis*-thiazolothiazoles **9** is favored, independent from the method used (*Entries 1–9; cf. Entries 10–12*⁵⁾).

C. Method d leads in case of poor carbenium ion stabilizing R from both *cis*-educts **7** and *trans*-educts **8** mainly to *trans*-products **10**⁶⁾ (*Entries 15,18,20,21–24; cf. Entries 10–12*⁵⁾).

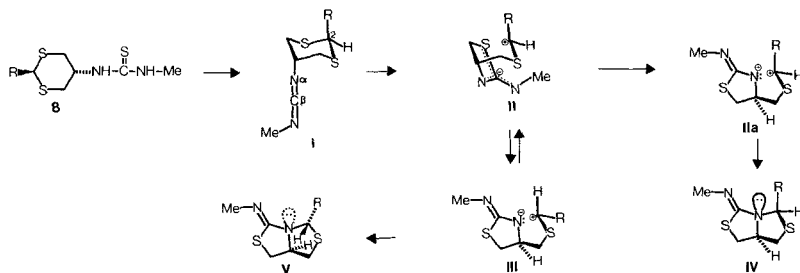
³⁾ Nor are these compounds equilibrated by $Et_3N \cdot HCl$.

⁴⁾ Most probably, also in this case the *cis*-fused compound is the thermodynamically more stable one. For some reason, the equilibration seems to be very slow with **10f**.

⁵⁾ The *p*-methoxyphenyl compounds **7c** and **8c** represent borderline cases.

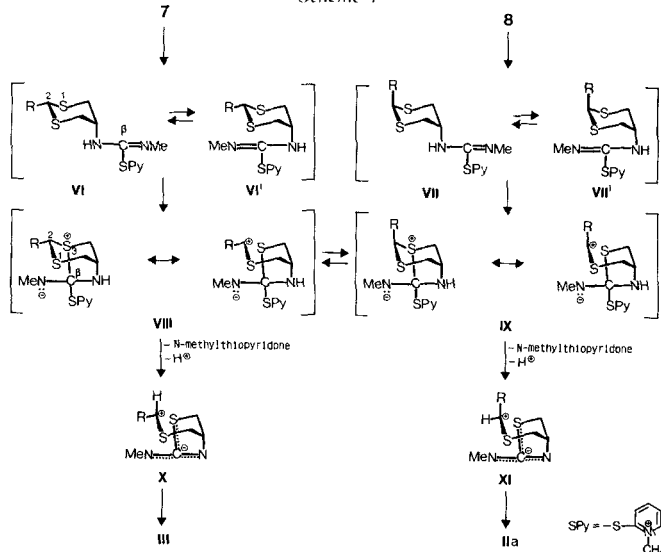
⁶⁾ This means inversion at C(2) in the case of the *cis*-compounds.

Scheme 3



The statements *A* and *B* can be explained by a mechanism as sketched in Scheme 3 for a *trans*-1,3-dithiane **8**: with *Methods a, b*, and *c* in a first step the thioureido residue is transformed into a carbodiimide grouping (**8**→**I**), which because of its high electrophilic power, reacts immediately with one of the ring S-atoms (**I**→**II**). The polar parts of **II** recombine under rotation, forming a bond between N(α) and C(2). The configuration at C(2) is retained by a close steric interaction of the cationic and the anionic part of **II**⁷⁾, if the positive charge is not too much spread (**II**→**IIa**→**IV**). In this case, the rearrangement is predominantly kinetically controlled (transition state similar to **IIa**). On the other hand, with a strongly resonance-stabilized cationic part of **II**, bond recombination is a relatively slow process, the configuration at C(2) is lost (**II**→**III**), and since **III** is thermodynamically more favorable than **IIa**, mainly or exclusively the *cis*-fused product **V** is formed (*via* a transition state similar to **III**).

Scheme 4



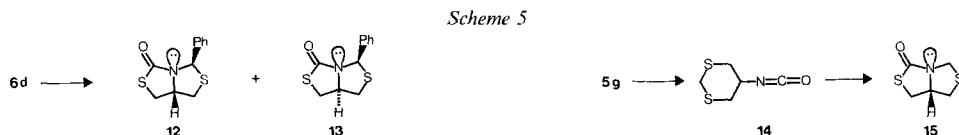
⁷⁾ As known for contact ion pairs, e.g. in the Stevens rearrangement.

⁸⁾ The stereochemical outcome could be explained likewise by the assumption of strong double-bond character of the C(2),S-bond in the zwitterion and retention of the *cis*- or *trans*-arrangement, respectively, of R and CH₂ on this bond.

A satisfactory hypothesis for the preferential formation of *trans*-thiazolothiazoles **10** from *cis*-1,3-dithianes **7** with *Method d* (if R is a substituent which poorly stabilizes carbenium ions; see statement *c*) has to define *i*) a mechanism, which allows transition from the *cis*- into the *trans*-1,3-dithiane series, and *ii*) a reaction step, which favors **10** over **9**. The pathways outlined in *Scheme 4* fulfill these requirements: In a first step, the thioureas **7** and **8** react with 2-chloro-1-methylpyridinium ion to the isothiurea derivatives **VI** and **VII**, respectively. The lifetime of these may be long enough to allow formation of the intermediates **VIII** and **IX** via the conformers **VI'** and **VII'**, respectively; **VIII** and **IX** can equilibrate because of their weakened 1,2-bond. Here, severe steric interference between R and the substituents at C(β) (MeS and PyS) in the *cis*-intermediate **VIII** strongly favors the *trans*-intermediate **IX**. In the latter, S(1) can further approach C(β) more easily and thereby facilitate the elimination of thiopyridone. Accordingly, a transition state similar to **IX** should be lower in energy than one similar to **VIII**. The route via **IX** and **XI**, running into **II** (*cf. Scheme 3*) is therefore the predominant one.

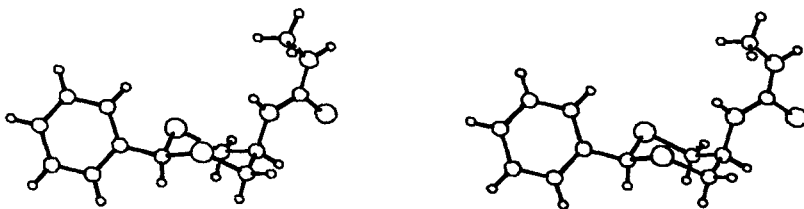
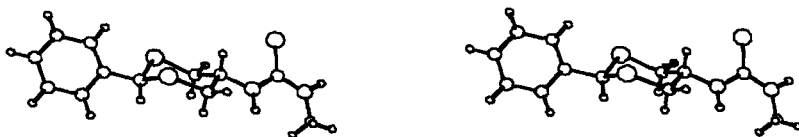
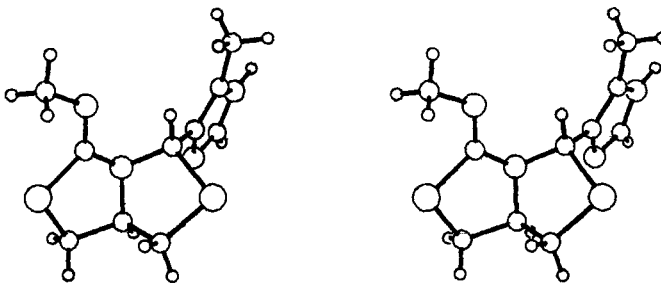
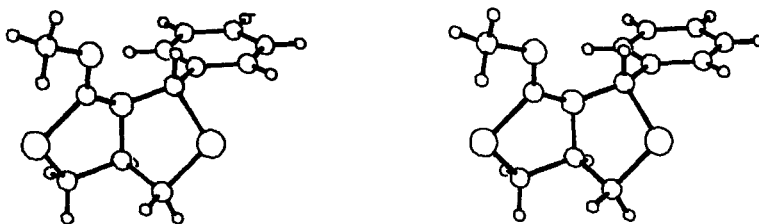
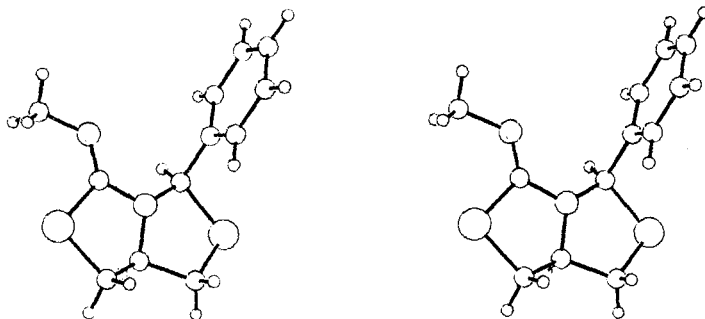
The fact that the imidazolyl- and *p*-(dimethylamino)phenyl-substituted 1,3-dithianes **7a** and **7b**, respectively, of the *cis*-series with the same method form *cis*-thiazolothiazoles is congruent with the intermediacy of **II** (which in these cases equilibrates with **III**; *cf. Scheme 3*). The *trans*-1,3-dithianes **8** under the conditions of *Method d* rearrange distinctly (*ca.* 5–6 times) faster than their *cis*-isomers. This may be explained by the assumption that starting from **VI**, the rate-limiting step is one before **IX**.

6. Reaction of 1,3-Dithian-5-amines with Phosgene or Trichloromethyl Chloroformate. – Considering its comparable electrophilicity an isocyanate substituent (or its precursor) in position 5 of a 1,3-dithiane should trigger a rearrangement to the corresponding thiazolo[3,4-*c*]thiazole skeleton about as easily as the carbodiimide grouping (or its precursor). This assumption was confirmed by experiments with the 1,3-dithian-5-amines **6d** and **5g** (*Scheme 5*). Compound **6d** reacts *e.g.* with trichloromethyl chloro-



formate and Et₃N in MeCN already at room temperature and delivers a 6:1 mixture of the *cis*- and *trans*-thiazolothiazolones **12** and **13**. The ratio **12/13** can be directed by the reaction conditions. For example, the hydrochloride of **6d** affords with phosgene in boiling toluene 62% of *trans*-product **13** and only 13.7% *cis*-product **12**. The configuration of **12** and **13** is deduced from the ¹H-NMR-spectra (chemical shift of H–C(5)). The simple 1,3-dithian-5-amine **5g** forms with trichloromethyl chloroformate/Et₃N/MeCN at 20° an isocyanate **14**, which in boiling diglyme rearranges to the thiazolothiazolone **15**.

7. X-Ray Structure Analyses of the 1-Methyl-3-(2-phenyl-1,3-dithian-5-yl)-2-thioureas 7d and 8d and of the 5-Aryl-3-(methylimino)-7,7a-dihydro-1H,3H,5H-thiazolo[3,4-*c*]thiazoles 9a, 9d, and 10d. – The crystal and molecular structures of com-

Fig. 1. Stereoscopic drawing of **7d**Fig. 2. Stereoscopic drawing of **8d**Fig. 3. Stereoscopic drawing of **9a**Fig. 4. Stereoscopic drawing of **9d**Fig. 5. Stereoscopic drawing of **10d**

pounds **7d**, **8d**, **9a**, **9d**, and **10d** have been determined by single-crystal X-ray structure analyses. All calculations were carried out with the SHELXTL [6] package of the *R3m* system. Stereoscopic drawings of all molecules are shown in *Fig. 1–5*⁹⁾.

The skillful assistance of *R. Roos* and *J. Wuhrlin* is acknowledged. The authors thank also Drs *W. Arnold*, *L. Chopard*, *A. Dirscherl*, *G. Englert*, *M. Grosjean*, *W. Vetter* and *Mr. W. Meister* for the spectroscopic determinations and microanalyses.

Experimental Part

General. All org. solvents used were dried over molecular sieves. Before evaporation, org. solutions were dried over Na_2SO_4 . Crystalline substances in all cases were dried *i.v.* (< 0.1 Torr). Silica gel F_{254} (*Merck*) plates were used for TLC. Column chromatography was carried out by using silica gel 60 (0.063–0.200 mm; *Merck*). Melting points (m.p.) were determined on a *Büchi-SMP-20* apparatus and are uncorrected. IR spectra (cm^{-1}) were obtained on a *Beckman-IR-9* instrument. $^1\text{H-NMR}$ spectra were recorded on a *Varian-A-60-D* and *EM-360* (60 MHz), *Bruker-Spectrospin-WP-80-CW* (80 MHz), *HX-90/15* (90 MHz), *HX-270* (270 MHz), and *WM-400* (400 MHz) spectrometer. Chemical shifts are given in ppm with TMS as internal standard ($= 0$ ppm); *s* = singlet; *d* = doublet; *t* = triplet; *q* = quadruplet; *m* = multiplet; *br.* = broad. Mass spectra were recorded on a *MS-9* (*ABI* Manchester) spectrometer. Signals in *m/z* (rel. intensities); signals $< 5\%$ mentioned only if of significance.

1. *tert-Butyl N-[2-Benzylthio-1-[(benzylthio)methyl]ethyl]carbamate (2)*. To the solution of **1**·HCl [7] (85.7 g, 0.25 mol) in DMF (750 ml), Et_3N (26.7 g, 0.26 mol) and then di(*tert*-butyl) dicarbonate (60.5 g, 0.28 mol) were added. The mixture was stirred at r.t. for 18 h. After evaporation of DMF *i.v.*, the residue was treated with EtOAc (500 ml) and H_2O (100 ml). The resulting org. layer was washed with H_2O and brine and then evaporated. The crude **2** was dissolved in petroleum ether (30–45°; 500 ml) and Et_2O (60 ml), shortly refluxed with active carbon and, after filtration, kept at 0° for crystallization: 93.9 g (92.3%) of colorless **2**, m.p. 61–63°. IR (KBr): 3337, 1684, 1650, 1601, 1535, 1169, 769, 756, 717. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 1.43 (*s*, $(\text{CH}_3)_3\text{C}$); 2.53 (*m*, $(\text{SCH}_2)_2\text{CH}$); 3.73 (*s*, 2 $\text{CH}_2\text{C}_6\text{H}_5$); 3.73 (*m*, H-C(1)); 6.85 (*d*, $J = 8.5$, HN); 7.20–7.44 (*m*, C_6H_5). MS: 312 (3, $M^+ - \text{C}_6\text{H}_5\text{CH}_2$), 256 (10), 238 (5), 166 (21), 149 (5), 91 (100), 57 (18), 41 (9). Anal. calc. for $\text{C}_{22}\text{H}_{29}\text{NO}_2\text{S}_2$ (403.60): C 65.47, H 7.24, N 3.47, S 15.89; found: C 65.44, H 7.04, N 3.39, S 16.03.

2. *tert-Butyl N-[2-Mercapto-1-(mercaptomethyl)ethyl]carbamate (4)*. A solution of **2** (93 g, 0.33 mol) in toluene (1.1 l) was dropped to a stirred solution of Na (16.1 g, 0.7 mol) in NH_3 at -70° . After addition of half of **2**, the color of the mixture turned from dark-blue to brown-yellow and, therefore, further Na (10 g, 0.43 mol) was added. Then, the rest of **2** was dropped in. After 30 min of further stirring, NH_4Cl (20.0 g, 0.37 mol) was added and the NH_3 evaporated over night. The residue was cooled to 0° and acidified with 10% $\text{KH}_2\text{SO}_4/\text{H}_2\text{O}$ (1950 ml). The toluene layer was washed with H_2O and evaporated *i.v.*: 60.6 g of crude **4** containing ca. 20% of bibenzyl (the preparation is very oxidizable and has to be kept under N_2). Crude **4** (1.04 g) was chromatographed over silica gel (20 g) with CH_2Cl_2 . By bulb-to-bulb distillation *i.v.*, bibenzyl (160 mg; b.p. 100–110°/0.1 Torr) and the viscous oily **4** (791 mg; b.p. 120–125°/0.02 Torr) were isolated. IR (film): 3334, 2977, 2931, 1692, 1510, 1168. $^1\text{H-NMR}$ (60 MHz, CDCl_3): 1.36 (*t*, $J = 9$, 2HS); 1.48 (*s*, $(\text{CH}_3)_3\text{C}$); 2.63–3.07 (*m*, 2 H_2C); 3.66–4.17 (*m*, 1HC); 4.9 (*br. m*, 1HN). Anal. calc. for $\text{C}_8\text{H}_{17}\text{NO}_2\text{S}_2$ (223.35): C 43.02, H 7.67, N 6.27, S 28.71; found: C 43.06, H 7.77, N 6.48, S 28.45.

3. *2-(5-Methylimidazol-4-yl)-1,3-dithian-5-amine (5a/6a)*. A solution of **4** (11.17 g, 50 mmol) and 5-methylimidazole-4-carboxaldehyde [8] (5.51 g, 50 mmol) in CHCl_3 (470 ml) and DMF (90 ml) was treated with dry HCl (gas) for 75 min at 50° and 90 min under reflux. After cooling, the mixture was first concentrated and then, after addition of toluene (200 ml), fully evaporated. The residue was suspended in CH_2Cl_2 (500 ml) and, under vigorous stirring, saturated with anh. NH_3 . The precipitate was filtered and the filtrate evaporated to dryness: crude **5a/6a** (10.5 g, 97.5%).

4. *2-[p-(Dimethylamino)phenyl]-1,3-dithian-5-amine (5b/6b)*. $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (66.2 g, 0.47 mol) in CH_2Cl_2 (50 ml) was dropped into a solution of *p*-(dimethylamino)benzaldehyde (31.6 g, 0.21 mol) and **4** (47.4 g, 0.21 mol) in CH_2Cl_2 (650 ml) within 25 min. The mixture was refluxed for 5 h. After cooling to r.t., 3*N* NaOH

⁹⁾ Coordinates and thermal parameters for all compounds have been deposited with the *Crystallographic Data Centre*, Cambridge University, University Chemical Lab, Cambridge CB2 1EW, England.

(250 ml) was added dropwise. The org. phase was washed with brine and evaporated. Then, 3N HCl (300 ml) was added to the residue and the mixture stirred overnight. The acidic solution was first washed with CH_2Cl_2 and then basified with 9N NaOH (130 ml). The resulting precipitate was dissolved in CH_2Cl_2 and washed with brine. After evaporation, the crude product was recrystallized from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$: 39.2 g (72.7%) of **5b/6b**, m.p. 129–135°. IR (KBr): 3345, 3325, 3247, 3156, 2802, 1611, 1579, 1562, 1523, 817. MS: 254 (36, M^+), 205 (17), 175 (13), 165 (96), 164 (67), 148 (100), 147 (93), 134 (17), 45 (13). Anal. calc. for $\text{C}_{12}\text{H}_{18}\text{N}_2\text{S}_2$ (254.41): C 56.65, H 7.16, N 11.01, S 25.20; found: C 56.31, H 7.15, N 10.95, S 25.25.

5. 2-(*p*-Methoxyphenyl)-1,3-dithian-5-amine (**5c/6c**). To a solution of **4** (29.0 g, 0.13 mol) and *p*-anisaldehyde (18.6 g, 0.137 mol) in CHCl_3 (325 ml) was added within 20 min under stirring $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (36.9 g, 0.26 mol) in CHCl_3 (40 ml). During the reaction, under evolution of 2-methyl-1-propene and CO_2 , the tetrafluoroborates of **5c/6c** precipitated as a white solid. After 90 min refluxing, the mixture was cooled to r.t., the precipitate was filtered off and washed with CHCl_3 . The dried salt was suspended in H_2O (150 ml). After adjusting to pH 10 with Na_2CO_3 solution, the mixture was extracted with CH_2Cl_2 . The org. layer was evaporated *i.v.* to give a crude mixture **5c/6c** (28.2 g, 89.9%), which was used in the next step without further purification.

6. 2-Phenyl-1,3-dithian-5-amine (**5d/6d**). Compound **4** (36.7 g, 164.5 mmol) and benzaldehyde (18.4 g, 173.4 mmol) were reacted as described under 5 to give 29.3 g (84.3%) of crude **5d/6d**.

7. 2-(*p*-Chlorophenyl)-1,3-dithiane-5-amine (**5e/6e**). Compound **4** (23.6 g, 105.7 mmol) and *p*-chlorobenzaldehyde (14.9 g, 106 mmol) were reacted as described under 5 to give 20.9 g (84.1%) of crude **5e/6e**.

8. 2-(*p*-Nitrophenyl)-1,3-dithian-5-amine (**5f/6f**), *N*-(*tert*-Butyl)-2-(*p*-nitrophenyl)-1,3-dithian-5-amine, and 2-(*tert*-Butylthio)-1-[(*tert*-butylthio)methyl]ethylamine Hydrochloride. To a solution of **4** (25.8 g, 115.5 mmol) and *p*-nitrobenzaldehyde (18.3 g, 121 mmol) in CHCl_3 (580 ml) was added within 25 min $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (32.8 g, 231 mmol) in CHCl_3 (35 ml). During the reaction, under evolution of 2-methyl-1-propene and CO_2 , a sticky tetrafluoroborate salt precipitated. After 60 min at r.t. and 2 h refluxing, the mixture was cooled to r.t. H_2O (200 ml) was added and then dropwise sat. Na_2CO_3 to reach pH *ca.* 9. The org. phase was washed with brine and evaporated. The residue (41.6 g) was chromatographed over silica gel (830 g) with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 95:5 to give the title compounds in the following sequence: 13.2 g (32.8%) of *cis*- and *trans*-*N*-(*tert*-Butyl)-2-(*p*-nitrophenyl)-1,3-dithian-5-amine, m.p. 82–84° (from MeCN). IR (KBr): 3269, 1597, 1523, 1490, 1346, 817. $^1\text{H-NMR}$ (80 MHz, CDCl_3): 2 s at 5.64 and 5.78 (H–C(2)) in a ratio of 2:3. MS: 312 (9, M^+), 255 (100), 209 (88), 177 (9), 161 (9), 130 (8), 105 (38), 104 (46), 73 (12), 57 (61), 45 (6), 41 (17), 23 (17). Anal. calc. for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_5\text{S}_2$ (312.45): C 53.82, H 6.45, N 8.97, S 20.52; found: C 53.74, H 6.55, N 8.97, S 20.42.

2-(*t*-Butylthio)-1-[(*tert*-butylthio)methyl]ethylamine, isolated as hydrochloride, 2.9 g (18.5%), m.p. 131–133° (from Et_2O). IR (KBr): 3185–2759 (br.), 1580, 1473, 1369, 1159. $^1\text{H-NMR}$ (80 MHz, CDCl_3): 1.36 (s, 2 $(\text{CH}_3)_2\text{C}$); 2.90–3.22 (*m*, 2 CH_2); 3.36 (br. *m*, H–C(1)). MS: 236 (100, M^+), 219 (17), 163 (18), 132 (35), 122 (8), 76 (43), 61 (21), 57 (6), 30 (7). Anal. calc. for $\text{C}_{11}\text{H}_{25}\text{NS}_2 \cdot \text{HCl}$ (271.91): C 48.59, H 9.27, Cl 13.03, N 5.15; found: C 48.65, H 9.46, Cl 12.72, N 5.18.

5f/6f: 9.1 g (30.7%), m.p. 142–144° (from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$). IR (KBr): 3365, 1604, 1595, 1579, 1518, 1492, 1348, 834. $^1\text{H-NMR}$ (90 MHz, CDCl_3): 2 s at 5.11 and 5.27 (H–C(2)) in a ratio of *ca.* 9:1. MS: 256 (9, M^+), 239 (23), 224 (14), 209 (11), 182 (38), 166 (11), 151 (7), 120 (6), 77 (8), 43 (100). Anal. calc. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_5\text{S}_2$ (256.34): C 46.86, H 4.72, N 10.93, S 25.01; found: C 46.60, H 4.95, N 10.83, S 24.98.

9. 1-Methyl-3-[*cis*-2-(5-methylimidazol-4-yl)-1,3-dithian-5-yl]-2-thiourea (**7a**) and 1-Methyl-3-[*trans*-2-(5-methylimidazol-4-yl)-1,3-dithian-5-yl]-2-thiourea (**8a**). Crude **5a/6a** (11.5 g, 53.4 mmol) and methyl isothiocyanate (3.95 g, 54 mmol) were refluxed in EtOH (100 ml) for 10 h. After evaporation *i.v.*, the mixture was separated by chromatography over silica gel (500 g) with *i*-PrOH. The *cis*-product **7a** was crystallized from *i*-PrOH/ Et_2O : 3.3 g (21.4%), m.p. 228–229°. IR (KBr): 3364, 3322, 3120, 1603, 1541, 1501. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.23 (s, CH_3C); 2.88 (*d*, $J = 4.5$, CH_3N); 2.90 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{vic}} = 4$, H–C(4) resp. H–C(6)); 3.38 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{vic}} = 2$, H–C(4) resp. H–C(6)); 4.59 (*m*, $\sum J \approx 26$, H–C(5)); 5.39 (s, H–C(2)); 7.39 (s, H–C=N); 7.44 (br. *d*, $J = 7$, HN–C(5)); 8.16 (br. *d*, $J = 4.5$, HNCH_3); 11.83 (br. *s*, HN (imidazole)). MS: 257 (18, $M^+ - \text{NH}_2 - \text{CH}_3$), 254 (5, $M^+ - \text{H}_2\text{S}$), 216 (15), 213 (24), 199 (16), 181 (20), 165 (29), 126 (82), 125 (100), 115 (93), 73 (55), 44 (29), 26 (35). Anal. calc. for $\text{C}_{10}\text{H}_{16}\text{N}_4\text{S}_3$ (288.45): C 41.64, H 5.59, N 19.42; found: C 41.68, H 5.78, N 19.32.

The *trans*-product **8a** was crystallized from EtOH: 3.1 g (20.1%), m.p. 235–237°. IR (KBr): 3365, 3260, 1604, 1560, 1502. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.25 (s, CH_3C); 2.84 (*d*, $J = 4.5$, CH_3N); 2.74–3.24 (*m*, 2 CH_2); 4.45 (*m*, $\sum J \approx 36$, H–C(5)); 5.38 (s, H–C(2)); 7.33–7.45 (*m*, HNCH_3 , HN–C(5)); 7.43 (s, H–C=N); 11.84 (br. *m*, HN (imidazole)). MS: 254 (6, $M^+ - \text{H}_2\text{S}$), 213 (22), 125 (40), 115 (100), 104 (16), 74 (25), 45 (30), 23 (24). Anal. calc. for $\text{C}_{10}\text{H}_{16}\text{N}_4\text{S}_3$ (288.45): C 41.64, H 5.59, N 19.42; found: C 41.75, H 5.76, N 19.32.

10. 1-[cis-2-(*p*-Dimethylamino)phenyl]-1,3-dithian-5-yl]-3-methyl-2-thiourea (**7b**) and 1-[trans-2-(*p*-Dimethylamino)phenyl]-1,3-dithian-5-yl]-3-methyl-2-thiourea (**8b**). A mixture of **5b/6b** (39.0 g, 0.15 mol), dry CHCl_3 (200 ml), and methyl isothiocyanate (11.9 g, 0.16 mol) was refluxed for 4 h. During this period, **8b** precipitated in crystalline form and was recrystallized from CHCl_3 : 11.3 g (22.4%), m.p. 212–214°. Chromatography (see below) gave an additional crop of 1.2 g (2.4%) **8b**, of the same m.p. IR (KBr): 1613, 1559, 1522, 812. $^1\text{H-NMR}$ (90 MHz, $(\text{D}_6)\text{DMSO}$): 2.33–2.72 (*m*, 2 CH_2); 2.83 (*d*, $J = 5$, CH_3NH); 2.90 (*s*, $(\text{CH}_3)_2\text{N}$); 4.43 (*br. m*, $\Sigma J \approx 36$, $\text{H-C}(5)$); 5.30 (*s*, $\text{H-C}(2)$); 6.56–6.80 (*m* (*AA'*), 2 arom. H); 7.16–7.40 (*m* (*BB'*), 2 arom. H); 7.40–7.85 (*m*, $\text{HN-C}(5)$, HNCH_3). MS: 327 (15, M^+), 296 (37), 255 (35), 252 (29), 205 (11), 165 (93), 164 (100), 148 (45), 147 (34), 134 (43), 115 (36), 73 (29), 45 (19), 28 (25). Anal. calc. for $\text{C}_{14}\text{H}_{21}\text{N}_3\text{S}_3$ (327.52): C 51.34, H 6.46, N 12.68, S 29.37; found: C 51.12, H 6.47, N 12.65, S 29.43.

The *cis*-compound **7b** was obtained after chromatography of the mother liquor (39 g) over silica gel (1300 g) with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 95:5: 31.5 g (62.4%), m.p. 187–189° (from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$). IR (KBr): 1618, 1553, 1513, 809, 768. $^1\text{H-NMR}$ (90 MHz, CDCl_3): 2.94 (*s*, $(\text{CH}_3)_2\text{N}$); 3.03 (*d*, $J = 5$, CH_3NH); 3.07 (*dd*, $J_{\text{gem}} = 13$, $J_{\text{ax,eq}} = 4$, $\text{H}_{\text{ax}}-\text{C}(4)$, $\text{H}_{\text{ax}}-\text{C}(6)$); 3.33 (*dd*, $J_{\text{gem}} = 13$, $J_{\text{eq,eq}} = 2.5$, $\text{H}_{\text{eq}}-\text{C}(4)$, $\text{H}_{\text{eq}}-\text{C}(6)$); 4.94 (*m*, $\Sigma J \approx 26$, $\text{H-C}(5)$); 5.08 (*s*, $\text{H-C}(2)$); 6.34 (*br. m*, HNCH_3); 7.03 (*d*, $J = 9$, $\text{HN-C}(5)$); 6.57–6.78 (*m* (*AA'*), 2 arom. H); 7.23–7.44 (*m* (*BB'*), 2 arom. H). MS: 327 (76, M^+), 296 (17), 252 (25), 165 (100), 164 (95), 148 (28), 134 (89), 115 (92), 73 (17), 57 (26), 45 (10), 28 (29). Anal. calc. for $\text{C}_{14}\text{H}_{21}\text{N}_3\text{S}_3$ (327.52): C 51.34, H 6.46, N 12.83, S 29.37; found: C 51.20, H 6.61, N 12.81, S 29.39.

11. 3-[*cis*-2-(*p*-Methoxyphenyl)-1,3-dithian-5-yl]-1-methyl-2-thiourea (**7c**) and 3-[*trans*-2-(*p*-Methoxyphenyl)-1,3-dithian-5-yl]-1-methyl-2-thiourea (**8c**). Crude **5c/6c** (28.2 g, 0.117 mol) and methyl isothiocyanate (9 g, 0.123 mol) in MeCN (280 ml) were refluxed for 2 h. Workup and chromatography as described under 9 yielded **7c** (1.1 g, 3.0%), m.p. 191–193° (from CH_2Cl_2) and **8c** (29.3 g, 79.4%), m.p. 214–216° (from MeCN). Data of **7c**: IR (KBr): 3392, 3377, 2841, 1605, 1533, 1508, 1299, 1256, 1240, 1226, 1174, 1024, 811. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.91 (*d*, $J = 4.5$, CH_3N); 2.96 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{ax,eq}} = 4$, $\text{H}_{\text{ax}}-\text{C}(4)$, $\text{H}_{\text{ax}}-\text{C}(6)$); 3.4 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{eq,eq}} = 2.0$, $\text{H}_{\text{eq}}-\text{C}(4)$, $\text{H}_{\text{eq}}-\text{C}(6)$); 3.79 (*s*, CH_3O); 4.69 (*m*, $\Sigma J \approx 27$, $\text{H-C}(5)$); 5.36 (*s*, $\text{H-C}(2)$); 6.8–7.06 (*m* (*AA'*), 2 arom. H); 7.2–7.6 (*m* (*BB'*), 2 arom. H); *ca.* 7.5 (*br. m*, HN); 8.16 (*br. m*, HN). MS: 314 (42, M^+), 239 (7), 191 (10), 162 (20), 129 (68), 121 (37), 115 (100), 91 (37), 73 (19), 57 (62), 45 (25), 41 (15), 28 (13). Anal. calc. for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_3\text{S}_3$ (314.48): C 49.65, H 5.77, N 8.91; found: C 49.65, H 5.82, N 8.87.

Data of **8c**: IR (KBr): 3341, 3227, 1611, 1567, 1514, 1254, 1168, 1024, 849, 825, 754. $^1\text{H-NMR}$ (90 MHz, $(\text{D}_6)\text{DMSO}$): 2.83 (*d*, $J = 4.5$, CH_3N); 2.74–3.22 (*m*, 2 CH_2); 3.74 (*s*, CH_3O); 4.47 (*m*, $\Sigma J \approx 40$, $\text{H}_{\text{ax}}-\text{C}(5)$); 5.38 (*s*, $\text{H-C}(2)$); 6.8–7.04 (*m* (*AA'*), 2 arom. H); 7.38–7.7 (*m* (*BB'*), 2 arom. H, 2 HN). MS: 314 (17, M^+), 283 (19), 242 (40), 239 (26), 152 (74), 151 (100), 115 (38), 73 (16), 45 (20). Anal. calc. for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_3\text{S}_3$ (314.48): C 49.65, H 5.77, N 8.91, S 30.58; found: C 49.59, H 5.74, N 8.81, S 30.87.

12. 1-Methyl-3-(*cis*-2-phenyl-1,3-dithian-5-yl)-2-thiourea (**7d**) and 1-Methyl-3-(*trans*-2-phenyl-1,3-dithian-5-yl)-2-thiourea (**8d**). Crude **5d/6d** (25.1 g, 118.8 mmol), methyl isothiocyanate (9.55 g, 130.6 mmol), and CHCl_3 (250 ml) were refluxed for 2 h. Workup and chromatography as described under 9 yielded 20.3 g (60.1%) of **7d**, m.p. 132–134° (from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$) and 6.0 g (17.8%) of **8d**, m.p. 247–249° (from MeCN). Data of **7d**: IR (KBr): 3385, 3220, 1556, 1511, 1498, 1226, 810, 739, 696. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.91 (*d*, $J = 4.5$, CH_3N); 2.98 (*dd*, $J_{\text{gem}} = 12$, $J_{\text{ax,eq}} = 4$, $\text{H}_{\text{ax}}-\text{C}(4)$, $\text{H}_{\text{ax}}-\text{C}(6)$); 3.43 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{eq,eq}} = 2.5$, $\text{H}_{\text{eq}}-\text{C}(4)$, $\text{H}_{\text{eq}}-\text{C}(6)$); 4.73 (*m*, $\Sigma J \approx 26$, $\text{H-C}(5)$); 5.48 (*s*, $\text{H-C}(2)$); 7.3–7.8 (*m*, 5 arom. H, 1 HN); 8.09–8.43 (*m*, HN). MS: 284 (28, M^+), 253 (12), 250 (6), 209 (22), 194 (13), 179 (5), 162 (15), 153 (7), 135 (14), 129 (47), 122 (63), 121 (78), 115 (45), 106 (20), 91 (48), 73 (53), 57 (29), 45 (50), 43 (100), 41 (24), 30 (24), 28 (18). Anal. calc. for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{S}_3$ (284.45): C 50.67, H 5.67, N 9.85, S 33.81; found: C 50.54, H 5.71, N 9.73, S 33.69.

Data of **8d**: IR (KBr): 3340, 3230, 1568, 1515, 1281, 1224, 1169, 810, 698. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.86 (*d*, $J = 4.5$, CH_3N); 2.93–3.30 (*m*, 2 CH_2); 4.51 (*m*, $\Sigma J \approx 40$, $\text{H-C}(5)$); 5.48 (*s*, $\text{H-C}(2)$); 7.33–7.75 (*m*, 5 arom. H, HN); 8.34 (*br.*, HN). MS: 284 (28, M^+), 253 (25), 250 (7), 212 (35), 209 (20), 194 (15), 179 (7), 161 (18), 129 (48), 122 (90), 121 (100), 115 (51), 91 (63), 73 (65), 57 (40), 43 (76), 30 (40), 28 (24). Anal. calc. for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{S}_3$ (284.45): C 50.67, H 5.67, N 9.85, S 33.81; found: C 50.71, H 5.85, N 10.00, S 34.12.

13. 1-[*cis*-2-(*p*-Chlorophenyl)-1,3-dithian-5-yl]-3-methyl-2-thiourea (**7e**) and 1-[*trans*-2-(*p*-Chlorophenyl)-1,3-dithian-5-yl]-3-methyl-2-thiourea (**8e**). Crude **5e/6e** (17.3 g, 70 mmol) and methyl isothiocyanate (5.66 g, 77 mmol) in MeCN (150 ml) were refluxed for 1 h. The pure thioureae were isolated by fractional crystallization: 11.5 g (51.2%) of **7e**, m.p. 153–155° (from CH_2Cl_2), and 3.0 g (13.4%) of **8e**, m.p. 264–266° (from MeCN). Data of **7e**: IR (KBr): 3360, 3296, 1539, 1509, 1488, 809, 702. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.91 (*d*, $J = 4.5$, CH_3N); 3.0 (*dd*, $J_{\text{gem}} = 13$, $J_{\text{ax,eq}} = 4.5$, $\text{H}_{\text{ax}}-\text{C}(4)$, $\text{H}_{\text{ax}}-\text{C}(6)$); 3.43 (*dd*, $J_{\text{gem}} = 14$, $J_{\text{eq,eq}} = 2.5$, $\text{H}_{\text{eq}}-\text{C}(4)$, $\text{H}_{\text{eq}}-\text{C}(6)$); 4.74 (*m*, $\Sigma J \approx 27$, $\text{H-C}(5)$); 5.50 (*s*, $\text{H-C}(2)$); 7.4–7.76 (*m*, 4 arom. H, HN); 8.06–8.41 (*m*, HN).

MS: 318 (43, M^+), 287 (17), 284 (7), 246 (31), 243 (25), 156 (77), 155 (95), 129 (81), 115 (100), 91 (45), 73 (55), 57 (35), 43 (66). Anal. calc. for $C_{12}H_{15}ClN_2S_3$ (318.90): C 45.20, H 4.74, Cl 11.12, N 8.78, S 30.16; found: C 45.16, H 4.69, Cl 11.23, N 8.75, S 30.34.

Data of **8e**: IR (KBr): 3310, 3246, 1552, 1509, 1486, 822, 801. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.85 (d , $J = 4.5$, CH_3N); 2.8–3.2 (m , 2 CH_2); 4.25–4.71 (m , $\Sigma J = 38$, $\text{H-C}(5)$); 5.48 (s , $\text{H-C}(2)$); 7.3–7.7 (m , 4 arom. H, HN); 8.13–8.25 (m , HN).

14. *1-Methyl-3-[cis-2-(p-nitrophenyl)-1,3-dithian-5-yl]-2-thiourea (7f) and 1-Methyl-3-[trans-2-(p-nitrophenyl)-1,3-dithian-5-yl]-2-thiourea (8f)*. A mixture of **5f/6f** (16.2 g, 63.2 mmol), methyl isocyanate (5.08 g, 69.5 mmol) and CHCl_3 (260 ml) was refluxed for 6 h. Compound **8f** crystallized from the mixture and was recrystallized from CHCl_3 : 1.6 g (7.7%), m.p. 213–215°. The first mother liquor was partly evaporated at r.t., whereupon **7f** crystallized: 18.5 g (88.9%), m.p. 203–205°.

Data of **7f**: IR (KBr): 3338, 3292, 1604, 1526, 1493, 1349, 861. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.93 (d , $J = 4.5$, CH_3N); 3.08 (dd , $J_{\text{gem}} = 14$, $J_{\text{eq,ax}} = 4.5$, $\text{H}_{\text{ax}}-\text{C}(4)$, $\text{H}_{\text{ax}}-(6)$); 3.42 (dd , $J_{\text{gem}} = 14$, $J_{\text{eq,eq}} = 2$, $\text{H}_{\text{eq}}-\text{C}(4)$, $\text{H}_{\text{eq}}-(6)$); 4.78 (m , $\Sigma J \approx 26$, $\text{H-C}(5)$); 5.69 (s , $\text{H-C}(2)$); 7.7 (br. m , HN); 7.7–8.0 (m (AA'), 2 arom. H); 8.0–8.5 (m (BB'), 2 arom. H, HN). MS: 329 (25, M^+), 298 (100), 257 (30), 254 (32), 239 (22), 224 (24), 182 (21), 167 (39), 129 (47), 115 (100), 91 (30), 73 (54), 57 (30), 43 (70), 30 (17), 28 (38). Anal. calc. for $C_{12}H_{15}N_3O_2S_3$ (329.45): C 43.75, H 4.59, S 29.19; found: C 43.34, H 4.77, S 28.81¹⁰.

Data of **8f**: IR (KBr): 1592, 1575, 1504, 1335, 819. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.86 (d , $J = 4.5$, CH_3N); 2.96–3.4 (m , 2 CH_2); 4.54 (m , $\Sigma J \approx 40$, $\text{H-C}(5)$); 5.68 (s , $\text{H-C}(2)$); 7.35–7.73 (m , 2 HN); 7.3–7.96 (m (AA'), 2 arom. H); 8.16–8.43 (m (BB'), 2 arom. H). MS: 329 (38, M^+), 298 (22), 257 (36), 239 (21), 224 (15), 206 (12), 182 (11), 166 (36), 162 (21), 151 (6), 129 (100), 115 (81), 91 (76), 73 (74), 57 (69), 43 (97), 30 (36), 28 (18). Anal. calc. for $C_{12}H_{15}N_3O_2S_3$ (329.45): C 43.75, H 4.59, N 12.75, S 29.19; found: C 43.42, H 4.64, N 12.68, S 29.00.

15. *1-(1,3-Dithian-5-yl)-3-methyl-2-thiourea (7g)*. The solution of **5g** [1] (1.35 g, 10 mmol) and methyl isothiocyanate (731 mg, 10.5 mmol) in MeCN (30 ml) was refluxed for 2 h. After evaporation of the solvent, the crude product was twice recrystallized from EtOAc: 1.8 g (86.4%) of **7g**, m.p. 139–141°. IR (KBr): 3332, 3190, 1567, 1514. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.56–3.18 (m , $\text{H}_2\text{C}(4)$, $\text{H}_2\text{C}(6)$); 2.84 (d , $J = 4.5$, CH_3N); 3.65–3.85 (2d (AB), $J = 15$, $\text{H}_2\text{C}(2)$); 4.49 (m , $\Sigma J \approx 32$, $\text{H-C}(5)$); 7.44 (d , $J = 8$, $\text{HN-C}(5)$); 7.75 ($ca. q$, HNCH_3). MS: 208 (58, M^+), 129 (100), 115 (54), 103 (23), 91 (84), 74 (37), 57 (27), 28 (47). Anal. calc. for $C_6H_{12}N_2S_3$ (208.36): C 34.59, H 5.81, N 13.45, S 46.16; found: C 34.78, H 5.85, N 13.20, S 45.80.

16. *7,7ax-Dihydro-5a-(5-methylimidazol-4-yl)-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-c]thiazole (9a)*. a) From **7a**. The mixture of **7a** (5.0 g, 17.3 mmol), MeCN (100 ml), DMF (40 ml), and lead oxide (3.87 g, 17.3 mmol) was refluxed for 68 h. The same amount of lead oxide was added every 12 h. Subsequently, the suspension was filtered through Speedex. The filtrate was evaporated to dryness. The residue was chromatographed over silica gel (110 g) with CH_2Cl_2 , saturated with anh. NH_3 : 2.9 g (65.8%) of **9a**, m.p. 164–166° (from i-PrOH). IR (KBr): 3458, 1645, 1495. $^1\text{H-NMR}$ (80 MHz, $(\text{D}_6)\text{DMSO}$): 2.13 (s , CH_3C); 2.64 (dd , $J_{\text{gem}} = J_{\text{vic}} = 10$, $\text{H-C}(1)$ or $\text{H-C}(7)$); 2.93 (s , CH_3N); 3.12 (dd , $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6$, $\text{H-C}(1)$ or $\text{H-C}(7)$); 3.33 (dd , $J_{\text{gem}} = 12$, $J_{\text{vic}} = 1.5$, $\text{H-C}(1)$ or $\text{H-C}(7)$); 3.63 (dd , $J_{\text{gem}} = 12$, $J_{\text{vic}} = 6$, $\text{H-C}(1)$ or $\text{H-C}(7)$); 4.84 (m , $\Sigma J \approx 24$, $\text{H-C}(7a)$); 6.45 (s , $\text{H-C}(5)$); 7.41 (s , 1 arom. H-C); 11.72 (br. m , HN). MS: 254 (27, M^+), 213 (100), 166 (21), 128 (31), 115 (29), 108 (28), 73 (17), 55 (14), 45 (21), 28 (45). Anal. calc. for $C_{10}H_{14}N_4S_2$ (254.37): C 47.22, H 5.55, N 22.03; found: C 47.21, H 5.61, N 21.71.

b) From **8a**. Under essentially the same conditions as described under a), 500 mg (1.73 mmol) of **8a** yielded 306 mg (69.6%) of **9a**, m.p. 165–167° (from 2-propanol), according to all spectroscopic data identical with **9a** described under a).

17. *5a-[p-(Dimethylamino)phenyl]-7,7ax-dihydro-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-c]thiazole (9b)*. a) From **7b**. A solution of **7b** (1.05 g, 3.2 mmol), 2-chloro-1-methylpyridinium iodide (981 mg, 3.8 mmol), and Et_3N (777 mg, 7.7 mmol) in MeCN (30 ml) was refluxed for 16 h. The mixture was evaporated and the residue treated with Et_2O (30 ml) and Na_2CO_3 (10%; 15 ml). The resulting org. phase was extracted with H_2O (10×15 ml) and then evaporated. Bulb-to-bulb distillation of the residue at 185–190°/0.09 Torr afforded 846 mg (90.1%) of **9b** as a viscous yellowish oil. IR (film): 1644, 1612, 1563, 1521, 840, 816. $^1\text{H-NMR}$ (80 MHz, CDCl_3): 2.96 (s , $(\text{CH}_3)_2\text{N}$); 3.14 (s , CH_3N); 2.89–3.76 (m , $\text{H}_2\text{C}(1)$, $\text{H}_2\text{C}(7)$); 4.20 (m , $\Sigma J \approx 24$, $\text{H-C}(7a)$); 6.65–6.87 (m (AA'), 2 arom. H); 7.27–7.53 (m (BB'), 2 arom. H). MS: 293 (23, M^+), 252 (100), 164 (20), 152 (17), 147 (13), 98 (14), 45 (20). Anal. calc. for $C_{14}H_{19}N_3S_2$ (293.45): C 57.30, H 6.53, N 14.32, S 21.85; found: C 56.90, H 6.50, N 14.19, S 21.92.

¹⁰) The substance contains 1.64% of CHCl_3 , although dried at 65° i.v. during 64 h.

b) From **8b**. With **8b**, the reaction was complete after 4 h of refluxing. Workup as above yielded 91% of **9b**, b.p. 185–190°/0.1 Torr, according to ¹H-NMR identical with **9b** described under a).

18. 7,7α-Dihydro-5α-(p-methoxyphenyl)-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-c]thiazole (**9c**) and 7,7α-Dihydro-5β-(p-methoxyphenyl)-3-(methylimino)-trans-1H,3H,5H-thiazolo[3,4-c]thiazole (**10c**) from **8c**. A solution of **8c** (3.22 g, 10.2 mmol), 2-chloro-1-methylpyridinium iodide (3.28 g, 12.3 mmol), and Et₃N (2.5 g, 24.6 mmol) in MeCN (40 ml) was refluxed for 5 h. After workup as described under 17, the crude product was chromatographed over silica gel (140 g). Upon elution with Et₂O, **9c** (1.48 g, 51.5%), crystallized from MeOH as fumarate, m.p. 163–165°, and **10c** (1.08 g, 37.6%), m.p. 121–122° (from Et₂O/petroleum ether), were isolated.

Data of **9c**-fumarate: IR (KBr): 2480, 1707, 1639, 1582, 1512, 1418, 1174, 1029, 825. ¹H-NMR (80 MHz, (D₆)DMSO): 2.74 (dd, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 2.98 (s, CH₃N); 3.18 (dd, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 5.5$, H–C(1) or H–C(7)); 3.33 (dd, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 1.5$, H–C(1) or H–C(7)); 3.64 (dd, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6.5$, H–C(1) or H–C(7)); 3.74 (s, CH₃O); 4.29 (m, $\Sigma J \approx 24$, H–C(7a)); 6.44 (s, H–C(5)); 6.62 (s, 3 olef. H); 6.75–6.96 (m (AA'), 2 arom. H); 7.16–7.40 (m (BB'), 2 arom. H). MS: 280 (85, M^+), 239 (100), 192 (28), 175 (21), 151 (67), 134 (73), 116 (30), 98 (87), 73 (32), 45 (80), 27 (62). Anal. calc. for C₁₃H₁₆N₂O₅·1.5 C₄H₄O₄ (454.51): C 50.21, H 4.88, N 6.16, S 14.11; found: C 50.27, H 4.90, N 6.10, S 14.01.

Data of **10c**: IR (KBr): 2770, 1653, 1610, 1584, 1512, 1250, 1173, 1027, 840, 799. ¹H-NMR (80 MHz, CDCl₃): 2.82 (s, CH₃N); 2.71–3.24 (m, H₂C(1), H₂C(7)); 3.84 (s, CH₃O); 4.48 (m, $\Sigma J \approx 31$, H–C(7a)); 5.54 (s, H–C(5)); 6.73–7.0 (m (AA'), 2 arom. H); 7.12–7.34 (m (BB'), 2 arom. H). MS: 280 (87, M^+), 239 (100), 192 (33), 175 (22), 151 (82), 134 (78), 121 (23), 106 (33), 91 (18), 73 (33), 45 (38), 41 (25), 38 (22), 28 (17). Anal. calc. for C₁₃H₁₆N₂O₅ (280.40): C 55.69, H 5.75, N 9.99, S 22.87; found: C 55.94, H 5.82, N 9.90, S 22.77.

19. 7,7α-Dihydro-3-(methylimino)-5α-phenyl-cis-1H,3H,5H-thiazolo[3,4-c]thiazole (**9d**) and 7,7α-dihydro-3-(methylimino)-5β-phenyl-trans-1H,3H,5H-thiazolo[3,4-c]thiazole (**10d**). a) From **7d**. The mixture of **7d** (2.54 g, 8.93 mmol), Ph₃P (4.68 g, 17.8 mmol), Et₃N (1.9 g, 18.8 mmol), CCl₄ (3.43 g, 22.3 mmol), and CH₂Cl₂ (50 ml) was heated under reflux for 20 h. After cooling to r.t. and adding of Et₂O (100 ml), the mixture was treated with 3N HCl (50 ml). After stirring for 30 min, the clear acidic phase was separated. The org. phase was extracted with H₂O (2 × 25 ml). The combined H₂O-phases were adjusted to pH 9 by careful addition of calcined Na₂CO₃ (14 g). The bases were extracted with CH₂Cl₂. After washing with H₂O and brine, the solution was evaporated. The crude product yielded, after chromatography with CH₂Cl₂/MeOH 98:2 over silica gel (120 g), 1.38 g (61.7%) of **9d**, m.p. 110–111° (from CH₂Cl₂/Et₂O), and 282 mg (12.6%) of **10d**, m.p. 124–126° (from Et₂O).

Data of **9d**: IR (KBr): 3427, 3267, 2990, 2932, 2765, 1644, 1494, 743, 717, 686. ¹H-NMR (400 MHz, CDCl₃): 2.94 (dd, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 3.08 (dd, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 5.5$, H–C(1) or H–C(7)); 3.11 (s, CH₃N); 3.19 (dd, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 1$, H–C(1) or H–C(7)); 3.62 (dd, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 6$, H–C(1) or H–C(7)); 4.21 (m, $\Sigma J \approx 25$, H–C(7a)); 6.67 (s, H–C(5)); 7.21–7.48 (m, 5 arom. H). MS: 250 (19, M^+), 209 (100), 162 (18), 145 (10), 121 (21), 104 (36), 77 (21), 55 (9), 45 (14). Anal. calc. for C₁₂H₁₄N₂S₂ (250.38): C 57.57, H 5.64, N 11.19, S 25.61; found: C 57.42, H 5.66, N 11.13, S 25.71.

Data of **10d**: IR (KBr): 3410, 3363, 2778, 1656, 1493, 694. ¹H-NMR (80 MHz, CDCl₃): 2.73–3.24 (m, H₂C(1), H₂C(7)); 2.83 (s, CH₃N); 4.48 (m, $\Sigma J = 32$, H–C(7a)); 5.55 (s, H–C(5)); 7.13–7.41 (m, 5 arom. H). MS: 250 (34, M^+), 209 (100), 162 (13), 121 (14), 104 (18), 73 (12), 45 (13). Anal. calc. for C₁₂H₁₄N₂S₂ (250.38): C 57.57, H 5.64, N 11.19, S 25.61; found: C 57.46, H 5.68, N 11.10, S 25.56.

b) From **8d**. Treatment of **8d** (1.50 g, 5.26 mmol) with Ph₃P (2.76 g, 10.5 mmol), Et₃N (1.12 g, 11.1 mmol), and CCl₄ (2.02 g, 13.1 mmol) and workup as described under a) led to **9d** (0.1 g, 7.6%), m.p. 110–111° (from CH₂Cl₂/Et₂O), and **10d** (1.0 g, 76.2%), m.p. 124–126°.

20. 5α-(p-Chlorophenyl)-7,7α-dihydro-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-c]thiazole (**9e**) from **7e**. Phosgene (460 mg, 4.65 mmol), dissolved in toluene (2.3 ml) was added at r.t. to a solution of **7e** (1.06 g, 3.32 mmol) in THF (10 ml). After 20 min, the stirred mixture was refluxed for 45 min. Cooled again to r.t., it was treated dropwise with Et₃N (672 mg, 6.64 mmol) in THF (3 ml). After 30 min of refluxing, the solvent was removed under reduced pressure. The residue was dissolved in CH₂Cl₂, washed with brine (4 × 10 ml), and evaporated. The crude product was purified by filtration through silica gel with CH₂Cl₂/MeOH 99.5:0.5 to furnish **9e** (707 mg, 74.7%). The compound crystallized as fumarate, m.p. 150–152° (from i-PrOH). IR (KBr): 3419, 2795, 2470, 1693, 1633, 1491, 1415, 1270, 1218, 840. ¹H-NMR (80 MHz, (D₆)DMSO): 2.74 (dd, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 2.95 (s, CH₃N); 3.21 (dd, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6$, H–C(1) or H–C(7)); 3.40 (dd, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 1.5$, H–C(1) or H–C(7)); 3.66 (dd, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 6$, H–C(1) or H–C(7)); 4.29 (m, $\Sigma J \approx 24$, H–C(7a)); 6.49 (s, H–C(5)); 6.62 (s, 3 olef. H); 7.4 (s, 4 arom. H). Anal. calc. for C₁₂H₁₃ClN₂S₂·1.5 C₄H₄O₄ (458.93): C 47.11, H 4.17, Cl 7.73, N 6.10, S 13.97; found: C 46.93, H 4.07, Cl 7.87, N 5.98, S 14.13.

21. 5 α -(*p*-Chlorophenyl)-7,7 α -dihydro-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-*c*]thiazole (**9e**) and 5 β -(*p*-Chlorophenyl)-7,7 α -dihydro-3-(methylimino)-trans-1H,3H,5H-thiazolo[3,4-*c*]thiazole (**10e**) from **8e**. The mixture of **8e** (3.09 g, 9.68 mmol), 2-chloro-1-methylpyridinium iodide (3.01 g, 11.62 mmol), Et₃N (2.35 g, 23.24 mmol), and MeCN (40 ml) was refluxed for 4 h. After workup as described under 17, the residue (2.95 g) was chromatographed over silica gel (140 g) with Et₂O to yield **9e** (226 mg, 5.1%), characterized as crystalline fumarate, m.p. 149–151°, as described under 20, and **10e** (2.1 g, 76.3%), m.p. 133–135° (from EtOH).

Data of **10e**: IR (KBr): 3416, 2925, 2865, 1649, 1592, 1581, 1488, 846, 827. ¹H-NMR (270 MHz, CDCl₃): 2.83 (s, CH₃N); 2.88 (dd, *J*_{gem} = 10, *J*_{vic} = 4.5, H–C(1) or H–C(7)); 3.07 (dd, *J*_{gem} = *J*_{vic} = 10.5, H–C(1) or H–C(7)); 3.0–3.1 (m, 2H–C(1) or 2H–C(7)); 4.49 (m, ΣJ = 32.5, H–C(7a)); 5.51 (s, H–C(5)); 7.22–7.33 (m, 4 arom. H). MS: 284 (34, *M*⁺), 245 (41), 243 (100), 196 (12), 155 (14), 138 (14), 89 (12), 73 (18), 45 (23), 41 (17), 27 (7). Anal. calc. for C₁₂H₁₃ClN₂S₂ (284.82): C 50.60, H 4.60, Cl 12.45, N 9.84, S 22.51; found: C 50.80, H 4.99, Cl 12.12, N 9.51, S 21.97¹¹⁾.

22. 7,7 α -Dihydro-3-(methylimino)-5 α -(*p*-nitrophenyl)-cis-1H,3H,5H-thiazolo[3,4-*c*]thiazole (**9f**) and 7,7 α -Dihydro-3-(methylimino)-5 β -(*p*-nitrophenyl)-trans-1H,3H,5H-thiazolo[3,4-*c*]thiazole (**10f**). A mixture of **7f** (14.8 g, 45 mmol), 2-chloro-1-methylpyridinium iodide (13.8 g, 54 mmol), anh. pulverized Na₂CO₃ (5.7 g, 54 mmol), and MeCN (450 ml) was refluxed for 24 h. After removal of the solvent under reduced pressure, CHCl₃ (500 ml) and H₂O (100 ml) were added to the residue. The org. phase was washed with H₂O and evaporated. The crude product was chromatographed with Et₂O over silica gel (1.4 kg) and yielded **9f** (3.15 g, 23.7%), m.p. 119–121° (from CH₂Cl₂/Et₂O), and **10f** (7.5 g, 56.5%), m.p. 199–201° (from CH₂Cl₂).

Data of **9f**: IR (KBr): 1640, 1603, 1515, 1346, 815. ¹H-NMR (80 MHz, (D₆)DMSO): 2.82 (dd, *J*_{gem} = *J*_{vic} = 10, H–C(1) or H–C(7)); 3.03 (s, CH₃N); 3.28 (dd, *J*_{gem} = 10, *J*_{vic} = 5.8, H–C(1) or H–C(7)); 3.44 (dd, *J*_{gem} = 11.5, *J*_{vic} = 2, H–C(1) or H–C(7)); 3.76 (dd, *J*_{gem} = 11.5, *J*_{vic} = 6.5, H–C(1) or H–C(7)); 4.38 (m, ΣJ = 24, H–C(7a)); 6.68 (s, H–C(5)); 7.6–7.9 (m (*AA'*), 2 arom. H); 8.1–8.4 (m (*BB'*), 2 arom. H). MS: 295 (30, *M*⁺), 254 (100), 208 (16), 124 (7), 45 (7), 28 (24). Anal. calc. for C₁₂H₁₃N₃O₂S₂ (295.38): C 48.80, H 4.44, N 14.23, S 21.71; found: C 48.89, H 4.45, N 14.05, S 21.59.

Data of **10f**: IR (KBr): 1644, 1608, 1597, 1525, 1489, 1346, 824. ¹H-NMR (80 MHz, (D₆)DMSO): 2.68 (s, CH₃N); 2.97–3.46 (m, 2 CH₂); 4.49 (m, ΣJ ≈ 31, H–C(7a)); 5.64 (s, H–C(5)); 7.6–7.8 (m (*AA'*), 2 arom. H); 8.08–8.4 (m (*BB'*), 2 arom. H). MS: 295 (68, *M*⁺), 254 (100), 224 (5), 208 (20), 175 (8), 129 (12), 73 (16), 45 (15), 41 (14), 28 (32). Anal. calc. for C₁₂H₁₃N₃O₂S₂ (295.38): C 48.80, H 4.44, N 14.23, S 21.71; found: C 48.83, H 4.46, N 14.09, S 21.56.

23. 7,7 α -Dihydro-3-(methylimino)-cis-1H,3H,5H-thiazolo[3,4-*c*]thiazole (**9g**). The mixture of **7g** (313 mg, 1.5 mmol), 2-chloro-1-methylpyridinium iodide (575 mg, 2.25 mmol), Et₃N (455 mg, 4.5 mmol), and MeCN (15 ml) was refluxed for 2.5 h. After addition of DMF (10 ml), the MeCN was removed by distillation, and the resulting DMF solution was stirred at 120° for 3 h. The solvent was then distilled off under reduced pressure. The CH₂Cl₂ solution of the residue was washed with Na₂CO₃ (10%), brine, and H₂O. After evaporation of the solvent, the crude product (207 mg) was chromatographed with Et₂O over silica gel (21 g). The resulting **9g** was crystallized as fumarate salt (214 mg, 40.9%), m.p. 131–133° (EtOH). IR (KBr): 3200–2400 (br.), 1697, 1653, 1546, 1450, 1283, 1255. ¹H-NMR (80 MHz, (D₆)DMSO): 2.60 (dd, *J*_{gem} = *J*_{vic} = 10, H–C(1) or H–C(7)); 2.97 (s, CH₃N); 3.08 (dd, *J*_{gem} = 10, *J*_{vic} = 6, H–C(1) or H–C(7)); 3.37 (dd, *J*_{gem} = 12, *J*_{vic} = 2.5, H–C(1) or H–C(7)); 3.65 (dd, *J*_{gem} = 12, *J*_{vic} = 6, H–C(1) or H–C(7)); 4.19 (m, ΣJ = 24.5, H–C(7a)); 4.14, 5.04 (2d (*AB*), *J* = 9.5, H₂C(5)); 6.70 (s, 3 olef. H); 12.1 (br. s, 3 HOOC). MS: 174 (39, *M*⁺), 133 (100), 116 (7), 98 (27), 87 (13), 69 (13), 55 (23), 45 (13), 41 (8), 27 (8). Anal. calc. for C₆H₁₀N₂S₂ · 1.5 C₄H₄O₄ (348.39): C 41.37, H 4.63, N 8.04, S 18.40; found: C 41.36, H 4.51, N 8.07, S 18.45.

24. 1-(1,3-Dithian-5-yl)-3-methylcarbodiimide (**11**) and 1-(1,3-Dithian-5-yl)-3-methylurea. The mixture of **7g** (1.0 g, 5 mmol), 2-chloro-1-methylpyridinium iodide (1.53 g, 6 mmol), Et₃N (1.21 g, 12 mmol), and CHCl₃ (10 ml) was refluxed for 23 h. The residue obtained after filtration and evaporation of the mixture was chromatographed with CHCl₃ over silica gel (105 g) and yielded crude **11** (45 mg, 5.1%) and the corresponding urea (615 mg, 63.9% crude product; 527 mg, 54.8% crystalline product), m.p. 231–233° (from MeOH).

Data of **11**: IR (film): 2186, 2105. ¹H-NMR (80 MHz, CDCl₃): 2.91 (dd, *J*_{gem} = 14, *J*_{vic} = 7.5, H–C(4), H–C(6)); 3.04 (s, CH₃N); 3.10 (dd, *J*_{gem} = 14, *J*_{vic} = 4, H–C(4), H–C(6)); 3.49, 4.15 (2d (*AB*), *J* = 14, H₂C(2)); 4.00 (m, ΣJ ≈ 25, H–C(7a)).

Data of 1-(1,3-Dithian-5-yl)-3-methylurea: IR (KBr): 3348, 3296, 1626, 1586, 1527. ¹H-NMR (80 MHz, (D₆)DMSO): 2.55 (d, *J* = 4.5, CH₃N); 2.60 (dd, *J*_{gem} = 14, *J*_{vic} = 7.5, H–C(4), H–C(6)); 2.93 (dd, *J*_{gem} = 14,

¹¹⁾ The substance holds tightly small amounts of EtOH.

$J_{\text{vic}} = 2.5$, H–C(4), H–C(6)); 3.83 (*m*, $\Sigma J \approx 30$, H–C(5)); 5.81–6.30 (*m*, 2HN). MS: 192 (8, M^+), 118 (11), 103 (12), 75 (100), 61 (12), 58 (15), 43 (49), 30 (7). Anal. calc. for $\text{C}_6\text{H}_{12}\text{N}_2\text{OS}_2$ (192.30): C 37.48, H 6.29, N 14.57, S 33.34; found: C 37.55, H 6.44, N 14.51, S 33.04.

25. *7,7 α -Dihydro-5 α -phenyl-cis-1H,3H,5H-thiazolo[3,4-*c*]thiazol-3-one (12) and 7,7 α -Dihydro-5 β -phenyl-trans-1H,3H,5H-thiazolo[3,4-*c*]thiazol-3-one (13).* a) From **6d**·HCl with Phosgene. A suspension of **6d**·HCl (248 mg, 1 mmol) in toluene (10 ml) was refluxed and 5 times (at intervals of 30 min) treated with phosgene (198 mg, 2 mmol) in toluene (1 ml). After further 15 h at r.t., the solvent was removed under reduced pressure. Chromatography of the residue with CH_2Cl_2 over silica gel yielded **12** (32.4 mg, 13.7%), b.p. 150–155°/0.04 Torr, and **13** (147.4 mg, 62.1%), m.p. 155–157° (from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$).

Data of **12**: IR (film): 1679, 1601, 1584, 1493, 1175, 754, 700. $^1\text{H-NMR}$ (90 MHz, CDCl_3): 3.02 (*dd*, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 3.14 (*dd*, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6.5$, H–C(1) or H–C(7)); 3.20 (*dd*, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 2.5$, H–C(1) or H–C(7)); 3.67 (*dd*, $J_{\text{gem}} = 12$, $J_{\text{vic}} = 7.5$, H–C(1) or H–C(7)); 4.35 (*m*, $\Sigma J = 26$, H–C(7a)); 6.42 (*s*, H–C(5)); 7.28–7.54 (*m*, 5 arom. H). MS: 237 (100, M^+), 236 (5), 209 (6), 196 (63), 162 (24), 132 (34), 122 (47), 121 (36), 117 (7), 104 (40), 103 (7), 89 (10), 77 (32), 73 (12), 51 (20), 45 (26), 39 (14), 27 (9). Anal. calc. for $\text{C}_{11}\text{H}_{11}\text{NOS}_2$ (237.34): C 55.67, H 4.67, N 5.90; found: C 55.88, H 4.72, N 5.79.

Data of **13**: IR (KBr): 1684, 1683, 1599, 1496, 753, 701. $^1\text{H-NMR}$ (80 MHz, CDCl_3): 2.90 (*dd*, $J_{\text{gem}} = 11$, $J_{\text{vic}} = 5$, H–C(1) or H–C(7)); 3.19 (*dd*, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6$, H–C(1) or H–C(7)); 3.21 (*dd*, $J_{\text{gem}} = J_{\text{vic}} = 11$, H–C(1) or H–C(7)); 3.45 (*dd*, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 4.86 (*m*, $\Sigma J \approx 32$, H–C(7a)); 5.23 (*s*, H–C(5)); 7.25–7.48 (*m*, 5 arom. H). MS: 237 (100, M^+), 209 (8), 196 (48), 162 (36), 160 (5), 132 (30), 122 (78), 121 (41), 117 (6), 104 (39), 103 (6), 89 (11), 77 (31), 73 (17), 69 (9), 59 (13), 45 (24), 39 (17), 27 (10).

b) From **6d**·HCl with Trichloromethyl Chloroformate. To a mixture of **6d**·HCl (248 mg, 1 mmol), Et_3N (213 mg, 2.1 mmol), and MeCN (10 ml), trichloromethyl chloroformate (139 mg, 0.7 mmol) was added under stirring at r.t. After 24 h, the solvent was evaporated and the residue dissolved in CH_2Cl_2 and washed with H_2O . The crude product (208 mg, 87.5%) obtained upon evaporation of CH_2Cl_2 was characterized by $^1\text{H-NMR}$ (80 MHz, CDCl_3) and shown to be a 6:1 mixture of **12** and **13**.

26. *7,7 α -Dihydro-cis-1H,3H,5H-thiazolo[3,4-*c*]thiazol-3-one (15).* A mixture of **5g** (3.43 g, 20 mmol), Et_3N (8.1 g, 80 mmol), trichloromethyl chloroformate (5.94 g, 30 mmol), and MeCN (100 ml) was refluxed for 5 h. The residue obtained upon evaporation of the solvent was refluxed with diglyme (100 ml) for 48 h. After removal of the solvent under reduced pressure, the material was dissolved in CH_2Cl_2 and washed with brine and H_2O . The crude product from the org. layer was purified by chromatography over silica gel with Et_2O and yielded, after bulb-to-bulb distillation, **15** (750 mg, 23.3%), b.p. 105–110°/0.03 Torr. IR (film): 1675. $^1\text{H-NMR}$ (80 MHz, CDCl_3): 2.83 (*dd*, $J_{\text{gem}} = J_{\text{vic}} = 10$, H–C(1) or H–C(7)); 3.05 (*dd*, $J_{\text{gem}} = 10$, $J_{\text{vic}} = 6$, H–C(1) or H–C(7)); 3.23 (*dd*, $J_{\text{gem}} = 11.5$, $J_{\text{vic}} = 2.5$, H–C(1) or H–C(7)); 3.68 (*dd*, $J_{\text{gem}} = 11.5$, $J_{\text{vic}} = 7.5$, H–C(1) or H–C(7)); 4.14 (*m*, $\Sigma J = 26$ H–C(7a)); 4.04, 4.96 (*2d*, $J = 9.0$, $\text{H}_2\text{C}(5)$). MS: 161 (100, M^+), 120 (10), 115 (35), 86 (38), 72 (8), 60 (20), 55 (51), 54 (10), 46 (18), 45 (26), 41 (20), 39 (9), 29 (8). Anal. calc. for $\text{C}_5\text{H}_7\text{NOS}_2$ (161.24): C 37.25, H 4.38, N 8.69, S 39.77; found: C 37.34, H 4.49, N 8.59, S 39.29.

27. *Equilibration Experiments with 7 and 8.* a) With Et_3N . Pure **7f** and pure **8f** were refluxed for 2 h in MeCN with an excess of Et_3N . After evaporation *i.v.*, the composition of the residues was estimated by TLC. In both cases a **7f/8f** ratio of 3:7 was found. The compounds **7d**, **7e**, **8d**, and **8e** were not changed under the above conditions.

b) With $\text{Et}_3\text{N} \cdot \text{HCl}$. A mixture of **8d** (100 mg, 0.34 mmol), $\text{Et}_3\text{N} \cdot \text{HCl}$ (53.2 mg, 0.39 mmol), and MeCN (2 ml) was refluxed for 72 h. After the usual workup, 97.1 mg (97.1%) of **8d**, in every respect identical with an authentic sample, was reisolated.

c) With NaOMe. Pure **7d** and pure **8d** (60 mg, 0.2 mmol) were refluxed for 24 h with NaOMe (10.8 mg, 0.2 mmol). After the usual workup, mixtures of **7d** and **8d** (84%) were isolated. In both cases, a **7d/8d** ratio of 2.5:7.5 was estimated by $^1\text{H-NMR}$ (90 MHz).

28. *Equilibration Experiments with 9 and 10.* a) With Strong Bases. Pure **9** or **10** or mixtures of both (0.1 or 0.2 mmol) were stirred under Ar with base (0.02 mmol or 0.04 mmol of NaOMe or sodium 2-methyl-2-butoxide ($\text{Na}[\text{O}i\text{Bu}(\text{Me})]$)) in DMSO (0.5 ml) at 20, 50, and 80° for 2 to 12 days. The reaction was monitored by TLC (comparison with authentic samples). After workup with $\text{H}_2\text{O}/\text{Et}_2\text{O}$ or $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2$, the crude products were obtained in almost quantitative yield. The **9/10** ratio was estimated by $^1\text{H-NMR}$ (80 or 90 MHz). The results are compiled in Table 4.

b) With $\text{Et}_3\text{N} \cdot \text{HCl}$. A mixture of **10d** (50.1 mg, 0.2 mmol), $\text{Et}_3\text{N} \cdot \text{HCl}$ (30.3 mg, 0.22 mmol), and MeCN (2 ml) was refluxed for 72 h, and 47.3 mg (94.5%) of **10d** contaminated with a small trace of **9d** were reisolated.

Table 4. *Equilibration Experiments with 9 and 10*

Type	Educts [%]		Base	Temperature [°C]	Reaction time [days]	Products [%]	
	9	10				9	10
d	—	100	NaOMe	20	2	95	5
	100	—	NaOMe	20	12	98	2
e	10	90	NaOMe	20	2	> 95	< 5
f	—	100	NaOMe	80	4	35	65
	—	100	Na[OBu(Me)]	20	4		100
	—	100	Na[OBu(Me)]	80	4	40	60
	100	—	Na[OBu(Me)]	80	4	100	

REFERENCES

- [1] A. Lüttringhaus & H. Prinzbach, *Justus Liebigs Ann. Chem.* 624, 79 (1959).
- [2] A. Williams & I. I. Ibrahim, *Chem. Rev.* 81, 589 (1981).
- [3] R. Appel, R. Kleinstück & K. D. Ziehn, *Chem. Ber.* 104, 1335 (1971).
- [4] H. Ulrich & A. A. Sayigh, *Angew. Chem.* 78, 761 (1966).
- [5] T. Shibanuma, M. Shiono & T. Mukaiyama, *Chem. Lett.* 1977, 575.
- [6] G. M. Sheldrick, University of Göttingen, SHELXT 3.0 (1981).
- [7] A. Thalen & G. Claeson, *Arkiv Kem.* 24, 463 (1965); *Chem. Abstr.* 63, 18061 (1965).
- [8] R. Paul, J. Menschik & B. L. Walworth (*American Cyanamid Co.*), *Ger. Offen.* 2804435 (17.8.1978).