Fused 1,2-Dithioles

Part VII

Synthesis and Reactions of 4*H*-1,2-Dithiolo[4,3-*c*]isothiazoles

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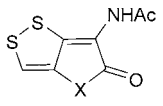
Dedicated to Professor *Rolf Huisgen* on the occasion of his 85th birthday

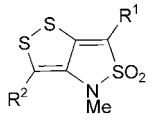
The 1,2-dithiolosultam derivative **14** was obtained from the (α-bromoalkylidene)propenesultam derivative **9** (*Scheme 1*). Regioselective cleavage of the two ester groups ($\rightarrow$ **1b** or **2b**) allowed the preparation of derivatives with different substituents at C(3) in the dithiole ring (see **27** and **28**) as well as at C(6) in the isothiazole ring (see **17**–**21**; *Scheme 2*). *Curtius* rearrangement of the 6-carbonyl azide **21** in Ac_2O afforded the 6-acetamide **22**, and saponification and decarboxylation of the latter yielded 'sulfothiolutin' (**30**). Hydride reductions of two of the bicyclic sultams resulted in ring opening of the sultam ring and loss of the sulfonyl group. Thus the reduction of the dithiolosultam derivative **14** yielded the alkylidenethiotetronic acid derivative **33** (tetronic acid = furan-2,4(3*H*,4*H*)-dione), and the lactam-sultam derivative **10** gave the alkylidenetetramic acid derivative **35** (tetramic acid = 1,5-dihydro-4-hydroxy-2*H*-pyrrol-2-one) (*Scheme 3*). Some of the new compounds (**14**, **22**, **26**, and **30**) exhibited antimycobacterial activity. The oxidative addition of 1 equiv. of [Pt(η^2-C_2H_4)L_2] (**36a**, L = PPh_3; **36b**, L = 1/2 dppf; **36c**, L = 1/2 (*R,R*)-diop) into the S–S bond of **14** led to the *cis*-(dithiolato)platinum(II) complexes **37a**–**c**. (dppf = 1,1′-bis(diphenylphosphino)ferrocene; (*R,R*)-diop = {[(4*R*,5*R*)-2,2-demithyl-1,3-dioxolane-4,5-diyl]bis(methylene)}bis[diphenylphosphine]).

Introduction. – The commercially available antibiotic thiolutin (=acetopyrrothin; **1a**) [1] was found to suppress tumor-induced angiogenesis and may be of value in tumor therapy [2]. Thiolutin has been synthesized by several working groups [3–5]. Recently, we have reported the synthesis and reactions of S- and O-analogs **1b**,**c** of thiolutin and derivatives therefrom [6][7]. Biological testing has shown high antimycobacterial activities in some of these compounds [8]. We describe here the synthesis and some reactions of 4*H*-1,2-dithiolo[4,3-*c*]isothiazoles of the general formula **2** which represent sulfonyl analogs of bicyclic lactams to which thiolutin (**1a**) belongs. Hence the sulfonyl analog **30** of thiolutin may be called 'sulfothiolutin'.

Results and Discussion. – The synthesis started from the (sulfonylamino)but-2-enedioate **3** which was prepared by acid-catalyzed condensation of dimethyl oxaloacetate (=dimethyl oxobutanedioate) and methyl (aminosulfonyl)acetate upon



1a X = NMe
b X = S
c X = O



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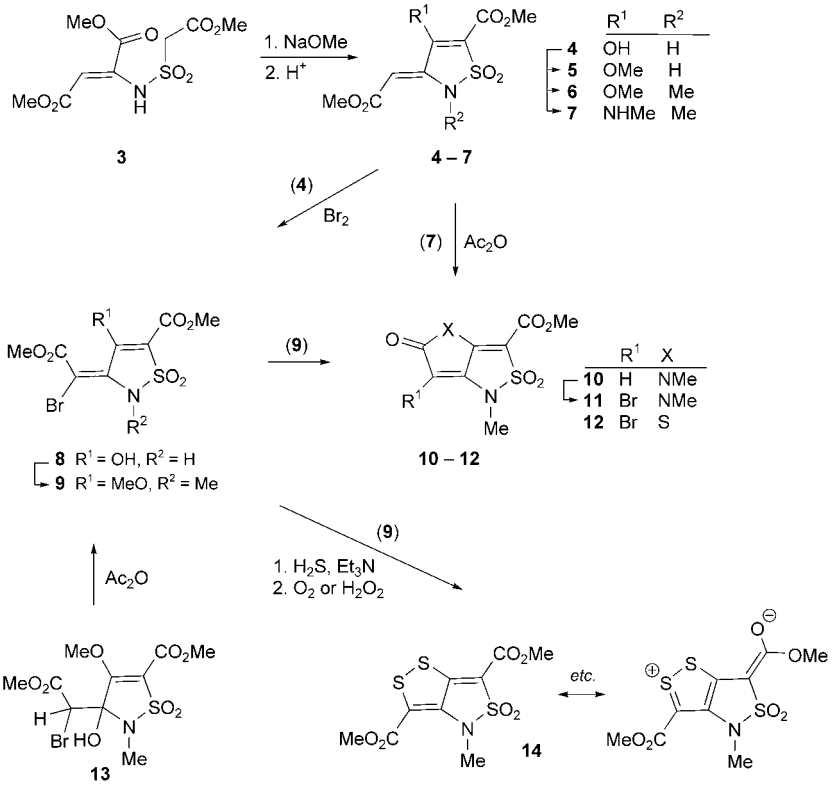
heating under a water trap. Compound **3** formed a monosodium salt which reacted in the presence of another equiv. of MeONa to give the disodium salt of the alkylidenepropenesultam derivative **4** in good yield (*Scheme 1*). There was no sign of a competitive internal *Dieckmann* condensation leading to an isomeric six-membered sultam. The five-membered-ring structure of compound **4** follows from the fact that stereoisomers appeared in the course of bromination of **4** as described below. The IR spectrum of compound **4** showed two ester carbonyl bands at 1685 and 1680 cm^{-1} indicating H-bridging of both esters on account of the (*Z*)-configuration of the side-chain. According to the ^{1}H-NMR spectrum ($CDCl_3$), **4** exists completely as an enol (H/D exchange of oldefinic H at δ(H) 5.47 ppm). This is an indication of the high polarity of the exocyclic C=C bond and its readiness to react with electrophiles. Heating of **4** with excess orthoformic acid methyl ester yielded the enol ether derivative **5**, whereas heating of **4** with orthocarbonic acid methyl ester gave the *N*-methylated enol ether derivative **6** in good yield. The same compound **6** was obtained upon reaction of **4** or **5** with diazomethane in practically quantitative yield. NOE Experiments with the alkylidenepropenesultam derivative **6** (correlation olefinic H/MeO) established the (*Z*)-configuration of the exocyclic C=C bond as well as that of its precursors **4** and **5**. In the ^{1}H-NMR spectra of both **5** and **6**, again H/D exchange of the olefinic proton with D_2O was observed. Nucleophilic substitution with $MeNH_2$ transformed **6** into enamine derivative **7**. Prolonged heating of **7** in Ac_2O caused isomerization into the (*E*)-isomer followed by cyclization to give the bicyclic compound **10**.

Compound **4** reacted with Br_2 to give the sultam derivative **8** but only in poor yield. (*Z*)-Configuration of this compound was deduced from its spectra (IR: 1685 and 1715 cm^{-1} for chelated and nonchelated ester) and from its methylation with diazomethane affording **9** as a sterically uniform compound. The (*Z*)-configuration of **9** was supported by the reaction with $MeNH_2$ leading exclusively to the pyrroloisothiazole derivative **11** which was also obtained by bromination of **10**. In the ^{1}H-NMR spectrum of **11**, the Br-atom caused a downfield shift of the signal of the neighboring MeN group.

To prepare the brominated enol ether derivative **9** in a better overall yield, the bromination was carried out in two steps *via* the bromohydrin **13**. The latter was obtained in good yield by the reaction of enol ether derivative **6** and *N*-bromosuccinimide (NBS) in aqueous acetone. The ^{1}H-NMR spectrum of **13** showed two sets of signals in a ratio of 1:4, indicating the presence of both diastereoisomers. However, acid-catalyzed dehydration of **13** with Ac_2O afforded (*Z*)-enol ether derivative **9** with

Scheme 1



only small amounts of its (*E*)-stereoisomer, which was easily distinguished in the NMR spectra (MeN signal of (*Z*)-downfield shifted by $\Delta\delta = 0.6$ due to the Br-atom).

Treatment of **9** with excess of hydrogen sulfide in the presence of Et_3N caused nucleophilic displacement of both the MeO group and the Br-atom by SH. The intermediate red dithiolate could not be isolated in pure form because of its ready oxidation in air. During prolonged stirring of the red solution exposed to air, the sparely soluble yellow dithioloisothiazole derivative **14** deposited. Oxidation of the intermediate was completed by addition of I_2 to reach a yield of *ca.* 35% of **14**. An intermediate of the sulfuration of **9** is probably the bicyclic thiolactone **12** which was isolated in low yield from the reaction of **9** with 1 equiv. of sodium sulfide.

The structure of **14** was established by single-crystal X-ray analysis (*Fig.*). Selected bond lengths and bond angles are given in the *Table.* The molecule is planar as anticipated. The bond lengths of the heterocyclic C-atoms distinctly alternate between C=C and C–C bonds. However, the formal double bonds C(2)=C(3) and C(4)=C(5) are extended to *ca.* 136 pm and the formal single bond C(3)–C(4) is shortened to 144.8 pm. The distance between S(1) and S(2) is in the usual range for cyclic disulfides [9] but the S(2)–C(4) bond (170.1 pm) is considerable shorter than the S(1)–C(2)

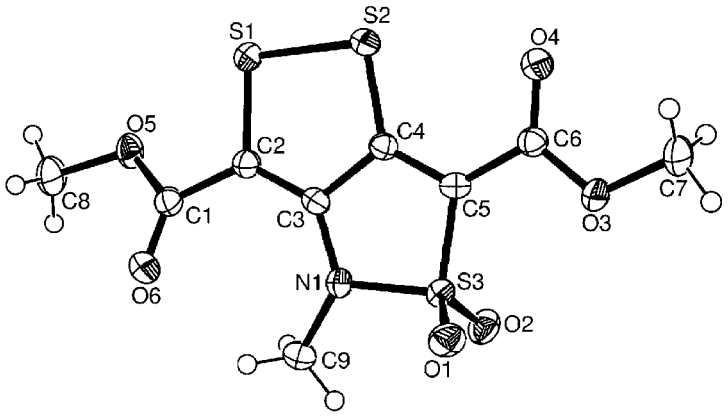


Figure. *Molecular structure of* **14** *with thermal ellipsoids at the 50% probability level.* Arbitrary numbering.

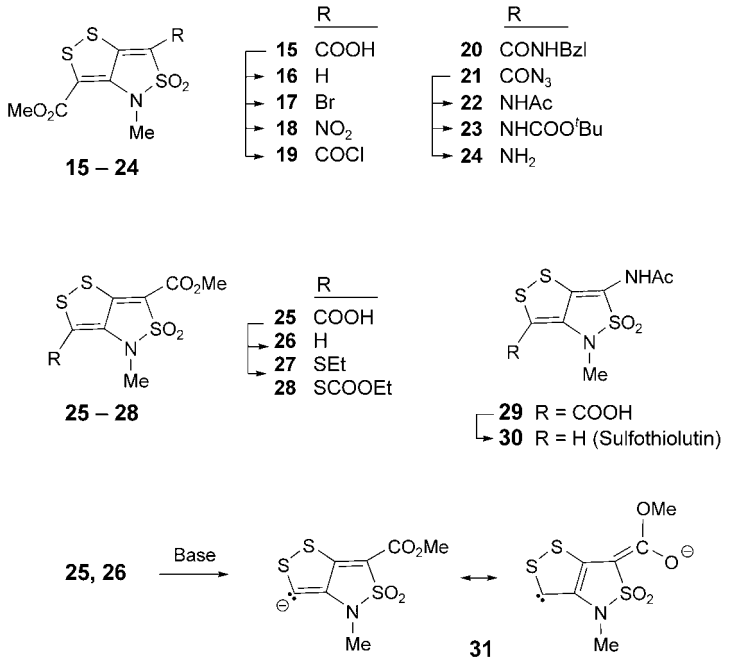
Table. *Selected Bond Distances* [pm] *and Bond Angles* [°] *of* **14**. For atom numbering, see *Figure*.

Bond distances			
S(1)–S(2)	206.8(1)	C(1)-C(2)	148.7(3)
S(1)–C(2)	174.9(2)	C(5)–C(6)	145.5(3)
S(2)–C(4)	170.1(2)	C(1)–O(6)	119.9(3)
S(3)–C(5)	173.3(2)	C(6)–O(4)	121.3(3)
C(2)–C(3)	136.3(3)	C(3)–N(1)	138.8(3)
C(3)–C(4)	144.8(3)	C(9)–N(1)	145.3(3)
C(4)–C(5)	135.9(3)	N(1)–S(3)	168.6(2)
Bond angles			
S(2)–S(1)–C(2)	95.35(8)	S(3)–C(5)–C(4)	109.25(18)
S(1)–S(2)–C(4)	95.05(8)	N(1)–S(3)–C(5)	93.61(11)
C(3)–C(4)–C(5)	114.8(2)	S(3)–N(1)–C(3)	112.26(16)
C(2)–C(3)–C(4)	115.9(2)	S(3)–C(5)–C(6)	126.72(18)

bond (174.9 pm). The usual C–S distance is 174 pm [10]. The C(5)–C(6) bond is shorter than the formally identical C(2)–C(1) bond, and the C–O distance of the C=O bonds is different in both ester groups. These data suggest that the stability of the dithiole system **14** is due to resonance which may adequately be expressed by a zwitterionic resonance formula.

The two carboxylate groups of **14** could be cleaved selectively. Upon treatment of the diester **14** with BBr_3 in CH_2Cl_2, the 6-carboxylic acid **15** was obtained, which was readily decarboxylated in refluxing nitromethane (*Scheme 2*). The formed 6-unsubstituted dithioloisothiazole derivative **16** easily underwent electrophilic substitution reactions. Thus decarboxylation in the presence of Br_2 yielded the 6-bromo derivative **17**. Analogously, decarboxylative nitration led to the 6-nitro derivative **18** which was also obtained from **17** and nitric acid by *ipso* substitution. Compound **18** could not be reduced to the amino compound **24**. Some remarks regarding the behavior of dithioloisothiazoles against reductive agents will be given below.

Scheme 2



Carboxylic acid **15** was derivatized by a number of textbook reactions. With phosphorus pentachloride, **15** was converted into the well-crystallizing acid chloride **19** from which we obtained the *N*-benzylamide **20**, and the azide **21** (*Scheme 2*). Heating of the latter in Ac_2O furnished acetamide **22** *via Curtius* rearrangement. Carrying out the thermal rearrangement of azide **21** in ^{t}BuOH yielded the carbamate **23,** which was thermically converted into the amine **24**.

The ester function in 3-position of **14** could be saponified by aqueous alkali. However, upon acidification, only small amounts of acid **25** were obtained; the main product was the 3-unsubstituted derivative **26** [11] (*Scheme 2*). The formation of **26** cannot be attributed to thermal decarboxylation of acid **25** because the latter proved thermally stable up to 120°. Thus **26** must be formed by decarboxylation of the anion of acid **25**, the driving force for this unusual reaction being the formation of the intermediate resonance-stabilized carbenoid anion **31** which also should be generated from **26** with suitable bases. In fact, **26** reacted in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) with sulfur to form an ammonium thiolate which yielded the thioether derivative **27** after addition of EtI. Reactions with S_8 are typical of nucleophilic carbenes [12]. A comparable reaction is the introduction of a mercapto group into 3-thioxo-1,2-dithiole-4-carboxylic acid methyl ester by sulfur in the presence of NaH [13]; in the ^{1}H-NMR spectrum of the starting dithiolecarboxylic acide, the reactive H–C(3) gave a signal at δ(H) 9.19 (DMSO). Similarly, the equally reactive olefinic proton in compound **26** exhibited a signal at δ(H) 7.71 (DMSO). The chemical

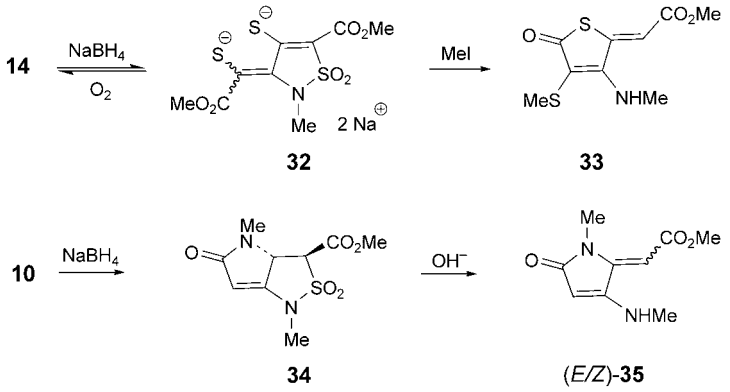
shift depends strongly on the polarity of the solvent. In $CDCl_3$, the olefinic proton of **26** gave a signal at δ(H) 6.66.

Another pathway to S-substituted derivatives of **26** was its reaction with ethoxyoxomethanesulfenyl chloride in the presence of weak bases which gave the thiocarbonate **28**.

Alkaline saponification of the ester group of acetamide **22** afforded the carboxylic acid **29**. In this case, no decarboxylation of the salt was observed because of absence of anion-stabilizing substituents. The acid decarboxylated upon refluxing its solution at 100° to yield amide **30**, *i.e.*, 'sulfothiolutin', the sulfonyl analogy of thiolutin. The ^{1}H-NMR spectrum ((D_6)DMSO) of **30** showed the olefinic proton at δ(H) 6.85 (thiolutin: δ(H) 7.33).

Reduction of compound **14** with $NaBH_4$ proceeded with cleavage of the disulfide bridge. From the violet solution of the resulting dithiolate **32** (not isolated), **14** was regenerated by air oxidation in up to 20% yield (*Scheme 3*). The remaining yellow solution contained, according to TLC, numerous substances. One of these was identified by derivatization with MeI yielding the thiolactone derivative **33**. Remarkably, the sulfonyl group of the sultam derivative **14** was lost during the reduction, presumably as a sulfite ion.

Scheme 3

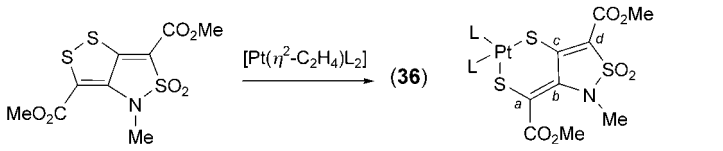


The same course took the reduction of the bicyclic sultam derivative **10**, leading to the lactam derivative **35** as a mixture of (*E*)/(*Z*)-isomers ((*E*)-isomer predominant) (*Scheme 3*). In this case, however, with two equiv. of $NaBH_4$, the primary hydrogenation product was isolated and identified by spectroscopic means as the bicyclic sultam derivative **34**. The hydrogenation had taken place only at the C=C bond of the isothiazole moiety. NOE Experiments showed the correlation Me–N(4)/H–C(3a). The latter coupled with H–C(3) ($J = 10.2$ Hz), and the signal for H–C(3) disappeared upon H/D-exchange. Upon addition of alkali, **34** was converted into the tetramic acid derivative **35** (tetramic acid = 1,5-dihydro-4-hydroxy-2*H*-pyrrol-2-one).

The preliminary testing of the new compounds for bioactivity has shown that the sultams **14**, **22**, **26**, and **30** exhibit antimycobacterial activities comparable to their lactam analogs [8][11][14].

In previous work [15], we have demonstrated extensively that N–S(O) as well as S–S(O)$_n$ ($n = 0, 1, 2$) bonds react with Pt^0 complexes [Pt(η^2-C_2H_4)(PR_3)$_2$] *via* oxidative addition to yield (sulfenato)(amido)- as well as (dithiolato)-, (sulfenato)(thiolato)-, and (sulfinato)(thiolato)platinum(II) complexes, respectively. In this paper, we were interested to study reactions of Pt^0 complexes [Pt(η^2-C_2H_4)L_2] (**36a**, L = PPh_3; **36b**, L = 1/2 dppf; **36c**, L = 1/2 (*R*,*R*)-diop)[1]) with compounds containing both a disulfide and a sulfonamido N–S(O)$_2$ group. Reactions of mixtures of a platinum(0) complex **36** with sultam **14** in toluene at room temperature under an inert atmosphere afforded the dithiolato complexes **37** after workup (*Scheme 4*). No insertion reaction of the Pt^0 in to the N–S(O)$_2$ bond was observed, even if the reaction mixture was heated up to 70° for several hours. Only decomposition of the starting material accompanied with the formation of triphenylphosphine sulfide was detected. The *cis*-configured complexes **37a–c** were characterized and their structures established by spectroscopic data (IR, ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra) and elemental analysis. The NMR data show that probably no zwitterionic resonance formulae must be formulated for **37a–c**, such as those postulated for **14**. In the IR spectra of **37a–c**, the medium to strong $\tilde{\nu}_{as}(SO_2)$ bands (1303–1312 cm^{-1}) and $\tilde{\nu}_s(SO_2)$ bands (1151–1183 cm^{-1}) were assigned to the intact sulfonamide group. This is also an important evidence that the Pt^0 inserted exclusively into the S–S bond of **14**, *via* an oxidative addition resulting in dithiolato complexes.

Scheme 4



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37a L = PPh_3
b L = $[dppf]_{1/2}$[1])
c L = $[(R,R)\text{-diop}]_{1/2}$[1])

The ^{31}P-NMR spectra of **37a–c** show the typical *AB* pattern expected for two chemically nonequivalent *cis*-positioned phosphine moieties with two '*d*' (^2J(P,P) = 29.3–33.1) and ^{195}Pt satellites (^1J(Pt,P) = 2819–3078 Hz). The similar values for the ^1J(Pt,P) coupling constants indicate that the Pt-atom inserted into the S–S bond rather than into the N–SO_2. Coordinated amido ligands *trans* to a phosphine would lead to a much higher ^1J(Pt,P) due to their weaker *trans*-influence compared with that of thiolato groups. In the ^{1}H-NMR spectra of **37a–c**, the MeN signals are shifted upfield by 0.6 ppm compared with that of **14**. Moreover, the ^{13}C-NMR spectra display resonances for the C_a-atoms which were shifted upfield by *ca.* 4 ppm compared to that of **14**. In contrast, remarkable downfield shifts of *ca.* 7 and 14 ppm are observed for the C_c- and C_d-atoms, respectively.

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[1]) Abbreviations: dppf = 1,1′-bis(diphenylphosphino)ferrocene, diop = 4,5-bis[(diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolane = [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis[diphenylphosphine].

Experimental Part

General. Flash chromatography (FC): 250-ml column (*Baker*), silica gel (0.040–0.063 mm; *Merck*). M.p.: *Büchi* melting-point apparatus; uncorrected. IR Spectra: *Perkin-Elmer Paragon 1000*; KBr pellets; in cm^{-1}. UV/VIS Spectra: *Kontron Uvikon-810 Anakomp-220* or *Perkin-Elmer Lambda-20*; λ_{max} in nm (log ε); in MeOH soln., unless stated otherwise. NMR Spectra: *Jeol GSX-400* (^1H), *Jeol EX-400* (^{13}C), and *Jeol GSX-270* (^{31}P); δ in ppm rel. to Me_4Si as internal standard (^1H,^{13}C) or to 85% aq. H_3PO_4 soln. as external standard (^{31}P), *J* in Hz; solvent: *A* = (D_6)DMSO, *B* = $CDCl_3$, unless indicated otherwise. MS: *Hewlett-Packard 5989A*; 70 eV. Elemental analysis: *Heraeus CHNO-Rapid* analyzer or carried out by *I. Beetz*, *Mikroanalytisches Laboratorium*, Kronach, Germany.

Dimethyl 2-{{[(Methoxycarbonyl)methyl]sulfonyl]}amino}but-2-enedioate (**3**). A soln. of methyl sulfamoylacetate (= methyl (aminosulfonyl)acetate) [16] (1.53 g, 10 mmol), dimethyl oxobutanedioate [17] (1.60 g, 10 mmol) and TsOH (0.35 g, 2 mmol) in benzene (70 ml) was heated to reflux under a water trap for 3 d. The solvent was evaporated and the residue crystallized from MeOH: 1.85 g (63%) of **3**. Colorless crystals. M.p. 98°. UV: 259 (3.981). IR: 3220, 3000, 2955, 1755, 1725, 1685. ^1H-NMR (*B*): 10.18 (*s*, 1 H, exchange with D_2O); 5.80 (*s*, 1 H); 4.50 (*s*, 2 H); 3.83 (*s*, 3 H); 3.77 (*s*, 3 H); 3.73 (*s*, 3 H). MS: 295 (M^+). Anal. calc. for $C_9H_{13}NO_8S$ (295.27): C 36.61, H 4.38, N 4.74, S 10.86; found: C 36.67, H 4.42, N 4.56, S 10.96.

Methyl (3Z)-2,3-Dihydro-4-hydroxy-3-[(methoxycarbonyl)methylene]isothiazole-5-carboxylate 1,1-Dioxide (**4**). Compound **3** (2.95 g, 10 mmol) was added slowly to a soln. of Na (0.46 g, 20 mmol) in dry MeOH (50 ml) and stirred at r.t. for 30 min. The precipitate was isolated. Its aq. soln. was acidified with dil. HCl soln. while cooling. The colorless precipitate was collected and crystallized from MeOH: 2.27 g (87%) of **4**. M.p. 250° (dec.). UV: 213 (4.011), 286 (4.255). IR: 3260, 1685, 1635, 1615. ^1H-NMR (*B*): 11.5 (*s*, 2 H, exchange with D_2O); 5.47 (*s*, 1 H, exchange with D_2O); 3.72 (*s*, 6 H). MS: 263 (M^+). Anal. calc. for $C_8H_9NO_7S$ (263.23): C 36.50, H 3.45, N 5.32, S 12.18; found: C 36.44, H 3.40, N 5.09, S 12.18.

Methyl (3Z)-2,3-Dihydro-4-methoxy-3-[(methoxycarbonyl)methylene]isothiazole-5-carboxylate 2,2-Dioxide (**5**). A soln. of **4** (0.52 g , 2 mmol) in trimethyl orthoformiate (30 ml) was heated to reflux for 2 h. The volatiles were evaporated, and the residue was crystallized from MeOH: 0.31 g (56%) of **5**. Yellowish crystals. M.p. 182°. UV: 285 (4.160), 213 (3.991). IR: 3260, 2965, 1723, 1675, 1655, 1615: ^1H-NMR (*A*): 5.62 (*s*, 1 H, exchange with D_2O); 4.27 (*s*, 3 H); 3.90 (*s*, 3 H); 3.73 (*s*, 3 H). MS: 277 (M^+). Anal. calc. for $C_9H_{11}NO_7S$ (277.25): C 38.99, H 4.00, N 5.05, S 11.66; found: C 38.99, H 3.91, N 5.10 , S 11.47.

Methyl (3Z)-2,3-Dihydro-4-methoxy-3-[(methoxycarbonyl)methylene]-2-methylisothiazole-5-carboxylate 1,1-Dioxide (**6**). *a*) An Et_2O soln. of CH_2N_2 (excess) was added at 0° to a stirred suspension of **4** (2.63 g, 10 mmol) in Et_2O (20 ml) (→ clear soln.). After evaporation of the volatiles, **6** was obtained in nearly quant. yield.

b) Compound **4** (0.52 g, 2 mmol) was heated with tetramethyl orthocarbonate (10 ml) to reflux for 15 min. The volatiles were evaporated, and the residue was crystallized: 0.32 g (55%) of **6**. Colorless crystals. M.p. 171° (MeCN). UV: 209 (3.996), 286 (4.166). IR: 3020, 2970, 1720, 1705, 1640, 1610. ^1H-NMR (*B*): 5.83 (*s*, 1 H): 4.33 (*s*, 3 H); 3.97 (*s*, 3 H); 3.77 (*s*, 3 H); 3.37 (*s*, 3 H). ^1H-NMR (*A*): 5.9 (*s*, 1 H, exchange with D_2O); 4.3 (*s*, 3 H); 3.93 (*s*, 3 H); 3.77 (*s*, 3 H); 3.22 (*s*, 3 H). MS: 291 (M^+). Anal. calc. for $C_{10}H_{13}NO_7S$ (291.28): C 41.24, H 4.50, N 4.81, S 11.01; found: C 41.41, H 4.49, N 4.80, S 11.02.

Methyl (3Z)-2,3-Dihydro-3-[(methoxycarbonyl)methylene]-2-methyl-4-(methylamino)isothiazole-5-carboxylate 1,1-Dioxide (**7**). A 40% aq. $MeNH_2$ soln. (5 ml) was added to a stirred soln. of compound **6** (2.91 g, (10 mmol) in EtOH (15 ml). The immediately appearing precipitate was collected and crystallized from MeOH: 2.55 g (88%) of **7**. Yellowish crystals. M.p. 170°. UV: 219 (3.990), 297 (4.166). IR: 3251, 2950, 1720, 1675, 1610. ^1H-NMR (*B*): 8.65 (*m*, 1 H, exchange with D_2O); 5.82 (*s*, 1 H); 3.93 (*s*, 3 H); 3.83 (*s*, 3 H); 3.35 (*d*, *J* = 6.1, *s* after exchange with D_2O); 3.25 (*s*, 3 H). MS: 290 (M^+). Anal. calc. for: $C_{10}H_{14}N_2O_6S$ (290.29): C 41.38, H 4.86, N 9.65, S 11.04; found: C 41.09, H 4.95, N 9.59, S 11.12.

Methyl (3Z)-3-[Bromo(methoxycarbonyl)methylene]-2,3-dihydro-4-hydroxy-2-methylisothiazole-5-carboxylate 1,1-Dioxide (**8**). To a soln. of **4** (0.26 g. 1 mmol) in AcOH (10 ml), Br_2 (0.2 ml) was added. After stirring for 3 h at r.t., the precipitate was collected and recrystallized from AcOH: 0.28 g (82%) of **8**. Colorless crystals. M.p. 220°. UV: 261 (3.996). IR: 3210, 1717, 1671, 1654, 1325, 1173. ^1H-NMR (*A*): 8.29 (*s*, 1 H, exchange with D_2O); 5.92 (*s*, 1 H, exchange with D_2O); 3.70 (*s*, 3 H); 3.56 (*s*, 3 H). MS: 341, 343 (M^+). Anal. calc. for $C_8H_8BrNO_7S$ (342.12): C 28.09, H 2.36, N 4.09, S 9.37, Br 23.36; found: C 27.84, H 2.42, N 4.08, S 9.53, Br 23.49.

Methyl (3Z)-3-[Bromo(methoxycarbonyl)methylene]-2,3-dihydro-4-methoxy-2-methylisothiazole-5-carboxylate 1,1 Dioxide (**9**). A soln. of **13** (3.88 g, 10 mmol) in Ac_2O (50 ml) was stirred for 30 min at r.t. after addition of 2 drops of conc. H_2SO_4 soln. The volatiles were evaporated and the residue was crystallized from

MeOH: 3.40 g (92%) of **9**. Colorless crystals. M.p. 117°. UV: 288 (4.109). IR: 2950, 1720, 1630, 1605. ^{1}H-NMR (*B*): 4.20 (*s*, 3 H); 4.00 (*s*, 3 H); 3.9 (*s*, 3 H); 3.4 (*s*, 3 H). MS: 369, 371 (M^+). Anal. calc. for $C_{10}H_{12}BrNO_7S$ (370.17): C 32.45, H 3.27, Br 21.59, N 3.78, S 8.66; found: C 32.48, H 3.29, Br 21.63, N 3.88, S 8.68.

*Methyl 4,5-Dihydro-1,4-Dimethyl-5-oxo-1*H*-pyrrolo[3,2-*c*]isothiazole-3-carboxylate 2,2-Dioxide* (**10**). A soln. of **7** (2.9 g, (10 mmol) in Ac_2O (50 ml) was heated for 30 min to 100° after addition of 2 drops of conc. H_2SO_4 soln. After cooling to r.t., the volatiles were evaporated. The residue was purified by FC (1. CH_2Cl_2, 2. $CHCl_3$/AcOEt 1:1): 1.65 g (65%) of **10**. Yellow crystals. M.p. 170° (MeOH). UV: 210 (3.821), 290 (4.362). IR: 3120, 2950, 1730, 1630. ^{1}H-NMR (*B*): 5.07 (*s*, 1 H); 4.00 (*s*, 3 H); 3.52 (*s*, 3 H); 3.27 (*s*, 3 H). MS: 258 (M^+). Anal. calc. for $C_9H_{10}N_2O_5S$ (258.25): C 41.85, H 3.90, N 10.85, S 12.41; found: C 41.96, H 3.97, N 10.80, S 12.44.

*Methyl 6-Bromo-4,5-dihydro-1,4-dimethyl-5-oxo-1*H*-pyrrolo[3,2-*c*]isothiazole-3-carboxylate 2,2-Dioxide* (**11**). A 40% aq. $MeNH_2$ soln. (5 ml) was added to a stirred soln. of **9** (3.7 g, 10 mmol) in MeOH (15 ml). The immediately appearing precipitate was collected and recrystallized from MeOH: 3.1 g (92%) of **11**. Yellow crystals. M.p. 205°. UV: 209 (3.922), 296 (4.282). IR: 2965, 1750, 1730, 1680, 1640. ^{1}H-NMR (*B*): 3.98 (*s*, 3 H); 3.55 (*s*, 3 H); 3.47 (*s*, 3 H). MS: 336, 338 (M^+). Anal. calc. for $C_9H_9BrN_2O_5S$ (337.15): C 32.06, H 2.69, Br 23.70, N 8.31, S 9.51; found: C 31.98, H 2.71, Br 23.74, N 8.20, S 9.36.

*Methyl 6-Bromo-1,5-dihydro-1-methyl-5-oxothieno[3,2-*c*]isothiazole-3-carboxylate 2,2-Dioxide* (**12**). A soln. of **9** (1.85 g, 5 mmol) in MeOH (30 ml) was cooled to −15°. Under stirring, $Na_2S \cdot 9\,H_2O$ (1.2 g, 5 mmol) was added portionwise. After 15 min, the solvent was evaporated and the residue extracted twice with $CHCl_3$. The soln. was purified by FC ($CHCl_3$): 0.43 g (25%) of **12**. Orange crystals. M.p. 151° (Et_2O). UV: 223 (3.833), 306 (4.406). IR: 1710, 1630, 1605. ^{1}H-NMR (*B*): 4.05 (*s*, 3 H), 3.63 (*s*, 3 H). MS: 339, 341 (M^+). Anal. calc. for $C_8H_6BrNO_5S_2$ (340.17): C 28.25, H 1.78, Br 23.49, N 4.12, S 18.85; found: C 28.26, H 1.91, Br 23.09, N 4.26, S 18.87.

Methyl α-Bromo-2,3-dihydro-3-hydroxy-4-methoxy-5-(methoxycarbonyl)-2-methylisothiazole-3-acetate 1,1 Dioxide (**13**). A soln. of **6** (2.91 g, 10 mmol) in acetone (20 ml) and H_2O (60 ml) was stirred at r.t. for 30 min, after addition of *N*-bromosuccinimide (1.78 g, 10 mmol). The acetone was evaporated, the remaining aq. soln. extracted twice with CH_2Cl_2, the org. phase dried (Na_2SO_4) and evaporated, and the residue recrystallized from Et_2O: 3.22 g (83%) of **13**. Colorless crystals. M.p. 144°. UV: 234 (3.907). IR: 3415, 3010, 2960, 1725, 1640. ^{1}H-NMR (*B*): 5.28 (*s*, 1 H, exchange with D_2O); 4.78 (*s*, 1 H); 4.35 (*s*, 3 H); 3.95 (*s*, 3 H); 3.88 (*s*, 3 H). MS: 387, 389 (M^+). Anal. calc. for $C_{10}H_{14}BrNO_8S$ (388.19): C 30.94, H 3.64, Br 20.58, N 3.61, S 8.26; found: C 30.60, H 3.53, Br 20.96, N 3.71, S 8.37.

*Dimethyl 4-Methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3,6-dicarboxylate 5,5-Dioxide* (**14**). A stirred soln. of **9** (3.70 g, 10 mmol) and Et_3N (4 ml, 29 mmol) in MeOH (50 ml) was saturated with H_2S during 10 min. After further vigorous stirring in contact with the air for 15 h, a yellow precipitate had formed. The precipitate was collected and recrystallized: 1.04 g (32%) of **14**. Yellow crystals. M.p. 202° (AcOEt/^{i}Pr$_2$O). UV: 212 (3.798), 247 (3.572), 410 (4.009), 429 (4.039). IR: 1728, 1700, 1666, 1580, 1321, 1178. ^{1}H-NMR (*B*): 3.97 (*s*, 3 H); 3.94 (*s*, 3 H); 3.57 (*s*, 3 H). ^{13}C-NMR (B): 161.0, 158.9 (COOMe); 160.9 (C(6a)); 135.6 (C(3a)); 116.4, 109.9 (C(6), C(3)); 53.4 (MeO); 30.6 (MeN). MS: 323 (M^+). Anal. calc. for $C_9H_9NO_6S_3$ (323.37): C 33.43, H 2.81, N 4.33, S 29.74; found: C 33.25, H 2.83, N 4.29, S 29.73.

X-Ray-Diffraction Analysis of **14**. Diffraction data were collected with MoK_α radiation (λ 0.71073 Å, graphite monochromator) on a *Nonius KappaCCD*. The structures were solved with SIR97 [18] and refined with full-matrix least squares on *F2* with SHELXL-97 [19]. The drawing (*Fig.*) was generated with ORTEP [20]. Further details are available under the depository number CCDC 247967 from the *Cambridge Crystallographic Data Centre*, 12, Union Road, Cambridge CB2 1EZ, UK (fax: +44 1233 336 033; E-mail: deposit@ccdc.cam.ac.uk).

*3-Methyl 6-Hydrogen 4-Methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3,6-dicarboxylate 5,5-Dioxide* (**15**). Boron tribromide (2 ml) was added to a stirred soln. of **14** (0.32 g, 1 mmol) in dry CH_2Cl_2 (30 ml) at −78°. After stirring at −78° for 1 h, the mixture was allowed to reach r.t. and kept at r.t. for 12 h. After recooling to −78°, the soln. was diluted first with Et_2O and then with MeOH (20 ml each) while stirring. The volatiles were evaporated, and the residue was dissolved in AcOEt (25 ml). The soln. was washed with 2N NaOH, dried (Na_2SO_4), and evaporated, and the residue crystallized from ^{i}Pr$_2$O: 0.23 g (74%) of **15**. Yellow crystals. M.p. 190°. UV: 246 (4.298), 409 (4.526), 427 (4.534). IR: 2955–2544 (br.), 1731, 1641. ^{1}H-NMR (*A*): 3.96 (*s*, 3 H); 3.50 (*s*, 3 H). MS: 265 ($[M-44]^+$). Anal. calc. for $C_8H_7NO_6S_3$ (309.34): C 31.06, H 2.28, N 4.53, S 31.10; found: C 31.02, H 2.32, N 4.47, S 31.18.

*Methyl 4-Methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**16**). A soln. of **15** (0.31 g, 1 mmol) in nitromethane (20 ml) was heated to reflux for 1 h. The solvent was evaporated and the residue purified by FC (petroleum ether/AcOEt 4:1): 0.05 g (19%) of **16**. Orange crystals. M.p. 199° (^{i}Pr$_2$O). UV: 304

(2.991), 380 (3.785). IR: 3108, 1724, 1594. ^{1}H-NMR (*B*): 6.36 (*s*, 1 H); 3.83 (*s*, 3 H); 3.45 (*s*, 3 H). MS: 265 (M^+). Anal. calc. for $C_7H_7NO_4S_3$ (265.33): C 31.69, H 2.66, N 5.28, S 36.26; found: C 31.76, H 2.72, N 5.09, S 36.21.

*Methyl 6-Bromo-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**17**). A soln. of **15** (0.31 g, 1 mmol) in AcOH (20 ml) and Br_2 (0.4 ml) were heated to 100° for 1 min. The solvent was evaporated and the residue crystallized from AcOEt: 0.15 g (44%). Yellowish brown crystals. M.p. 179°. UV: 235 (3.643), 386 (3.887). IR: 2955, 1725, 1593, 1344, 1186. ^{1}H-NMR (*B*): 3.83 (*s*, 3 H); 3.50 (*s*, 3 H). MS: 343, 345 (M^+). Anal. calc. for $C_7H_6BrNO_4S_3$ (344.23): C 24.42, H 1.76, Br 23.21, N 4.07, S 27.95; found: C 24.57, H 1.82, Br 22.96, N 4.11, S 27.95.

*Methyl 4-Methyl-6-nitro-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**18**). A soln. of *a*) **15** (0.31 g, 1 mmol) or *b*) **17** (0.34 g, 1 mmol) in AcOH (10 ml) and conc. HNO_3 soln. (1 ml) were heated to 100° for 1 min. While cooling, the crude product precipitated and was recrystallized from hexane/AcOEt 20:1: *a*) 0.17 g (55%) of **18** or *b*) 0.12 g (39%) of **18**. Yellow-orange crystals. M.p. 233° . UV: 460 (3.756). IR: 2927, 1729, 1582, 1309, 1246, 1179. ^{1}H-NMR (*B*): 3.92 (*s*, 3 H); 3.54 (*s*, 3 H). MS: 310 (M^+). Anal. calc. for $C_7H_6N_2O_6S_3$ (310.33): C 27.09, H 1.95, N 9.03, S 31.00; found: C 27.20, H 1.90, N 9.02, S 31.08.

*Methyl 6-(Chlorocarbonyl)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**19**). A soln. of **15** (0.3 g, 1 mmol) in dry benzene (20 ml) and PCl_5 (0.23 g, 1 mmol) were heated to reflux for 3 h. After cooling, the soln. was washed with H_2O several times, dried (Na_2SO_4), and evaporated and the residue crystallized from ^{i}Pr$_2$O: 0.23 g (70%) of **19**. Dark green crystals. M.p. 138°. UV: 429 (4.100). IR: 2957, 1728, 1673, 1321, 1170. MS: 299, 301 ([$M-28$]$^+$). Anal. calc. for $C_8H_6ClNO_5S_3$ (327.79): C 29.31, H 1.84, N 4.27, S 29.35; found: C 29.43, H 1.94, N 4.36, S 29.45.

*Methyl 6-(Benzylcarbamoyl)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**20**). A soln. of **19** (0.33 g, 1 mmol) in dry THF (20 ml) and benzylamine (0.5 ml) were stirred at 0° for 30 min. The soln. was concentrated to half of its initial volume, acidified with 2N HCl (30 ml) and extracted twice with AcOEt. The org. phase was dried (Na_2SO_4) and evaporated: 0.16 g (40%) of **20**. Yellow crystals. M.p. 174° (^{i}Pr$_2$O). UV: 206 (4.420), 248 (3.910), 410 (4.187), 431 (4.187). IR: 3371, 1728, 1627, 1312. ^{1}H-NMR (*B*): 7.35–7.26 (*m*, 5 H); 6.23 (br. *s*, 1 H, exchange with D_2O); 4.61 (*d*, $J = 6.1$, 2 H); 3.93 (*s*, 3 H), 3.54 (*s*, 3 H). MS: 398 (M^+). Anal. calc. for $C_{15}H_{14}N_2O_5S_3$ (398.48): C 45.21, H 3.54, N 7.03, S 24.14; found: C 45.21, H 3.47, N 7.06, S 24.10.

*Methyl 6-(Azidocarbonyl)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**21**). A soln. of NaN_3 (0.70 g, 1.1 mmol) in H_2O (5 ml) was added dropwise to a stirred soln. of **19** (0.33 g, 1 mmol) in acetone (10 ml). After further stirring for 45 min, the mixture was diluted with AcOEt (30 ml) and washed with H_2O. The org. layer was dried (Na_2SO_4) and evaporated and the residue purified by FC (petroleum ether/AcOEt 1:1): 0.25 g (75%) of **21**. Yellow crystals. M.p. 168° (^{i}Pr$_2$O). UV: 254 (3.916), 446 (4.337). IR: 2190, 2143, 1727, 1621. ^{1}H-NMR (*B*): 3.95 (*s*, 3 H); 3.57 (*s*, 3 H). MS: 334 (M^+). Anal. calc. for $C_8H_6N_4O_5S_3$ (334.36): C 28.74, H 1.81, N 16.76, S 28.77; found: C 28.66, H 1.71, N 16.72, S 28.79.

*Methyl 6-(Acetylamino)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**22**). A soln. of *a*) **21** (0.33 g, 1 mmol) or *b*) **24** (0.28 g, 1 mmol) in Ac_2O (15 ml) was heated to 140° for 4 h. The solvent was evaporated and the residue purified by FC (petroleum ether/AcOEt 2:1): *a*) 0.12 g (37%) of **22** or *b*) 0.19 g (59%) of **22**. Yellow crystals. M.p. 216° (^{i}Pr$_2$O). UV: 245 (3.816), 394 (3.901). IR: 3289, 1729, 1673, 1613, 1357, 1179. ^{1}H-NMR (*B*): 7.36 (*s*, 1 H, exchange with D_2O); 3.81 (*s*, 3 H); 3.41 (*s*, 3 H); 2.15 (*s*, 3 H). MS: 322 (M^+). Anal. calc. for $C_9H_{10}N_2O_5S_3$ (322.38): C 33.53, H 3.13, N 8.69, S 29.84; found: C 33.60, H 3.09, N 8.69, S 29.89.

*Methyl 6-{[(*tert*-Butoxy)carbonyl]amino}-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**23**). A soln. of **21** (0.33 g, 1 mmol) in freshly distilled ^{t}BuOH (50 ml) was heated to reflux for 3 d. The solvent was evaporated and the residue purified by FC (petroleum ether/AcOEt 1:1): 0.17 g (45%) of **23**. Yellow crystals. M.p. 179° (^{i}Pr$_2$O). UV: 244 (3.892), 389 (3.967). IR: 3285, 1728, 1706, 1626, 1600. ^{1}H-NMR (*B*): 6.45 (br., 1 H, exchange with D_2O); 3.87 (*s*, 3 H); 3.47 (*s*, 3 H); 1.51 (*s*, 9 H). MS: 380 (M^+). Anal. calc. for $C_{12}H_{16}N_2O_6S_3$ (380.46): C 37.88, H 4.24, N 7.36, S 25.28; found: C 37.90, H 4.46, N 7.39, S 25.19.

*Methyl 6-Amino-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylate 5,5-Dioxide* (**24**). A soln. of **23** (0.33 g, 1 mmol) in benzene (50 ml) was heated to reflux for 2 d. The solvent was evaporated and the residue purified by FC (petroleum ether/AcOEt 3:1): 0.12 g (42%) of **24**. Red-brown crystals. M.p. 149° (^{i}Pr$_2$O). UV: 239 (3.926), 401 (3.842). IR: 3402, 3328, 3219, 1706, 1646. ^{1}H-NMR (*B*): 3.78 (*s*, 3 H); 3.41 (*s*, 3 H). MS: 280 (M^+). Anal. calc. for $C_7H_8N_2O_4S_3$ (280.35): C 29.99, H 2.88, N 9.99, S 34.31; found: C 29.90, H 3.01, N 9.95, S 34.25.

*6-Methyl 3-Hydrogen 4-Methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3,6-dicarboxylate 5,5-Dioxide* (**25**). As described for **26**, **25** was obtained as a by-product in the alkaline aq. phase. The latter was separated, acidified with 2N HCl, and extracted twice with CH_2Cl_2. The combined org. phase was dried (Na_2SO_4) and evaporated and the residue crystallized from AcOEt: 30 mg (10%) of **25**. Orange crystals. M.p. 130–135° (dec.). UV: 212

(3.697), 242 (sh), 403 (4.219), 420 (sh). IR: 3600–3300, 3150–2750, 1710, 1675. ^{1}H-NMR (*A*): 5.73 (*s*, 1 H, exchange with D_2O); 3.92 (*s*, 3 H); 3.28 (*s*, 3 H). MS: 309 (*M*$^+$). Anal. calc. for $C_8H_7NO_6S_3$ (309.34): C 31.06, H 2.28, N 4.53, S 31.09; found: C 31.08, H 2.38, N 4.48, S 31.01.

*Methyl 4-Methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-6-carboxylate 5,5-Dioxide* (**26**). A soln. of **14** (0.32 g, 1 mmol) in THF (10 ml) was stirred with 2N NaOH (2 ml) at r.t. for 3 h. The mixture was concentrated to half of the initial volume, diluted with H_2O (25 ml), and extracted twice with AcOEt (25 ml). The alkaline aq. phase contained compound **25**. The combined org. phase was dried (Na_2SO_4) and evaporated and the residue purified by FC ($CHCl_3$/AcOEt 1:1): 0.17 g (64%) of **26**. Dark yellow crystals. M.p. 189° (^{i}Pr$_2$O). UV: 218 (3.670), 299 (2.970), 392 (4.254). IR: 3038, 1706, 1588, 1326, 1181. ^{1}H-NMR (*B*): 6.66 (*s*, 1 H): 3.96 (*s*, 3 H); 3.31 (*s*, 3 H). ^{1}H-NMR (*A*): 7.71 (*s*, 1 H); 3.84 (*s*, 3 H); 3.21 (*s*, 3 H); NOE H–C(3) (6.66) MeN (3.31). MS: 265 (*M*$^+$). Anal. calc. for $C_7H_7NO_4S_3$ (265.33): C 31.69, H 2.66, N 5.28, S 36.25; found: C 31.68, H 2.62, N 5.33, S 36.15.

*Methyl 3-(Ethylthio)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-6-carboxylate 5,5-Dioxide* (**27**). Under N_2, a soln. of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.3 ml, 2 mmol) in THF (3 ml) was dropwise added to a stirred mixture of **26** (265 mg, 1 mmol) and S_8 (260 mg, 8 mmol) in THF (20 ml). After 15 min, EtI (0.47 g, 3 mmol) was added and the mixture stirred for 2 h. After dilution with AcOEt (40 ml), the mixture was washed with 2N HCl (15 ml) and the aq. layer re-extracted with AcOEt (15 ml). The combined org. phase was dried (Na_2SO_4) and evaporated and the residue purified by FC (cyclohexane/AcOEt 2:1): 260 mg (80%) of **27**. Yellow crystals. M.p. 124° (^{i}Pr$_2$O). UV: 208 (3.951), 240 (3.856), 409 (4.411). IR: 1659, 1221, 1171. ^{1}H-NMR (*B*): 3.94 (*s*, 3 H); 3.58 (*s*, 3 H); 3.07 (*q*, *J* = 6.9, MeC*H*$_2$); 1.41 (*t*, *J* = 6.9, *Me*CH$_2$). MS: 325 (*M*$^+$). Anal. calc. for $C_9H_{11}NO_4S_4$ (325.45): C 33.21, H 3.41, N 4.30, S 39.41); found: C 33.08, H 3.34, N 4.24, S 39.51.

*Methyl 3-[(Ethoxycarbonyl)thio]-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-6-carboxylate 5,5-Dioxide* (**28**). A soln. of **26** (0.27 g, 1 mmol) in THF (10 ml), ethoxyoxomethanesulfenyl chloride (= carbonothioic acid anhydrosulfide with thiohypochlorous acid *O*-ethyl ester; 0.8 ml, 8 mmol [21], and Et_3N (0.7 ml, 5 mmol) were stirred for 24 h at r.t. The volatiles were evaporated and the residue extracted with AcOEt (20 ml). The soln. was washed with 2N HCl, dried (Na_2SO_4), and evaporated and the residue purified by FC (petroleum ether/AcOEt 3:1): 0.31 g (84%) of **28**. Yellow crystals. M.p. 145° (^{i}Pr$_2$O). UV: 397 (4.089), 414 (4.122). IR 2938, 1724, 1671, 1301, 1179. ^{1}H-NMR (*B*): 4.33 (*q*, *J* = 7.3, 2 H); 3.89 (*s*, 3 H); 3.42 (*s*, 3 H); 1.30 (*t*, *J* = 7.3, 3 H). MS: 369 (*M*$^+$). Anal. calc. for $C_{10}H_{11}NO_6S_4$ (369.46): C 32.51 H 3.00 N 3.79 S 34.72; found: C 32.30 H 3.20 N 3.96 S 34.69.

*6-(Acetylamino)-4-methyl-4*H*-1,2-dithiolo[4,3-*c*]isothiazole-3-carboxylic Acid 5,5-Dioxide* (**29**). A soln. of **22** (0.64 g, 2 mmol) in MeOH (20 ml) and KOH (6.1 g, 55 mmol) were heated to reflux for 30 min. The mixture was acidified with 2N HCl (30 ml) and extracted with AcOEt (30 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue crystallized from ^{i}Pr$_2$O: 0.36 g (59%) of **29**. Orange crystals. M.p. 120–125° (dec.). UV: 374 (3.970). IR: 3306, 2960–2500 (br.), 1686, 1208. ^{1}H-NMR (*A*): 10.10 (*s*, 1 H), 3.41 (*s*, 3 H), 2.15 (*s*, 3 H). MS: 264 ([*M* – 44]$^+$). Anal. calc. for $C_8H_8N_2O_5S_3$ (308.36): C 31.16, H 2.61, N 9.08, S 31.20; found: C 31.26, H 2.66, N 9.20, S 31.08.

N-*(4-Methyl-5,5-dioxido-4*H*-1,2-dithiolo[4,3-*c*]isothiazol-6-yl)acetamide 5,5-Dioxide* (= '*Sulfothiolutin*') (**30**). A soln. of **29** (0.31 g, 1 mmol) in nitromethane (15 ml) was heated to reflux for 30 min. The solvent was evaporated and the residue purified by FC (petroleum ether/AcOEt 1:1): 0.14 g (53%) of **30**. Orange needles. M.p. 187° (^{i}Pr$_2$O). UV: 349 (4.098). IR: 3271, 3181, 3075, 1667, 1181. ^{1}H-NMR (*B*): 7.10 (br. *s*, 1 H, exchange with D_2O); 6.00 (*s*, 1 H); 3.15 (*s*, 3 H); 2.11 (*s*, 3 H). ^{1}H-NMR (*A*): 10.62 (*s*, 1 H, exchange with D_2O); 6.85 (*s*, 1 H); 3.16 (*s*, 3 H); 2.06 (s, 3 H); NOE H–C(3) (6.85)/Me–N(4) (3.16). MS: 264 (*M*$^+$). Anal. calc. for $C_7H_8N_2O_3S_3$ (264.35): C 31.81, H 3.05, N 10.60, S 36.39; found: C 31.81, H 3.00, N 10.63, S 36.11.

*Methyl (2Z)-[3-(Methylamino)-4-(methylthio)-5-oxo-2(5*H*)-thienylidene]acetate* (**33**). A soln. of 0.32 g (1 mmol) **14** in dry MeOH (20 ml) and $NaBH_4$ (0.113 g, 3 mmol) were heated to 60° for 1 h. After addition of of MeI (0.13 ml, 2 mmol) the mixture was stirred at r.t. for 60 min. The soln. was concentrated to half of the initial volume, diluted with H_2O, acidified with 2N HCl, and extracted with AcOEt. The org. phase was dried (Na_2SO_4) and evaporated and the residue purified by FC (cyclohexane/AcOEt 2:1): 60 mg (24%) of **33**. Orange crystals. M.p. 166° (^{i}Pr$_2$O). UV: 232 (4.133), 304 (4.254), 411 (3.378). IR: 3364, 3057, 1700, 1654. ^{1}H-NMR (*B*): 6.46 (*s*, 1 H); 5.75 (br. *s*, 1 H, exchange with D_2O); 3.83 (*s*, 3 H); 3.42 (*d*, *J* = 6.0, 3 H); 2.26 (*s*, 3 H); NOE H–C=C(2) (6.46)/MeN (3.42). MS: 245 (*M*$^+$). Anal. calc. for $C_9H_{11}NO_3S_2$ (245.32): C 44.06, H 4.52, N 5.71, S 26.14; found: C 44.16, H 4.59, N 5.69, S 26.18.

*Methyl (3*R**,3a*R**)-3,3a,4,5-Tetrahydro-1,4-dimethyl-oxo-1*H*-pyrrolo[3,2-*c*]isothiazole-3-carboxylate 2,2-Dioxide* (**34**). A soln. of **10** (0.26 g, 1 mmol) in MeOH (15 ml), and $NaBH_4$ (0.05 g, 1.3 mmol) was stirred for 12 h at r.t. The soln. was concentrated to half of the initial volume, diluted with H_2O, acidified with 2N HCl, and extracted with $CHCl_3$. The org. phase was washed with H_2O, dried (Na_2SO_4) and evaporated, and the residue

(containing **34** and (*E*/*Z*)-**35**) was purified by column chromatography (cyclohexane/AcOEt 1:3; R_f 0.18): 0.05 g (19%) of **34**. Pale yellow crystals. M.p. 185° (MeOH). IR: 3082, 2950, 1754, 1688, 1353, 1179. ^{1}H-NMR (*A*): 5.39 (*s*, H–C(6)); 5.21 (*d*, *J* = 10.6, H–C(3)); 4.93 (*d*, *J* = 10.6, H–C(3a)); 3.07 (*s*, Me–N(1)); 2.80 (*s*, Me-N(4)); NOEs H–C(6) (5.39)/Me–N(1) (3.07), and H–C(3a) (4.93)/H–C(3) (5.21) and Me–N(4) (2.80). MS: 260 (M^+). Anal. calc. for $C_9H_{12}N_2O_5S$ (260.27): C 41.53, H 4.65, N 10.76, S 12.32; found: C 41.42, H 4.56, N 10.59, S 12.09.

*Methyl [1,5-Dihydro-1-methyl-3-(methylamino)-5-oxo-2*H*-pyrrol-2-ylidene)acetate* (**35**). A soln of **34** (0.26 g, 1 mmol) and MeONa (0.11 g, 2 mmol) in MeOH (20 ml) was kept at r.t. for 15 min. The mixture was concentrated to half of the initial volume, diluted with H_2O, acidified with 2N HCl, and extracted with AcOEt. The org. phase was washed with H_2O, dried (Na_2SO_4), and evaporated, and the residue (containing (*E*)- and (*Z*)-**35**) was purified by column chromatography (cyclohexane/AcOEt 1:3).

*Data of (*E*)-***35***: Yield 0.12 g (61%). R_f 0.56. Yellow crystals. M.p. 125° (MeOH). UV: 403 (3.091), 301 (4.349), 218 (4.197). IR: 3270, 3189, 3097, 2950, 1690. ^{1}H-NMR (*B*): 9.50 (br. *s*, 1 H, exchange with D_2O); 5.39 (*s*, 1 H); 4.73 (*s*, 1 H); 3.76 (*s*, 3 H); 3.00 (*s*, 3 H), 2.89 (*d*, *J* = 4.7, 3 H); NOEs H–C(4) (5.39)/*Me*NH (2.89), and H–C=C(2) (4.73)/Me–N(1) (3.00). MS: 196 (M^+). Anal. calc. for $C_9H_{12}N_2O_3$ (196.20): C 55.08, H 6.16. N 14.27; found: C 55.19, H 6.17, N 14.13.

*Data of (*Z*)-***35***: Yield 0.03 g (15%). R_f 0.45. Yellow crystals. M.p. 155° (MeOH). UV: 383 (3.383), 291 (4.342), 213 (4.987). IR: 3339, 3050, 2951, 1720, 1684, 1645. ^{1}H-NMR (*B*): 5.14 (*s*, 1 H); 4.83 (*s*, 1 H); 4.73 (br. *s*, 1 H, exchange with D_2O); 3.74 (*s*, 3 H); 3.26 (*s*, 3 H); 2.88 (*d*, *J* = 4.7, 3 H). MS: 196 (M^+). Anal. calc. for $C_9H_{12}N_2O_3$ (196.20): C 55.08, H 6.16, N 14.27; found: C 55.13, H 6.12, N 14.31.

*{[Methyl 2,3-Dihydro-4-(mercapto-*κS*)-3-[1-(mercapto-*κS*)-2-methoxy-2-oxoethylidene]-2-methylisothiazole-5-carboxylate 1,1-Dioxidato}(2–)}bis(triphenylphosphine)platinum* (**37a**). Compound **14** (22 mg, 0.067 mmol) was added to a soln. of [Pt(η^2-C_2H_4)(PPh_3)$_2$] [22] (**36a**; 50 mg, 0.067 mmol) in toluene (10 ml). The color changed immediately from yellow to dark brown, and a brown-ochre solid began to precipitate. After stirring for 1 h at r.t., hexane (20 ml) was added. The crude material was collected by centrifugation, washed twice with Et_2O (20 ml), and dried *in vacuo:* **37a** (86%). Brown-ochre powder. M.p. 272–273°. IR: 1731*ms*, 1703*ms*, 1684*m*, 1312*m*, 1183*ms*. ^{1}H-NMR (CD_2Cl_2): 7.00–7.42 (*m*, 30 arom. H); 3.66 (*s*, COOMe); 3.49 (*s*, COOMe); 2.90 (*s*, MeN). ^{31}P-NMR (CH_2Cl_2): 19.77; 20.98; ^1J(Pt,P) = 3001, 2988; ^2J(P,P) = 30.7. Anal. calc. for $C_{45}H_{39}NO_6P_2PtS_3$ (1042.28): C 51.80, H 3.74, N 1.34, S 9.22; found: C 52.39, H 3.89, N 1.27, S 9.02.

*Bis[1,1′-bis(diphenylphosphino-*κP*)ferrocene]{[methyl 2,3-Dihydro-4-(mercapto-*κS*)-3-[1-(mercapto-*κS*)-2-methoxy-2-oxoethylidene]-2-methylisothiazole-5-carboxylate 1,1-Dioxidato}(2–)}platinum* (**37b**). As described for **37a**, with **14** (22 mg, 0.067 mmol) and [Pt(η^2-C_2H_4)(dppf)][1]) [23] (**36b**; 52 mg, 0.067 mmol) in toluene (10 ml): **37b** (50%). Brown-ochre solid. M.p. 181–183°. IR: 1724*s*, 1699*ms*, 1681*s*, 1301*m*, 1151*s*. ^{1}H-NMR (CD_2Cl_2): 7.00–7.42 (*m*, 30 arom. H), 3.65 (*s*, COOMe), 3.52 (*s*, COOMe), 2.87 (*s*, MeN). ^{13}C-NMR (CD_2Cl_2): 167.61 (*J* = 9.1); 161.75; 138.12; 135.52; 131.50; 129.80; 128.33; 125.40; 111.95 (*J* = 6.1); 76.61 (*J* = 10); 76.11 (*J* = 10); 74.58 (*J* = 7.2); 74.03 (*J* = 7.2); 52.92; 51.11; 34.63. ^{31}P-NMR (CH_2Cl_2): 18.36; 19.96; ^1J(Pt,P) = 3078, 3055; ^2J(P,P) = 30.6. Anal. calc. for $C_{43}H_{37}FeNO_6P_2PtS_3$ (1072.12): C 48.13, H 3.45, N 1.31, S 8.97; found: C 47.68, H 3.62, N 1.10, S 8.52.

*{[[(4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl]bis(methylene)}bis[diphenylphosphine-*κP*]]{[methyl 2,3-Dihydro-4-(mercapto-*κS*)-3-[1-(mercapto-*κS*)-2-methoxy-2-oxoethylidene]-2-methylisothiazole-5-carboxylate 1,1-Dioxidato}(2–)}platinum* (**37c**). As described for **37a**, with **14** (22 mg, 0.067 mmol) and [Pt(η^2-C_2H_4){*R*,*R*)-diop}][1]) [24] (**36c**; 48 mg, 0.067 mmol) in toluene (10 ml): **37c** (43%). Brown-ochre solid. M.p. 157–159°. IR: 1725*ms*, 1700*ms*, 1681*ms*, 1303*ms*, 1152*s*. ^{1}H-NMR (CD_2Cl_2): 7.00–7.42 (*m*, 30 arom. H); 3.66 (*s*, COOMe); 3.59 (*s*, COOMe); 2.84 (s, MeN). ^{13}C-NMR (CD_2Cl_2): 167.77 (*J* = 8.9); 161.76; 138.22; 138.22–132.44; 129.22–128.41; 127.98; 111.97 (*J* = 6.3); 52.94; 51.19; 34.47. ^{31}P-NMR (CH_2Cl_2): 1.33; 2.99; ^1J(Pt,P) = 2875, 2847; ^2J(P,P) = 33.1. Anal. calc. for $C_{40}H_{41}NO_8P_2PtS_3$ (1016.99): C 47.24, H 4.06, N 1.38, S 9.46; found: C 47.14, H 3.78, N 1.11, S 9.16.

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Received December 15, 2004