

# 1-Thiacyclooct-4-yne (= 5,6-Didehydro-3,4,7,8-tetrahydro-2*H*-thiocin), and Its Sulfoxide and Its Sulfone

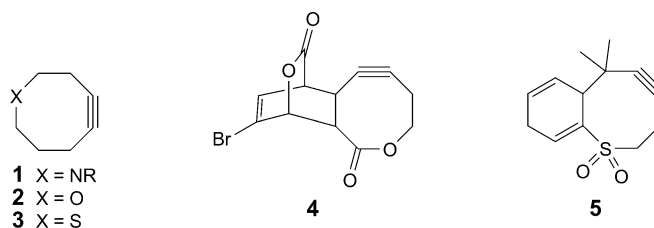
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1-Thiacyclooct-4-yne (= 5,6-didehydro-3,4,7,8-tetrahydro-2*H*-thiocin; **9**) can be prepared from thiocan-5-one (**6**) in three steps by applying the so-called selenadiazole method. The heterocyclic alkyne can be oxidized to the corresponding sulfoxide **16** and sulfone **17**. Due to their geometrical strain, all three cyclic alkynes show high reactivities in *Diels–Alder* and 1,3-dipolar cycloadditions. Moreover, tetrathiafulvalenes can be prepared from **9** and **16** by the reaction with CS<sub>2</sub>.

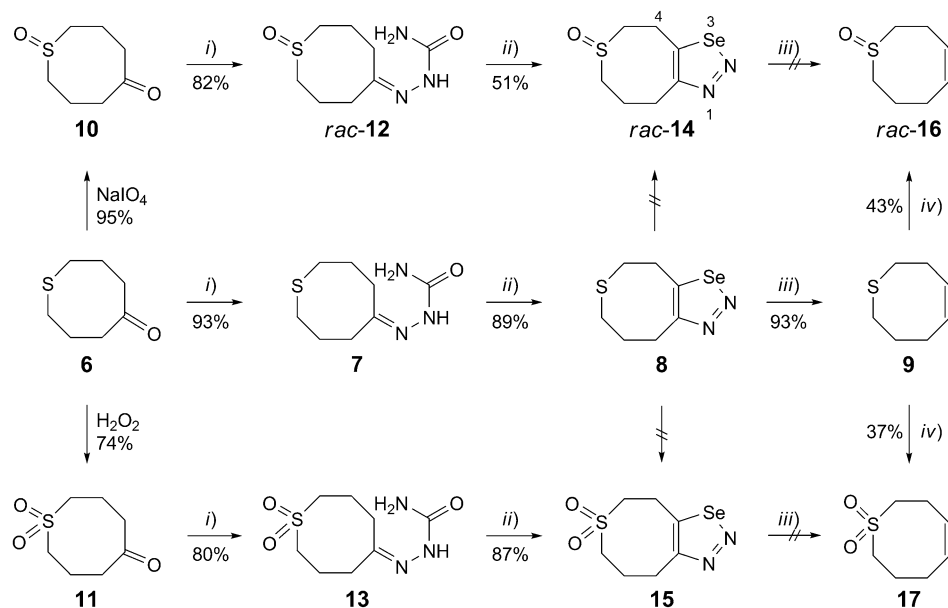
**Introduction.** – Due to their high reactivity in addition and cycloaddition reactions, strained cycloalkynes have a high actuality in click processes and bioorthogonal reactions [1–14]. In the previous five years, many studies of azacyclooct-5-yne (**1**) appeared [8][11][15–42].

To the best of our knowledge, only one example exists for 1-oxacyclooct-4-yne (**2**) and one for 1-thiacyclooct-4-yne **3**, namely the tricyclic lactone **4** [42] and the bicyclic sulfone **5** [43], respectively. This prompted us to report our results on the parent compound **3**.



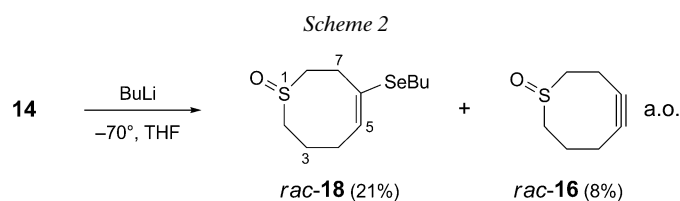
**Results and Discussion.** – A convenient and high-yield preparation of strained cyclic alkynes is based on the fragmentation of 1,2,3-selenadiazoles [44]. We used the conversion of thiocanone **6** to the 1,2,3-selenadiazole **8** *via* the semicarbazone **7** [45]. Thermolysis of **8** on Cu powder gave the desired 1-thiacyclooct-4-yne (= 5,6-didehydro-3,4,7,8-tetrahydro-2*H*-thiocin; **9**) in almost quantitative yields (*Scheme 1*).

The 1,2,3-selenadiazole ring is sensitive towards oxidation. Therefore, we tried to oxidize its precursor, the thiocanone **6** with NaIO<sub>4</sub> to the sulfoxide **10** and with H<sub>2</sub>O<sub>2</sub> to the sulfone **11**. The corresponding 1,2,3-selenadiazoles **14** and **15** were then obtained *via* the semicarbazones **12** and **13**, respectively. However, the thermal fragmentation of **14** and **15** failed. The volatility of the desired products is not high enough, so that decompositions occurred in the hot zone.

Scheme 1. Preparation of 5-Thiacyclooctyne (**9**), and Its Sulfoxide (**16**) and Its Sulfone (**17**)

i)  $\text{H}_2\text{NNHCONH}_2$ , EtOH, AcONa. ii)  $\text{SeO}_2$ , aqueous dioxane. iii) Cu, 165–175°, 100 Pa. iv)  $\text{NaIO}_4$ , 0°.

Therefore, we tried the alkaline fragmentation of the 1,2,3-selenadiazole **14** with BuLi. The reaction led to a mixture of several Se-containing products. Selenio sulfoxide **18** was the major component, and the desired alkyne **16** was a minor product, in an unsatisfying yield (Scheme 2).



Finally, we realized that the stability of 1-thiacyclooct-4-yne (**9**) is sufficient for the oxidation to its sulfoxide **16** and its sulfone **17**. A fourfold excess of  $\text{NaIO}_4$  yielded 80% of the oxidation-productmixture **16/17** in a 43:37 ratio (Scheme 1). A higher excess of  $\text{NaIO}_4$  increased the portion of the sulfone **17**, but reduced the overall yield.

One- and two-dimensional NMR experiments were performed for the characterization of the new alkynes. A  $^1\text{H}$ ,  $^1\text{H}$ -shift-correlated NMR spectrum of *rac*-**16** is depicted in the Figure. The COSY 45 technique is suitable to distinguish between the geminal and vicinal couplings [46]. A control for the assignment of geminal H-atoms was achieved by a HSQC measurement.

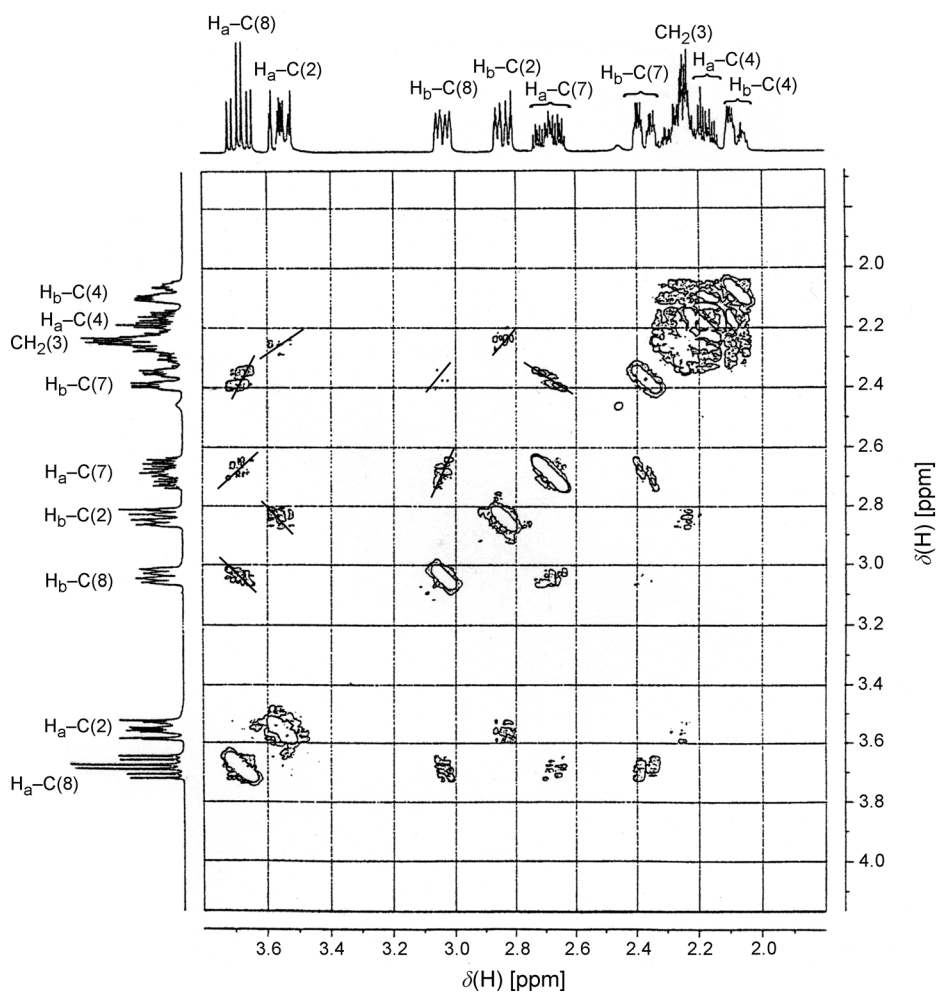


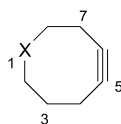
Figure.  $^1\text{H}, ^1\text{H}$ -COSY-45-NMR Spectrum of *rac*-**16**. The cross-peaks, which are characterized by a positive slope, correspond to vicinal couplings, the cross-peaks marked with a negative slope correspond to geminal couplings.

The  $^1\text{H}$  and  $^{13}\text{C}$  chemical shifts of the alkynes **9**, **16**, and **17** are compiled in the Table.

An easy anchor point for the interpretation of the NMR spectra is always  $\text{CH}_2(3)$  with two adjacent  $\text{CH}_2$  groups,  $\text{CH}_2(2)$  and  $\text{CH}_2(4)$ . Due to the geometrical strain, the  $\text{sp}$ -atoms C(5) and C(6) exhibit signals with relatively high  $\delta$  values. Their difference  $\Delta\delta$  is small, which is in accordance with the small polarization of the  $\text{C}\equiv\text{C}$  bonds and the small regioselectivity of certain cycloadditions shown below.

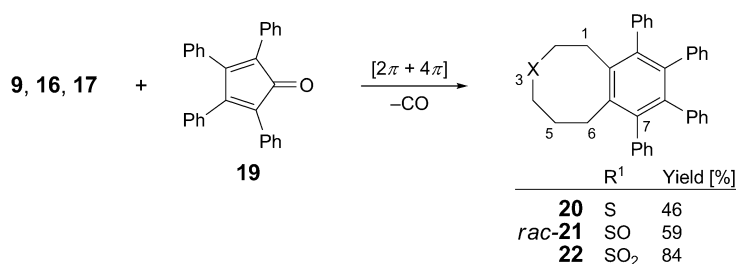
The strain energies of the eight-membered rings of **9**, **16**, and **17** should be comparable to that of cyclooctyne [44]. Hence, a high reactivity of **9**, **16**, and **17** in cycloaddition reactions can be expected. We studied first the reactions with 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (**19**) at room temperature (Scheme 3). The Diels–

Table.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ) Data of the Heterocyclic Alkynes **9**, **16**, and **17**.  $\delta$  in ppm relative to  $\text{Me}_4\text{Si}$  as internal standard,  $J$  in Hz. The atom numbering corresponds to the 2*H*-thiocin nomenclature.



Compound	X	NMR	$\text{CH}_2(2)$	$\text{CH}_2(3)$	$\text{CH}_2(4)$	C(5,6)	$\text{CH}_2(7)$	$\text{CH}_2(8)$
<b>9</b>	S	$\delta(\text{H})$	2.76–2.72	2.19–2.12	2.24–2.19		2.35–2.29	2.97–2.93
		$\delta(\text{C})$	35.5	35.9	19.6	94.1, 92.2	23.6	41.9
<i>rac</i> - <b>16</b>	SO	$\delta(\text{H})$	3.59–3.50	2.23–2.30	2.22–2.14		2.74–2.65	3.72–3.65
			2.88–2.80	2.23–2.30	2.12–2.04		2.42–2.32	3.06–3.02
		$\delta(\text{C})$	62.0	25.8	18.5	92.1, 88.7	15.6	60.8
<b>17</b>	$\text{SO}_2$	$\delta(\text{H})$	3.37–3.33	2.36–2.28	2.26–2.20		2.61–2.55	3.55–3.51
		$\delta(\text{C})$	61.9	25.3	18.7	92.1, 88.9	16.0	59.9

Scheme 3

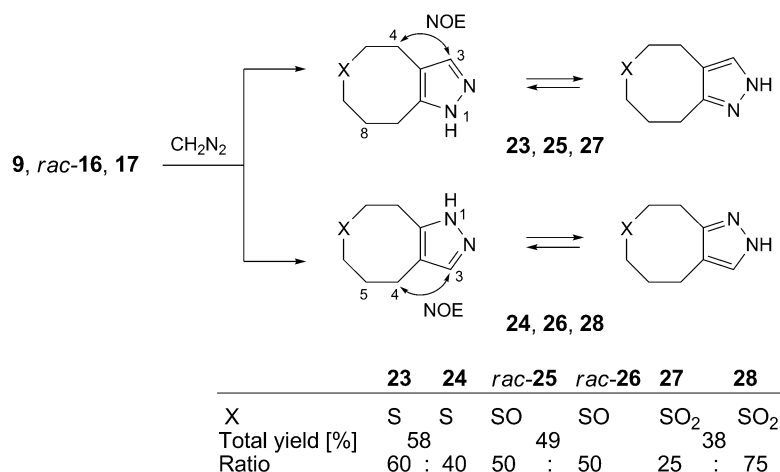


*Alder* reactions with subsequent aromatization according to the *Alder–Rickert* rule furnished the cycloadducts **20**, **21**, and **22**, respectively, in reasonable-to-good yields.

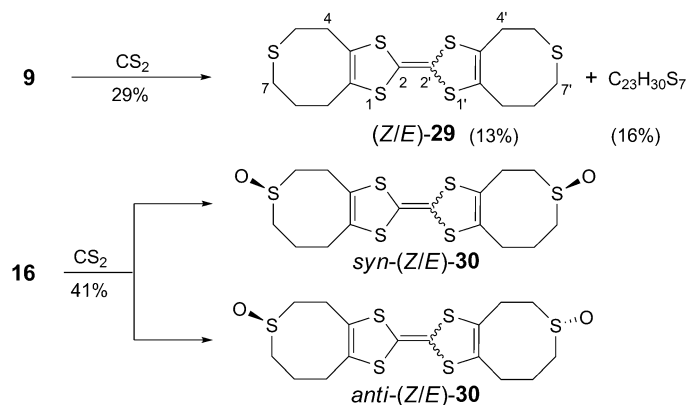
From a synthetic point of view, the 1,3-dipolar cycloaddition, another  $[2\pi + 4\pi]$  cycloaddition, of **8**, **16**, and **17** with  $\text{CH}_2\text{N}_2$  is more attractive. The tautomeric pyrazoles **23**–**28** were obtained (Scheme 4). The regioselectivities **23/24**, **25/26**, and **27/28** change from 3:2 for the reaction of **9** to 1:3 for the reaction of the sulfone **17**. NOE Experiments served for the distinction between the isomeric pyrazoles. Irradiation into the signal of  $\text{H}-\text{C}(3)$  led to a positive NOE for  $\text{CH}_2(4)$ , which is a part of the ethylene ‘chain’ in **23**, **25**, and **27**, whereas it is a part of the trimethylene ‘chain’ in **24**, **26**, and **28**.

Finally, we studied the behavior of the alkynes toward  $\text{CS}_2$  (Scheme 5). Alkyne **9** furnished, after 12 d in boiling  $\text{CS}_2$ , tetrathiafulvalene **29** in low yield. This reaction type is restricted to strained cycloalkynes and to electron-deficient linear alkynes [47][48]. A second reaction product of **9** (obtained in a yield of 16%) had the formula  $\text{C}_{23}\text{H}_{30}\text{S}_7$ , which corresponds to a 3:2-adduct of **9** and  $\text{CS}_2$ . Sulfoxide **16** gave 41% of the tetrathiafulvalene **30**. (*Z/E*)-Isomers have to be considered for **29** and **30**. It is known that the separation of (*Z/E*)-isomeric tetrathiafulvalenes is extremely difficult – even a spectroscopic identification of these isomers is challenging [49]. We found a single set of  $^{13}\text{C}$ -NMR signals among which the broad signal at  $\delta(\text{C})$  108.2 looked like two superimposed signals for C(2) of **29**. All other  $^{13}\text{C}$ -NMR signals of **29** did not show a

Scheme 4



Scheme 5



splitting. Apart from the (*Z/E*)-isomerism, **30** exhibits a stereoisomerism owing to the sulfoxide functionalities. Compounds *syn*-(*E*)-**30** and *anti*-(*Z*)-**30** are chiral, and *anti*-(*E*)-**30** and *syn*-(*Z*)-**30** are *meso*-forms. Chiral tetrathiafulvalenes have recently gained a high actuality [50][51]. Most of the <sup>13</sup>C-NMR signals of **30** are split into pairs of equal intensity. This corresponds to a *syn*-**30**/*anti*-**30** ratio of 1:1. The resonance region at  $\delta(C)$  47.3–47.7 for one of the C-atoms neighboring to the SO group is even split into four signals (*syn*-(*Z*), *anti*-(*Z*), *syn*-(*E*), and *anti*-(*E*); see *Exper. Part*). The other C-atom neighboring to the SO group gives two signals of 52.6 ppm. Sulfone **17** did not show an addition of CS<sub>2</sub> with subsequent tetrathiafulvalene generation.

**Conclusions.** – In principle, three isomeric thiacyclooctynes (=didehydrotetrahydro-2*H*-thiocins), and their sulfoxides and sulfones should exist. 1-Thiacyclooct-2-yne and -3-yne were synthesized much earlier; here we report the preparation of 1-

thiacyclooct-4-yne (**9**) by applying the selenadiazole method for the formation of the C≡C bond. Oxidation of **9** with NaIO<sub>4</sub> generated the sulfoxide **16** and the sulfone **17**.

	$\begin{array}{c c} \diagup \text{X} \diagdown \\ n \end{array}$	S	SO	SO <sub>2</sub>
0	[52]	–	–	–
1	[52][53]	–	–	–
2	<b>9</b>	<i>rac</i> - <b>16</b>	<b>17</b>	

Other sulfoxides or sulfones ( $n = 0, 1$ ) of thiacyclooctynes are not known. All three heterocyclic alkynes, **9**, **16**, and **17**, have high reactivities as  $2\pi$  components toward  $4\pi$  components in *Diels–Alder* reactions and 1,3-dipolar cycloadditions. Moreover, the tetrathiafulvalenes **29** and **30** could be obtained from **9** and **16** by the reaction with CS<sub>2</sub>. The new cyclic alkynes **9**, **16**, and **17** are stimulating candidates for click reactions and should be also interesting species for applications in bioorthogonal processes.

We are grateful to the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* for financial support.

### Experimental Part

*General.* 4,7,8,9-Tetrahydro-5H-thiocino[5,4-d][1,2,3]selenadiazole (**8**) was prepared as described in [45] from 5-thiocanone (**6**) via semicarbazone **7**. M.p.: Büchi melting-point apparatus. IR: Beckman Acculab 4;  $\bar{\nu}$  in cm<sup>−1</sup>. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra: AM-400 spectrometer from Bruker; CDCl<sub>3</sub> as solvent and Me<sub>4</sub>Si as internal standard;  $\delta$  in ppm and  $J$  in Hz. EI-MS: Finnigan-MAT-95 spectrometer, 70-eV ionization energy; in  $m/z$  (rel. %).

*Thermal Fragmentation of 1,2,3-Selenadiazole 8.* To 2.0 g (31.5 mmol) of Cu powder, 467 mg (2.0 mmol) of **8** dissolved in 2 ml of CH<sub>2</sub>Cl<sub>2</sub> was added. The solvent was removed, and the residue was heated under reduced pressure of 100 Pa to 170 ± 5°. 5-Thiacyclooctyne (5,6-didehydro-3,4,7,8-tetrahydro-2H-thiocin; **9**) distilled off as a colorless oil. Yield 235 mg (93%). IR (CDCl<sub>3</sub>): 2240 (C≡C). NMR: see the Table. EI-MS: 126 (62,  $M^+$ ), 111 (51), 98 (52), 97 (100). According to the NMR spectra, the product was pure, but, due to the volatility, a correct combustion analysis could not be conducted.

*Thiocan-5-one 1-Oxide (=1-Oxo-1 $\lambda^4$ -thiocan-5-one) (10).* The preparation was performed according to a modified procedure described by Leonard and Johnson [54]. Thiocanone **8** (1.00 g, 6.93 mmol) was dissolved in 10 ml of MeOH and added at 0° within 20 min to a soln. of 1.58 g (7.39 mmol) of NaIO<sub>4</sub> in 10 ml of H<sub>2</sub>O. The product was isolated by extraction with CHCl<sub>3</sub>. The hygroscopic compound melted at 105° (m.p. 91–92° [54]) and was analytically pure. Yield 1.05 g (95%). IR (CDCl<sub>3</sub>): 1030 (S=O), 1695 (C=O). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.17–3.08 (ddd, <sup>2</sup> $J$  = 14.4, <sup>3</sup> $J$  = 8.8, <sup>3</sup> $J$  = 2.6, 1 H each, CH<sub>2</sub>(2,8)); 2.73–2.57 (m, 1 H each, CH<sub>2</sub>(2,4,6,8)); 2.43–2.28 (m, 1 H each, CH<sub>2</sub>(3,4,6,7)); 2.15–2.04 (m, 1 H each, CH<sub>2</sub>(3,7)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 213.4 (C(5)); 51.1 (C(2,8)), 40.5 (C(4,6)); 18.1 (C(3,7)). EI-MS: 160 (7,  $M^+$ ), 118 (24), 90 (100). Anal. calc. for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>S (160.2): C 52.47, H 7.55; found: C 52.58, H 7.57.

*Thiocan-5-one 1,1-Dioxide (=1,1-Dioxo-1 $\lambda^6$ -thiocan-5-one) (11).* The preparation was conducted according to a modified procedure described by Leonard *et al.* [54][55]. Thiocanone **8** (1.00 g, 6.93 mmol) dissolved in 20 ml of acetone was treated with H<sub>2</sub>O<sub>2</sub> (30%, 1.40 g, 73.6 mmol) at r.t. The reaction was monitored by TLC (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>). At the end, the volatile parts were removed and the residue was recrystallized from EtOH. Yield 904 mg (74%). M.p. 106° ([55]: 124–127°). IR (KBr): 1690 (C=O), 1325 (SO<sub>2</sub>), 1125 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.15–3.08 (m, 4 H, CH<sub>2</sub>(2,8)); 2.66–2.60 (m, 4 H, CH<sub>2</sub>(4,6)); 2.33–2.24 (m, 4 H, CH<sub>2</sub>(3,7)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 212.8 (C(5)); 54.8 (C(2,8)); 39.8 (C(4,6)); 19.9 (C(3,7)). EI-MS: 176 (8,  $M^+$ ), 70 (56), 55 (42), 42 (100). The compound was identical with an authentic sample [54][55].

*rac*-2-(1-Oxidothiocan-5-ylidene)hydrazinecarboxamide (*rac*-**12**). Semicarbazide hydrochloride (950 mg, 8.5 mmol) and AcONa (1.08 g, 13.2 mmol) were briefly refluxed in 20 ml of dry EtOH. The hot filtrate was added to **10** (1.12 g, 7.0 mmol) dissolved in 5 ml of dry EtOH. After 2 h, the mixture was cooled to 0°. A crystalline precipitate was formed which was recrystallized from MeOH. Yield: 1.25 g (82%). Colorless, fine crystals. M.p. 138°. IR (KBr): 1660 (C=O), 1010 (S=O). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 9.12 (s, NH); 6.26 (s, NH<sub>2</sub>); 3.10–3.01 (m, 1 H); 2.95–2.83 (m, 2 H); 2.63–2.52 (m, 2 H); 2.35–2.27 (m, 1 H); 2.27–2.08 (m, 3 H); 2.06–1.95 (m, 2 H); 1.92–1.81 (m, 1 H). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO): 157.1 (CO); 150.2 (C(5)); 51.3, 50.6 (C(2,8)); 35.6 (C(6)); 26.4 (C(4)); 18.9, 16.4 (C(3,7)). EI-MS: 217 (91, *M*<sup>+</sup>), 166 (56), 160 (100). Anal. calc. for C<sub>8</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>S (217.3): S 44.22, H 6.69, N 19.34; found: C 44.16, H 6.98, N 19.29.

2-(1,1-Dioxidothiocan-5-ylidene)hydrazinecarboxamide (**13**). The preparation was performed as described for **12**. Ketone **11** (2.33 g, 13.2 mmol) yielded 2.46 g (80%) of **13**. Colorless crystals. M.p. 184° (MeOH). IR (KBr): 1680 (C=O), 1110 (SO<sub>2</sub>). <sup>1</sup>H-NMR ((D<sub>6</sub>)DMSO): 9.10 (s, NH); 6.30 (s, NH<sub>2</sub>); 3.22–3.14 (m, 2 H); 3.05–2.96 (m, 2 H); 2.54–2.45 (m, 2 H); 2.38–2.29 (m, 2 H); 2.08–1.95 (m, 4 H). <sup>13</sup>C-NMR ((D<sub>6</sub>)DMSO): 157.2 (CO); 149.7 (C(5)); 53.6, 53.1 (C(2,8)); 35.5, 25.8 (C(4,6)); 20.8, 17.6 (C(3,7)). EI-MS: 233 (8, *M*<sup>+</sup>), 97 (24), 83 (37), 67 (30), 44 (43), 41 (100). Anal. calc. for C<sub>8</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>S (233.3): C 41.19, H 6.48, N 18.01; found: C 41.08, H 6.49, N 17.97.

*rac*-4,7,8,9-Tetrahydro-5H-thiocino[5,4-d][1,2,3]selenadiazole 6-Oxide (*rac*-**14**). To semicarbazone **12** (870 mg, 4.0 mmol) in 55 ml of dioxane, SeO<sub>2</sub> (0.89 g, 8.0 mmol) and 0.25 ml of H<sub>2</sub>O were added. The reaction in the dark was monitored by TLC (SiO<sub>2</sub>, toluene). After *ca.* 2 d, when the formation of gas (CO<sub>2</sub>, NH<sub>3</sub>) was completed, the mixture was filtered and concentrated to *ca.* 3 ml. The remaining red oil was purified by column chromatography CC (SiO<sub>2</sub> (2 × 50 cm); toluene/AcOEt 10:1). Yield: 510 mg (51%). Beige crystals. M.p. 107–108° (dec.). IR (KBr): 1300, 1275, 1025 (S=O), 1000, 990, 780. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.78–3.69 (m, 1 H of CH<sub>2</sub>(4)); 3.43–3.35 (m, 1 H, CH<sub>2</sub>(4)); 3.35–3.29 (m, 1 H, CH<sub>2</sub>(9)); 3.29–3.25 (m, 1 H, CH<sub>2</sub>(9)); 3.25–3.20 (m, 1 H of CH<sub>2</sub>(5)); 3.09–3.03 (m, 1 H of CH<sub>2</sub>(7)); 3.03–2.96 (m, 1 H, CH<sub>2</sub>(5)); 2.50–2.41 (m, 1 H, CH<sub>2</sub>(7)); 2.41–2.31 (m, 1 H, CH<sub>2</sub>(8)); 2.31–2.20 (m, 1 H, CH<sub>2</sub>(8)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 159.3 (C(9a)); 157.0 (C(3a)); 53.6, 48.1 (C(5,7)); 25.2, 23.6, 17.7 (C(4,8,9)). EI-MS: 205 (100, [*M* – C<sub>3</sub>H<sub>8</sub>]<sup>+</sup>), 166 (38), 143 (11, [*M* – N<sub>2</sub> – Se]<sup>+</sup>), 124 (72), 91 (52). Anal. calc. for C<sub>7</sub>H<sub>10</sub>N<sub>2</sub>OSe (249.2): C 33.74, H 4.04, N 11.24; found: C 33.66, H 4.00, N 11.27.

4,7,8,9-Tetrahydro-5H-thiocino[5,4-d][1,2,3]selenadiazole 6,6-Dioxide (**15**). The preparation was performed as described for **14**. Semicarbazone **13** (0.93 g, 4.0 mmol) yielded 920 mg (87%) of **15**. Yellow crystals. M.p. 163°. IR (KBr): 1270 (SO<sub>2</sub>), 1165, 1110 (SO<sub>2</sub>), 795, 680. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.60–3.54 (m, CH<sub>2</sub>(4)); 3.47–3.42 (m, CH<sub>2</sub>(9)); 3.33–3.27 (m, CH<sub>2</sub>(5)); 2.89–2.83 (m, CH<sub>2</sub>(7)); 2.19–2.27 (m, CH<sub>2</sub>(8)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 159.2, 156.1 (C(3a,9a)); 58.6, 53.3 (C(5,7)); 23.9, 22.9, 21.0 (C(4,8,9)). EI-MS: 186 (1, [*M* – Se]<sup>+</sup>), 119 (39), 92 (39), 91 (100). Anal. calc. for C<sub>7</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>Se (317.8): C 31.70, H 3.80, N 10.56; found: C 31.78, H 3.61, N 10.58.

Oxidation of 4,5-Didehydro-3,6,7,8-tetrahydro-2H-thiocine (**9**). Alkyne **9** (100 mg, 0.79 mmol) was dissolved in 4 ml of MeOH and cooled to 0°. NaIO<sub>4</sub> (712 mg, 3.32 mmol) in 4 ml of H<sub>2</sub>O was added, and the mixture was stirred overnight at 0°. Further 6 ml of MeOH were added, and the mixture was cooled to –20°. The inorg. salts precipitated and were filtered off. The soln. was dried (MgSO<sub>4</sub>), concentrated, and subjected to CC (SiO<sub>2</sub> (1 × 20 cm); AcOEt/EtOH 2:1). The first fraction consisted of 46 mg (37%) of 4,5-didehydro-3,6,7,8-tetrahydro-2H-thiocine 1,1-dioxide (**17**). Colorless crystals. M.p. 113°. The second fraction consisted of 48 mg (43%) of 4,5-didehydro-3,6,7,8-tetrahydro-2H-thiocine 1-oxide (*rac*-**16**). Colorless crystals. M.p. 56°.

Data of *rac*-**16**. IR (KBr): 1010 (S=O), 2240 (C≡C). <sup>1</sup>H- and <sup>13</sup>C-NMR: see the Table. EI-MS: 142 (54, *M*<sup>+</sup>), 91 (48), 79 (75), 77 (100). Anal. calc. for C<sub>17</sub>H<sub>10</sub>OS (142.2): C 59.12, H 7.09, S 22.54; found: C 59.23, H 7.11, S 22.50.

Data of **17**. IR (KBr): 1110 (SO<sub>2</sub>), 1275, 1310 (SO<sub>2</sub>), 2260 (C≡C). <sup>1</sup>H- and <sup>13</sup>C-NMR: see the Table. EI-MS: 158 (100, *M*<sup>+</sup>), 117 (57), 83 (100). Anal. calc. for C<sub>7</sub>H<sub>10</sub>O<sub>2</sub>S (158.2): C 53.14, H 6.37; found: C 53.03, H 6.28.

Alkaline Fragmentation of *rac*-**14**. To *rac*-**14** (250 mg, 1.0 mmol) in 10 ml of dry THF, 0.6 ml (1.5 mmol) of a 15% soln. of BuLi in hexane was added at –70°. After 10 min, the reaction was quenched by addition of 1.2 ml of MeOH and 1.2 ml of H<sub>2</sub>O. Extraction with CHCl<sub>3</sub> at r.t. gave a yellow

soln., which was dried ( $\text{MgSO}_4$ ), concentrated, and purified by CC ( $\text{SiO}_2$  ( $1 \times 20$  cm);  $\text{AcOEt/EtOH}$  2 : 1). The first fraction consisted of *rac*-**18** (yield 60 mg (21 %), yellow oil), and the second fraction of *rac*-**16** (yield 11.5 mg (8 %)).

*rac*-(5*E*)-6-(*Butylselanyl*)-3,4,7,8-tetrahydro-2*H*-thiocine 1-Oxide (*rac*-**18**). IR (neat): 1025 ( $\text{S=O}$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 5.62 (*t*,  $^3J = 9.0$ ,  $\text{H-C(5)}$ ); 3.34–3.25 (*m*, 1 H,  $\text{CH}_2(8)$ ); 3.25–3.15 (*m*, 1 H,  $\text{CH}_2(2)$ ); 3.00–2.89 (*m*, 1 H each,  $\text{CH}_2(7,8)$ ); 2.80–2.73 (*m*, 1 H,  $\text{CH}_2(2)$ ); 2.67 (*t*,  $^3J = 7.5$ ,  $\alpha\text{-CH}_2$ ); 2.60–2.52 (*m*, 1 H,  $\text{CH}_2(7)$ ); 2.44–2.33 (*m*, 1 H of  $\text{CH}_2(4)$ ); 2.20–2.08 (*m*, 1 H,  $\text{CH}_2(4)$ ); 2.02–1.91 (*m*, 1 H,  $\text{CH}_2(3)$ ); 1.62 (*quint.*,  $^3J = 7.5$ ,  $\beta\text{-CH}_2$ ); 1.38 (*sext.*,  $^3J = 7.8$ ,  $\gamma\text{-CH}_2$ ); 0.90 (*t*,  $^3J = 7.8$ , Me).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 130.9 (C(6)); 128.8 (C(5)); 52.9, 51.4 (C(2,8)); 31.9, 27.2, 25.3, 25.1, 23.0, 23.0 (other  $\text{CH}_2$ ); 13.5 (Me). EI-MS: 280 (3,  $M^+$ , Se pattern), 143 (100,  $[M - \text{C}_4\text{H}_9]^+$ ). Anal. calc. for  $\text{C}_{11}\text{H}_{20}\text{OSSe}$  (279.3): C 47.30, H 7.22; found: C 47.43, H 7.12.

Reaction of **9**, *rac*-**16**, and **17** with 2,3,4,5-Tetraphenylcyclopenta-2,4-dien-1-one (**19**). Alkyne **9**, *rac*-**16** or **17** (0.20 mmol), and **19** (154 mg, 0.40 mmol) were stirred overnight at r.t. in 4 ml of toluene. The violet soln. was concentrated and purified by CC ( $\text{SiO}_2$  ( $1 \times 60$  cm); toluene for **20**,  $\text{AcOEt/EtOH}$  1 : 1 for **21**, and  $\text{CHCl}_3$  for **22**).

1,4,5,6-Tetrahydro-7,8,9,10-tetraphenyl-2*H*-3-benzothiociene (**20**). Yield: 45 mg (46 %). Colorless crystals. M.p. 224°. IR (KBr): 700, 740.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 7.19–7.00 (*m*, 10 arom. H); 6.80–6.66 (*m*, 10 arom. H); 3.10–2.98 (*m*,  $\text{CH}_2(1,6)$ ); 2.68–2.61, 2.60–2.50 (2*m*,  $\text{CH}_2(2,4)$ ); 1.65–1.56 (*m*,  $\text{CH}_2(5)$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 141.2, 141.2, 141.1, 141.0, 140.7, 140.6, 139.9, 139.6, 137.7, 137.2 (arom.  $\text{C}_q$ ); 131.1, 130.7, 130.4, 127.4, 127.2, 126.3, 126.1, 126.0, 125.0 (arom. CH, partly superimposed); 35.1, 33.9, 32.5, 31.0, 27.5 (aliph.  $\text{CH}_2$ ). EI-MS: 482 (89,  $M^+$ ), 440 (100). Anal. calc. for  $\text{C}_{35}\text{H}_{30}\text{S}$ : C 87.09, H 6.26; found: C 87.21, H 6.52.

1,4,5,6-Tetrahydro-7,8,9,10-tetraphenyl-2*H*-3-benzothiociene 3-Oxide (**21**). Yield 59 mg (59 %). Colorless crystals. M.p. 227°. IR (KBr): 700, 740, 1025 ( $\text{S=O}$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 7.34–6.97 (*m*, 10 arom. H); 6.82–6.66 (*m*, 10 arom. H); 3.31–3.15, 3.08–2.85, 2.81–2.63 (3*m*,  $\text{CH}_2(1,2,4,6)$ ); 1.97–1.79 (*m*,  $\text{CH}_2(5)$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 141.5, 141.4, 140.8, 140.4, 140.3, 140.2, 140.1, 140.1, 135.7, 135.4 (arom.  $\text{C}_q$ ); 130.9, 130.3, 130.2, 130.1, 127.7, 127.5, 127.3, 126.5, 126.4, 126.3, 125.2 (arom. CH, partly superimposed); 58.3, 55.3 (C(2,4)); 28.5, 23.5, 22.8 (C(1,5,6)). EI-MS: 498 (97,  $M^+$ ), 407 (100). Anal. calc. for  $\text{C}_{35}\text{H}_{30}\text{OS}$  (498.7): C 84.30, H 6.06; found: C 84.05, H 6.05.

1,4,5,6-Tetrahydro-7,8,9,10-tetraphenyl-2*H*-3-benzothiociene 3,3-Dioxide (**22**). Yield: 87 mg (84 %). Colorless crystals. M.p. 255°. IR (KBr): 700, 740, 1120 ( $\text{SO}_2$ ), 1280 ( $\text{SO}_2$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 7.21–7.00 (*m*, 10 arom. H); 6.83–6.68 (*m*, 10 arom. H); 3.15–2.97 (*m*,  $\text{CH}_2(1,2,4,6)$ ); 1.71–1.67 (*m*,  $\text{CH}_2(5)$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 141.6, 141.5, 141.0, 140.4, 140.2, 140.1, 140.0, 139.9, 135.5, 135.2 (arom.  $\text{C}_q$ ); 130.8, 130.2, 129.9, 127.8, 127.5, 126.7, 126.5, 125.3 (arom. CH, partly superimposed); 58.7, 52.5 (C(2,4)); 27.1, 24.6, 22.6 (C(1,5,6)). EI-MS: 514 (43,  $M^+$ ), 349 (56), 348 (50), 347 (100). Anal. calc. for  $\text{C}_{35}\text{H}_{30}\text{O}_2\text{S}$  (514.7): C 81.68, H 5.87; found: C 81.51, H 5.68.

Reaction of **9**, *rac*-**16**, and **17** with  $\text{CH}_2\text{N}_2$ . To 0.50 mmol of the **9**, *rac*-**16**, or **17**, dissolved in 10 ml of dry  $\text{Et}_2\text{O}$ , a 0.1 M soln. of  $\text{CH}_2\text{N}_2$  in  $\text{Et}_2\text{O}$  (ca. 10 ml, ca. 1.0 mmol) was added. The yellow soln. was stirred for 24 h, and then the excess  $\text{CH}_2\text{N}_2$  was removed by passing compressed air through the flask (the air is then introduced to a trap with aq. HCl). The remaining soln. was concentrated, and the product was purified by CC ( $\text{SiO}_2$  ( $2 \times 38$  cm);  $\text{Et}_2\text{O}$ /petroleum ether (b.p. 40–70°) 3 : 1). The separation of the regioisomeric cycloadducts **23/24**, *rac*-**25/26**, and **27/28** by CC was not successful. The correlation of the NMR signals was based on NOE experiments and  $^1\text{H}$ ,  $^1\text{H}$ -COSY 45 spectra.

1,4,5,7,8,9-Hexahydrothiocieno[5,4-*c*]pyrazole (**23**)/1,4,5,6,8,9-Hexahydrothiocieno[4,5-*c*]pyrazole (**24**). Yield: 49 mg (58 %). Colorless crystals. M.p. 96°. Ratio **23/24** according to the  $^1\text{H-NMR}$  signals 60 : 40.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) of **23**: 7.25 (*s*,  $\text{H-C(3)}$ ); 3.04–2.99 (*m*,  $\text{CH}_2(9)$ ); 2.88–2.85 (*m*,  $\text{CH}_2(4)$ ); 2.67–2.63 (*m*,  $\text{CH}_2(5)$ ); 2.47–2.43 (*m*,  $\text{CH}_2(7)$ ); 1.89–1.81 (*m*,  $\text{CH}_2(8)$ ).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) of **24**: 7.28 (*s*,  $\text{H-C(3)}$ ); 3.07–3.03 (*m*,  $\text{CH}_2(9)$ ); 2.76–2.81 (*m*,  $\text{CH}_2(4)$ ); 2.71–2.67 (*m*,  $\text{CH}_2(8)$ ); 2.43–2.39 (*m*,  $\text{CH}_2(6)$ ); 1.78–1.70 (*m*,  $\text{CH}_2(5)$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ) of **23**: 144.8 (C(9a)); 133.4 (C(3a)); 118.1 (C(3)); 37.3, 31.4, 31.2, 28.0, 21.3 (C(4,5,7,8,9)).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ) of **24**: 146.4 (C(9a)); 132.4 (C(3a)); 116.9 (C(3)); 35.4, 32.4, 31.5, 30.1, 19.2 (C(4,5,6,8,9)). EI-MS: 168 (100,  $M^+$ ), 121 (39), 107 (50), 94 (84). Anal. calc. for  $\text{C}_8\text{H}_{12}\text{N}_2\text{S}$  (168.3): C 57.11, H 7.19, N 16.65; found: C 57.00, H 7.18, N 16.68.



*rac*-1,4,5,7,8,9-Hexahydrothiocino[5,4-*c*]pyrazole 6-Oxide (**25**)/*rac*-1,4,5,6,8,9-Hexahydrothiicino[4,5-*c*]pyrazole 7-Oxide (**26**). Yield: 45 mg (49%). Viscous oil. Ratio **25/26** according to the <sup>1</sup>H-NMR signals 50:50. IR (neat): 1010 (S=O). <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 7.35 (s, H–C(3)) and 7.25 (s, H–C(3)); 3.32–2.95 (m, 9 H), 2.92–2.78 (m, 2 H), 2.73–2.62 (m, 4 H), 2.52–2.42 (m, 1 H), 2.21–2.05 (m, 3 H), 2.04–1.93 (m, 1 H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 145.3, 144.6 (C(9a)); 132.5, 130.9 (C(3a)); 115.6, 115.5 (C(3)); 55.8, 54.0, 51.5, 51.2 (C(5,7) of **25** and C(6,8) of **26**); 25.0, 23.6, 23.2, 21.1, 18.2, 16.0 (C(4,8,9) of **25** and C(4,5,9) of **26**). EI-MS: 184 (22, *M*<sup>+</sup>), 108 (12), 85 (66), 84 (21), 83 (100). Anal. calc. for C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>OS (184.3): C 52.15, H 6.56, N 15.20; found: C 52.40, H 6.85, N 15.17.

1,4,5,7,8,9-Hexahydrothiicino[5,4-*c*]pyrazole 6,6-Dioxide (**27**)/1,4,5,6,8,9-hexahydrothiicino[4,5-*c*]pyrazole 7,7-Dioxide (**28**). Yield 38 mg (38%). Viscous oil. Ratio **27/28** according to the <sup>1</sup>H-NMR signals 25:75. IR (CHCl<sub>3</sub>): 1105 (SO<sub>2</sub>), 1270 (SO<sub>2</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, **27**): 7.40 (s, H–C(3)); 3.21–3.14, 3.02–2.90, 2.03–2.01 (3m, CH<sub>2</sub>(4,5,7,8,9)). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, **28**): 7.32 (s, H–C(3)), 3.28–3.23, 3.21–3.14, 2.96–2.88, 2.83–2.77, 2.01–1.93 (5m, CH<sub>2</sub>(4,5,6,8,9)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, **27**): 145.2 (C(9a)); 130.2 (C(3a)); 116.1 (C(3)); 59.7, 52.9 (C(5,7)); 23.1, 21.4, 18.2 (C(4,8,9)). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, **28**): 147.0 (C(9a)); 129.8 (C(3a)); 115.9 (C(3)); 58.2, 52.5 (C(6,8)); 24.5, 20.8, 19.1 (C(4,5,9)). EI-MS: 200 (1, *M*<sup>+</sup>), 84 (93), 66 (100). Anal. calc. for C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S (200.3): C 47.98, H 6.04, N 13.99; found: C 47.88, H 6.30, N 14.02.

Reaction of the **9** or *rac*-**16** with CS<sub>2</sub>. Alkyne (1.0 mmol) and CS<sub>2</sub> (4 ml, 5.08 g, 66.7 mmol) were refluxed under N<sub>2</sub> for 12–15 d. The colorless soln. turned orange and then redbrown. The soln. was concentrated, and the products were purified by CC (SiO<sub>2</sub> (3 × 40 cm); toluene/petroleum ether (b.p. 40–70°) 2:1 for **29** and AcOEt/EtOH 1:1 for product **30**).

(2*Z*/E)-4,7,8,9-Tetrahydro-2-(4,7,8,9-tetrahydro-5H-1,3-dithiolo[4,5-*d*]thiicin-2-ylidene)-5H-1,3-dithiolo[4,5-*d*]thiicine; **29**). Yield: 53 mg (13%). Red-orange crystals. M.p. 195°. IR (CDCl<sub>3</sub>): 1270, 1445. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 2.75–2.63 (m, CH<sub>2</sub>(4,5,7,9,4',5',7',9')); 1.91–1.81 (m, CH<sub>2</sub>(8,8')). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 128.8, 128.7 (C(3a,9a,3a',9a')); 108.2 (C(2,2')); 34.7, 32.0, 31.4, 31.1, 25.1 (C(4,5,7,8,9,4',5',7',8',9')). EI-MS: 404 (100, *M*<sup>+</sup>), 202 (4, *M*<sup>2+</sup>). Anal. calc. for C<sub>16</sub>H<sub>20</sub>S<sub>6</sub> (404.7): C 47.49, H 4.98; found: C 47.39, H 4.89. As second fraction, a dark-red solid C<sub>23</sub>H<sub>30</sub>S<sub>7</sub> (85 mg, 16%) was obtained. The structure was not determined.

syn-(2*Z*/E)- and anti-(2*Z*/E)-4,7,8,9-Tetrahydro-2-(4,7,8,9-tetrahydro-6-oxido-5H-1,3-dithiolo[4,5-*d*]thiicin-2-ylidene)-5H-1,3-dithiolo[4,5-*d*]thiicine 6-Oxide; **30**). Yield: 179 mg (41%). Red-orange solid. M.p. 204°. IR (KBr): 1010, 1445, 1625. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 3.30–3.19 (m, 2 H); 3.19–3.07 (m, 4 H); 3.00–2.89 (m, 2 H); 2.88–2.73 (m, 4 H); 2.55–2.45 (m, 2 H); 2.42–2.30 (m, 2 H); 2.26–2.20 (m, 2 H); 2.20–2.13 (m, 2 H) (CH<sub>2</sub> groups). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 129.0, 129.0, 127.3, 127.2 (C(3a,9a,3a',9a')); 108.3, 108.2 (C(2,2')); 52.6, 52.6, 47.7, 47.6, 47.4, 47.3 (C(5,7,5',7')); 26.5, 26.4, 23.0, 22.8, 18.9, 18.8 (C(4,8,9,4',8',9')). EI-MS: 436 (30, *M*<sup>+</sup>), 142 (100), 97 (56), 85 (49), 72 (58), 71 (84). Anal. calc. for C<sub>16</sub>H<sub>20</sub>O<sub>2</sub>S<sub>6</sub> (436.7): C 44.01, H 4.62, S 44.05; found: C 43.89, H 4.61, S 43.87.

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