New NO-Donors with Antithrombotic and Vasodilating Activities, VI:

Thiazole-2-nitrosimines

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24 new thiazole-2-nitrosimines were prepared and described by means of spectroscopical methods (NMR, IR, MS, UV). At pH 7 in cell free systems as well as in platelet rich plasma the compounds are stable against hydrolysis and do not react with the platelet glutathione. The chemical stability is underlined by the mass spectra: $M^{+\cdot}$ is of high intensity and sometimes even forms the base peak (*e.g.* **8a**). Thermal elimination of N_2 is of minor importance. The =N-NO bond in solution is susceptible to cleavage by visible light. The metabolite so formed is able to inhibit the platelet aggregation induced by collagen (*Born*-test). Five compounds exhibit this activity in concentrations below 10 µmol/L (IC_{50}). This is due to the release of a NO species, as could be demonstrated by the stimulation of soluble guanylate cyclase in a cell free system (*e.g.* **8a**, K_M = 72 µmol/L). *In vivo* the nitrosimines show antithrombotic properties. Two h after a single oral dose of **8g** (60 mg/kg) a 57% inhibition of the laser induced thrombus formation in the mesenteric arterioles of rats is observed. After 8 h a 43% inhibition still is seen.

Neue NO-Pharmaka mit antithrombotischen und gefäßerweiternden Eigenschaften, 6. Mitt.: Thiazol-2-nitrosimine

24 neue Thiazolnitrosimine wurden dargestellt und mit spektroskopischen Methoden (NMR, IR, MS, UV) charakterisiert. Sie waren bei pH 7 sowohl in einem zellfreien System als auch in plättchenreichem Plasma (PRP) hydrolysestabil. Mit dem Glutathion des PRP reagieren sie ebenfalls nicht. Ihre chemische Stabilität wird auch dadurch unterstrichen, daß im MS $M^{+\cdot}$ sehr intensiv ist und gelegentlich sogar den Basispeak bildet (z.B. **8a**). Die thermische Eliminierung von N_2 ist von untergeordneter Bedeutung. Die =N-NO-Bindung kann in Lösung mit Hilfe von sichtbarem Licht gespalten werden. Der hierdurch gebildete Metabolit hemmt im *Born*-Test die durch Collagen ausgelöste Plättchenaggregation. Fünf Verbindungen zeigten diese Wirkung schon in Konzentrationen unterhalb von 10 µmol/L (IC_{50}). Ursache ist die Bildung von NO, wie durch die Stimulation löslicher Guanylatcyclase (s-GC) in einem zellfreien System gezeigt werden konnte (z.B. **8a**, K_M = 72 µmol/L). *In vivo* zeigen die Thiazolnitrosimine antithrombotische Eigenschaften. 2 h nach einmaliger oraler Verabreichung von **8a** (60 mg/kg) wird die durch Laserlicht induzierte Thrombusbildung in Mesenterialarteriolen von Ratten zu 57% gehemmt. Nach 8 h ist noch eine 43proz. Hemmung zu beobachten.

Having observed strong antiplatelet, antithrombotic and vasodilating activities in sydnone nitrosimines we were interested to extend our investigations on nitrosimines derived from other heterocyclic moieties. In the thiazole series the preparation of 3-methyl-thiazole-2-nitrosimine (**8a**) was reported in 1891 by *Näf*[1]. For decades those thiazole derivatives found no further interest until *Beyer* and *Drews*[2] synthesized 3-methyl-4-phenyl-thiazole-2-nitrosimine (**8l**). The thiazole-2-nitrosimines then continued to be a forgotten class of compounds and no further chemical or even pharmacologic investigations were performed.

The results obtained with sydnone nitrosimines, therefore prompted us to elucidate systematically synthesis and stability of thiazole nitrosimines as well as their potential function as NO-donors. The synthetic routes which we applied to get the type **8** nitrosimines are compiled in Scheme 1.

Firstly some intermediate thiazole-2-imines of type **7** which are not yet described in the lit. were prepared by alkylation of thiazole-2-amines (**A**) which are obtained according to *Hantzsch*[3,4] and *Traumann*[5] from α-haloketones (**1**) and thiourea (**7f, i, x, y**). In 1957 *Beyer*[6] established a more elegant method when he found, that compounds of type **7** are formed directly from **1** and **2** (**B**) under acidic conditions (applied for **7g, m, n, p, q, r, s, t, u, w**). A third method (**C**) reacts α-rhodanoketones **3** with amine salts **4**[6,7]. This method was used for the synthesis of the bisnitrosimine **9** (*v.i.*). The methods reported for the nitrosation of **7a**[1] and **7l**[2] were unsatisfactory. Good yields were not obtained, but we developed a two phase nitrosation method by which the nitrosimine formed was transferred immediately into a chloroform layer. So the desired compounds **8** were removed from the equilibrium between **7** and **8** and simultaneously protected from degradation to 2-thiazolones. The structures of **8a-y** are thoroughly backed by spectral data. Characteric examples are summarized in Table 1.

The successful nitrosation of **7** is demonstrated by a downfield shift of 4-H from 7.49 (**7b** x HCl/**8b**) to 7.96 ppm and 5-H from 7.05 to 7.27 ppm. The signal of the methylene group in 3-position is shifted from 4.03 to 4.48 ppm.

The same direction with similar shift differences are found for the pairs **7c/8c** and **7d/8d**. In the UV-spectra a characteristic absorption maximum appears at 330-340 nm with high intensity (log ε ~ 4). The formation of the nitrosimines can be demonstrated quite well by the IR-spectra.

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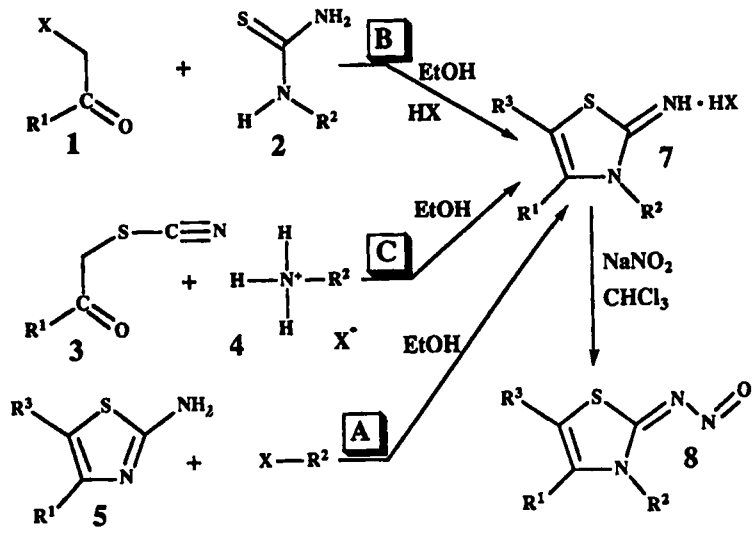
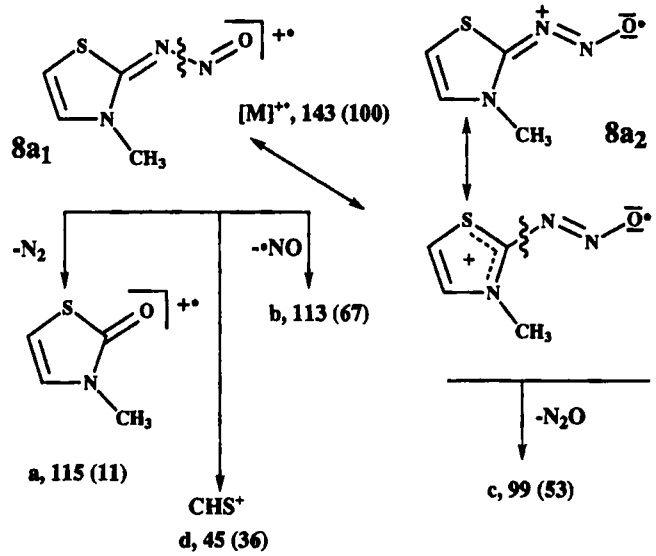


Scheme 1: Synthesis of thiazole-2-nitrosimines; R^1, R^2, R^3: cf. Table 2, cpds. **8**

Tab. 1: Selected spectral data of type **8** nitrosimines in comparison to the parent imines of type **7**

Method	Spectral data	7b	8b	7c	8c	7d	8d
NMR	H-4 [ppm]	7.49	7.96	7.45	7.87	7.50	8.03
	H-5 [ppm]	7.05	7.27	7.09	7.28	7.08	7.33
	3-CH_2[ppm]	4.03	4.48	4.98	5.00	5.30	5.61
UV	λ_{max} [nm]	2.22	3.32	2.56	3.34	2.56	3.38
	log ε	4.16	3.96	4.16	3.98	3.87	4.00
IR	=N^+H_2[cm^{-1}]	3249	-	3253	-	3255	-
	N=O [cm^{-1}]	-	1398	-	1420	-	1411
	C=N [cm^{-1}]	1621	1548	1620	1544	1625	1545



Scheme 2: Mass spectral fragmentation of **8a** (EI-ionization, 40°C)

The N-H vibration at 3250 cm^{-1} (type **7**) is replaced by the N=O valence vibration at ~1400 cm^{-1}.

The shift of the C=N double bond from ~1620 to ~1550 cm^{-1} clearly demonstrates its partial single bond character in thiazole-2-nitrosimines (see $\mathbf{8a_2}$ in Scheme 2).

The behaviour of thiazole-2-nitrosimines in the mass spectrometer after electron impact is examplified by **8a** (see Scheme 2). It was very surprising that the spectrum is dominated by the peak of $M^{+\cdot}$. This is quite different from the results which were obtained with sydnone nitrosimines,

Tab. 2: Inhibition of platelet aggregation by thiazole-2-nitrosimines. An asterisk means that DMSO had to be added to achieve sufficient solubility of type **8** compounds. At the IC_{50} documented DMSO itself has no effect on platelet aggregation (*Born*-test).

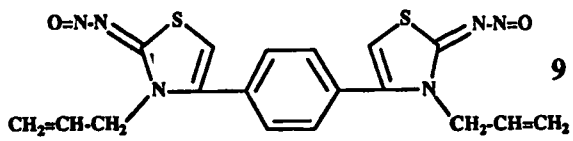
8	R^2	R^1	R^3	IC_{50} [µmol/L]
a	CH_3	H	H	3
b	C_2H_5	H	H	55
c	allyl	H	H	95
d	Ph-CH_2	H	H	35
e	CH_3	CH_3	H	21
f	C_2H_5	CH_3	H	21
g	allyl	CH_3	H	4
h	Ph	CH_3	H	41
i	Ph-CH_2	CH_3	H	20
k	Ph-$(CH_2)_2$	CH_3	H	22
l	CH_3	Ph	H	62,5*
m	C_2H_5	Ph	H	16*
n	allyl	Ph	H	40*
o	Ph	Ph	H	42*
p	CH_3	4-OCH_3-Ph	H	12*
q	C_2H_5	4-OCH_3-Ph	H	8*
r	allyl	4-OCH_3-Ph	H	9*
s	allyl	4-CH_3-Ph	H	38*
t	CH_3	4-NO_2-Ph	H	38*
u	allyl	4-NO_2-Ph	H	7,5*
v	CH_3	2,5-$(OCH_3)_2$-Ph	H	16*
w	CH_3	$(Ph)_2$-CH	H	46*
x	CH_3	$COOC_2H_5$	H	16*
y	CH_3	Ph	$C_{14}H_{29}$	41*

where the intensity of this ion is low. The high stability of **8a** correlates with the low intensity of ion **a** which is formed by thermal decomposition of the parent molecule, the ionization of which occurs afterwards. Even at higher temp. up to 440°C the intensity of this ion never exceeds 30% of the base peak. The elimination of radical nitrogen oxide is demonstrated by the formation of m/z = 113. Another striking feature is the abundant elimination of dinitrogen oxide (see ion **c**, m/z = 99) which again is different to sydnone nitrosimines.

The results obtained with **8a-y** in the *Born*-test are summarized in Table 2. All compounds tested were able to inhibit the aggregation of blood platelets induced by collagen in concentration between 3 and 95 µmol/L.

In the sydnone nitrosimines we had experienced that this effect could be enhanced by lipophilic substituents. Comparison of **8a-d** shows that this is not the case in the thiazole series. The reason might be that the mesoionic sydnones are so polar that additional hydrophobic interactions are necessary for attachement to the platelet membrane. Compound **8c** suggests that an alkyl substituent in 3-position is unfavourable as well. Comparison of **8a** with **8e** leads to the conclusion that a second substituent in 4-position is unfavourable. A look on **8g**, however, where these two properties are combined, gives us one of the most active compounds of the whole series. Aryl- or arylalkyl substituents in 4-position (**8h-k**) only have low inhibitory properties.

The same was true for a phenyl ring in 3-position (**8l-o**). It, therefore, was surprising that the 4-methoxyphenyl compounds **8p** and **8q** as well as the 4-nitrophenyl derivative **8u** inhibit the platelet aggregation in concentrations < 10 µmol/L. A benzhydryl rest in 4-position is not favourable (**8w**), while a carboxylic acid ester in this position (**8x**) results in a compound of medium activity. An additional rest in 5-position only has little influence (compare **8l** with **8y**). As we had observed a dramatic rise in activity in the sydnone series when two nitrosimine moieties were connected by a benzene ring we synthesized the bis-derivative **9**.



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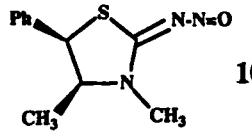

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An IC_{50} = 10 µmol/L was found. Finally we included the thiazolidine derivative **10** into our investigations. This compound was obtained from the corresponding imine which is part of the antiasthmatic drug Priatan®. An IC_{50} = 69 µmol/L was measured.

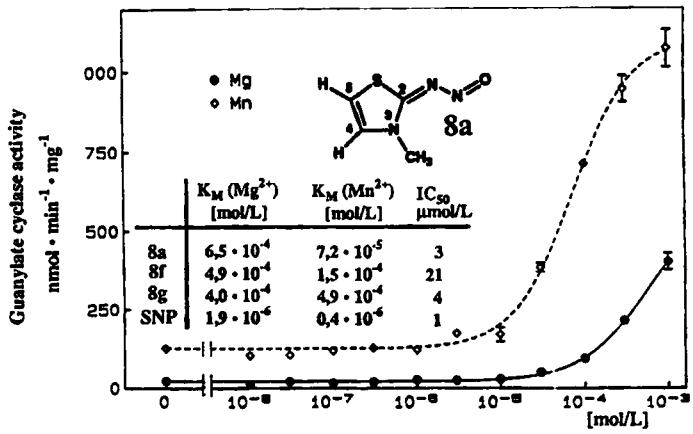

Fig. 1: Activation of guanylate cyclase by **8a**, **f**, **g** and sodium nitroprusside (SNP).

Tab. 3: Inhibition of thrombus formation in an in vivo thrombosis model. Statistics: *Man* and *Whitney* U-test[12].

Compound No.	IC_{50} [µmol/L]	dose [mg/kg]	time after p.o. application [h]	venoles % inhibition ± SEM	α	arterioles % inhibition ± SEM	α
8a	3	60	2	3 ± 1	0,1	2 ± 2	n.s.
8e	21	60	2	22 ± 5	0,002	44 ± 9	0,002
8e		30	2	3 ± 6	n.s.	18 ± 6	0,02
8g	4	60	2	29 ± 8	0,002	57 ± 9	0,002
8g		30	2	11 ± 6	n.s.	27 ± 13	0,02
8g		60	8	19 ± 5	0,002	43 ± 8	0,002
ASA	50	60	1	20 ± 5	0,002	48 ± 10	0,002

In order to characterize the mechanism of action three compounds (**8a**, **f**, **g**) were selected for assaying their influence on soluble guanylate cyclase (s-GC). As shown in Fig. 1 all three compounds do activate the enzyme. Full activation is only observed in the presence of Mn^{2+} as a cofactor. The addition of Mg^{2+} is less effective. The results are expressed quantitatively as the *Michaelis-Menten* constant. Its value with **8a**, **f**, **g** in general is two orders of magnitude higher than with sodium nitroprusside (SNP) indicating a slow release of NO from the nitrosimines in this cell free system. The IC_{50} values of the *Born*-test are poorly correlated to the K_M values. So **8g** (IC_{50} = 4 µmol/L) has a higher K_M (Mn^{2+}) than **8f** (IC_{50} = 21 µmol/L) indicating a lower activity of **8g** in the s-GC assay. These results suggest either an important role of the platelet in liberating the active metabolite or a much higher affinity of **8g** to the platelet membrane.

The antithrombotic effects of **8f** and **8g** were investigated in an *in vivo* thrombosis model[8].

In short, thrombus formation in arterioles and venoles of rats is induced by a laser beam of defined energy and time. The average number of "shots" needed is called thrombus formation index (TFI). It is transformed into the percentage of inhibition of thrombus formation by the following equation:

$$\% \text{ inhibition} = \frac{\text{TFI test - TFI control}}{6 - \text{TFI control}} \times 100$$

The results obtained with three compounds are compiled in Tab. 3. For comparison acetylsalicylic acid (ASA) is included. Again there is no correlation between the *in vitro* and *in vivo* results: while **8a** and **8g** *in vitro* are equipotent, *in vivo* **8a** is inactive. In contrast **8g** exhibits pronounced and long lasting antithrombotic properties in venoles and in arterioles. Compound **8e** which has a small *in vitro* activity surprisingly was nearly as effective as **8g**. The reason for this lack of *in vitro* - *in vivo* correlation is a different mechanism by which the active metabolite is formed[9]. The *in vitro* results demonstrate how easily the =N-NO bond can be cleaved by visible light. No hydrolysis of type **8** compounds to the imines **7** occurs in aqueous solution or PRP. It, therefore, is most probable that *in vivo* the active metabolite is formed in the liver presumably by a reductive mechanism involving suitable enzymes.

Experimental Part

Devices and test methods correspond to the previous communications of this series[10,11].- ^{1}H-NMR spectra: 300 MHz in [D_6]DMSO.- IR spectra: KBr.- Temp. in °C.

Synthesis of new thiazol-2-imines

The thiazolimines **7a-d**[13], **7e**[6], **7h**[14], **7l**[14] and **7o**[6] are already described.

Method **A**

20 mmol 2-thiazolamine are dissolved in 40 ml absol. EtOH, 30 mmol alkyl halogenide are added and the mixture is refluxed overnight. When cooled to room temp. Et_2O is added until turbidity occurs. The mixture is kept at 5° for 3 h. The precipitate is sucked off, dissolved in MeOH, purified with charcoal and recrystallized.

3-Ethyl-4-methyl-2(3H)-thiazolimine hydrochloride (**7f**)

From 4-methyl-2-thiazolamine and EtI. Crystals (methanol/ether), mp. 246°, yield 51%.- $C_6H_{10}N_2S \cdot HI$ (270.1) Calcd. C 26.7 H 4.10 N 10.4 Found C 26.6 H 4.30 N 10.4.- IR: 3157; 3045; 1620; 1603; 1524; 1464; 1455; 1439; 1399; 1378; 1346; 1160; 1080; 842; 778; 721 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 222 (4.21), 260 nm (3.83).- ^{1}H-NMR: δ (ppm) = 9.37 (bs, 2H, NH_2^+, D_2O exchange), 6.73 (s, 1H, 5-H), 3.99 (q, J = 7 Hz, 2H, 3-CH_2), 2.28 (s, 3H, 4-CH_3), 1.22 (t, J = 7 Hz, 3H, CH_2-$C\underline{H}_3$).- MS (130°): m/z = 142 (54%, $M^{+\cdot}$), 128 (90), 127 (44), 114 (100), 100 (10), 73 (15), 72 (28), 71 (21), 69 (15), 45 (24), 43 (12), 42 (56).

3-Benzyl-4-methyl-2(3H)-thiazolimine hydrobromide (**7i**)

From 4-methyl-2-thiazolamine and benzylbromide. Crystals (methanol/ether), mp. 239°, yield 50%.- $C_{11}H_{12}N_2S \cdot HBr$ (285.2) Calcd. C 46.3 H 4.59 N 9.8 Found C 46.3 H 4.64 N 9.9.- UV (CH_3OH): λ max (log ε) = 206 (4.08), 260 nm (3.84).- ^{1}H-NMR: δ (ppm) = 9.74 (bs, 2H, NH_2^+, D_2O exchange), 7.45-7.33 (m, 3H aromat.), 7.13 (d, J = 7.2 Hz, 2H aromat.), 7.13 (d, J = 7.2 Hz, 2H aromat.), 6.84 (s, 1H, 5-H), 5.39 (s, 2H, 3-CH_2), 2.14 (s, 3H, 4-CH_3).- MS (100°): m/z = 204 (32%, $M^{+\cdot}$), 203 (12), 113 (11), 100 (9), 91 (100), 82 (12), 80 (12), 65 (20).

3-Methyl-4-phenyl-5-tetradecyl-2(3H)-thiazolimine hydroidide (**7y**)

From 4-phenyl-5-tetradecyl-2-thiazolamine and MeI. Crystals (methanol/ether), mp. 110°, yield 35%.- $C_{24}H_{38}N_2S \cdot HI$ (514.6) Calcd. C 56.0 H 7.64 N 5.4 Found C 56.2 H 8.02 N 5.7.- UV (CH_3OH): λ max (log ε) = 206 (4.10), 258 nm (3.80).- ^{1}H-NMR: δ (ppm) = 9.48 (bs, 2H, NH_2^+, D_2O exchange), 8.05-7.47 (m, 5H aromat.), 3.24 (s, 3H, 3-CH_3), 2.47 (t, 2H, 5-CH_2-), 1.44 (bs, 2H, 5-CH_2-$C\underline{H}_2$-), 1.24 (bs, 22 H, -$(C\underline{H}_2)_{11}$-CH_3), 0.84 (t, 3H, -$(CH_2)_{13}$-$C\underline{H}_3$).- MS (140°): m/z = 386 (35%, $M^{+\cdot}$), 385 (11), 357 (16), 343 (16), 329 (15), 315 (12), 301 (10), 287 (10), 273 (11), 259 (11), 231 (13), 218 (19), 217 (100), 205 (15), 204 (94), 203 (94), 177 (11), 176 (88), 147 (12), 128 (10), 118 (36), 103 (10), 91 (13), 77 (20), 46 (12), 43 (17), 41 (12).

4-Methyl-3-(2-phenylethyl)-2-(3H)-thiazolimine hydrobromide (**7k**)

Crystals (methanol/ether), mp. 249° (decompn.), yield 37%.- $C_{12}H_{14}N_2S \cdot HBr$ (299.2) Calcd. C 48.2 H 5.05 N 9.4 Found C 48.2 H 5.14 N 9.4.- UV (CH_3OH): λ max (log ε) = 206 (4.11), 260 nm (3.76).- ^{1}H-NMR: δ (ppm) = 9.57 (bs, 2H, NH_2^+, D_2O exchange), 7.34-7.24 (m, 5H aromat.), 6.65 (s, 1H, 5-H), 4.20 (t, J = 7.3 Hz, 2H, 3-CH_2), 2.95 (t, J = 7.3 Hz, 2H, 3-CH_2-$C\underline{H}_2$), 1.98 (s, 3H, 4-CH_3).- MS (110°): m/z = 218 (8%, $M^{+\cdot}$), 114 (100).

Method **B**

10 mmol α-haloketone, 10 mmol N-substituted thiourea and 1 ml conc. HCl or HBr are dissolved in 10 ml EtOH and refluxed for 1 h. After cooling the precipitate is sucked off, purified with charcoal and recrystallized.

3-Allyl-4-methyl-2(3H)-thiazolimine hydrochloride (**7g**)

From chloroacetone and *N*-allylthiourea. Purified by liquid chromatography. Plates (isopropanol), mp. 148°, yield 27%.- $C_7H_{10}N_2S \cdot HCl$ (190.7) Calcd. C 44.1 H 5.81 N 14.7 Found C 43.7 H 5.85 N 14.7.- IR: 3253; 3136; 3098; 2983; 2775; 1630; 1599; 1554; 1435; 1413; 1395; 1382; 1353; 1324; 1229; 1158; 988; 962; 934; 841; 836; 738; 720; 653 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 204 (3.37), 224 (3.37), 260 nm (3.81).- ^{1}H-NMR: δ (ppm) = 10.08 (bs, 2H, NH_2^+, D_2O exchange), 6.75 (s, 1H, 5-H), 5.98-5.86 (m, 1H, $C\underline{H}$=CH_2), 5.25 (d, J = 10 Hz, 1H, *trans* CH=$C\underline{H}_2$), 5.00 (d, J = 17 Hz, 1H, *cis* CH=$C\underline{H}_2$), 4.80 (d, J = 5 Hz, 2H, 3-CH_2), 2.22 (s, 3H, 4-CH_3).- MS (200°): m/z = 154 (100%, $M^{+\cdot}$), 153 (50), 139 (63), 127 (22), 126 (29), 121 (16), 114 (16), 113 (44), 100 (11), 99 (10), 86 (22), 80 (10), 73 (14), 72 (19), 71 (51), 69 (77), 67 (13), 56 (16), 54 (12).

3-Ethyl-4-phenyl-2(3H)-thiazolimine hydrobromide (**7m**)

From 2-bromo-acetophenone and *N*-ethylthiourea. Cubes (methanol/ether), mp. 238-246°, yield 83%.- $C_{11}H_{12}N_2S \cdot HBr$ (285.2) Calcd. C 46.3 H 4.59 N 9.8 Found C 46.1 H 4.54 N 9.8.- UV (CH_3OH): λ max (log ε) = 206 (4.25), 258 nm (3.99).- ^{1}H-NMR: δ (ppm) = 10.01 (bs, 2H, NH_2^+, D_2O exchange), 7.56 (s, 5H aromat.), 7.03 (s, 1H, 5-H), 3.96 (q, J = 7 Hz, 2H, 3-CH_2), 1.06 (t, J = 7 Hz, 3H, CH_2-$C\underline{H}_3$).- MS (260°): m/z = 204 (54%, $M^{+\cdot}$), 203 (78), 191 (10), 177 (12), 176 (100), 172 (24), 135 (11), 134 (66), 129 (11), 104 (28), 102 (22), 89 (12), 77 (16), 74 (12), 71 (10).

3-Allyl-4-phenyl-2(3H)-thiazolimine hydrobromide (**7n**)

From 2-Bromo-acetophenone and *N*-allylthiourea. Needles (methanol/ether), mp. 202°, yield 53%.- $C_{12}H_{12}N_2S \cdot HBr$ (297.2) Calcd. C 48.5 H 4.41 N 9.4 Found C 48.3 H 4.43 N 9.3.- UV (CH_3OH): λ max (log ε) = 206 (4.36), 232 (4.20), 266 nm (4.03).- ^{1}H-NMR: δ (ppm) = 9.67 (bs, 2H, NH_2^+, D_2O exchange), 7.58-7.45 (m, 5H aromat.), 7.07 (s, 1H, 5-H), 5.82-5.70 (m, 1H, $C\underline{H}$=CH_2), 5.20 (d, J = 10 Hz, 1H, *trans* CH=$C\underline{H}_2$), 4.84 (d, J = 17 Hz, 1H, *cis* CH=$C\underline{H}_2$), 4.52 (d, J = 5 Hz, 2H, 3-CH_2).- MS (110°): m/z = 216 (100%, $M^{+\cdot}$), 215 (65), 201 (40), 189 (13), 188 (20), 183 (12), 175 (12), 148 (11), 135 (13), 134 (99), 121 (10), 104 (11), 102 (13), 89 (13), 82 (33), 81 (12), 80 (33), 79 (12), 77 (19), 51 (11), 45 (11), 41 (24), 39 (19).

4-(4-Methoxyphenyl)-3-methyl-2(3H)-thiazolimine hydrobromide (**7p**)

From 4-methoxyphenacyl bromide and *N*-methylthiourea. Stars (methanol/ether), mp. 188°, yield 57%.- $C_{11}H_{12}N_2OS \cdot HBr$ (301.2) Calcd. C 43.9 H 4.35 N 9.3 Found C 43.6 H 4.33 N 9.2.- UV (CH_3OH): λ max (log ε) = 202 (4.46), 254 nm (4.24).- ^{1}H-NMR: δ (ppm) = 9.81 (bs, 2H, NH_2^+, D_2O exchange), 7.47 (d, J = 9 Hz, 2H, 4-Ph-2-H and 6-H), 7.09 (d, J = 9 Hz, 2H, 4-Ph-3-H and 5-H), 6.92 (s, 1H, 5-H), 3.83 (s, 3H, 3-CH_3), 3.40 (s, 3H, O-CH_3).- MS (165°): m/z = 220 (100%, $M^{+\cdot}$), 219 (57), 177 (38), 149 (32), 148 (28), 133 (14), 132 (17), 121 (14), 77 (13), 36 (20).

3-Ethyl-4-(4-methoxyphenyl)-2(3H)-thiazolimine hydrobromide (**7q**)

From 4-methoxyphenacyl bromide and *N*-ethylthiourea. Crystals (methanol/ether), mp. 266° (decompn.), yield 67%.- $C_{12}H_{14}N_2OS \cdot HBr$ (315.2) Calcd. C 45.7 H 4.80 N 8.9 Found C 45.6 H 4.92 N 8.9.- UV (CH_3OH): λ max (log ε) = 202 (4.21), 236 nm (3.96).- ^{1}H-NMR: δ (ppm) = 9.92 (bs, 2H, NH_2^+, D_2O exchange), 7.47 (d, J = 9 Hz, 2H, 4-Ph-2-H and 6-H), 7.11 (d, J = 9 Hz, 2H, 4-Ph-3-H and 5-H), 6.95 (s, 1H, 5-H), 3.93 (q, 2H, 3-CH_2), 3.84 (s, 3H, O-CH_3), 1.06 (t, 3H, CH_2-$C\underline{H}_3$).- MS (140°): m/z = 234

(64%, $M^{+\cdot}$), 233 (82), 207 (13), 206 (100), 191 (48), 164 (28), 149 (44), 134 (24), 132 (18), 121 (20), 103 (10), 91 (10), 82 (15), 80 (15), 77 (18), 46 (10), 45 (23), 36 (13), 31 (46).

3-Allyl-4-(4-methoxyphenyl)-2(3H)-thiazolimine hydrobromide (**7r**)

From 4-methoxyphenacyl bromide and *N*-allylthiourea. Needles (methanol/ether), mp. 208°, yield 78%.- $C_{13}H_{14}N_2OS \cdot HBr$ (327.2) Calcd. C 47.7 H 4.62 N 8.6 Found C 47.5 H 4.66 N 8.7.- UV (CH_3OH): λ max (log ε) = 204 (4.35), 240 nm (4.17).- ^{1}H-NMR: δ (ppm) = 9.65 (bs, 2H, NH_2^+, D_2O exchange), 7.41 (d, J = 9 Hz, 2H, 4-Ph-2-H and 6-H), 7.07 (d, J = 9 Hz, 2H, 4-Ph-3-H and 5-H), 6.99 (s, 1H, 5-H), 5.82-5.70 (m, 1H, C<u>H</u>=CH_2), 5.21 (d, J = 10 Hz, 1H, *trans* CH=C<u>H</u>$_2$), 4.85 (d, J = 17 Hz, 1H, *cis* CH=C<u>H</u>$_2$), 4.51 (d, J = 5 Hz, 2H, 3-CH_2), 3.82 (s, 3H, O-CH_3).- MS (180°): m/z = 246 (100%, $M^{+\cdot}$), 245 (31), 231 (27), 218 (14), 205 (10), 164 (61), 149 (31), 132 (17), 121 (12), 82 (21), 80 (21), 77 (10), 41 (20), 39 (13).

3-Allyl-4-(4-tolyl)-2(3H)-thiazolimine hydrobromide (**7s**)

From 4-methylphenacyl bromide and *N*-allylthiourea. Crystals (methanol/ether), mp. 118°, yield 36%.- $C_{13}H_{14}N_2S \cdot HBr$ (311.2) Calcd. C 50.2 H 4.86 N 9.0 Found C 50.0 H 4.91 N 9.0.- UV (CH_3OH): λ max (log ε) = 206 (4.40), 240 nm (4.25).- ^{1}H-NMR: δ (ppm) = 9.56 (bs, 2H, NH_2^+, D_2O exchange), 7.65 (d, J = 9 Hz, 2H, 4-Ph-2-H and 6-H), 7.31 (d, J = 9 Hz, 2H, 4-Ph-3-H and 5-H), 7.20 (s, 1H, 5-H), 5.99-5.87 (m, 1H, C<u>H</u>=CH_2), 5.36 (d, J = 17 Hz, 1H, *cis* CH=C<u>H</u>$_2$), 5.27 (d, J = 10 Hz, 1H, *trans* CH=C<u>H</u>$_2$), 4.12 (d, J = 5 Hz, 2H, 3-CH_2), 2.35 (s, 3H, CH_3).- MS (90°): m/z = 230 (100%, $M^{+\cdot}$), 229 (51), 215 (31), 203 (14), 202 (21), 197 (10), 189 (10), 149 (11), 148 (54), 147 (35), 116 (13), 115 (13), 91 (11), 82 (30), 81 (10), 80 (30), 79 (11), 41 (15).

3-Methyl-4-(4-nitrophenyl)-2(3H)-thiazolimine hydrobromide (**7t**)

From 4-nitrophenacyl bromide and *N*-methylthiourea. Light yellow crystals (methanol/ether), mp. 290° (decompn.), yield 32%.- $C_{10}H_9N_3O_2S \cdot HBr \cdot H_2O$ (334.2) Calcd. C 35.9 H 3.62 N 12.6 Found C 35.4 H 3.62 N 12.4.- UV (CH_3OH): λ max (log ε) = 204 (4.21), 260 (3.97), 372 nm (3.49).- ^{1}H-NMR: δ (ppm) = 10.17 and 9.58 (s, 1+1 H, NH_2^+, D_2O exchange), 8.32 (d, J = 9 Hz, 1H aromat.), 8.27 (d, J = 9 Hz, 1H aromat.), 8.09 (d, J = 9 Hz, 1H aromat.), 7.83 (d, J = 9 Hz, 1H aromat.), 7.50 (s, 1H, 5-H), 2.94 (s, 3H, 3-CH_3).- MS (80°): m/z = 235 (100%, $M^{+\cdot}$), 207 (44), 189 (20), 174 (22), 149 (10), 147 (10), 121 (11), 89 (34), 82 (31), 81 (11), 80 (32), 79 (11), 63 (10), 31 (19), 30 (21), 28 (12).

3-Allyl-4-(4-nitrophenyl)-2(3H)-thiazolimine hydrobromide (**7u**)

From 4-nitrophenacyl bromide and *N*-allylthiourea. Light yellow stars (methanol/ether), mp. 202° (decompn.), yield 24%.- $C_{12}H_{11}N_3O_2S \cdot HBr$ (342.2) Calcd. C 42.1 H 3.53 N 12.2 Found C 41.9 H 3.55 N 12.2.- IR: 3092; 1680; 1625; 1605; 1525; 1436; 1362; 1307; 1206; 1122; 1072; 1062; 1002; 926; 870; 790; 760; 700 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 208 (4.53), 266 (4.36), 372 nm (4.01).- ^{1}H-NMR: δ (ppm) = 8.28 (d, J = 9 Hz, 2H, 4-Ph-3-H and 5-H), 8.07 (d, J = 9 Hz, 2H, 4-Ph-2-H and 6-H), 7.52 (s, 1H, 5-H), 6.01-5.88 (m, 1H, C<u>H</u>=CH_2), 5.31 (d, J = 18 Hz, 1H, *cis* CH=C<u>H</u>$_2$), 5.19 (d, J = 10 Hz, 1H, *trans* CH=C<u>H</u>$_2$), 5.07 (bs, NH_2^+/H_2O, D_2O exchange), 4.03 (d, J = 5 Hz, 2H, 3-CH_2).- MS (130°): m/z = 261 (100%, $M^{+\cdot}$), 260 (37), 246 (33), 234 (12), 233 (17), 214 (10), 174 (31), 147 (12), 146 (13), 103 (10), 89 (18), 82 (24), 80 (25), 56 (10), 41 (23).

4-(2,5-Dimethoxyphenyl)-3-methyl-2-(3H)-thiazolimine hydrobromide (**7v**)

Needles (methanol/ether), mp. 238° (decompn.), yield 56%.- $C_{12}H_{14}N_2O_2S \cdot HBr \cdot 1/4\ H_2O$ (335.7) Calcd. C 42.9 H 4.65 N 8.3 Found C 42.8 H 4.53 N 8.3.- UV (CH_3OH): λ max (log ε) = 206 (4.40), 228 (3.92), 304 nm (3.71).- ^{1}H-NMR: δ (ppm) = 9.60 (bs, 2H, NH_2^+, D_2O exchange), 7.15 (s, 1H, Ph-6-H and 5-H), 7.00 (s, 1H, Ph-3-H), 6.94 (s, 1H, Ph-4-H), 3.78 (s, 3H, Ph-2-O-CH_3), 3.75 (s, 3H, Ph-5-O-CH_3), 3.27 (s, 3H, 3-CH_3).- MS (130°): m/z = 250 (100%, $M^{+\cdot}$), 249 (16), 219 (16), 179 (12), 178 (12), 177 (27), 176 (10), 162 (10), 161 (32), 148 (25), 82 (18), 80 (18).

4-(Diphenylmethyl)-3-methyl-2(3H)-thiazolimine hydrobromide (**7w**)

From 1-bromo-3,3-diphenylpropan-2-one and *N*-methylthiourea. Crystals (ethanol/ether), mp. 189°, yield 72%.- $C_{17}H_{16}N_2S \cdot HBr$ (361.3) Calcd. C 56.5 H 4.74 N 7.8 Found C 56.6 H 4.81 N 7.8.- IR: 3429; 3047; 1625; 1590; 1550; 1490; 1449; 1424; 1392; 1176; 1154; 1111; 1076; 1029; 928; 862; 838; 779; 742; 719; 699; 681; 629 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 206 (4.40), 232 (3.98), 304 nm (3.71).- ^{1}H-NMR: δ (ppm) = 9.49 (bs, 2H, NH_2^+, D_2O exchange), 7.43-7.19 (m, 10 H aromat.), 6.03 (s, 1H, 5-H), 5.73 (s, 1H, 4-CH), 3.28 (s, 3H, 3-CH_3).- MS (150°): m/z = 280 (100%, $M^{+\cdot}$), 191 (14), 190 (13), 189 (88), 178 (10), 167 (27), 166 (10), 165 (36), 152 (19), 147 (43), 130 (11), 115 (10), 103 (11), 82 (17), 80 (17), 45 (10), 42 (16).

[4-[2-(3H)-Imino-3-methyl-thiazole]]-carboxylic acid ethylester hydrobromide (**7x**)

Crystals (methanol/ether), mp. 126°, yield 31%.- $C_7H_{10}N_2O_2S \cdot HBr$ (267.1). Calcd. C 31.5 H 4.15 N 10.5 Found C 31.4 H 4.24 N 10.5.- UV (CH_3OH): λ max (log ε) = 212 (4.13), 242 nm (3.83).- ^{1}H-NMR: δ (ppm) = 7.68 (s, 1H, 5-H), 5.47 (bs, 2H, NH_2^+, D_2O exchange), 4.28 (q, J = 7 Hz, 2H, O-C<u>H</u>$_2$-CH_3), 2.96 (s, 3H, 3-CH_3), 1.29 (t, J = 7 Hz, 3H, O-CH_2-C<u>H</u>$_3$).- MS (150°): m/z = 186 (100%, $M^{+\cdot}$), 158 (11), 141 (40), 140 (13), 139 (10), 114 (69), 113 (10), 112 (34), 82 (41), 81 (13), 80 (42), 79 (13), 74 (27), 73 (26), 72 (11), 58 (52), 57 (12).

4,4'-p-Phenylene-bis-[3-allyl-2(3H)-thiazolimine hydrobromide]

From 10 mmol 1,4-bis-(2-bromoacetyl)benzene and 20 mmol *N*-allylthiourea. Crystals (methanol/aceton/ether), mp. 243° (decompn.), yield 34%.- $C_{18}H_{18}N_4S_2 \cdot 2HBr$ (516.3) Calcd. C 41.9 H 3.90 N 10.9 Found C 41.8 H 3.86 N 10.9.- UV (CH_3OH): λ max (log ε) = 206 (4.31), 254 nm (4.14).- ^{1}H-NMR: δ (ppm) = 7.88 (s, 4H aromat.), 7.35 (s, 2H, 5 and 5'-H), 6.79 (bs, 4H, 2 and 2' NH_2^+, D_2O exchange), 6.01-5.88 (m, 2H, 3 and 3'-CH_2-C<u>H</u>), 5.35 (d, J = 18 Hz, 2H, *cis* 3 and 3'-CH_2-CH=C<u>H</u>$_2$), 5.25 (d, J = 10 Hz, 2H, *trans* 3 and 3'-CH_2-CH=C<u>H</u>$_2$), 4.10 (d, J = 5 Hz, 4H, 3 and 3'-CH_2).- MS (255°): m/z = 354 (100%, $M^{+\cdot}$), 353 (19), 272 (22), 230 (10), 82 (47), 81 (17), 80 (48), 79 (18), 41 (13).

Synthesis of thiazole-2-nitrosimines

General procedure: 10 mmol thiazolimine hydrohalogenide are dissolved in 100 ml H_2O and 100 ml $CHCl_3$ and 15 mmol $NaNO_2$ added. The mixture is kept at room temp. overnight and stirred vigorously. Then the org. layer is washed twice with 100 ml H_2O, dried with Na_2SO_4 and the solvent removed below 40°. The residue is recrystallized from the solvent stated.

3-Methyl-N-nitroso-2(3H)-thiazolimine (**8a**)

Light yellow crystals (H_2O/isopropanol), mp. 160°[1], yield 32%.- $C_4H_5N_3OS$ (143.2) Calcd. C 33.6 H 3.52 N 29.4 Found C 34.1 H 3.41 N 29.4.- IR: 3422; 3133; 3062; 3039; 1807; 1666; 1568; 1554; 1495; 1416; 1370; 1297; 1276; 1266; 1246; 1219; 1131; 1085; 970; 852; 817; 765; 687; 640 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 210 (4.03), 332 nm (3.93).- ^{1}H-NMR: δ (ppm) = 7.88 (s, 1H, 4-H), 7.24 (s, 1H, 5-H), 3.97 (bs, 3H, 3-CH_3).- MS (80°): m/z = 143 (100%, $M^{+\cdot}$), 113 (67), 99 (53), 86 (24), 72 (15), 69 (54), 59 (20), 55 (61), 45 (19), 42 (41).

3-Ethyl-N-nitroso-2(3H)-thiazolimine (**8b**)

Light yellow crystals (ethanol/ether), mp. 123° (decompn.), yield 57%.- $C_5H_7N_3OS$ (157.2) Calcd. C 38.2 H 4.49 N 26.7 Found C 37.9 H 4.47 N 26.6.- UV (CH_3OH): λ max (log ε) = 212 (4.10), 332 nm (3.96).- ^{1}H-NMR: δ (ppm) = 7.96 (s, 1H, 4-H), 7.27 (s, 1H, 5-H), 4.48 (bs, 2H, 3-CH_2), 1.38 (bs, 3H, CH_3).- MS (30°): m/z = 157 (38%, $M^{+\cdot}$), 129 (64), 127 (18), 113 (11), 101 (24), 86 (22), 72 (27), 59 (31), 54 (45), 44 (54), 30 (23).

3-Allyl-N-nitroso-2(3H)-thiazolimine (**8c**)

Light yellow crystals (methanol/ether), mp. 58°, yield 62%.- $C_6H_7N_3OS$ (169.2) Calcd. C 42.6 H 4.17 N 24.8 Found C 42.7 H 4.16 N 25.1.- UV (CH_3OH): λ max (log ε) = 206 (3.94), 248 (3.81), 334 nm (3.98).- ^{1}H-NMR: δ (ppm) = 7.87 (s, 1H, 4-H), 7.28 (s, 1H, 5-H), 6.03 (m, 1H, C<u>H</u>=CH_2), 5.27 (d, J = 10 Hz, 1H, *trans* CH=C<u>H</u>$_2$), 5.11 (d, J = 16 Hz, 1H, *cis* CH=C<u>H</u>$_2$), 5.05-4.60 (bs, 2H, 3-CH_2).- MS (75°): m/z = 169 (5%, $M^{+\cdot}$), 139 (16), 111 (12), 59 (10), 45 (12), 41 (100), 39 (30).

3-Benzyl-N-nitroso-2(3H)-thiazolimine (**8d**)

Orange platelets (isopropanol), mp. 111°, yield 87%.- $C_{10}H_9N_3OS$ (219.3) Calcd. C 54.8 H 4.14 N 19.2 Found C 54.3 H 4.07 N 19.2.- UV (CH_3OH): λ max (log ε) = 210 (4.09), 248 (3.82), 338 nm (4.00).- ^{1}H-NMR: δ (ppm) = 8.03 (s, 1H, 4-H), 7.33 (bs, 6H, 5-H and Ph), 5.61 (bs, 2H, 3-CH_2).- MS (120°): m/z = 219 (7%, $M^{+\cdot}$), 189 (23), 91 (100), 65 (18), 45 (11).

3,4-Dimethyl-N-nitroso-2(3H)-thiazolimine (**8e**)

Yellow orange crystals (isopropanol), mp. 176°[2] (dec.), yield 46%.- $C_5H_7N_3OS$ (157.2) Calcd. C 38.2 H 4.49 N 26.7 Found C 38.3 H 4.53 N 26.6.- UV (CH_3OH): λ max (log ε) = 210 (3.87), 338 nm (3.54).- ^{1}H-NMR: δ (ppm) = 6.90 (bs, 1H, 5-H), 3.88 (bs, 3H, 3-CH_3), 2.42 (s, 3H, 4-CH_3).- MS (120°): m/z = 157 (52%, $M^{+\cdot}$), 127 (47), 113 (18), 86 (18), 83 (13), 73 (17), 71 (15), 69 (12), 56 (100), 45 (35), 42 (48), 39 (12), 30 (11).

3-Ethyl-4-methyl-N-nitroso-2(3H)-thiazolimine (**8f**)

Yellow orange needles (isopropanol), mp. 124°, yield 69%.- $C_6H_9N_3OS$ (171.2) Calcd. C 42.1 H 5.30 N 24.5 Found C 41.9 H 5.33 N 24.5.- IR: 3422; 3068; 2991; 2969; 2935; 2920; 1595; 1570; 1506; 1457; 1434; 1394; 1381; 1365; 1343; 1332; 1305; 1255; 1220; 1178; 1138; 1121; 1084; 1074; 1036; 965; 871; 841; 810; 788; 773 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 206 (4.09), 338 nm (3.92).- ^{1}H-NMR: δ (ppm) = 6.91 (s, 1H, 5-H), 4.37 (bs, 2H, 3-CH_2), 2.46 (s, 3H, 4-CH_3, 1.31 (bs, 3H, CH_2-C<u>H</u>$_3$).- MS (80°): m/z = 171 (100%, $M^{+\cdot}$), 143 (10), 141 (89), 127 (16), 114 (30), 99 (19), 86 (16), 83 (14), 73 (33), 72 (16), 71 (46), 70 (19), 69 (67), 67 (15), 54 (10), 45 (43), 43 (15), 42 (59), 39 (13), 30 (11).

3-Allyl-4-methyl-N-nitroso-2(3H)-thiazolimine (**8g**)

Light orange cubes (isopropanol), mp. 87°, yield 71%.- $C_7H_9N_3OS$ (183.2) Calcd. C 45.9 H 4.95 N 22.9 Found C 45.6 H 4.97 N 22.9.- UV (CH_3OH): λ max (log ε) = 212 (3.88), 338 nm (3.50).- ^{1}H-NMR: δ (ppm) = 6.95 (s, 1H, 5-H), 5.99 (m, 1H, C<u>H</u>=CH_2), 5.23-4.87 (bs, 2H, 3-CH_2), 5.22 (d, J = 10.4 Hz, 1H, *trans* CH=C<u>H</u>$_2$), 4.90 (d, J = 17.4 Hz, 1H, *cis* CH=C<u>H</u>$_2$), 2.39 (s, 3H, 4-CH_3).- MS (80°): m/z = 183 (11%, $M^{+\cdot}$), 155 (4), 153 (53), 139 (13), 125 (19), 73 (12), 71 (12), 45 (20), 41 (100), 39 (32).

4-Methyl-N-nitroso-3-phenyl-2(3H)-thiazolimine (**8h**)

Yellow needles (isopropanol), mp. 146°, yield 71%.- $C_{10}H_9N_3OS$ (219.3) Calcd. C 54.8 H 4.14 N 19.2 Found C 54.4 H 4.05 N 19.1.- UV (CH_3OH): λ max (log ε) = 208 (4.39), 346 nm (4.05).- ^{1}H-NMR: δ (ppm) = 7.62 (m, 3H aromat.), 7.50 (m, 2H aromat.), 7.04 (s, 1H, 5-H), 2.08 (s, 3H, 4-CH_3).- MS (100°): m/z = 219 (55%, $M^{+\cdot}$), 191 (16), 189 (100), 174 (50), 130 (87), 118 (28), 103 (31), 77 (58).

3-Benzyl-4-methyl-N-nitroso-2(3H)-thiazolimine (**8i**)

Orange crystals (isopropanol), mp. 140°, yield 82%.- $C_{11}H_{11}N_3OS$ (233.3) Calcd. C 56.6 H 4.75 N 18.0 Found C 56.4 H 4.65 N 18.1.- UV (CH_3OH): λ max (log ε) = 210 (4.26), 340 nm (3.81).- ^{1}H-NMR: δ (ppm) = 7.40-7.29 (m, 3H aromat.), 7.16 (d, J = 6.8 Hz, 2H aromat.), 6.98 (s, 1H, 5-H), 5.65 (bs, 2H, 3-CH_2), 2.33 (s, 3H, 4-CH_3).- MS (110°): m/z = 233 (6%, $M^{+\cdot}$), 205 (4), 203 (21), 91 (100), 65 (16).

4-Methyl-N-nitroso-3-(2-phenylethyl)-2(3H)-thiazolimine (**8k**)

Green yellow needles (isopropanol), mp. 149°, yield 15%.- $C_{12}H_{13}N_3OS$ (247.3) Calcd. C 58.3 H 5.30 N 17.0 Found C 58.3 H 5.29 N 16.9.- UV (CH_3OH): λ max (log ε) = 210 (4.19), 340 nm (3.55).- ^{1}H-NMR: δ (ppm) = 7.33-7.19 (m, 3H aromat.), 7.17 (d, J = 6.6 Hz, 2H, aromat.), 6.83 (s, 1H, 5-H), 4.51 (bs, 2H, 3-CH_2-), 3.08 (bs, 2H, 3-CH_2-C<u>H</u>$_2$-), 2.17 (s, 3H, 4-CH_3).- MS (80°): m/z = 247 (19%, $M^{+\cdot}$), 219 (7), 217 (66), 209 (15), 202 (12), 178 (10), 164 (16), 138 (12), 114 (40), 105 (100), 91 (38), 79 (32), 77 (40), 71 (11), 65 (12), 51 (14), 45 (30), 39 (15), 30 (11).

3-Methyl-N-nitroso-4-phenyl-2(3H)-thiazolimine (**8l**)

Yellow needles (isopropanol), mp. 188°[2], yield 39%.- $C_{10}H_9N_3OS$ (219.3) Calcd. C 54.8 H 4.14 N 19.2 Found C 54.8 H 3.92 N 19.2.- UV (CH_3OH): λ max (log ε) = 206 (4.28), 340 nm (4.01).- ^{1}H-NMR: δ (ppm) = 7.63-7.56 (m, 5H aromat.), 7.23 (s, 1H, 5-H), 3.74 (bs, 3H, 3-CH_3).- MS (240°): m/z = 219 (7%, $M^{+\cdot}$), 191 (78), 189 (12), 162 (25), 134 (34), 118 (100), 103 (10), 91 (12), 89 (13), 77 (36), 51 (18), 45 (19).

3-Ethyl-N-nitroso-4-phenyl-2(3H)-thiazolimine (**8m**)

Yellow needles (isopropanol), mp. 151°, yield 58%.- $C_{11}H_{11}N_3OS$ (233.3) Calcd. C 56.6 H 4.75 N 18.0 Found C 56.5 H 4.63 N 18.1.- UV (CH_3OH): λ max (log ε) = 206 (4.32), 338 nm (3.91).- ^{1}H-NMR: δ (ppm) = 7.60 (s, 5H aromat.), 7.22 (s, 1H, 5-H), 4.23 (bs, 3H, 3-CH_2), 1.18 (s, 3H, CH_3).- MS (90°): m/z = 233 (52%, $M^{+\cdot}$), 205 (17), 203 (41), 188 (30), 176 (58), 174 (41), 161 (11), 148 (38), 134 (100), 121 (13), 104 (24), 102 (14), 89 (14), 77 (32), 51 (17), 45 (15).

3-Allyl-N-nitroso-4-phenyl-2(3H)-thiazolimine (**8n**)

Orange needles (isopropanol), mp. 103°, yield 67%.- $C_{12}H_{11}N_3OS$ (245.3) Calcd. C 58.8 H 4.52 N 17.1 Found C 58.5 H 4.34 N 17.3.- UV (CH_3OH): λ max (log ε) = 206 (4.25), 260 (3.85), 340 nm (3.58).- ^{1}H-NMR: δ (ppm) = 7.56 (bs, 5H aromat.), 7.26 (s, 1H, 5-H), 5.14-4.70 (bs, 2H, 3-CH_2), 5.13 (d, J = 10.4 Hz, 1H, *trans* CH=C$\underline{H}_2$), 4.74 (d, J = 17.4 Hz, 1H, *cis* CH=C$\underline{H}_2$).- MS (80°): m/z = 245 (12%, $M^{+\cdot}$), 217 (13), 215 (100), 201 (16), 174 (48), 148 (13), 134 (33), 102 (11), 77 (22), 51 (11), 41 (93), 39 (20).

N-Nitroso-3,4-diphenyl-2(3H)-thiazolimine (**8o**)

Yellow orange needles (methanol), mp. 155°, yield 39%.- $C_{15}H_{11}N_3OS$ (281.3) Calcd. C 64.0 H 3.94 N 14.9 Found C 64.0 H 3.81 N 14.8.- IR: 3084; 3045; 1594; 1496; 1455; 1444; 1322; 1296; 1196; 1110; 1056; 1024; 999; 968; 942; 918; 852; 844; 773; 750; 694; 637 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 210 (4.31), 250 (4.04), 338 nm (3.40).- ^{1}H-NMR: δ (ppm) = 7.43-7.27 (m, 11 H, 5-H, 3-Ph, 4-Ph).- MS (150°): m/z = 281 (18%, $M^{+\cdot}$), 253 (70), 251 (46), 236 (17), 224 (31), 223 (15), 181 (13), 180 (95), 165 (15), 134 (44), 89 (13), 77 (100), 51 (39).

4-(4-Methoxyphenyl)-3-methyl-N-nitroso-2(3H)-thiazolimine (**8p**)

Yellow orange crystals (isopropanol), mp. 170°, yield 69%.- $C_{11}H_{11}N_3O_2S$ (249.3) Calcd. C 53.0 H 4.45 N 16.9 Found C 52.7 H 4.28 N 16.8.- UV (CH_3OH): λ max (log ε) = 206 (4.37), 234 (4.25), 342 nm (3.86).- ^{1}H-NMR: δ (ppm) = 7.54 (d, J = 8.7 Hz, 2H, 4-Ph-2-H and 6-H), 7.13 (m, 3H, 5-H and 4-Ph-3-H and 5-H), 3.90-3.77 (bs, 3H, 3-CH_3), 3.35 (s, 3H, O-CH_3).- MS (140°): m/z = 249 (55%, $M^{+\cdot}$), 221 (25), 219 (60), 204 (15), 192 (74), 189 (15), 164 (100), 149 (50), 148 (21), 146 (11), 132 (32), 121 (15), 89 (13), 77 (16), 63 (16).

3-Ethyl-4-(4-methoxyphenyl)-N-nitroso-2(3H)-thiazolimine (**8q**)

Yellow orange needles (isopropanol), mp. 139°, yield 65%.- $C_{12}H_{13}N_3O_2S$ (263.3) Calcd. C 54.7 H 4.98 N 16.0 Found C 54.6 H 4.88 N 16.1.- UV (CH_3OH): λ max (log ε) = 206 (4.37), 234 (4.26), 342 nm (3.98).- ^{1}H-NMR: δ (ppm) = 7.52 (d, J = 8.4 Hz, 2H, 4-Ph-2-H and 6-H), 7.13 (m, 3H, 5-H and 4-Ph-3-H and 5-H), 4.22 (bs, 2H, 3-CH_2), 3.84 (s, 3H, O-CH_3), 1.18 (bs, 3H, CH_2-C$\underline{H}_3$).- MS (100°): m/z = 263 (53%, $M^{+\cdot}$), 235 (20), 233 (55), 218 (19), 206 (56), 204 (41), 191 (15), 189 (14), 178 (14), 164 (100), 149 (36), 134 (16), 132 (10), 121 (13), 89 (10), 77 (14), 45 (17), 31 (25).

3-Allyl-4-(4-methoxyphenyl)-N-nitroso-2(3H)-thiazolimine (**8r**)

Yellow orange needles (isopropanol), mp. 127°, yield 85%.- $C_{13}H_{13}N_3O_2S$ (275.3) Calcd. C 56.7 H 4.76 N 15.3 Found C 56.8 H 4.72 N 15.2.- UV (CH_3OH): λ max (log ε) = 206 (4.40), 234 (4.19), 342 nm (3.86).- ^{1}H-NMR: δ (ppm) = 7.48 (d, J = 8.7 Hz, 2H, 4-Ph-2-H and 6-H), 7.18 (s, 1H, 5-H), 7.10 (d, J = 8.7 Hz, 2H, 4-Ph-3-H and 5-H), 5.15-4.71 (bs, 2H, 3-CH_2), 5.13 (d, J = 10.4 Hz, 1H, *trans* CH=C$\underline{H}_2$), 4.74 (d, J = 17.4 Hz, 1H, *cis* CH=C$\underline{H}_2$), 3.83 (s, 3H, O-CH_3).- MS (110°): m/z = 275 (8%, $M^{+\cdot}$), 247 (100), 245 (60), 206 (97), 204 (37), 191 (31), 178 (10), 175 (12), 164 (48), 149 (20), 121 (11), 89 (10), 77 (14), 63 (10), 45 (14), 41 (92), 39 (29).

3-Allyl-N-nitroso-4-(4-tolyl)-2(3H)-thiazolimine (**8s**)

Yellow orange needles (isopropanol), mp. 109°, yield 67%.- $C_{13}H_{13}N_3OS$ (259.3) Calcd. C 60.2 H 5.05 N 16.2 Found C 59.8 H 5.05 N 16.3.- IR: 3051; 3020; 2971; 1642; 1617; 1574; 1502; 1446; 1419; 1404; 1366; 1335; 1237; 1212; 1201; 1184; 1156; 1138; 1095; 1007; 943; 925; 811; 792; 713; 616 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 206 (3.88), 342 nm (3.04).- ^{1}H-NMR: δ (ppm) = 7.44 (d, J = 8 Hz, 2H, 4-Ph-2-H and 6-H), 7.35 (d, J = 8 Hz, 2H, 4-Ph-3-H and 5-H), 7.20 (s, 1H, 5-H), 5.12 (d, J = 10 Hz, 1H, *trans* CH=C$\underline{H}_2$), 5.05-4.71 (bs, 2H, 3-CH_2), 4.73 (d, J = 17 Hz, 1H, *cis* CH=C$\underline{H}_2$), 2.39 (s, 3H, 4'-CH_3).- MS (80°): m/z = 259 (8%, $M^{+\cdot}$), 231 (37), 229 (78), 215 (12), 190 (31), 188 (47), 175 (13), 162 (12), 148 (31), 115 (14), 91 (17), 65 (11), 45 (12), 41 (100), 39 (19).

3-Methyl-4-(4-nitrophenyl)-N-nitroso-2(3H)-thiazolimine (**8t**)

Yellow crystals (methanol), mp. 168° (dec.), yield 29%.- $C_{10}H_8N_4O_3S$ (264.3) Calcd. C 45.5 H 3.05 N 21.2 Found C 45.9 H 2.83 N 20.9.- UV (CH_3OH): λ max (log ε) = 204 (4.23), 228 (4.14), 330 nm (4.27).- ^{1}H-NMR: δ (ppm) = 8.35-8.22 (m, 5H, 5-H and 4-Ph), 4.51, 3.62 (2s, 3H, 3-CH_3, ratio *Z*:*E* = 35:65).- MS (90°): m/z = 264 (4%, $M^{+\cdot}$), 236 (9), 234 (100), 217 (15), 188 (79), 173 (18), 146 (16), 121 (10), 89 (19), 45 (15), 30 (19).

3-Allyl-4-(4-nitrophenyl)-N-nitroso-2(3H)-thiazolimine (**8u**)

Yellow crystals (isopropanol), mp. 153° (dec.), yield 32%.- $C_{12}H_{10}N_4O_3S$ (290.3) Calcd. C 49.7 H 3.47 N 19.3 Found C 50.1 H 3.44 N 19.5.- UV (CH_3OH): λ max (log ε) = 206 (4.26), 218 (4.16), 224 (4.16), 330 nm (4.28).- ^{1}H-NMR: δ (ppm) = 8.35-8.22 (m, 5H, 5-H and 4-Ph), 6.35-6.22, 5.88-5.76 (2m, 1H, C$\underline{H}$=CH_2, ratio *Z*:*E* = 44:56), 5.65, 4.87 (2d, J = 6 Hz, 2H, 3-CH_2-, ratio *Z*:*E* = 44:56), 5.43, 5.12 (2d, J = 17 Hz, 1H, *cis* CH=C$\underline{H}_2$, ratio *Z*:*E* = 44:56), 5.35, 5.18 (2d, J = 10 Hz, 1H, *trans* CH=C$\underline{H}_2$, ratio *Z*:*E* = 44:56).- MS (90°): m/z = 290 (1%, $M^{+\cdot}$), 262 (5), 260 (51), 214 (14), 89 (10), 41 (100).

4-(2,5-Dimethoxyphenyl)-3-methyl-N-nitroso-2(3H)-thiazolimine (**8v**)

Yellow needles (isopropanol), mp. 91°, yield 53%.- $C_{12}H_{13}N_3O_3S$ (279.3) Calcd. C 51.6 H 4.69 N 15.0 Found C 51.4 H 4.63 N 15.0.- UV (CH_3OH): λ max (log ε) = 208 (4.40), 230 (4.31), 256 (4.23), 318 nm (4.00).- ^{1}H-NMR: δ (ppm) = 7.96, 7.87 (2s, 1H, 5-H, ratio *E*:*Z* = 34:66), 7.72 (m, 1H, 4-Ph-6-H), 7.10 (d, J = 9 Hz, 1H, 4-Ph-3-H), 6.95 (m, 1H, 4-Ph-4-H), 4.48, 3.62 (2s, 3H, 3-CH_3, ratio *Z*:*E* = 34:66), 3.89 (s, 3H, 2'-O-CH_3), 3.77 (s, 3H, 5'-O-CH_3).- MS (40°): m/z = 279 (11%, $M^{+\cdot}$), 251 (6), 249 (100), 218 (25), 208 (18), 194 (41), 179 (20), 30 (10).

4-(Diphenylmethyl)-3-methyl-N-nitroso-2(3H)-thiazolimine (**8w**)

Orange needles (isopropanol), mp. 134°, yield 46%.- $C_{17}H_{15}N_3OS$ (309.4) Calcd. C 66.0 H 4.89 N 13.6 Found C 66.1 H 4.87 N 13.3.- IR: 3400; 3060; 3004; 2953; 1620; 1594; 1560; 1507; 1492; 1443; 1418; 1383; 1321; 1299; 1282; 1240; 1209; 1137; 1120; 1099; 1060; 883; 876; 831; 771; 740; 699; 624 cm^{-1}.- UV (CH_3OH): λ max (log ε) = 206 (4.49), 338 nm (3.71).- ^{1}H-NMR: δ (ppm) = 7.43-7.21 (m, 10 H aromat.), 6.28 (s, 1H, 5-H), 5.93 (s, 1H, 4-CH), 3.62 (bs, 3H, 3-CH_3).- MS (60°): m/z = 309 (3%, $M^{+\cdot}$), 281 (100), 279 (14), 221 (10), 220 (36), 204 (10), 191 (14), 189 (40), 179 (15), 178 (12), 167 (49), 166 (16), 165 (54), 152 (26), 147 (24), 144 (15), 115 (13), 103 (14), 45 (62), 42 (20), 31 (15).

[4-[2(3H)-Imino-3-methyl-N-nitroso-thiazole]]-carboxylic acid ethylester (**8x**)

Yellow stars (isopropanol), mp. 78°, yield 35%.- $C_7H_9N_3O_3S$ (215.2) Calcd. C 39.1 H 4.21 N 19.5 Found C 38.7 H 4.20 N 19.6.- UV (CH_3OH):

λ max (log ε) = 206 (4.07), 222 (4.09), 308 nm (3.81).- ^{1}H-NMR: δ (ppm) = 8.31, 8.26 (2s, 1H, 5-H, ratio *E*:*Z* = 33:67), 4.42, 3.52 (2s, 3H, 3-CH_3, ratio *Z*:*E* = 67:33), 4.33 (q, J = 7 Hz, 2H, 4-COO-CH_2), 1.33 (t, J = 7 Hz, 3H, CH_2-C<u>H</u>$_3$).- MS (150°): m/z = 215 (4%, $M^{+\cdot}$), 187 (6), 185 (100), 139 (14), 72 (18), 70 (10), 58 (99).

3-Methyl-N-nitroso-4-phenyl-5-tetradecyl-2(3H)-thiazolimine (**8y**)

Light yellow needles (methanol/water), mp. 72°, yield 23%.- $C_{24}H_{37}N_3OS$ (415.6) Calcd. C 69.4 H 8.97 N 10.0 Found C 69.4 H 9.09 N 10.0.- UV (CH_3OH): λ max (log ε) = 206 (4.02), 338 nm (3.97).- ^{1}H-NMR: δ (ppm) = 7.58-7.53 (bs, 5H aromat.), 3.36 (s, 3H, 3-CH_3), 2.49 (bs, 2H, 5-CH_2), 1.47 (bs, 2H, 5-CH_2-C<u>H</u>$_2$), 1.19 (bs, 22H, (C<u>H</u>$_2$)$_{11}$-CH_3), 0.85 (t, 3H, $(CH_2)_{13}$-C<u>H</u>$_3$).- MS (140°): m/z = 415 (5%, $M^{+\cdot}$), 389 (8), 388 (30), 387 (98), 205 (23), 204 (100), 176 (20), 118 (36).

3,4-Dimethyl-N-nitroso-5-phenyl-2-thiazolidinimine (**10**)

From 3,4-dimethyl-5-phenyl-2-thiazolidinimine hydrorhodanine in chloroform/water. Light orange needles (isopropanol), mp. 114°, yield 32%.- $C_{11}H_{13}N_3OS$ (235.3) Calcd. C 56.2 H 5.57 N 17.9 Found C 56.3 H 5.62 N 17.5.- UV (CH_3OH): λ max (log ε) = 206 (4.18), 290 (4.14), 476 nm (1.54).- ^{1}H-NMR: δ (ppm) = 7.49-7.36 (m, 5H aromat.), 4.82 (d, J = 5.4 Hz, 1H, 5-H), 4.51 (m, 1H, 4-H), 3.23 (s, 3H, 3-CH_3), 1.48 (d, J = 5.4 Hz, 3H, 4-CH_3).- MS (90°): m/z = 235 (24%, $M^{+\cdot}$), 207 (29), 205 (1), 192 (12), 150 (23), 132 (10), 122 (41), 118 (100), 115 (13), 91 (20), 89 (11), 83 (24), 77 (14), 58 (66), 56 (23), 42 (45).

4,4'-p-Phenylene-bis-[3-allyl-N-nitroso-2(3H)-thiazolimine] (**9**)

From 10 mmol 4,4'-*p*-Phenylene-bis-(3-allyl-2(3*H*)-thiazolimine · HBr) (see above) in 200 ml H_2O and 150 ml chloroform. The crude product was purified by liquid chromatography in SiO_2 (column 30 cm, eluent CH_2Cl_2).

Yellow crystals (acetone/isopropanol), mp. 145° (dec.), yield 10%.- $C_{18}H_{16}N_6O_2S_2$ (412.5) Calcd. C 52.4 H 3.91 N 20.4 Fournd C 52.4 H 3.85 N 20.6.- UV (CH_3CN): λ max (log ε) = 200 (4.53), 222 (4.31), 304 nm (4.54).- ^{1}H-NMR: δ (ppm) = 8.08 (m, 4H aromat.), 8.04, 7.96 (2s, 2H, 5-H, ratio *Z*:*E* = 48:52), 6.33-6.22, 5.87-5.76 (2m, 2H, C<u>H</u>=CH_2, ratio *Z*:*E* = 48:52), 5.65, 4.89 (2d, J = 7 Hz, 4H, 3'-CH_2, ratio *Z*:*E* = 48:52), 5.44, 5.14 (2d, J = 17 Hz, 2H, *cis* CH=C<u>H</u>$_2$, ratio *Z*:*E* = 48:52), 5.36, 5.18 (2d, J = 10 Hz, 2H, *trans* CH=C<u>H</u>$_2$, ratio *Z*:*E* = 48:52).- MS (150°): m/z = 342 (5%, $M^{+\cdot}$), 314 (20), 288 (11), 287 (17), 286 (100), 285 (26), 226 (54), 198 (18), 197 (74), 196 (16), 182 (30), 157 (25), 155 (19), 144 (32), 143 (67), 142 (37), 130 (18), 109 (12), 85 (16), 83 (25), 73 (13), 69 (16), 43 (30), 41 (14).

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[Ph209]