Reactions of Stable α-Chlorosulfanyl Chlorides with C=S-Functionalized Compounds

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The smooth reaction of 3-chloro-3-(chlorosulfanyl)-2,2,4,4-tetramethylcyclobutanone (**3**) with 3,4,5-trisubstituted 2,3-dihydro-1*H*-imidazole-2-thiones **8** and 2-thiouracil (**10**) in CH_2Cl_2/Et_3N at room temperature yielded the corresponding disulfanes **9** and **11** (*Scheme 2*), respectively, *via* a nucleophilic substitution of Cl^- of the sulfanyl chloride by the S-atom of the heterocyclic thione. The analogous reaction of 3-cyclohexyl-2,3-dihydro-4,5-diphenyl-1*H*-imidazole-2-thione (**8b**) and **10** with the chlorodisulfanyl derivative **16** led to the corresponding trisulfanes **17** and **18** (*Scheme 4*), respectively. On the other hand, the reaction of **3** and 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**12**) in CH_2Cl_2 gave only 4,4-dimethyl-2-phenyl-1,3-thiazol-5(4*H*)-one (**13**) and the trithioorthoester derivative **14**, a bis-disulfane, in low yield (*Scheme 3*). At $-78°$, only bis(1-chloro-2,2,4,4-tetramethyl-3-oxocyclobutyl)polysulfanes **15** were formed. Even at $-78°$, a 1:2 mixture of **12** and **16** in CH_2Cl_2 reacted to give **13** and the symmetrical pentasulfane **19** in good yield (*Scheme 5*). The structures of **11**, **14**, **17**, and **18** have been established by X-ray crystallography.

Introduction. – Recently, it has been shown that the reaction of 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**1**) and the corresponding dithione **2** with Cl_2 at room temperature leads smoothly to stable α-chlorosulfanyl chlorides **3** and **4**, respectively [1] (*Scheme 1*). Replacement of gaseous Cl_2 by PCl_5 afforded the same products, which, surprisingly, were stable during aqueous workup [2]. Compounds **3** and **4** react easily with thioacetic acid to give acetylated disulfanes [1]. Furthermore, they add to **1** and adamantanethione yielding the corresponding α,α'-dichloro-disulfanes [2][3].

In contrast to the unexpected formation of α-chlorosulfanyl chlorides from **1** and **2**, and PCl_5, the analogous reaction with 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**) was reported as a convenient synthesis of 1,1,3,3-tetrachloro-2,2,4,4-tetramethylcyclobutane (**6**) [4]. Surprisingly, the expected formation of dichloro ketone **7** has not been mentioned. On the other hand, **7** was used in a photochemical study, but neither details of its preparation nor physico-chemical properties were mentioned [5].

In the present paper, we describe the results of the reactions of **3** and the corresponding disulfanyl chloride **16** with some compounds containing C=S groups.

Results. – The starting material **3** was prepared by the known method with PCl_5 [2]. In analogy to the reported smooth reaction **5** → **6**, we treated **3** with excess PCl_5 in

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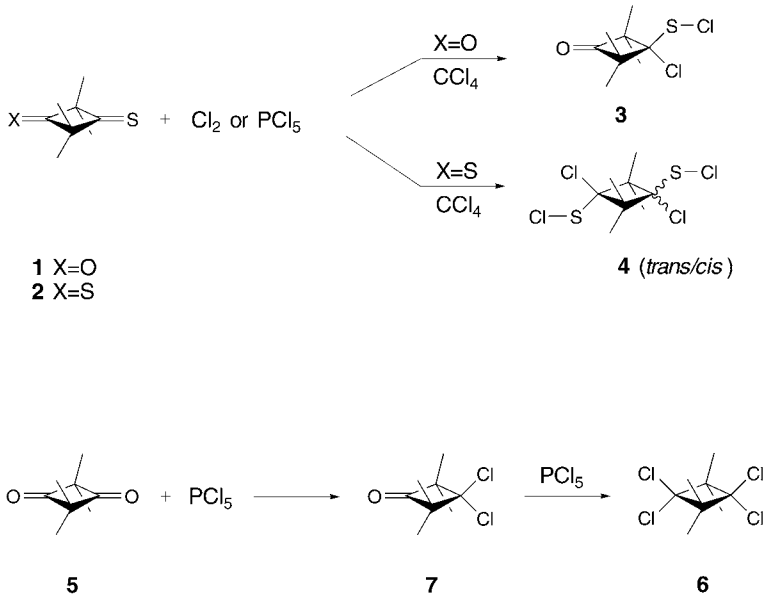
[1]) Part of the planned Ph.D. thesis of *A. M.*, Universität Zürich.
[2]) In part from the Diploma thesis of *A. J.*, University of Łódź, 2002.

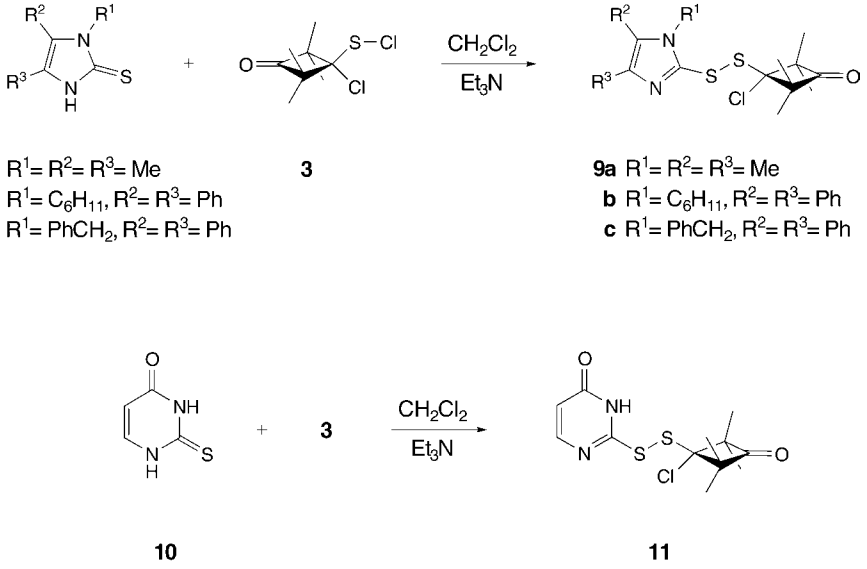
Scheme 1



refluxing CCl_4. After 18 h and aqueous workup, **3** was the only compound obtained. Based on this result, we repeated the reaction of **5** with a threefold excess of PCl_5 in boiling CCl_4, and the progress of the reaction was monitored by ^{1}H-NMR spectroscopy. After 1 h, the dichloro derivative **7** was the main product, accompanied by **5** and **6** (ratio 7:1:2). Prolonged heating (3 h) led to a 3:1 mixture of **7** and **6**, and, only after 18 h, **6** was the main product. The analogous reaction of **5** with 1.1 equiv. of PCl_5 afforded after 6 h a *ca.* 9:1 mixture of **7** and **6**. Their separation by fractional crystallization was unsuccessful, and chromatography on SiO_2 led to almost complete hydrolysis of **7**. Nevertheless, small amounts of pure **7** were obtained and fully characterized.

Reactions with α-Chlorosulfanyl Chloride **3**. The easily available 2,3-dihydro-1*H*-imidazole-2-thiones **8** [6] reacted smoothly with **3** in the presence of Et_3N at room temperature. After a few min, **8** was completely consumed (TLC), and, after aqueous workup, the crude mixture was analyzed by ^{1}H-NMR spectroscopy. In each case, only one product was formed, which was identified as a disulfane of type **9** (*Scheme 2*). Purification by crystallization gave yellowish solids in good yields. The characteristic data of **9a** are a strong IR absorption at 1791 cm^{-1} (C=O) and, in the ^{1}H-NMR spectrum, two signals for two Me groups at 1.61 and 1.55 ppm, attributed to the tetramethylcyclobutane moiety, and three Me signals at 2.36, 2.37, and 3.86 ppm for the trimethylimidazole. In the ^{13}C-NMR spectrum, the signals of C=O, and C(2) and C(4) of the tetramethylcyclobutanone appear at 216.2 and 69.2 ppm, respectively, and C(3) absorbs at 86.5 ppm. The EI-MS shows the molecular ion ($M^{+\bullet}$) at *m/z* 332.

Scheme 2



8a $R^1 = R^2 = R^3 = Me$
b $R^1 = C_6H_{11}$, $R^2 = R^3 = Ph$
c $R^1 = PhCH_2$, $R^2 = R^3 = Ph$

3

9a $R^1 = R^2 = R^3 = Me$
b $R^1 = C_6H_{11}$, $R^2 = R^3 = Ph$
c $R^1 = PhCH_2$, $R^2 = R^3 = Ph$

10 **11**

The analogous reaction of **3** with thiouracil (**10**) gave again only one product, isolated in 78% yield as colorless crystals. The structure of **11** (*Scheme 2*) was elucidated on the basis of its spectroscopic data and elemental analysis, and confirmed by an X-ray crystal-structure determination (*Fig. 1*).

Disulfanes with heterocyclic residues, in particular those with imidazoles, are well known as biologically active compounds (*cf.* [8][9] and refs. cit. therein). The method used for the synthesis of symmetrical disulfanes is the oxidation of the corresponding imidazole-thiones. Reactions with sulfanyl chlorides leading to unsymmetrical disul-

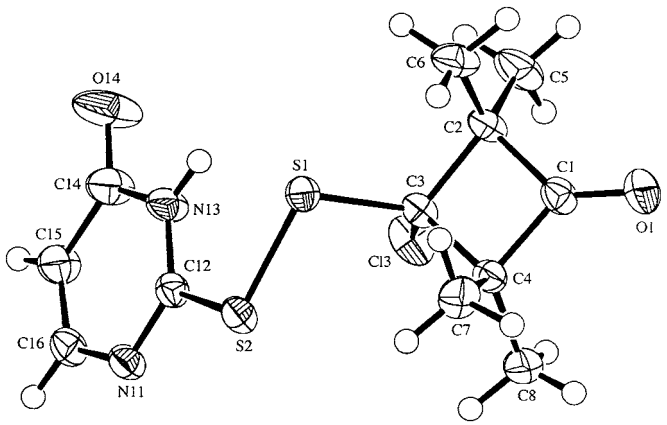


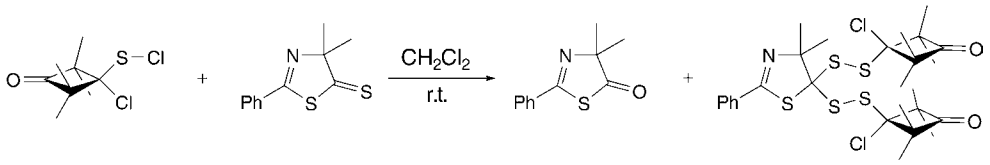
Fig. 1. *ORTEP Plot* [7] *of the molecular structure of* **11** (50% probability ellipsoids, arbitrary numbering of atoms)

fanes have also been reported [9–11], but, to the best of our knowledge, no reaction with an α-chlorosulfanyl chloride has been described.

In the last few years, 1,3-thiazole-5(4*H*)-thiones of type **12** have frequently been used as model compounds for reactions with C=S groups [12][13]. Unlike imidazole-thiones **8** and thiouracil (**10**), no tautomerism to 'thiol' derivatives is possible in the case of **12**; its structure corresponds rather to that of a dithiolactone (cyclic dithioester). As reactions of dithioesters with α-chlorosulfanyl chlorides are almost unknown, we decided to include **12** in the present study.

The reaction of equimolar amounts of **3** and 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**12**) in CH_2Cl_2 at room temperature for 24 h afforded a mixture of **12**, the corresponding oxo compound **13**, and a product **14**, containing both starting materials (*Scheme 3*)[3]). After chromatographic separation and crystallization from hexane, **14** was obtained as colorless crystals. In the IR spectrum, a very strong band at 1785 cm^{-1} confirmed the presence of the cyclobutanone unit. The NMR spectra revealed typical signals for the 2,5-dihydro-1,3-thiazole ring (Ph substituent, C=N absorption at 160.0 ppm). Both the ^1H- and ^{13}C-NMR spectra showed five *singlets* for two Me groups each. These data indicated that structure **14** contains two cyclobutanone units and one 1,3-thiazole ring. The elemental analysis suggested that **14** also contains five S-atoms. Finally, an X-ray crystal-structure determination established the structure of **14** (*Fig. 2*), which is a trithioorthoester derivative of 1,3-thiazole-5(4*H*)-thione **12**.

Scheme 3



3 **12** **13** **14**

Reactions with α-Chlorodisulfanyl Chloride **16**. As already reported, the reaction of **1** with SCl_2 is the method of choice for preparing the stable α-chlorodisulfanyl chloride **16** [2]. As an extension of the experiments described above, reactions of **16** with **8b** and **10**, as well as with **12**, were carried out. In the cases of **8b** and **10**, under typical conditions (CH_2Cl_2, Et_3N, r.t.) only one product, **17** and **18**, respectively, was formed.

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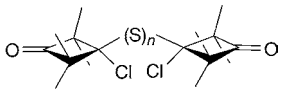
[3]) The reaction of **3** and **12** in a ratio of 2:1 at $-78°$ led to the disappearance of **12** after 4 h. Workup after stirring for 24 h at room temperature gave **13**, and a mixture of di-, tri-, and tetrasulfanes of type **15** (*cf.* [2][3]).



15 $n = 2–4$

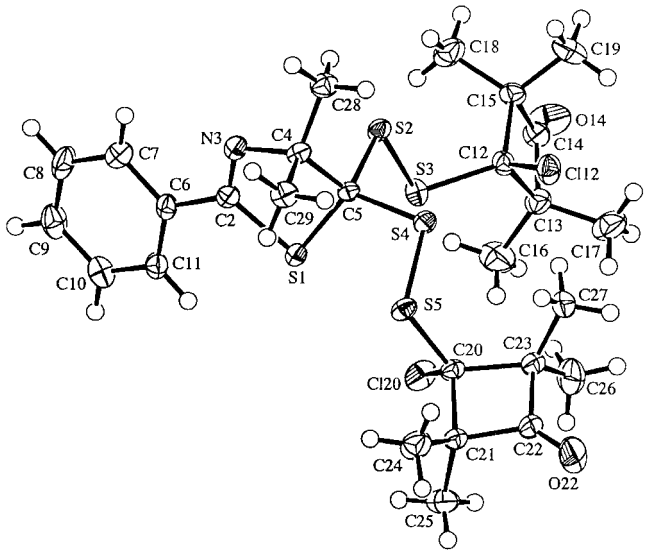


Fig. 2. *ORTEP Plot* [7] *of the molecular structure of one of the two symmetry-independent molecules of* **14** (50% probability ellipsoids, arbitrary numbering of atoms)

Whereas **17** was isolated as yellow crystals, the crystals of **18** were colorless (*Scheme 4*). The structures of the two products were established on the basis of their spectroscopic data, elemental analyses, and by X-ray crystallography (*Fig. 3*). These compounds are the first examples of imidazole and uracil derivatives with a trisulfanyl side chain.

Disulfanyl chloride **16** reacted with **12** in CH_2Cl_2 even at $-78°$. After stirring a 1:2 mixture for 6 h at this temperature and 24 h at room temperature, chromatographic separation gave **13** and pentasulfane **19** (*Scheme 5*) in comparable yields (*ca.* 76%). The structure of **19** was unambigously determined by X-ray crystallography[4]). An analogous experiment carried out at room temperature led to similar results. In both cases, no product containing fragments of both starting materials could be detected.

Discussion. – Sulfanyl chlorides are well-known as electrophilic reaction partners [14]. The presented results show that α-chlorosulfanyl chloride **3** reacts with imidazole-2-thiones analogously to typical sulfanyl chlorides, *e.g.*, (*tert*-butyl)- or (2-nitrophenyl)sulfanyl chlorides (*cf.* [9–11]), to yield unsymmetrical disulfanes **9**. The mechanism of the formation of **9** corresponds to known reactions of imidazole-2-thiones (*cf.* [15]), *i.e.*, the nucleophilic attack occurs *via* the S-atom. The reactions of imidazole-2-thione **8b** and thiouracil (**10**) with disulfanyl chlorides, which have not been reported to date, follow the same reaction pathway, leading to trisulfanes. It is worth mentioning that products **9**, **11**, **17**, and **18** are stable compounds, although they contain an sp^3-C-atom bearing an S- and a Cl-atom. This stability – like that of **3** [1] – can be rationalized by the unfavorable formation of an sp^2-C-atom in a small ring [16].

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[4]) The structure determination will be published elsewhere.

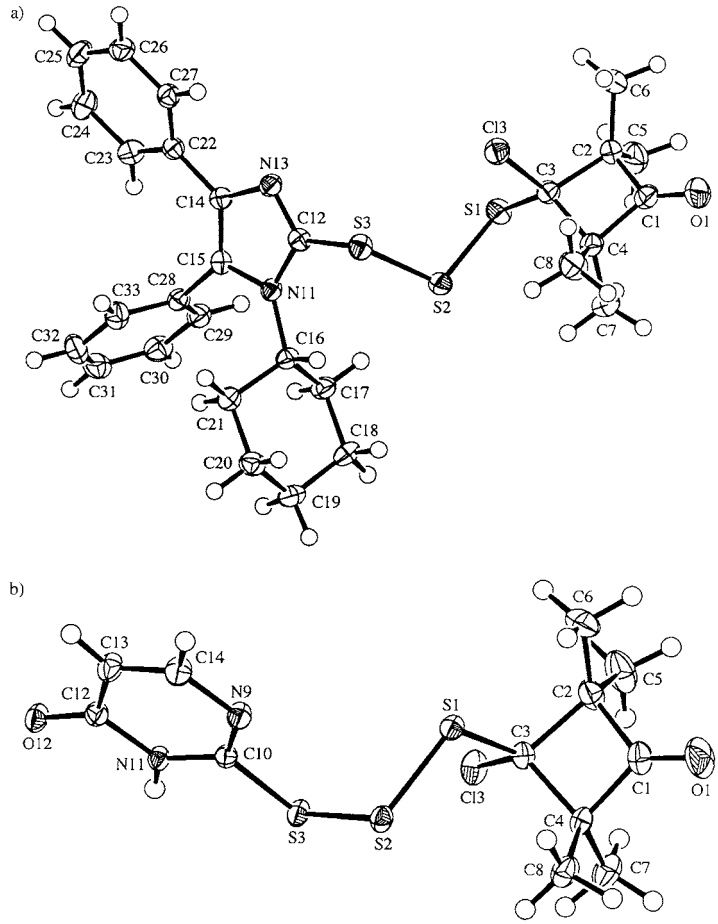
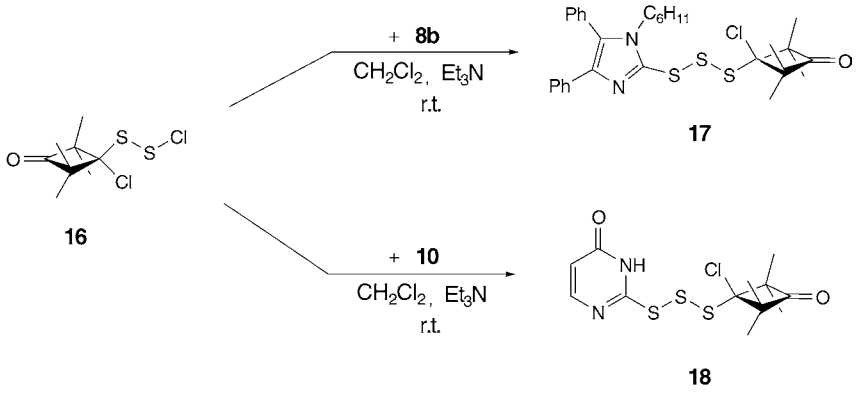


Fig. 3. *ORTEP Plots* [7] *of the molecular structures of* a) **17** *and* b) **18** (50% probability ellipsoids, arbitrary numbering of atoms)

The driving force for the formation of **9** and **11** is the elimination of HCl from the intermediate thiocarbonylium chlorides of type **20**.

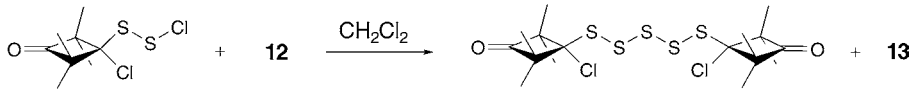
In the case of the reactions with **12**, the initial formation of similar thiocarbonylium salts of type **21** is likely. However, in these cases, no stabilization *via* deprotonation is possible. Therefore, the reactive salts **21** react with traces of H_2O and decompose into **13** and polysulfanes **22**. According to this interpretation, 1,3-thiazole-5(4*H*)-thiones can be used as efficient S-transfer reagents. This procedure can be regarded as an extension of *Senning*'s method, where the elongation of a sulfane chain is achieved by the reaction of a sulfanyl chloride with thioacetic acid and subsequent deacylation using morpholine [17]. The *in situ* formed sulfanes **22** can easily react with sulfanyl chlorides **3** and **16** leading to symmetrical sulfanes **15** and **19**, respectively. In the case of the reaction of **3** with **12**, **22** ($n=1$) apparently reacts faster with the thiocarbonylium salt **21** ($n=1$) to give **14**.

Scheme 4



16 **17** **18**

Scheme 5



16 **12** **19** **13**

With the aim of obtaining further support for the above interpretation, **3** was also reacted with thiobenzophenone in CH_2Cl_2 at room temperature. After a few min, the blue color of the mixture disappeared, and, after typical workup, benzophenone was isolated chromatographically as the sole product [18]. In line with our proposals, the initially formed **23**, which cannot be stabilized by deprotonation, is easily hydrolyzed by traces of H_2O.

20 **21** *n*=1,2

22 *n*=1,2 **23**

In conclusion, α-chlorosulfanyl chlorides **3** and **16** smoothly form new S,S bonds with C=S groups to give reactive thiocarbonylium salts. Further conversion depends on the structure of the thiocarbonyl substrate.

We thank the analytical sections of our institutes for spectra and elemental analyses, and Mrs. *M. Celeda*, Łódź, for excellent technical assistance. Financial support of the *Rector of the University of Łódź* (Research Grant No. 505/465), the *Swiss National Science Foundation*, and *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged.

Experimental Part

1. *General.* See [19]. M.p.: in capillary; *Melt-Temp II* apparatus (*Aldrich*); uncorrected. IR (KBr): *NEXUS FT-IR* spectrophotometer. ^{1}H- and ^{13}C-NMR ($CDCl_3$): *Bruker-AC-300* (300 and 75.5 MHz, resp.) or *Tesla BS 687* (80 and 20 MHz, resp.). MS: *Finnigan-MAT-90* (EI, 70 eV, or CI (NH_3)). Elemental analyses were performed by the Mikroanalytisches Laboratorium des Organisch-chemischen Instituts der Universität Zürich.

2. *Starting Materials. 2,2,4,4-Tetramethylcyclobutane-1,3-dione* (**5**) (dimethylketene dimer) was prepared by treatment of isobutyryl chloride with Et_3N by using CH_2Cl_2 as solvent [20]. Thioketones **1** and **2** were obtained from **5** by treatment with P_4S_{10} in pyridine according to a known protocol [21]. *2,3-Dihydro-1*H*-imidazole-2-thiones* **8** were obtained from the corresponding imidazole *N*-oxides by treatment with dithione **2** as described in [22]. *3-Chloro-3-(chlorosulfanyl)-2,2,4,4-tetramethylcyclobutanone* (**3**) and *3-chloro-3-(chlorodisulfanyl)-2,2,4,4-tetramethylcyclobutanone* (**16**) were synthesized from **1** and PCl_5 and SCl_2, respectively; the crude products were purified by distillation *in vacuo* as described in [2]. The synthesis of 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**12**) was performed according to [23].

3. *Reaction of* **5** *with* PCl_5. A soln. of **5** (2.0 g, 14 mmol) and PCl_5 (5.9 g, 28 mmol) in CCl_4 (10 ml) was heated under reflux, and the progress of the reaction was monitored by ^{1}H-NMR. After 3 h, **5** was completely converted into a mixture **7**/**6** (*ca.* 3:1). The soln. was cooled to r.t. and poured on ice/H_2O. The org. phase was washed three times with an aq. soln. of $NaHCO_3$ (5%) and subsequently dried ($MgSO_4$). The product mixture was separated chromatographically (CC; SiO_2, petroleum ether with increasing amounts of CH_2Cl_2). Tetrachlorocyclobutane **6** was isolated as the less polar fraction, followed by **7**, which partially hydrolyzed during chromatography to give **5**.

1,1,3,3-Tetrachloro-2,2,4,4-tetramethylcyclobutane (**6**). Yield: 290 mg (8%). Colorless crystals. M.p. 232–234° (MeOH) ([4]: 234–236°, MeOH). IR: 3011*s*, 2984*s*, 2943*s*, 1470v*s*, 1455*s*, 1443*s*, 1387*m*, 1371*m*, 1205*m*, 952*m*, 881v*s*, 839v*s*, 517*s*, 431*s*. ^{1}H-NMR: 1.54 (*s*, 4 Me). ^{13}C-NMR: 26.2 (*q*, 4 Me); 61.6 (*s*, C(2), C(4)); 96.9 (*s*, C(1), C(3)).

3,3-Dichloro-2,2,4,4-tetramethylcyclobutan-1-one (**7**). Yield: 680 mg (25%). Colorless plates. M.p. 72–73° (MeOH, dry ice). IR: 2983*s*, 2939*m*, 2872*w*, 1794v*s* and 1769*s* (C=O), 1462*s*, 1451*s*, 1383*m*, 1369*m*, 1249*m*, 1030*s*, 935v*s*, 837*s*. ^{1}H-NMR: 1.43 (*s*, 4 Me). ^{13}C-NMR: 22.8 (*q*, 4 Me); 70.1 (*s*, C(2), C(4)); 94.1 (*s*, C(3)); 215.3 (*s*, C=O). Anal. calc. for $C_8H_{12}Cl_2O$ (195.09): C 49.25, H 6.20; found: C 49.50, H 6.38.

4. *Reactions of* **8a**–**8c** *with* **3**. A soln. of **3** (272 mg, 1.2 mmol) in CH_2Cl_2 (2 ml) was added in portions at r.t. to a stirred soln. of **8** (1 mmol) and Et_3N (2 ml, 1.45 g, 14.3 mmol) in CH_2Cl_2 (2 ml). When the addition was complete, stirring was continued for 15 min, and subsequently CH_2Cl_2 (20 ml) was added. The mixture was washed with H_2O (20 ml, 2 ×), the org. phase was dried ($MgSO_4$), the solvent was evaporated, and the crude products were purified by crystallization.

*3-Chloro-3-[(1,4,5-trimethyl-1*H*-imidazol-2-yl)disulfanyl]-2,2,4,4-tetramethylcyclobutanone* (**9a**). Yield: 218 mg (65%). Yellowish crystals. M.p. 120–122° (hexane/CH_2Cl_2). IR: 1791v*s* (C=O), 1462*m*, 1381*w*, 1029*w*, 835*w*. ^{1}H-NMR: 1.55 (*s*, 2 Me); 1.61 (*s*, 2 Me); 2.36, 2.37 (2*s*, 2 Me); 3.86 (*s*, MeN). ^{13}C-NMR: 9.4, 12.6 (2*q*, 2 Me); 22.2, 23.1 (2*q*, 4 Me); 31.8 (*q*, MeN); 69.2 (*s*, C(2), C(4)); 86.5 (*s*, C(3)); 127.4, 135.4, 135.7 (3*s*, 3 arom. C); 216.2 (*s*, C=O). EI-MS: 332 (30, $M^{+\cdot}$), 142 (57), 141 (100). Anal. calc. for $C_{14}H_{21}ClN_2OS_2$ (332.91): C 50.51, H 6.36, N 8.41; found: C 51.09, H 6.45, N 7.90.

*3-Chloro-3-[(1-cyclohexyl-4,5-diphenyl-1*H*-imidazol-2-yl)disulfanyl]-2,2,4,4-tetramethylcyclobutanone* (**9b**). Yield: 217 mg (41%). Yellowish crystals. M.p. 163–165° (MeOH/CH_2Cl_2). IR: 2933v*s*, 2855*s*, 1789v*s* (C=O), 1444*s*, 1381*m*, 1325*s*, 1027*m*, 775*s*, 724v*s*. ^{1}H-NMR: 0.90–1.77 (*m*, 10 H); 1.32 (*s*, 2 Me); 1.36 (*s*, 2 Me); 4.10–4.55 (*m*, 1 H); 6.98–7.38 (10 arom. CH). ^{13}C-NMR: 22.5 (*q*, 2 Me); 23.0 (*q*, 2 Me); 25.0, 26.2, 33.1 (3*t*, 5 CH_2); 59.0 (*d*, CH); 69.3 (*s*, C(2), C(4)); 86.6 (*s*, C(3)); 126.4, 126.6, 127.8, 128.7, 129.1, 131.6 (6*d*, 10 arom. CH); 127.8, 132.0, 133.9, 138.1, 139.8 (5*s*, 5 arom. C); 216.3 (*s*, C=O). EI-MS: 525 (5, $M^{+\cdot}$), 524 (17, $[M-1]^+$),

334 (53), 275 (13), 252 (100), 193 (43), 165 (12), 156 (9), 86 (26). Anal. calc. for $C_{29}H_{33}ClN_2OS_2$ (525.18): C 66.32, H 6.33, N 5.33; found: C 65.97, H 5.90, N 5.25.

3-[(1-Benzyl-4,5-diphenylimidazol-2-yl)disulfanyl]-3-chloro-2,2,4,4-tetramethylcyclobutanone (**9c**). Yield: 217 mg (41%). Yellowish crystals. M.p. 137–139° (MeOH/CH_2Cl_2). IR: 1786v*s* (C=O), 1603*m*, 1497*s*, 1443*s*, 1381*s*, 1352*s*, 1027*s*, 917*m*, 832*m*, 775*s*, 728*s*, 695v*s*. ^{1}H-NMR: 1.35 (*s*, 2 Me); 1.43 (*s*, 2 Me); 5.25 (*s*, CH_2). ^{13}C-NMR: 22.4 (*q*, 2 Me); 23.1 (*q*, 2 Me); 48.7 (*t*, CH_2); 69.3 (*s*, C(2), C(4)); 86.3 (*s*, C(3)); 126.3, 126.7, 127.6, 128.0, 128.6, 128.9, 129.1, 130.7 (8*d*, 15 arom. CH); 130.3, 132.5, 133.6, 136.7, 139.1, 140.1 (6*s*, 6 arom. C); 216.3 (*s*, C=O). EI-MS: 532 (27, $[M-1]^+$), 283 (21), 252 (9), 193 (35), 156 (11), 91 (100). Anal. calc. for $C_{30}H_{29}ClN_2OS_2$ (533.14): C 67.58, H 5.48, N 5.25; found: C 67.47, H 5.44, N 5.58.

5. *Reaction of Thiouracil* (=*2,3-Dihydro-2-thioxopyrimidin-4(1*H*)-one*; **10**) *with* **3**. To a stirred suspension of **10** (192.0 mg, 1.5 mmol) and Et_3N (152 mg, 1.5 mmol) in CH_2Cl_2 (1 ml) was added a soln. of freshly distilled **3** (218.0 mg, 1 mmol) in CH_2Cl_2 (2 ml) at r.t. When the addition was complete, stirring was continued for 20 min, then CH_2Cl_2 (5 ml) was added, the soln. was washed with 2% HCl (10 ml) and H_2O (10 ml, 2 ×). The org. phase was separated, dried ($MgSO_4$), and evaporated. The crude product was purified by recrystallization.

*2-[(1-Chloro-2,2,4,4-tetramethyl-3-oxocyclobutyl)disulfanyl]pyrimidin-4(3*H*)-one* (**11**). Yield: 210 mg (66%). Colorless crystals. M.p. 142–144° (hexane/CH_2Cl_2). IR: 1790*s* (C=O, ketone), 1690v*s* (C=O, pyrimidone), 1480*s*, 1430*s*, 1250*s*, 980*m*, 820*s*. ^{1}H-NMR: 1.46 (*s*, 2 Me); 1.55 (*s*, 2 Me); 6.27, 7.80 (*AB*, *J* = 7.95, 2 H). ^{13}C-NMR: 22.2 (*q*, 2 Me); 23.6 (*q*, 2 Me); 69.6 (*s*, C(2′), C(4′)); 87.2 (*s*, C(1′)); 113.1, 153.8 (2*d*, C(5), C(6)); 161.0, 158.2 (2*s*, C(2), C(4)); 214.0 (*s*, C=O). EI-MS: 318 (4, $M^{+\cdot}$), 249 (16), 224 (29), 213 (100), 197 (24), 148 (11), 131 (66). Anal. calc. for $C_{12}H_{15}ClN_2O_2S_2$ (318.85): C 45.20, H 4.74, N 8.78; found: C 44.77, H 4.62, N 8.74.

6. *Reaction of* **12** *with* **3**. A soln. of **12** (221 mg, 1 mmol) in CH_2Cl_2 (5 ml) was added to a stirred soln. of freshly distilled **3** (227 mg, 1 mmol) in CH_2Cl_2 (5 ml). During the addition, the reaction flask was cooled in a H_2O/ice bath, then, the cooling bath was removed, and the mixture was stirred at r.t. After 24 h, the solvent was evaporated, and the solid residue was separated by prep. TLC (SiO_2; hexane/Et_2O 20 :1). Along with recovered starting material **12** (92 mg, 42%), the oxo analogue **13** (54 mg, 26%) and a solid identified as **14** (22 mg, 7%) were isolated as main fractions.

*4,4-Dimethyl-2-phenyl-1,3-thiazol-5(4*H*)-one* (**13**). Yield: 54 mg (26%). Yellowish oil. The ^{1}H-NMR spectrum of the isolated material was identical with that of an original sample of **12** [24].

5,5-Bis[1-chloro-2,2,4,4-tetramethyl-3-oxocyclobutyl)disulfanyl]-4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-thiazole (**14**). Yield: 22 mg (7%). Colorless crystals. M.p. 145–147° (hexane). IR: 2977*m*, 1785v*s* (C=O), 1447*m*, 1381*m*, 1260*w*, 949*m*, 835*w*, 767*m*. ^{1}H-NMR: 1.39 (*s*, 2 Me); 1.41 (*s*, 2 Me); 1.43 (*s*, 2 Me); 1.49 (*s*, 2 Me); 1.60 (*s*, 2 Me); 7.38–7.47 (*m*, 3 arom. H); 7.83–7.86 (*m*, 2 arom. H). ^{13}C-NMR: 22.2, 22.3, 22.9, 23.5, 24.0 (5*q*, 10 Me); 69.0, 69.7 (2*s*, 2 C(2′), 2 C(4′)); 84.5, 85.5, 95.1 (3*s*, 2 C(1′), C(4), C(5)); 128.1, 128.4, 128.7 (3*d*, 5 arom. CH); 131.5 (*s*, 1 arom. C); 160.0 (*s*, C=N); 216.0 (*s*, C=O). Anal. calc. for $C_{27}H_{35}Cl_2NO_2S_5$ (635.06): C 50.92, H 5.54, N 2.20; found: C 50.04, H 5.43, N 2.01.

7. *Reaction of* **8b** *with* **16**[5]). A soln. of freshly distilled **16** (52.0 mg, 0.20 mmol) in CH_2Cl_2 (0.5 ml) was added dropwise to a stirred soln. of **8b** (70 mg, 0.21 mmol) and Et_3N (20 mg, 0.20 mmol) cooled in a H_2O/ice bath. The exothermic reaction was complete after 15 min. Then, the mixture was diluted with 10 ml CH_2Cl_2, extracted with H_2O (10 ml, 3 ×), and the org. phase was dried ($MgSO_4$). The solvent was evaporated, and the solid residue was purified by crystallization.

*3-Chloro-3-[(1-cyclohexyl-4,5-diphenyl-1*H*-imidazol-2-yl)trisulfanyl]-2,2,4,4-tetramethylcyclobutanone* (**17**). Yield: 79 mg (70%). Yellow crystals. M.p. 180–182° (hexane/CH_2Cl_2). IR: 2933*s*, 1792v*s* (C=O), 1444*m*, 1332*w*, 1027*w*, 825*w*, 776*w*, 699*s*. ^{1}H-NMR: 0.75–1.90 (*m*, 10 H); 1.39 (*s*, 2 Me); 1.41 (*s*, 2 Me); 4.10–4.40 (*m*, 1 H); 7.04–7.42 (*m*, 10 arom. H). ^{13}C-NMR: 22.9 (*q*, 2 Me); 23.6 (*q*, 2 Me); 25.2, 26.4, 33.6 (3*t*, 5 CH_2); 59.0 (*d*, CH); 69.6 (2*s*, C(2), C(4)); 88.3 (*s*, C(3)); 127.0, 127.2, 128.3, 129.2, 129.6 (5*d*, 10 arom. CH); 132.0, 132.8, 134.0, 139.5, 140.8 (5*s*, 5 arom. C); 216.2 (*s*, C=O). EI-MS: 557 (< 1, $M^{+\cdot}$), 556 (4, $[M-1]^+$), 334 (100), 333 (32). Anal. calc. for $C_{29}H_{33}ClN_2OS_3$ (557.24): C 62.51, H 5.97, N 5.03; found: C 62.10, H 5.98, N 5.24.

8. *Reaction of* **10** *with* **16**. To a stirred suspension of **10** (192 mg, 1.50 mmol) and Et_3N (152 mg, 1.50 mmol) in CH_2Cl_2 (1 ml) was added dropwise at r.t. a soln. of freshly distilled **16** (259 mg, 1.00 mmol) in CH_2Cl_2 (2 ml). After 20 min stirring, CH_2Cl_2 (5 ml) was added, and the mixture was washed with 2% HCl (10 ml) and H_2O (10 ml, 2 ×). The org. phase was dried ($MgSO_4$) and evaporated to give a crystalline, colorless solid. Crystallization of the crude product afforded an anal. pure sample.

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[5]) Experiment performed by *K. Tegos*, University of Łódź, 2002.

*2-[(1-Chloro-2,2,4,4-tetramethyl-3-oxocyclobutyl)trisulfanyl]pyrimidin-4(3*H*)-one* (**18**). Yield: 230 mg (65%). Colorless crystals. M.p. 169–170° (hexane/CH_2Cl_2). IR: 3100–2614 (br., NH), 1790*s* (C=O), 1683v*s* (C=O, pyrimidone), 1524*s*, 1448*s*, 1270*s*, 980*s*, 830*m*. ^{1}H-NMR: 1.45 (*s*, 2 Me); 1.46 (*s*, 2 Me); 6.31, 7.90 (*AB*, *J* = 6.6, 2 H). ^{13}C-NMR: 22.5 (*q*, 2 Me); 23.4 (*q*, 2 Me); 69.4 (*s*, C(2′), C(4′)); 112.8, 154.4 (2*d*, C(5), C(6)); 158.9, 162.8 (2*s*, C(2), C(4)); 215.0 (*s*, C=O). CI-MS (NH_3): 253 (16), 251 (35, $[M+1]^+$), 289 (15), 288 (13), 287 (100), 238 (8), 221 (10), 144 (15). Anal. calc. for $C_{12}H_{15}ClN_2O_2S_3$ (350.91): C 41.07, H 4.31, N 7.98, S 27.41; found C 40.95, H 4.40, N 7.95, S 27.53.

9. *Reaction of* **12** *with* **16**. To a soln. of freshly distilled **16** (155 mg, 0.60 mmol) in CH_2Cl_2 (5 ml), which was cooled in acetone/dry ice bath (−78°), was added dropwise a soln. of **12** (66 mg, 0.30 mmol) in CH_2Cl_2 (2 ml) at −78°, and the mixture was stirred at this temp. for 6 h. After 24 h at r.t., the solvent was evaporated, and the residue was separated by prep. TLC (SiO_2; hexane/Et_2O 20:1). Along with a small amount of recovered **12** (10 mg, 16%), 1,3-thiazolone **13** (47 mg, 78%) and pentasulfane **19** were obtained.

1,5-Bis(1-Chloro-2,2,4,4-tetramethyl-3-oxocyclobutyl)pentasulfane (**19**). Yield: 112 mg (78%). Colorless crystals. M.p. 136–138° (hexane). IR: 2969*m*, 2867*m*, 1790v*s* (C=O), 1460*s*, 1455*s*, 1379*s*, 1363*s*, 1245*m*, 1168*s*, 1134*m*, 1030*s*, 911*s*, 887*s*, 830*m*, 780*m*. ^{1}H-NMR: 1.44 (*s*, 4 Me); 1.47 (*s*, 4 Me). ^{13}C-NMR: 22.8 (*q*, 4 Me); 23.4 (*q*, 4 Me); 69.2 (*s*, 4 Me_2C); 87.1 (*s*, 2 C(1)); 215.4 (*s*, 2 C=O). CI-MS: 285 (27, $[C_8H_{12}OS_5+1]^+$), 284 (100, $C_8H_{12}OS_5^+$), 267 (17), 266 (6). Anal. calc. for $C_{16}H_{24}Cl_2O_2S_5$ (479.60): C 40.07, H 5.04, S 33.43; found: C 40.11, H 5.09, S 33.17.

10. *X-Ray Crystal-Structure Determination of* **11**, **14**, **17**, *and* **18** (see *Table* and *Figs. 1–3*)[6]). All measurements were performed on a *Nonius KappaCCD* diffractometer [25] with graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. Data reduction was performed with *HKL Denzo* and *Scalepack* [26]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multiscan method [27] was applied. Equivalent reflections were merged, except that for **14**, *Friedel* pairs were not merged. Data collection and refinement parameters are given in the *Table*, and views of the molecules are shown in *Figs. 1–3*. Each structure was solved by direct methods with SIR92 [28], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. In the cases of **11** and **18**, the amine H-atom was placed in the position indicated by a difference electron density map, and its position was allowed to refine together with an isotropic displacement parameter. All remaining H-atoms, as well as all H-atoms of **14** and **17**, were placed in geometrically calculated positions and refined with a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent C-atom (1.5U_{eq} for the Me groups). Refinement of each structure was carried out on F^2 by full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. Corrections for secondary extinction were not applied. In the case of **11**, one reflection, whose intensity was considered to be an extreme outlier, was omitted from the final refinement. Two significant peaks of residual electron density (1.52 and 1.40 e Å^{-3}; next peak is 0.36 e Å^{-3}) remain in the vicinity of O(1). These features could not be rationalized, but may be the result of poor crystal quality, as it was necessary to cut a fragment from a large brittle block. In the case of **14**, there are two independent molecules in the asymmetric unit. The molecules have very similar conformations, although molecule B is inverted with respect to molecule A. The atomic coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group with the program PLATON [29], but none could be found. Ten reflections, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Refinement of the absolute structure parameter [30] yielded a value of 0.51(3), which indicates that the crystals are inversion twins. Neutral-atom-scattering factors for non-H-atoms were taken from [31a], and the scattering factors for H-atoms were taken from [32]. Anomalous dispersion effects were included in F_c [33]; the values for f' and f'' were those of [31b]. The values of the mass attenuation coefficients are those of [31c]. All calculations were performed using the SHELXL97 [34] program.

In **11**, the NH group forms bifurcated H-bonds. One interaction is an intramolecular H-bond with the most distant S(1)-atom of the molecule. This forms a five-membered loop with a graph set motif [35] of S(5). The other interaction is an intermolecular H-bond with the cyclobutanone O(1)-atom of a neighboring molecule and links the molecules into centrosymmetric dimeric units which have a graph set motif of $R_2^2(8)$. The NH group of

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[6]) CCDC-200712–200714 and 203557 contain the supplementary crystallographic data for this paper. These data can be obtained, free of charge, *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB21EZ, U.K.; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Table. *Crystallographic Data of* **11**, **14**, **17**, *and* **18**

		11	**14**	**17**	**18**
Crystallized from		hexane/CH_2Cl_2	benzene	hexane/CH_2Cl_2	hexane/CH_2Cl_2
Empirical formula		$C_{12}H_{15}ClN_2O_2S_2$	$C_{27}H_{35}Cl_2NO_2S_5$	$C_{29}H_{33}ClN_2OS_3$	$C_{12}H_{15}ClN_2O_2S_3$
Formula weight [g mol^{-1}]		318.83	636.78	557.23	350.89
Crystal color, habit		colorless, prism	colorless, prism	yellow, needle	colorless, plate
Crystal dimensions [mm]		0.15 × 0.20 × 0.25	0.15 × 0.20 × 0.20	0.08 × 0.13 × 0.18	0.05 × 0.22 × 0.25
Temp. [K]		160(1)	160(1)	160(1)	160(1)
Crystal system		triclinic	monoclinic	monoclinic	monoclinic
Space group		$P\bar{1}$	$P2_1$	$P2_1/c$	$P2_1/c$
Z		2	4	4	4
Reflections for cell determination		19095	72062	21410	46013
2θ Range for cell determination [°]		4–60	4–60	2–55	4–60
Unit cell parameters	a [Å]	7.9038(2)	11.4713(1)	28.3425(6)	19.9472(3)
	b [Å]	8.0878(2)	23.5861(2)	11.2684(2)	7.5302(1)
	c [Å]	12.2811(3)	12.5495(1)	8.5224(1)	10.8067(2)
	α [°]	99.5214(9)	90	90	90
	β [°]	98.9073(9)	114.1797(4)	93.5783(6)	105.6430(8)
	γ [°]	100.922(1)	90	90	90
	V [Å^3]	746.04(3)	3097.54(5)	2716.53 (8)	1563.11(4)
D_x [g cm^{-3}]		1.419	1.365	1.362	1.491
μ(MoK_α) [mm^{-1}]		0.534	0.572	0.397	0.646
Scan type		ϕ and ω	ϕ and ω	ϕ and ω	ϕ and ω
$2\theta_{(max)}$ [°]		60	60	55	60
Transmission factors (min; max)		0.842; 0.925	0.874; 0.919	0.883; 0.972	0.848; 0.971
Total reflections measured		22598	76350	46572	31233
>Symmetry independent reflections		4339	17916	6213	4548
Reflections with $I > 2\sigma(I)$		3360	13899	4115	3835
Reflections used in refinement		4338	17906	6213	4548
Parameters refined		180	688	329	189
Final $R(F)$ [$I > 2\sigma(I)$ reflections]		0.0476	0.0405	0.0466	0.0327
$wR(F^2)$ (all data)		0.1357	0.0915	0.1262	0.0850
Weighting parameters [a; b][a])		0.0715; 0.3563	0.0444; 0	0.0612; 0.3487	0.0411; 0.6041
Goodness-of-fit		1.070	1.025	1.050	1.056
Final Δ_{max}/σ		0.001	0.001	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]		1.52; −0.40	0.68; −0.42	0.55; −0.48	0.40; −0.47

[a]) $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$ where $P = (F_o^2 + 2F_c^2)/3$

18 forms an intermolecular H-bond with the amide O-atom of a neighboring molecule and thereby links the molecules into infinite chains, which run parallel to the *y*-axis and have a graph set motif of C(4).

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Received February 12, 2003