184. Synthesis and Addition Reactions of 1,3-Thiazole-5(4*H*)-thione Oxides

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Dedicated to Prof. Dr. *Fritz Sauter* on the occasion of his 65th birthday

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1,3-Thiazole-5(4*H*)-thione oxides **2** were prepared by oxidation of the corresponding 1,3-thiazole-5(4*H*)-thiones **1** with *m*-chloroperbenzoic acid (*Table 1*). Addition reactions of **2** with organolithium and *Grignard* reagents yielded 4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yl methyl sulfoxides of type **4** *via* thiophilic attack (*Table 2*). Whereas the reaction with the organolithium compounds proceeded with fair-to-excellent yields, the *Grignard* reagents reacted only very sluggishly. The sulfoxides **4** could also be prepared *via* oxidation of 4,5-dihydro-4,4-dimethyl-5-(methylthio)-1,3-thiazoles of type **3** with *m*-chloroperbenzoic acid, together with the corresponding sulfones **5** (*Scheme 1*).

1. Introduction. – Sulfines (thioketone oxides) are compounds containing the S-centered heterocumulene structure with the general formula XYC=S=O [1] [2]. Though the first stable sulfine was isolated as early as 1923 [3], the systematic investigation of sulfines started only in the sixties. Nowadays, the chemistry of sulfines is well known, including their preparations and chemical properties (for reviews, see [4–6]).

In our preliminary contribution [7], two sulfines, 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione oxide (**2a**) and 2,4,4-trimethyl-1,3-thiazole-5(4*H*)-thione oxide (**2b**), were described. They have been prepared from the corresponding 1,3-thiazole-5(4*H*)-thiones **1** by oxidation of the C=S group. Now, we report on the generalization of this synthesis and some reactions of organometallic reagents with these sulfines.

2. Preparation of 1,3-Thiazole-5(4*H*)-thione Oxides by Oxidation. – The thione oxides **2a–e** were prepared from the corresponding 1,3-thiazole-5(4*H*)-thiones **1a–e** by oxidation with *m*-chloroperbenzoic acid (*m*-CPBA) at 0° in Et_2O (*Table 1*). The reaction occurred smoothly, and the typical orange color of the thiones **1** disappeared within a few seconds. The thione oxides **2** were isolated as colorless crystals (**2a–c, e**) or as a pale yellow oil (**2d**) in high yield (> 80%). The structure of the products has been elucidated by comparing the spectral data with those of **2a**, whose structure was established by X-ray crystallography [7].

In each reaction, only one geometric isomer of **2** was isolated. As confirmed already by X-ray crystallography for **2a** [7], we assume that all compounds are (*Z*)-configurated. Because **1e** has an oxidizable (methylthio) group at C(2), the reaction mixture was worked up after 5 min in order to avoid side reactions. It is well known that sulfides are

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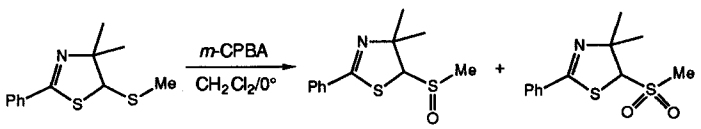
Table 1. *Preparation of Thione Oxides* **2**

1 **2**

1	R	Reaction time [min]	2	Yield [%]
1a	Ph	30	**2a**	98 [7]
1b	Me	30	**2b**	94 [7]
1c	*t*-Bu	30	**2c**	89
1d	$PhCH_2$	30	**2d**	80
1e	MeS	5	**2e**	80

easily oxidized to sulfoxides and sulfones under similar conditions. *E.g.*, sulfide **3** was converted to sulfoxide **4a** and/or sulfone **5** by *m*-CPBA in CH_2Cl_2 at 0° (*Scheme 1*). The ratio **4a**/**5** depends on the amount of oxidizing reagent: when 1 equiv. of *m*-CPBA was used, the sulfoxide **4a** was obtained as the main product (85%); with 3 equiv. of *m*-CPBA, the sulfone **5** is formed as the predominant product (56%).

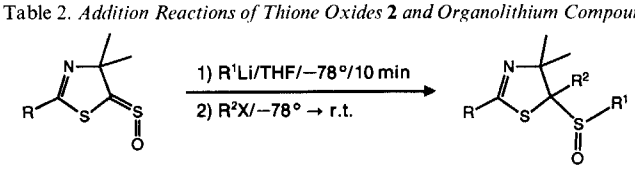
Scheme 1



3 **4a** **5**

3. Addition Reactions of 1,3-Thiazole-5(4*H*)-thione Oxides and Organometallic Compounds. – Thione oxides are known to give *S*-addition products in the reaction with organometallic reagents (*cf.* [8]). On treatment of 1,3-thiazole-5(4*H*)-thione oxides **2** with alkyl and aryllithium compounds at −78°, followed by alkylation or protonation, sulfoxides of type **4** were formed as the exclusive products (*Table 2*), formed *via* a thiophilic addition of the organolithium compound.

Table 2. *Addition Reactions of Thione Oxides* **2** *and Organolithium Compounds*



2 **4**

2	R	R^1	R^2	4 Yield [%]
2a	Ph	Me	H	**4a**[a]) (68)
2a	Ph	Me	Me	**4b** (95)
2a	Ph	Me	CH_2=$CHCH_2$	**4c** (78)
2a	Ph	Bu	H	**4d** (94)
2a	Ph	Ph	H	**4e** (71)
2a	Ph	*t*-Bu	H	**4f** (24)
2b	Me	Bu	H	**4g** (72)
2c	*t*-Bu	Me	H	**4h** (66)
2d	$PhCH_2$	Me	H	**4i** (25)
2e	MeS	Me	H	**4j** (88)

[a]) Ratio of the diastereoisomers **4a**/**4a'** 6:1.

In most of the reactions, the yields of **4** were good. Only the two products **4f** and **4i**, prepared from 2-phenyl-4,4-dimethyl-1,3-thiazole-5(4*H*)-thione oxide (**2a**) and *t*-BuLi, and 2-benzyl-4,4-dimethyl-1,3-thiazole-5(4*H*)-thione oxide (**2d**) and MeLi, respectively, were obtained in lower yields. Steric hindrance in the reaction with *t*-BuLi could be the reason for the low yield of **4f**, and that of sulfoxide **4i** could be the result of a side reaction of the benzyl group in **2c**. As in the thione analogue, the relatively acidic benzyl protons may interfere with the addition reaction under basic conditions [9].

It is worth noting that two diastereoisomers **4a** and **4a′** were isolated from the reaction of **2a** and MeLi followed by protonation, while the other reactions yielded only one isomer (as a racemate). The structure of **4a′**, the minor diastereoisomer, was confirmed by X-ray crystallography (*Fig.*, see *Exper. Part*).

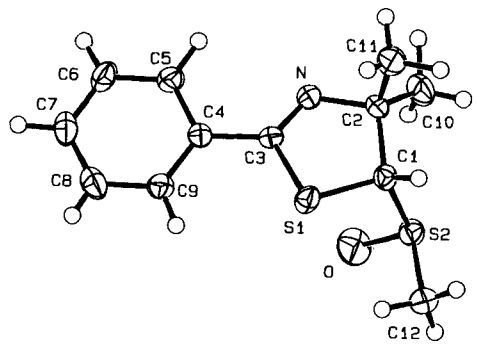
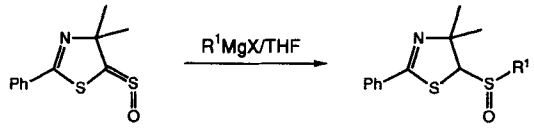


Figure. *ORTEP Diagram* [10] *of the crystal structure of sulfoxide* **4a′**

In contrast to 1,3-thiazole-5(4*H*)-thione **1a**, thione oxide **2a** reacted sluggishly with *Grignard* reagents. The reactions with MeMgI and (1-methylallyl)magnesium chloride gave products **4a** and **4k**, respectively, in poor yields (*Scheme 2*).

Scheme 2



2a R^1 = Me **4a** (10%)

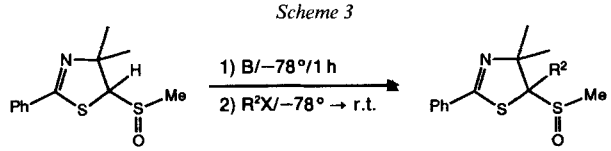
R^1 = CH_2=CHCH(Me) **4k** (11%)

Organocuprates did not react with **2a**. After treatment of **2a** with methyl cuprate and butyl cuprate at r.t. for 2 days, respectively, no addition product could be observed; only the reduction product, 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**1a**), and starting material **2a**, were isolated each in *ca.* 30% yields.

4. Alkylation of the Sulfoxide. – Usually, sulfoxides with α-protons are easily deprotonated and alkylated (*cf.* [11]). In contrast, the alkylation of 4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl methyl sulfoxide (**4a**) – even with the reactive allyl bromide – was

very difficult. Treatment of **4a** in THF at −78° with LDA and trapping the anionic intermediate with allyl bromide, gave **4c** in only 8% yield (*Scheme 3*). A control experiment showed the successful deprotonation: after addition of 2.5 equiv. of BuLi into a solution of **4a** in THF at −78°, the mixture was maintained at this temperature for 1 h and then quenched with D_2O. Only 42% of **4a**, deuterated at C(5), were isolated. The low yield must be the result of the instability of the starting material or the intermediate under the reaction conditions.

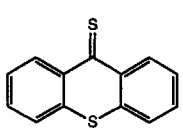
Scheme 3



4a B = BuLi, $R^2X = D_2O$ **4l** $R^2 = D$ (42%)

B = LDA, $R^2X = CH_2$=$CHCH_2Br$ **4c** $R^2 = CH_2$=$CHCH_2$ (8%)

5. Discussion. – The oxidation of 1,3-thiazole-5(4*H*)-thiones **1** gives the corresponding (*Z*)-configurated thione oxides **2** in high yields. It is worth mentioning that the oxidation proceeds selectively, *i.e.*, only the C=S group is oxidized even in the case of **1e** with a MeS group at C(2). This result corresponds to those of previous work: *e.g.* *Zwanenburg* reported on the stepwise oxidation of compound **6** with *m*-CPBA to give successively the thione oxide, the sulfoxide, and the sulfone [12]. A second example is the selective oxidation of the C=S group in methyl dithionaphthoate (**7**) [13].



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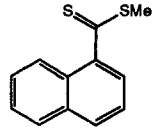

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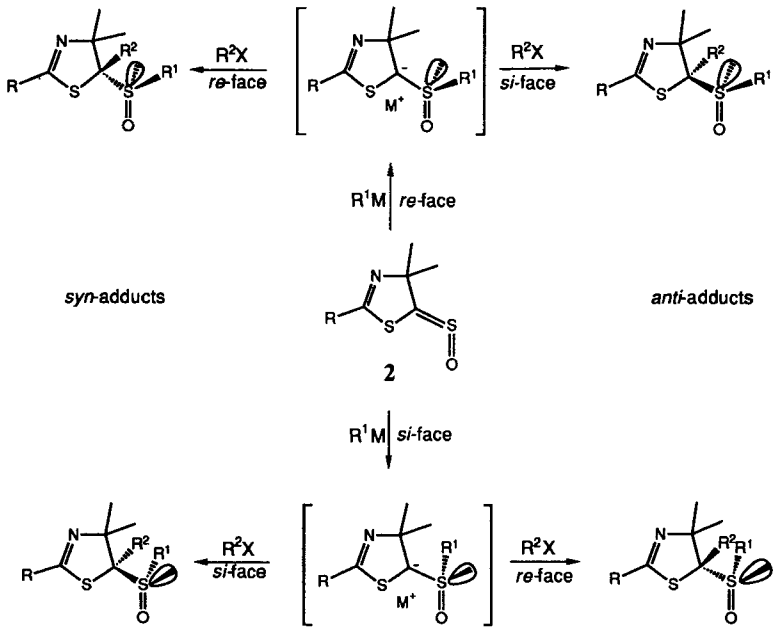
Usually, sulfides are oxidized either to sulfoxides or sulfones depending on the reaction conditions, the oxidation of sulfoxides to sulfones being more difficult and requiring stronger conditions [14]. Thus, by controlling the amount of the oxidizing agent, the desired product can be prepared selectively. This rule holds also in the case of 4,5-dihydro-5-(methylthio)-1,3-thiazole **3** (*Scheme 1*). In summary, the following order of reactivity against oxidants is found for 1,3-thiazole-5(4*H*)-thione derivatives: C=S > alkylthio > thiazole S-atom.

The thiophilic addition of organolithium reagents to 1,3-thiazole-5(4*H*)-thione oxides **2** (*Table 2*) is a characteristic reaction of thione oxides. Since the S-atom of sulfines, with its lone electron pair, is a prochiral center, the addition of an organolithium compound to an unsymmetrical sulfine creates two new chiral centers. In principle, 2^2 isomers could be formed, as shown in *Scheme 4*.

Because of the planarity of 1,3-thiazole-5(4*H*)-thione oxides, organolithium reagents attack S=O from either face of the ring, and for the symmetrical thione oxides **2**, the

Scheme 4



attacks occur equally well. However, the opportunities for the second addition, the alkylation or protonation, are then different for each face. Because of the steric effect of R^1, it is obvious that the alkylation or protonation from the opposite side is more favorable, especially when R^1 or R^2 is a bulky group. In other words, *anti*-addition products are always predominantly, if not exclusively, formed. Indeed, only one of the reactions leads to a mixture of *anti*- and *syn*-addition products (**4a**/**4a'**), in which the *anti*-product predominates. All of the other reactions afford exclusively the *anti*-adducts.

Reactions of sulfines with *Grignard* reagents and organocuprates have not been reported so far. Generally, *Grignard* reagents and organocuprates are less nucleophilic than organolithium compounds, while sulfines seem to be less reactive towards nucleophilic reagents than the corresponding thiones. This may explain the low yield of sulfoxides **4a** and **4k** in the reaction of **2a** with the corresponding *Grignard* reagents and the failure of the reaction of organocuprates with **2a**.

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Experimental Part

General. See [15].

1. Preparation of 1,3-Thiazole-5(4*H*)-thione Oxides 2. – *General Procedure.* Into a soln. of 230 mg (1.2 mmol) of *m*-CPBA (90%) in 10 ml of Et_2O, a soln. of 1,3-thiazole-5(4*H*)-thione **1** (1 mmol) in 5 ml of Et_2O was added dropwise and the mixture stirred at 0° for 30 min. Then, 30 ml of Et_2O were added, the soln. was washed with 5%

$NaHSO_3$, sat. aq. $NaHCO_3$, and brine. The Et_2O phase was dried, the solvent evaporated *i.v.*, and the residue chromatographed with hexane/Et_2O 3:1. For **2a** and **2b**, see [7].

1.1. *2-(*tert*-Butyl)-4,4-dimethyl-1,3-thiazole-5(4*H*)-thione Oxide* (**2c**). The oxidation of *2-(*tert*-butyl)-4,4-trimethyl-1,3-thiazole-5(4*H*)-thione* (**1c**) (201 mg, 1 mmol) with *m*-CPBA afforded 192 mg (89%) of **2c**. White crystals. M.p. 56–57.5°. IR: 2960*s*, 2920*m*, 2900*m*, 2860*m*, 1630*m*, 1470*m*, 1450*m*, 1445*m*, 1395*w*, 1380*m*, 1365*m*, 1250*m*, 1235*m*, 1195*m*, 1145*m*, 1025*s*, 995*s*, 935*m*, 910*s*, 860*w*, 650*m*. ^{1}H-NMR: 1.50 (*s*, Me_2C); 1.23 (*s*, *t*-Bu). ^{13}C-NMR: 206.6 (*s*, C(5)); 169.3 (*s*, C(2)); 84.2 (*s*, C(4)); 38.1 (*s*, Me_3C); 31.2 (*q*, Me_2C); 28.7 (*q*, Me_3C). CI-MS: 237 (8), 236 (11), 235 (94, $[M + 1 + NH_3]^+$), 220 (9), 219 (12), 218 (100, $[M + 1]^+$). Anal. calc. for $C_9H_{15}NOS_2$ (217.35): C 49.73, H 6.96, N 6.44, S 29.50; found: C 50.01, H 7.10, N 6.22, S 29.26.

1.2. *2-Benzyl-4,4-dimethyl-1,3-thiazole-5(4*H*)-thione Oxide* (**2d**). The oxidation of *2-benzyl-4,4-dimethyl-1,3-thiazole-5(4*H*)-thione* (**1d**) (235 mg, 1 mmol) with *m*-CPBA afforded 202 mg (80%) of **2d**. Pale-yellow oil. IR: 2980*m*, 2920*w*, 1630*s*, 1600*w*, 1505*w*, 1490*m*, 1450*m*, 1430*w*, 1380*w*, 1360*m*, 1230*m*, 1180*m*, 1145*m*, 1090*m*, 1025*s*, 945*m*, 905*m*, 890*m*, 850*w*, 700*s*, 660*w*, 605*m*. ^{1}H-NMR: 7.3–7.15 (*m*, 5 arom. H); 3.87 (*s*, PhCH_2); 1.54 (*s*, Me_2C). ^{13}C-NMR: 206.0 (*s*, C(5)); 160.3 (*s*, C(2)); 134.0 (*s*, 1 arom. C); 129.0, 128.9, 127.7 (3*d*, 5 arom. CH); 84.1 (*s*, C(4)); 40.3 (*t*, PhCH$_2$); 31.1 (*q*, $(CH_3)_2$C). CI-MS: 269 (19, $[M + 1 + NH_3]^+$), 253 (15), 252 (100, $[M + 1]^+$), 236 (15).

1.3. *4,4-Dimethyl-2-(methylthio)-1,3-thiazole-5(4*H*)-thione Oxide* (**2e**). The oxidation of *4,4-dimethyl-2-(methylthio)-1,3-thiazole-5(4*H*)-thione* (**1e**) (96 mg, 0.5 mmol) with *m*-CPBA (96 mg, 0.5 mmol) at 0° for 5 min afforded 83 mg (80%) of **2e**. White crystals. M.p. 65.5–65.9°. IR: 2980*m*, 2920*m*, 1575*s*, 1455*m*, 1445*m*, 1425*m*, 1410*w*, 1380*m*, 1360*m*, 1310*m*, 1235*m*, 1190*m*, 1140*m*, 1030*s*, 980*s*, 960*s*, 905*s*, 840*m*, 660*w*, 640*m*. ^{1}H-NMR: 2.60 (*s*, MeS); 1.63 (*s*, Me_2C). ^{13}C-NMR: 205.7 (*s*, C(5)); 156.2 (*s*, C(2)); 84.4 (*s*, C(4)); 31.5 (*q*, Me_2C); 15.4 (*q*, MeS). CI-MS: 227 (10), 226 (7), 225 (75, $[M + 1 + NH_3]^+$), 210 (13), 209 (10), 208 (100, $[M + 1]^+$). Anal. calc. for $C_6H_9NOS_3$ (207.34): C 34.76, H 4.38, N 6.76, S 46.39; found: C 34.96, H 4.51, N 6.50, S 46.11.

2. Reactions of 1,3-Thiazole-5(4*H*)-thione Oxides 2 with Organolithium Reagents. – *General Procedure.* Into a soln. of 0.5 mmol of **2** in 5 ml of THF at −78°, 0.6 mmol of organolithium reagent were added dropwise. After 10 min, 1 mmol of an electrophile (alkyl halide or redistilled H_2O) was added, the temp. allowed to rise to r.t. within 3 h, and the reaction mixture maintained at r.t. for another 3 h. The soln. was poured into a mixture of sat. aq. NH_4Cl (20 ml) and Et_2O (50 ml). The Et_2O phase was separated, dried, evaporated *i.v.*, and chromatographed with hexane/AcOEt 1:4.

2.1. *4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Methyl Sulfoxides* (**4a** and **4a'**). The reaction of **2a** [7] (140 mg, 0.59 mmol) with MeLi (1.6M soln.; 0.47 ml, 0.75 mmol) followed by hydrolysis afforded 101 mg (68%) of **4a**/**4a'** 6:1. By column chromatography, **4a** and **4a'** were separated.

Data of **4a**: white crystals. M.p. 75.1–75.4°. IR: 3005*m*, 2990*m*, 1615*m*, 1580*w*, 1490*w*, 1450*m*, 1365*w*, 1260*m*, 1240*w*, 1180*w*, 1040*s*, 950*s*, 690*m*. ^{1}H-NMR: 7.8–7.75 (*m*, 2 arom. H); 7.55–7.4 (*m*, 3 arom. H); 4.51 (*s*, H–C(5)); 2.66 (*s*, MeS); 1.84, 1.54 (2*s*, Me_2C). ^{13}C-NMR: 160.8 (*s*, C(2)); 131.9 (*s*, 1 arom. C); 131.6, 128.5, 128.1 (3*d*, 5 arom. CH); 81.0 (*s*, C(4)); 79.5 (*d*, C(5)); 37.9 (*q*, MeS); 28.7, 24.4 (2*q*, Me_2C). CI-MS: 255 (7), 254 (51, $[M + 1]^+$), 192 (9), 191 (13), 190 (100). Anal. calc. for $C_{12}H_{15}NOS_2$ (253.39): C 56.88, H 5.97, N 5.53, S 25.31; found: C 56.77, H 5.83, N 5.64, S 25.26.

Data of **4a'**: white crystals. M.p. 175.1–175.5°. IR: 3005*m*, 2985*m*, 1615*m*, 1580*w*, 1490*w*, 1450*m*, 1365*w*, 1300*w*, 1260*m*, 1240*w*, 1180*w*, 1105*w*, 1060*s*, 950*s*, 690*m*. ^{1}H-NMR: 7.9–7.85 (*m*, 2 arom. H); 7.5–7.35 (*m*, 3 arom. H); 4.27 (*s*, H–C(5)); 2.53 (*s*, MeS); 1.95, 1.51 (2*s*, Me_2C). ^{13}C-NMR: 161.8 (*s*, C(2)); 132.2 (*s*, 1 arom. C); 131.3, 128.5, 128.3 (3*d*, 5 arom. CH); 81.2 (*s*, C(4)); 79.9 (*d*, C(5)); 37.2 (*q*, MeS); 28.5, 24.5 (2*q*, Me_2C). CI-MS: 256 (10), 255 (14), 254 (100, $[M + 1]^+$), 208 (7), 206 (7), 192 (36), 190 (11), 174 (37). Anal. calc. for $C_{12}H_{15}NOS_2$ (253.39): C 56.88, H 5.97, N 5.53, S 25.31; found: C 56.96, H 6.18, N 5.63, S 25.04.

2.2. *4,5-Dihydro-4,4,5-trimethyl-2-phenyl-1,3-thiazol-5-yl Methyl Sulfoxide* (**4b**). The reaction of **2a** (119 mg, 0.5 mmol) with MeLi (1.6M soln.; 0.3 ml, 0.6 mmol) followed by alkylation with MeI (97 mg, 0.68 mmol) afforded 127 mg (95%) of **4b**. Pale-yellow oil. IR: 3010*m*, 2985*m*, 2930*w*, 1610*m*, 1580*w*, 1490*w*, 1450*m*, 1420*w*, 1390*w*, 1375*w*, 1360*w*, 1295*w*, 1260*m*, 1240*m*, 1205*w*, 1180*m*, 1050*m*, 950*s*, 690*m*, 660*m*, 615*m*. ^{1}H-NMR: 7.8–7.75 (*m*, 2 arom. H); 7.4–7.35 (*m*, 3 arom. H); 2.51 (*s*, MeS); 1.82, 1.63 (2*s*, Me_2C); 1.36 (*s*, Me–C(5)). ^{13}C-NMR: 162.2 (*s*, C(2)); 132.5 (*s*, 1 arom. C); 131.4, 128.4, 128.2 (3*d*, 5 arom. CH); 85.8 (*s*, C(4)); 81.7 (*s*, C(5)); 33.8 (*q*, MeS); 25.1, 22.6 (2*q*, Me_2C); 15.3 (*q*, *Me*–C(5)). CI-MS: 268 ($[M + 1]^+$).

2.3. *5-Allyl-4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Methyl Sulfoxide* (**4c**). The reaction of **2a** (119 mg, 0.5 mmol) with MeLi (0.3 ml, 0.6 mmol) followed by alkylation with allyl bromide (80 mg, 0.66 mmol) afforded 114 mg (78%) of **4c**. Pale-yellow oil. IR: 3005*m*, 2985*m*, 2945*w*, 1640*w*, 1610*m*, 1580*w*, 1550*w*, 1490*w*, 1465*w*, 1450*m*, 1420*w*, 1410*w*, 1385*w*, 1365*w*, 1310*w*, 1300*w*, 1260*m*, 1235*m*, 1200*w*, 1180*m*, 1045*m*, 1000*w*, 950*s*, 930*m*, 910*s*, 690*m*, 665*m*. ^{1}H-NMR: 7.8–7.75 (*m*, 2 arom. H); 7.5–7.35 (*m*, 3 arom. H); 5.95 5.85 (*m*, CH_2=C*H*–CH_2);

5.35–5.2 (*m*, CH_2=CH–CH_2); 3.15 (*B* of *ABX*, J_{AB} = 15.1, J_{BX} = 7.5, CH_2=CH–CH_2, 1 H); 2.85 (*A* of *ABX*, J_{AB} = 15.1, J_{AX} = 6.7, CH_2=CH–CH_2, 1 H); 2.61 (*s*, MeS); 1.92, 1.44 (2*s*, Me_2C). ^{13}C-NMR: 161.7 (*s*, C(2)); 132.5 (*s*, 1 arom. C); 132.4 (*d*, CH_2=CH–CH_2); 131.5, 128.5, 128.1 (3*d*, 5 arom. CH); 120.1 (*t*, CH_2=CH–CH_2); 87.3 (*s*, C(4)); 82.0 (*s*, C(5)); 34.9 (*t*, CH_2=CH–CH_2); 32.8 (*q*, MeS); 25.2, 23.4 (2*q*, Me_2C). CI-MS: 294 ([*M* + 1]$^+$).

2.4. *Butyl 4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Sulfoxide* (**4d**). The reaction of **2a** (119 mg, 0.5 mmol) with BuLi (2.5M soln. in hexane; 0.2 ml, 0.6 mmol) followed by hydrolysis afforded 140 mg (94%) of **4d**. Pale-yellow oil. IR: 3010*m*, 2970*s*, 2930*m*, 2880*w*, 1625*w*, 1615*w*, 1600*w*, 1580*w*, 1490*w*, 1465*w*, 1450*m*, 1385*w*, 1365*w*, 1260*m*, 1240*m*, 1200*w*, 1180*w*, 1065*w*, 1030*s*, 1000*w*, 945*s*, 910*m*, 690*m*, 660*w*, 610*w*. ^{1}H-NMR: 7.8–7.75 (*m*, 2 arom. H); 7.5–7.4 (*m*, 3 arom. H); 4.43 (*s*, H–C(5)); 2.85–2.75 (*m*, MeS); 1.9–1.7 (*m*, CH_2CH_2S); 1.85, 1.56 (2*s*, Me_2C); 1.55–1.45 (*m*, $MeCH_2$); 0.97 (*t*, *J* = 7.5, $MeCH_2$). ^{13}C-NMR: 160.2 (*s*, C(2)); 132.2 (*s*, 1 arom. C); 131.7, 128.6, 128.3 (3*d*, 5 arom. CH); 81.5 (*s*, C(4)); 77.0 (*d*, C(5)); 51.9 (*t*, CH_2S); 29.0, 24.5 (2*q*, Me_2C); 24.3 (*t*, CH_2CH_2S); 21.9 (*t*, $MeCH_2$); 13.6 (*q*, $MeCH_2$). CI-MS: 296 ([*M* + 1]$^+$).

2.5. *4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Phenyl Sulfoxide* (**4e**). The reaction of **2a** (100 mg, 0.42 mmol) with PhLi (2M soln.; 0.32 ml, 0.63 mmol) followed by hydrolysis afforded 95 mg (71%) of **4e**. Colorless crystals. M.p. 106.5–107.5°. IR (KBr): 2965*w*, 1615*m*, 1445*m*, 1255*m*, 1045*s*, 945*s*, 770*m*, 735*m*, 690*m*, 610*m*. ^{1}H-NMR: 7.85–7.35 (*m*, 10 arom. H); 4.47 (*s*, H–C(5)); 2.01, 1.60 (2*s*, Me_2C). ^{13}C-NMR: 160.3 (*s*, C(2)); 143.6, 131.6 (2*s*, 2 arom. C); 132.0, 131.4, 128.8, 128.4, 128.0, 126.1 (6*d*, 10 arom. CH); 81.8 (*d*, C(5)); 80.8 (*s*, C(4)); 29.1, 24.6 (2*q*, Me_2C). CI-MS: 316 ([*M* + 1]$^+$). Anal. calc. for $C_{17}H_{17}NOS_2$ (315.46): C 64.73, H 5.43, N 4.44; found: C 64.55, H 5.68, N 4.69.

2.6. tert-*Butyl 4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Sulfoxide* (**4f**). The reaction of **2a** (100 mg, 0.42 mmol) with *t*-BuLi (1.4M soln.; 0.45 ml, 0.63 mmol) followed by hydrolysis afforded 30 mg (24%) of **4f**. Colorless crystals. M.p. 93–94°. IR: 2980*s*, 1610*m*, 1460*m*, 1450*m*, 1365*m*, 1255*m*, 1175*m*, 1150*m*, 1040*s*, 1030*s*, 945*s*, 690*m*. ^{1}H-NMR: 7.8–7.75 (*m*, 2 arom. H); 7.5–7.4 (*m*, 3 arom. H); 4.23 (*s*, H–C(5)); 1.76, 1.67 (2*s*, Me_2C); 1.37 (*s*, *t*-Bu). ^{13}C-NMR: 160.7 (*s*, C(2)); 132.4 (*s*, 1 arom. C); 131.4, 128.5, 128.1 (3*d*, 5 arom. CH); 83.6 (*s*, C(4)); 68.8 (*d*, C(5)); 55.6 (*s*, Me_3C); 30.0, 21.6 (2*q*, Me_2C); 23.6 (*q*, Me_3C). CI-MS: 297 (18), 296 (100, [*M* + 1]$^+$), 280 (2), 240 (20). Anal. calc. for $C_{15}H_{21}NOS_2$ (295.47): C 60.98, H 7.16, N 4.74, S 21.70; found: C 60.88, H 6.99, N 4.89, S 21.42.

2.7. *Butyl 4,5-Dihydro-2,4,4-trimethyl-1,3-thiazol-5-yl Sulfoxide* (**4g**). The reaction of **2b** [7] (88 mg, 0.5 mmol) with BuLi (2.5M soln. in hexane; 0.2 ml, 0.6 mmol) followed by hydrolysis afforded 83 mg (72%) of **4g**. Pale-yellow oil. IR: 3000*m*, 2970*s*, 2930*m*, 2870*m*, 1670*m*, 1645*m*, 1505*w*, 1465*m*, 1430*w*, 1385*m*, 1375*m*, 1365*m*, 1240*m*, 1200*m*, 1185*m*, 1145*w*, 1095*w*, 1065*w*, 1030*s*, 910*m*, 870*w*, 660*w*. ^{1}H-NMR: 4.31 (*s*, H–C(5)); 2.75–2.65 (*m*, CH_2S); 2.20 (*s*, Me–C(2)); 1.8–1.7 (*m*, CH_2CH_2S); 1.74, 1.46 (2*s*, Me_2C); 1.55–1.4 (*m*, $MeCH_2$); 0.97 (*t*, *J* = 7.5, $MeCH_2$). ^{13}C-NMR: 159.2 (*s*, C(2)); 81.2 (*s*, C(4)); 78.1 (*s*, C(5)); 52.2 (*t*, CH_2S); 29.1, 24.32 (2*q*, Me_2C); 24.27 (*t*, CH_2CH_2S); 21.9 (*t*, $MeCH_2$); 20.1 (*q*, Me–C(2)); 13.6 (*q*, $MeCH_2$). CI-MS: 234 ([*M* + 1]$^+$).

2.8. *2-(*tert-*Butyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yl Methyl Sulfoxide* (**4h**). The reaction of **2c** (175 mg, 0.806 mmol) with MeLi (1.6M soln.; 0.60 ml, 0.96 mmol) followed by hydrolysis afforded 124 mg (66%) of **4h**. White crystals. M.p. 61.8–62.1°. IR: 2960*s*, 2920*m*, 2900*w*, 2860*w*, 1620*m*, 1470*m*, 1460*m*, 1420*w*, 1380*w*, 1360*m*, 1295*w*, 1260*m*, 1240*m*, 1175*m*, 1145*w*, 1105*w*, 1030*s*, 990*m*, 950*m*, 880*m*, 660*m*. ^{1}H-NMR: 4.32 (*s*, H–C(5)); 2.61 (*s*, MeS); 1.71, 1.41 (2*s*, Me_2C); 1.24 (*s*, *t*-Bu). ^{13}C-NMR: 172.4 (*s*, C(2)); 80.3 (*s*, C(4)); 79.3 (*d*, C(5)); 38.1 (*q*, MeS); 37.7 (*s*, Me_3C); 28.8 (*q*, Me_3C); 28.6, 24.1 (2*q*, Me_2C). CI-MS: 236 (10), 235 (14), 234 (100, [*M* + 1]$^+$), 187 (6), 170 (26). Anal. calc. for $C_{10}H_{19}NOS_2$ (233.40): C 51.46, H 8.21, N 6.00, S 27.48; found: C 51.46, H 8.40, N 6.10, S 27.26.

2.9. *2-Benzyl-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yl Methyl Sulfoxide* (**4i**). The reaction of **2d** (126 mg, 0.5 mmol) with MeLi (1.6M soln.; 0.38 ml, 0.6 mmol) followed by hydrolysis afforded 33 mg (25%) of **4i**. Pale-yellow powder. M.p. 123–125°. IR: 2980*m*, 2960*m*, 1630*m*, 1600*w*, 1490*m*, 1465*w*, 1450*m*, 1420*w*, 1405*w*, 1380*w*, 1360*m*, 1295*w*, 1235*m*, 1145*m*, 1100*m*, 1060*s*, 960*m*, 870*w*, 700*m*, 610*w*. ^{1}H-NMR: 7.6–7.3 (*m*, 5 arom. H); 4.08 (*s*, H–C(5)); 3.94, 3.85 (*AB*, *J* = 15.8, $PhCH_2$); 2.40 (*s*, MeS); 1.87, 1.41 (2*s*, Me_2C). ^{13}C-NMR: 164.3 (*s*, C(2)); 135.2 (*s*, 1 arom. C); 129.0, 128.6, 127.2 (3*d*, 5 arom. CH); 80.7 (*s*, C(4)); 80.6 (*d*, C(5)); 40.5 (*t*, $PhCH_2$); 37.2 (*q*, MeS); 28.4, 24.3 (2*q*, Me_2C). CI-MS: 270 (10), 269 (17), 268 (100, [*M* + 1]$^+$), 252 (5), 206 (7).

2.10. *4,5-Dihydro-4,4-dimethyl-2-(methylthio)-1,3-thiazol-5-yl Methyl Sulfoxide* (**4j**). The reaction of **2e** (109 mg, 0.5 mmol) with MeLi (1.6M soln.; 0.38 ml, 0.6 mmol) followed by hydrolysis afforded 98 mg (88%) of **4j**. White crystals. M.p. 87.3–88.0°. IR: 3400*m*, 2970*s*, 2920*m*, 2850*w*, 2450*w*, 1725*m*, 1570*s*, 1560*s*, 1460*m*, 1425*m*, 1410*m*, 1400*m*, 1380*m*, 1360*m*, 1310*m*, 1290*m*, 1235*m*, 1170*m*, 1140*m*, 1100*m*, 1030*s*, 980*s*, 935*s*, 870*m*, 815*w*, 705*w*, 675*w*, 655*m*. ^{1}H-NMR: 4.47 (*s*, H–C(5)); 2.61 (*s*, MeSO); 2.54 (*s*, MeS); 1.74, 1.45 (2*s*, Me_2C). ^{13}C-NMR: 159.6 (*s*, C(2)); 80.8 (*d*, C(5)); 80.7 (*s*, C(4)); 37.6 (*q*, *Me*SO); 28.7, 24.4 (2*q*, Me_2C); 15.3 (*q*, MeS). CI-MS: 226 (14), 225 (10), 224 (100, [*M* + 1]$^+$), 208 (7), 160 (20). Anal. calc. for $C_7H_{13}NOS_3$ (223.38): C 37.64, H 5.87, N 6.27, S 43.06; found: C 37.87, H 5.59, N 6.13, S 42.80.

3. Reactions of 1,3-Thiazole-5(4*H*)-thione Oxide 2a with *Grignard* Reagents. – 3.1. *With MeMgI.* Into a soln. of **2a** (100 mg, 0.42 mmol) in THF (3 ml), a freshly prepared MeMgI soln. (0.63 mmol) was added at 0°. The mixture was stirred at 0° for 1 h and poured into a mixture of sat. aq. NH_4Cl (20 ml) and Et_2O (30 ml). The org. phase was separated, dried, and the solvent evaporated *i.v.* After chromatography, 11 mg (10%) of **4a** were obtained.

3.2. *With (1-Methylallyl)magnesium Chloride.* In analogy to *Exper. 3.1*, the reaction of **2a** (100 mg, 0.42 mmol) with (1-methylallyl)magnesium chloride (0.63 mmol) at −20° for 30 min afforded 14 mg (11%) of *4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl 1-methylallyl sulfoxide* (**4k**). Pale-yellow oil. IR: 2985*s*, 1615*s*, 1580*m*, 1490*m*, 1450*s*, 1385*m*, 1365*m*, 1260*s*, 1180*m*, 1050*s*, 1020*s*, 950*s*, 690*s*, 615*m*. ^{1}H-NMR: 7.85–7.75 (*m*, 2 arom. H); 7.5–7.35 (*m*, 3 arom. H); 6.05–5.65 (2*m*, CH_2=C*H*); 5.55–5.35 (*m*, C*H*$_2$=CH); 4.55, 4.47, 4.29, 4.23 (4*s*, intensity 6:3:3:8, H–C(5) of 4 diastereoisomers); 3.6–3.35 (*m*, MeC*H*); 1.9–1.8 (*m*, *Me*CH); 1.6–1.4 (*m*, Me_2C). CI-MS: 294 (< 1, $[M + 1]^+$), 278 (10), 262 (11), 238 (16), 222 (100), 208 (8), 192 (5), 190 (5).

4. Alkylation of 4a. – 4.1. *4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-(5-$^2H_1$)thiazol-5-yl Methyl Sulfoxide* (**4l**). Into a soln. of **4a** (50 mg, 0.20 mmol) in THF (3 ml) at −78°, BuLi (1.6M soln. in hexane; 0.31 ml, 0.5 mmol) was added dropwise, and the mixture maintained at −78° for 1 h. Then, D_2O (8 mg, 0.4 mmol) was added and the temp. allowed to rise to r.t. within 6 h. The mixture was poured into a mixture of Et_2O (30 ml) and sat. aq. NH_4Cl (10 ml), the org. phase separated, dried, and evaporated *i.v.* After chromatography with hexane/AcOEt 1:1, 21 mg (42%) of **4l** were obtained. Colorless crystals. ^{1}H-NMR: 7.85–7.8 (*m*, 2 arom. H); 7.5–7.4 (*m*, 3 arom. H); 2.67 (*s*, MeS); 1.84, 1.55 (2*s*, Me_2C). CI-MS: 257 (4), 256 (9), 255 (31, $[M + 1]^+$), 193 (7), 192 (15), 191 (100), 190 (9).

4.2. *5-Allyl-4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Methyl Sulfoxide* (**4c**). In analogy to *Exper. 4.1*, the reaction of **2a** (80 mg, 0.316 mmol) with LDA (0.41 mmol) at −78° for 1 h afforded, after alkylation with allyl bromide (50 mg, 0.41 mmol), 7 mg (8%) of **4c**.

5. Oxidation of 4,5-Dihydro-4,4-dimethyl-5-(methylthio)-2-phenyl-1,3-thiazole. – 5.1. *Sulfoxides* **4a** and **4a′**. Into a soln. of *m*-CPBA (90%; 106 mg, 0.55 mmol) in CH_2Cl_2 (5 ml) at 0°, a soln. of *4,5-dihydro-4,4-dimethyl-5-(methylthio)-2-phenyl-1,3-thiazole* (**3**) (119 mg, 0.5 mmol) in CH_2Cl_2 (2 ml) was added. After stirring for 1 h at 0°, CH_2Cl_2 (40 ml) was added, the soln. washed with 5% Na_2SO_3, 5% $NaHCO_3$, and brine, subsequently, dried, and the solvent evaporated *i.v.* After chromatography with hexane/AcOEt 1:1, 81 mg (64%) of **4a** and 27 mg (21%) of **4a′**, as well as 9 mg (7%) of sulfone **5** were obtained.

5.2. *4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-thiazol-5-yl Methyl Sulfone* (**5**). In analogy to *Exper. 5.1*, the reaction of **3** (119 mg, 0.5 mmol) with *m*-CPBA (90%; 288 mg, 1.5 mmol) afforded, after chromatographed with hexane/Et_2O 2:1, 75 mg (56%) of **5** and 7 mg (6%) of **4a**.

Data of **5**: pale-yellow crystals. M.p. 87–88.5°. IR: 3020*m*, 3000*m*, 2980*m*, 1665*m*, 1625*m*, 1610*m*, 1580*m*, 1485*m*, 1450*m*, 1365*m*, 1315*s*, 1260*s*, 1240*m*, 1180*m*, 1175*m*, 1140*s*, 1120s, 950*s*, 690*s*, 615*m*. ^{1}H-NMR: 7.85–7.7 (*m*, 2 arom. H); 7.55–7.4 (*m*, 3 arom. H); 4.61 (*s*, H–C(5)); 2.97 (*s*, MeS); 1.97, 1.52 (2*s*, Me_2C). ^{13}C-NMR: 160.9 (*s*, C(2)); 131.9 (*s*, 1 arom. C); 131.9, 128.6, 128.3 (3*d*, 5 arom. CH); 80.9 (*s*, C(4)); 78.5 (*d*, C(5)); 38.9 (*q*, MeS); 28.8, 24.0 (2*q*, *Me*$_2$C). CI-MS: 270 (100, $[M + 1]^+$), 190 (47), 176 (9). Anal. calc. for $C_{12}H_{15}NO_2S_2$ (269.39): C 53.50, H 5.61, N 5.20; found: C 53.41, H 5.49, N 5.41.

6. Crystal-Structure Determination of 4a′ (see *Table 3* and *Fig.*)[4]). – The intensities were collected on a *Nicolet R3* diffractometer using graphite-monochromated CuK_α radiation ($\lambda = 1.54059$ Å) and *Wyckoff* ω scans. The intensities were corrected for *Lorentz* and polarisation effects, and an empirical absorption correction was applied using DIFABS [16]. Data collection and refinement parameters are listed in *Table 3*, a view of the molecule is shown in the *Figure*. The structure was solved by direct methods using SHELXS86 [17] which revealed the positions of all non-H-atoms. All of the H-atoms were located in a difference-electron-density map. Refinement of the non-H-atoms with anisotropic temp. factors and the H-atoms with individual isotropic temp. factors was carried out on *F* using full-matrix least-squares procedures [18]. A correction for secondary extinction was applied (coefficient 2.1×10^{-6}). Neutral atom-scattering factors for non-H-atoms were taken from [19a] and the scattering factors for H-atoms from [20]. Anomalous dispersion effects were included in F_{calc} [21]; the values for $\Delta f'$ and $\Delta f''$ were those of [19b]. All calculations were performed using the TEXSAN [22] crystallographic software package.

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[4]) Atomic coordinates, bond lengths and angles have been deposited with the *Cambridge Crystallographic Data Center*, 12 Union Road, Cambridge CB2 1EZ, England.

Table 3. *Crystallographic Data for Compound* **4a'**

Crystallized from	hexane/Et_2O	Space group	$P2_1/c$
Empirical formula	$C_{12}H_{15}NOS_2$	Z	4
Formula weight	253.38	D_x [g cm^{-3}]	1.299
Crystal color, habit	colorless, prism	Absorption coefficient μ(MoK_α) [cm^{-1}]	34.97
Crystal temp. [K]	213(1)	Absorption correction min, max	0.910, 1.431
Crystal dimensions [mm]	0.26 × 0.34 × 0.50	2θ (max) [°]	116
Crystal system	monoclinic	Total reflections measured	2491
Lattice parameters		Symmetry independent reflections	1745
Reflections for		Reflections observed ($I > 3\sigma(I)$)	1634
cell determination	25	Variables	206
2θ range [°]	$80 < 2\theta < 85$	Final R	0.0307
a [Å]	11.402(4)	R_w[a])	0.0558
b [Å]	9.657(3)	Goodness of fit s	2.769
c [Å]	11.911(3)	Final Δ_{max}/σ	0.0005
β [°]	98.85(2)	$\Delta\rho$ (max, min) [e Å^{-3}]	0.23, −0.20
V [Å^3]	1295.9(6)		

[a]) Function minimized $\Sigma w(|F_o| - |F_c|)^2$; $w = [\sigma^2(F_o) + 0.015\,F_o^2]^{-1}$.

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