New Contributions to the Chemistry of 2-Chloro-2-(chlorothio)propanedioic Diesters and Diamides

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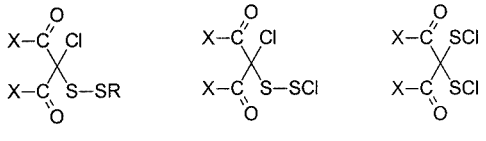
The pyridine-catalyzed reaction between a number of propanedioic acid derivatives **1** and thionyl chloride has been investigated in detail. Contrary to popular belief the straightforward formation of the corresponding α-chloro sulfenyl chlorides **2** is the exception rather than the rule. The propanediamide **2e**, not available by the "standard" reaction of **1e** with thionyl chloride, is surprisingly formed by reaction of **1e** with sulfur dichloride. The usefulness of **2** as thiosulfine **4** precursors has been demonstrated.

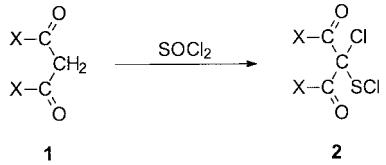
Our renewed interest in active methylene compound **1** derived α-chloroalkanesulfenyl chlorides **2**,[1–6] [see Equation (1)] stems from the following considerations:
1) Compounds **2** are in principle convenient intermediates for the generation of transient dithiiranes/thiosulfines **3/4**,[3,7] i.e. via their conversion with thiocarboxylic acids to the corresponding acyldithio compounds **5**, which subsequently can be "unzipped" with morpholine[3,7] to form **3/4**, or chlorinated with formation of the corresponding chlorodithio compounds **6**, which in turn upon dechlorination under the proper conditions might generate **3/4** [Scheme 1 and Equation (2)].



5 **6** **15**

a, R = MeCO
b, R = PhCO
c, R = Ph

Scheme 1



1 **2**

(1)

a, X = MeO
b, X = EtO
c, X = CCl_3CH_2O
d, X = CBr_3CH_2O
e, X = *t*BuNH

3 **4**

(2)

Thiosulfines **4** typically suffer disproportionation according to Equation (3): and in subsequent cycloadditions yield 1,2,4-trithiolanes **9** and/or 1,2,4,5-tetrathianes **10** [Equation (4) and (5)].

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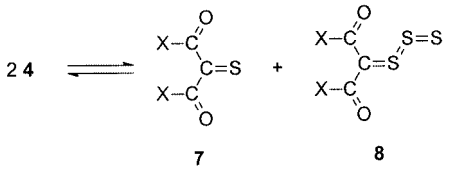
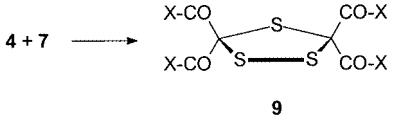
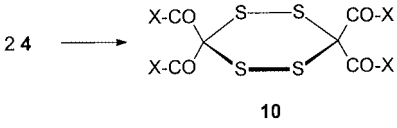


(3)

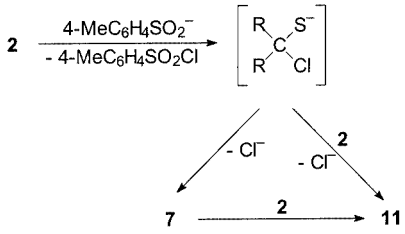


(4)



(5)

2) Dechlorination of **2** would, in principle, generate the highly reactive thiones **7**,[8] which are useful for cycloadditions etc. (Scheme 2).



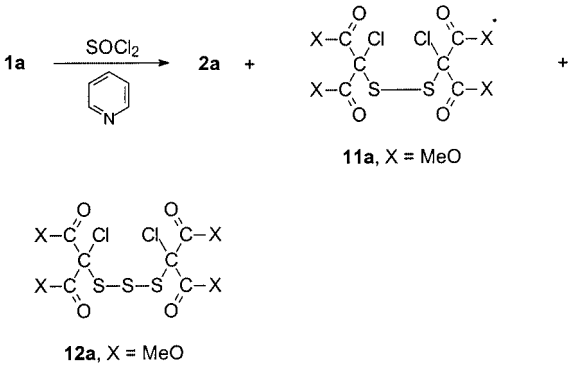
Scheme 2

3) The persistent failure of closely related α-chloroalkanesulfenyl chlorides to form the corresponding disulfides **11** upon reduction[4,5] (otherwise a standard reaction of sulfenyl chlorides[9]) suggested a need for a better understanding of the substitution/reduction pattern of α-chloroalkanesulfenyl chlorides including **2**.

Results and Discussion

The standard procedure for the preparation of **2** from **1** is treatment of the latter with thionyl chloride in the presence of a catalytic amount of pyridine [Equation (1) and Table 1].[1]

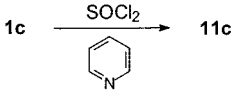
The preparation of **2a** differs significantly from that of the known **2b**[1] in that **2a** can be purified by column chromatography (yield 58%), which also yields the corresponding disulfide **11a** (yield 25%) and trisulfide **12a** (yield 10%) [Equation (6)].



(6)

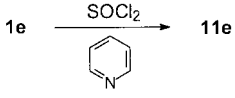
It seems safe to assume that the impurities in crude **2b** are therefore **11b** and **12b**.

We were unable to prepare bis(2,2,2-trichloroethyl)-2-chloro-2-(chlorothio)propanedioate (**2c**) and the corresponding 2,2,2-tribromoethyl compound **2d**: the diester **1c**, seemingly highly analogous with other compounds **1**, only yielded the corresponding disulfide **11c** (a remarkable Cl_{14} compound) while **1d** failed to react with thionyl chloride [Equation (7)].



(7)

The propanediamide **1e** gave the disulfide **11e** when treated with thionyl chloride [Equation (8)].



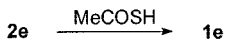
(8)

Table 1. Reactions of propanedioic acid derivatives **1** with $SOCl_2$

Starting material	Product(s) (yield, %)	Comments
1a	**2a** (58), **11a** (25), **12a** (10)	after column chromatography, analytically pure
1b	**2b** (99)	crude product, satisfactory for synthetic purposes; decomposes upon attempted column chromatography; can be distilled[1]
1c	**11c** (71)	analytically pure
1d	**1d**	no reaction
1e	**11e** (66)	analytically pure; **2e** can be prepared from **1e** and SCl_2 in boiling benzene

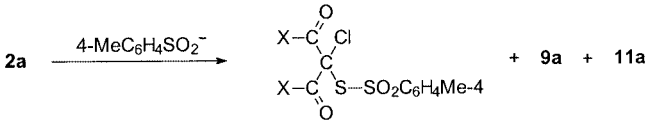
However, **2e** could be obtained in an unorthodox fashion from **1e** and sulfur dichloride in boiling benzene.

When we treated **2a,b** with thioacetic acid, thiobenzoic acid, or thiophenol all substitutions proceeded in the expected uneventful fashion, yielding **5aa**, **5ab**, **5ac**, **5bb**, and **5bc**, respectively. An unorthodox result was the formation of **1e** from **2e** and thioacetic acid [Equation (9)].

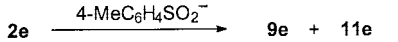


(9)

The substitution/reduction reactions of **2** with various nucleophiles were also difficult to predict. Thus, treatment of **2a** with *p*-toluenesulfinate led to three products: the simple substitution product **12a**, the disulfide **11a**, and the 1,2,4-trithiolane **9a** [Equation (10)], whereas the corresponding reaction of **2e** gave disulfide **11e** and 1,2,4-trithiolane **9e** [Equation (11)].



(10)



(11)

While the formation of **11a** from **2a** may or may not involve the thione **7a** as intermediate (Scheme 2), it is not very likely that the 1,2,4-trithiolane **9a** can be formed in any other way than by cycloaddition of the thione **7a** and the thiosulfine **4a** [Equation (4)]. Although a spontaneous disproportionation of the S_1 compound **7a** to the S_2 compound **4a** and, presumably, an unspecified sulfur-free species is not exactly trivial, reactions of this kind do have precedent in the literature, especially in the presence of oxidants.[10] While a number of reducing agents convert **2** efficiently to **11**, the corresponding electrochemical reduction yields **11** in analytical purity without chromatographic workup.

The solid-state structure of the key compound **11a** was determined by X-ray crystallography (Figure 1, Table 2). The structure appears to be devoid of strain and largely determined by the electrostatic repulsions of the chlorine atoms and the geminal carbonyl groups.

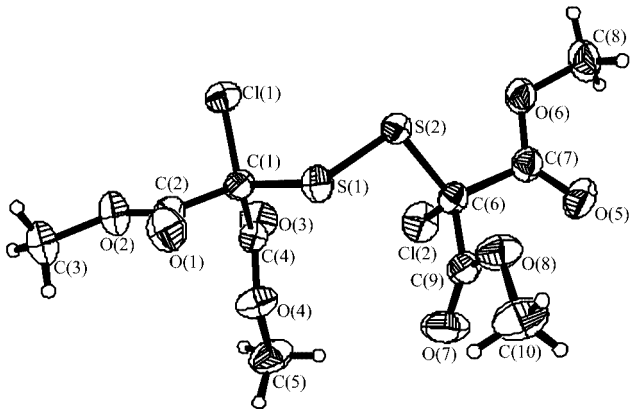
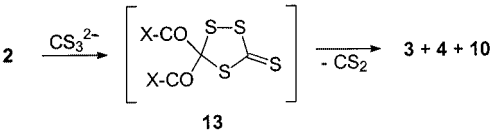


Figure 1. The molecular structure of **11a** with 50% probability ellipsoids

Table 2. Crystal data for compound **11a**

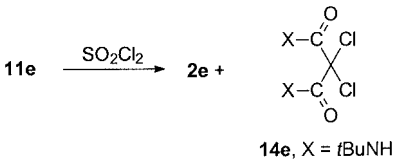
	11a
Formula	$C_{10}H_{12}Cl_2O_8S_2$
Mol. wt.	395.24
M.p. (°C)	72.5−73.5
Cryst. system	monoclinic
Space group	$P2_1/c$
a (Å)	10.98520(10)
b (Å)	18.0271(2)
c (Å)	8.26470(10)
α (°)	–
β (°)	90.94
γ (°)	–
V (Å^3)	1636.45(3)
Z	4
Total number of unique refl.	4078
[$I > 2\sigma(I)$]	3469
θ range (°)	1.85−29.49
R (obs. data)	0.0344
*wR*2 (all data)	0.0933

Although the reaction of **2** with aqueous trithiocarbonate leading to the 1,2,4,5-tetrathiane **10** could be formulated as a straightforward reduction it is tempting to consider the intermediate formation of **3/4** via a labile 1,2,4-trithiolane-3-thione precursor **13** [Equation (12)].



(12)

Chlorination of the disulfides **11** leads, as expected, to the corresponding compounds **2**. However, in the case of **11e** the α-chloro sulfenyl chloride thus formed is accompanied by the dichloromethylene compound **14e** [Equation (13)].

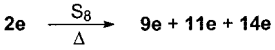


(13)

The chlorination of the 1,2,4-trithiolane **9a** yields, as expected, **2a** and the corresponding *gem*-disulfenyl dichloride **15a** while the analogous treatment of **9e** leads to **2e** and **14e**.

The chlorination of **5aa** was followed in small-scale qualitative experiments: it is relatively fast with chlorine and relatively slow (and requiring heating) with sulfuryl chloride. In both cases (as judged by MS) varying amounts of thiosulfenyl chloride **6a** and *gem*-disulfenyl dichloride **15a** (cf. Scheme 1) were obtained, along with disulfide **11a**, trisulfide **12a**, and tetrasulfide **16a**, i.e. tetramethyl 1,6-dichloro-2,3,4,5-tetrathiahexane-1,1,6,6-tetracarboxylate. Because of the very similar polarities of the components of these mixtures small-scale column chromatography could not effect complete separations. We chose not to pursue this matter any further even though the formation of the sulfur-rich compounds **12a** and **16a** is puzzling.

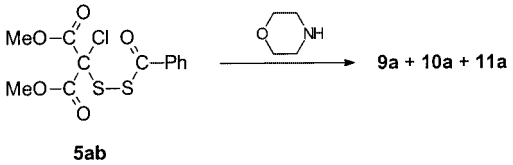
Upon heating with elemental sulfur compounds **2** all behave differently: **2a** gives the disulfide **11a** and the trisulfide **12a** as well as the 1,2,4-trithiolane **9a**; compound **2b** is cleanly oxidized to the disulfide **11b**; and **2e** forms **11e** as well as the 1,2,4-trithiolane **9e** and the dichloromethylene compound **14e** [Equation (14)].



(14)

In particular, the formation of **14e** in the absence of an external source of chlorine is baffling.

When the unsymmetrical disulfide **5ab** was subjected to our standard "unzipping" reaction with morpholine[11,3,7] we obtained the 1,2,4-trithiolane **9a**, the 1,2,4,5-tetrathiane **10a**, and, contrary to expectation, the disulfide **11a** [Equation (15)].



(15)

The observation of the two first compounds clearly indicates the intermediacy of the corresponding thiosulfine **4a**. The corresponding "unzipping" of **5aa** with morpholine was unrewarding. An inconveniently large number of ill-defined products was formed, none of which was the expected **9a**,**10a**, and/or **11a**.

Experimental Section

All commercial chemicals and solvents were used as received except sulfur dichloride which was distilled immediately prior to use. Bis(2,2,2-trichloroethyl) propanedioate (**1c**),[12] bis(2,2,2-tribromoethyl) propanedioate (**1d**),[13] *N,N*-di-*tert*-butylpropanediamide (**1e**),[14] and diethyl 2-chloro-2-(chlorothio)propanedioate (**2b**)[1] were prepared according to literature procedures. The electrochemical reductions were performed in a three-compartment H cell at constant potential by means of a home-built potentiostat.[13] The stationary phase for column chromatography was Merck silica gel 60, particle size 0.040−0.063 mm. The eluent for TLC was hexane/ether (1:1), and the eluent for column chromatography petroleum ether (b.p. 40−60 C)/diethyl ether (10:1). The NMR spectra were recorded in $CDCl_3$ solution with a Bruker AC 250 or Bruker AM 500 apparatus. IR spectra were recorded on a Perkin−Elmer FTIR 1700 with KBr wafers, those of liquids neat between NaCl windows. The mass spectra were obtained with a VG (Mass Lab) Trio-2 quadrupole instrument. Chemical ionization spectra were recorded with NH_3 as reagent gas. The elemental analyses were carried out by the Microanalytical Laboratory of the Department of Physical Chemistry, University of Vienna, A-1090 Vienna, Austria.

Reaction of Dimethyl Propanedioate (1a) with $SOCl_2$: Dimethyl propanedioate **1a** (1.50 mL, 13 mmol), thionyl chloride (12.4 mL, 170 mmol), and pyridine (0.20 mL, 2.6 mmol) were refluxed for 7.5 h. The reaction mixture was allowed to cool, then filtered, and the solvents evaporated in vacuo. Yield 2.76 g of crude product which was column chromatographed. The following products (in order of elution) were obtained: **2a** (1.74 g, 58%), **11a** (0.64 g, 25%), **12a** (0.28 g, 10%).

Dimethyl 2-Chloro-2-(chlorothio)propanedioate (2a): Yellow oil, b.p. 87−91 °C/0.5 Torr. IR: $\tilde{\nu}$ = 2957 (aliph. CH), 1748 (C=O), 1435, 1354, 1250, 1109, 1007, 947, 905, 846, 763, 624, 523 cm^{-1}. ^1H NMR: δ = 3.95 (s) ppm. ^{13}C NMR: δ = 54.8 (2 CH_3), C-2 signal not observed, 164.2 (2 C=O) ppm. MS (EI): *m*/*z* (%) = 232 (12) [M], 197 (0.6) [$C_5H_6ClO_4S$], 173 (15) [$C_3H_3Cl_2O_2S$], 162 (10) [$C_5H_6O_2S$], 153 (18), 138 (23) [$C_3H_3ClO_2S$], 109 (25), 103 (25) [$C_3H_3O_2S$], 79 (32), 59 (100) [$C_2H_3O_2$], 45 (10). $C_5H_6Cl_2O_4S$ (233.07): calcd. C 25.77, H 2.60; found C 25.91, H 2.56.

Tetramethyl 1,4-Dichloro-2,3-dithiabutane-1,1,4,4-tetracarboxylate (11a): Colorless crystals, m.p. 72.5−73.5 °C. IR: $\tilde{\nu}$ = 2957 (aliph. CH), 2848 (aliph. CH), 1742 (C=O), 1435, 1248, 1435, 1248, 1109, 1007, 947, 905, 846, 763, 706, 635 cm^{-1}. ^1H NMR: δ = 3.85 (s) ppm. ^{13}C NMR: δ = 54.8 (4 CH_3), C-1, C-4 signals not observed, 164.2 (4 C=O) ppm. MS (EI): *m*/*z* (%) = 394 (14) [M], 335 (4) [$C_8H_9Cl_2O_6S_2$], 330 (2) [$C_{10}H_{12}Cl_2O_8$], 229 (12), 194 (4) [$C_5H_6O_4S_2$], 180 (8) [$C_4H_4O_4S_2$], 162 (12), 153 (22), 137 (42), 109 (30), 103 (27), 95 (25), 79 (18), 59 (100) [$C_2H_3O_2$], 45 (8). $C_{10}H_{12}Cl_2O_8S_2$ (395.24): calcd. C 30.39, H 3.06, S 16.23; found C 30.38, H 3.04, S 18.15. In light of the overwhelming structural proof for **11a**, including X-ray data, we consider the low sulfur analysis unimportant. An X-ray single crystal structure determination was performed (cf. Figure 1, Table 2).

Tetramethyl 1,5-Dichloro-2,3,4-trithiapentane-1,1,5,5-tetracarboxylate (12a): Colorless crystals, m.p. 79.5−80.5 °C. IR: $\tilde{\nu}$ = 2961 (aliph. CH), 1738 (C=O), 1436, 1252, 1018, 948, 843, 763, 706, 635 cm^{-1}. ^1H NMR: δ = 3.85 (s) ppm. ^{13}C NMR: δ = 54.6 (4 CH_3), C-1, C-5 signals not observed, 163.9 (4 C=O) ppm. MS (EI): *m*/*z* (%) = 426 (3) [M], 394 (22) [$C_{10}H_{12}Cl_2O_8S_2$], 335 (9) [$C_8H_9Cl_2O_6S_2$], 330 (6) [$C_{10}H_{12}Cl_2O_8$], 261 (8), 229 (81) [$C_5H_6ClO_4S_2$], 197 (10) [$C_5H_6ClO_4S$], 180 (9) [$C_4H_4O_4S_2$], 162 (12) [$C_5H_6O_4S$], 153 (23), 137 (43), 109 (23), 103 (19), 79 (16), 59 (100)

[$C_2H_3O_2$]. $C_{10}H_{12}Cl_2O_8S_3$ (427.30): calcd. C 28.11, H 2.83; found C 27.84, H 2.60%.

Reaction of Bis(2,2,2-trichloroethyl) Propanedioate (1c) with $SOCl_2$: Bis(2,2,2-trichloroethyl) propanedioate[12] (47.3 g, 130 mmol), thionyl chloride (124 mL, 1.70 mol), and pyridine (0.20 mL, 2.6 mmol) were stirred at room temperature until TLC showed that the reaction was complete (10 h). The reaction mixture was allowed to cool, filtered, and the solvents evaporated in vacuo. It was then cooled and triturated with diethyl ether/petroleum ether (1:1). Yield 40.5 g (73%) crude product, m.p. 109−114 °C, which was recrystallized from diethyl ether/petroleum ether (1:2) to give colorless crystals (39.4 g, 71%) of tetrakis(2,2,2-trichloroethyl) 1,4-dichloro-2,3-dithiabutane-1,1,4,4-tetracarboxylate (**11c**), m.p. 116.5−117.5 °C. IR: $\tilde{\nu}$ = 2980 (aliph. CH), 1753 (C=O), 1188, 763, 718, 575 cm^{-1}. ^1H NMR: δ = 4.85 (d, ^2J = 12.5 Hz, 2 H, 2 CH_aH$_b$), 5.00 (d, ^2J = 12.5 Hz, 2 H, 2 CH$_a$$H_b$) ppm. ^{13}C NMR: δ = 76.0 (4 CCl_3), 76.6 (4 CH_2), 93.4 (C-1, C-4), 161.8 (4 CO) ppm. MS (EI): *m*/*z* (%) = 858 [M], 683 [$C_{11}H_6Cl_{11}O_6S_2$], 394 (1) [$C_7H_4Cl_6O_4S$], 362 (6) [$C_7H_4Cl_6O_4$], 131 (100) [$C_2H_2Cl_3$], 117 (32) [CCl_3], 95 (63), 79 (34), 61 (28), 45 (24), 36 (17), 26 (3). $C_{14}H_8Cl_{14}O_8S_2$ (864.68): calcd. C 19.45, H 0.93, Cl 57.40, S 7.42; found C 19.74, H 0.89, Cl 57.26, S 7.68.

Reaction of Bis(2,2,2-tribromoethyl) Propanedioate (1d) with $SOCl_2$: No reaction could be observed after up to 20 h reflux of **1d** with $SOCl_2$ with or without pyridine as catalyst.

Reaction of *N,N′*-Di-*tert*-butylpropanediamide (1e) with $SOCl_2$: *N,N′*-Di-*tert*-butylpropanediamide (**1e**)[14] (27.80 g, 130 mmol), thionyl chloride (124 mL, 1700 mmol), and pyridine (0.20 mL, 2.6 mmol) were stirred at room temperature until TLC showed that the reaction was complete (10 h). The reaction mixture was then allowed to cool, filtered, and the solvents evaporated in vacuo. It was then triturated with diethyl ether/petroleum ether (1:1). Yield 25.0 g (69%) crude product, m.p. 137−141 °C, which was recrystallized from diethyl ether to give 24.0 g (66%) colorless crystals of *N,N,N′,N′*-tetra-*tert*-butyl-1,4-dichloro-2,3-dithiabutane-1,1,4,4-tetracarboxamide (**11e**). M.p. 142.5−143.5 °C. IR: $\tilde{\nu}$ = 3425 (NH), 3275 (NH), 2290 (aliph. CH), 1712 (C=O), 1540, 1240 cm^{-1}. ^1H NMR: δ = 1.40 (s, 36 H, 12 CH_3), 7.15 (br. s, 4 H, 4 NH) ppm. ^{13}C NMR: δ = 28.3 (12 CH_3), 52.9 (4 C_t), 81.3 (C-1, C-4), 162.8 (4 C=O) ppm. MS (CI): *m*/*z* (%) = 559 (2) [M + H^+], 352 (4), 245 (100). $C_{22}H_{40}Cl_2N_4O_4S_2$ (559.62): calcd. C 47.22, H 7.20, N 10.01, S 11.46; found C 47.48, H 7.38, N 10.12, S 11.05. An X-ray single crystal structure determination confirming the structure was performed. However, the poor quality of the single crystals which could be grown prevented a full-scale determination of the molecular dimensions.

***N,N*-Di-*tert*-butyl-2-chloro-2-(chlorothio)propanediamide (2e):** *N,N*-Di-*tert*-butylpropanediamide (**1e**)[14] (8.35 g, 390 mmol) was suspended in benzene (250 mL). Sulfur dichloride (17.7 mL, 279 mmol) was added, evolution of hydrogen chloride occurred immediately, and the mixture formed a thick paste. Benzene (75 mL) was added and the mixture heated at reflux until TLC showed that the reaction was complete (4.5 h). The cooled mixture was filtered. Yield 8.70 g (71%) of crude product, m.p. 141−146 °C, which was recrystallized from benzene to give **2e**. Final yield 7.50 g (61%) of pale yellow needles, m.p. 147.5−148.5 °C. IR: $\tilde{\nu}$ = 3287 (NH), 2976 (aliph. CH), 1704 (C=O), 1511, 1394, 1364, 1215, 946, 834, 631 cm^{-1}. ^1H NMR: δ = 1.40 (s, 18 H, 6 CH_3), 6.80 (br. s, 2 H, 2 NH) ppm. ^{13}C NMR: δ = 28.3 (6 CH_3), 52.9 (2 C_t), 81.3 (C-2), 162.8 (2 CO), ppm. $C_{11}H_{20}Cl_2N_2O_2S$ (315.26): calcd. C 41.91, H 6.39, N 8.86, S 10.17; found C 42.06, H 6.54, N 8.90, S 10.78.

Reactions Between 2 and Mercapto Compounds. General Procedure:[11] Equimolar amounts (10 mmol each) of **2** and the mercapto compound (thioacetic acid, series **a**, thiobenzoic acid, series **b**, or thiophenol, series **c**) were dissolved in tetrachloromethane and heated at 50−60 °C until TLC showed that the reaction was complete (3 h). In the case of **5aa** rapid reaction took place at room temperature and was complete after 1 h. After evaporation of the solvent **6aa** (2.72 g, 100%) was obtained by recrystallization from diethyl ether while **5ab** (2.45 g, 73%), **5ac** (2.30 g, 75%), **5bb** (2.80 g, 77%), and **5bc** (2.50 g, 75%) were obtained after column chromatography.

Dimethyl 2-(Acetyldithio)-2-chloropropanedioate (5aa): Colorless crystals, m.p. 67.0−68.0 °C. IR: $\tilde{\nu}$ = 2961 (CH), 1760 (OC=O), 1733 (SC=O), 1436, 1350, 1270, 1228, 1113, 1023, 948, 849, 763, 660 cm^{-1}. ^1H NMR: δ = 2.43 (s, 3 H, CH_3CO), 3.90 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR: δ = 54.8 (2 CH_3), C-2 signal not observed, 128.1, (C-2, C-6), 129.1 (C-3, C5), 134.6 (C-1), 135.0 (C-4), 164.2 (COO), 186.8 (COS) ppm. MS (EI): *m*/*z* (%) = 272 (0.1) [M], 230 (4) [$C_5H_7ClO_4S_2$], 166 (7) [$C_5H_7ClO_4$], 134 (5) [$C_4H_3ClO_3$], 103 (1) [C_3ClO_2], 79 (2) [CClS], 59 (11) [$C_2H_3O_2$], 43 (100) [C_2H_3O]. $C_7H_9ClO_5S_2$ (272.73): calcd. C 30.83, H 3.33, Cl 13.00, S 23.35; found C 30.76, H 3.19, Cl 12.96, S 23.38.

Dimethyl 2-(Benzoyldithio)-2-chloropropanedioate (5ab): Colorless crystals, m.p. 88.5−89.0 °C. IR: $\tilde{\nu}$ = 3035 (arom. CH), 2995 (aliph. CH), 1777 (OC=O), 1751 (SC=O), 1437, 1203, 1022, 949, 873, 773, 689, 678, 643 cm^{-1}. ^1H NMR: δ = 3.90 (s, 6 H, 2 CH_3), 7.6−8.0 (m, 5 H, ArH) ppm. ^{13}C NMR: δ = 29.0 (CH_3CO), 54.7 (2 CH_3O), C-2 signal not observed, 164.2 (COO), 191.8 (COS) ppm. MS (CI): *m*/*z* (%) = 352 (54) [M + NH_4^+], 335 (10) [M + H^+], 105 (100) [C_7H_5O]. $C_{12}H_{11}ClO_5S_2$ (334.80): calcd. C 43.05, H 3.31, S 19.16; found C 43.04, H 3.25, S 19.10.

Dimethyl 2-Chloro-2-(phenyldithio)propanedioate (5ac): Colorless crystals, m.p. 81.5−82.0 °C. IR: $\tilde{\nu}$ = 3040 (arom. CH), 2995 (aliph. CH), 1743 (C=O), 1439, 1256, 1023, 744, 687 cm^{-1}. ^1H NMR: δ = 3.90 (s, 6 H, 2 CH_3), 7.6−8.0 (m, 5 H, ArH) ppm. ^{13}C NMR: δ = 54.7 (2 CH_3), C-2 signal not observed, 128.1, (C-2, C-6), 129.0 (C-3, C5), 134.5 (C-1), 135.0 (C-4), 164.1 (2 CO) ppm. MS (EI): *m*/*z* (%) = 306 (15) [M], 218 (8) [$C_{12}H_{10}S_2$], 141 (100) [$C_6H_5S_2$], 109 (45) [C_6H_5S], 77 (29) [C_6H_5], 65 (18), 59 (17) [$C_2H_3O_2$]. $C_{11}H_{11}ClO_4S_2$ (306.79): calcd. C 43.07, H 3.61, S 20.90; found C 42.95, H 3.17, S 20.74.

Diethyl 2-(Benzoyldithio)-2-chloropropanedioate (5bb): Colorless crystals, m.p. 87.5−88.5 °C. IR: $\tilde{\nu}$ = 3040 (arom. CH), 2983 (aliph. CH), 1741 (OC=O), 1721 (SC=O), 1596, 1581, 1448, 1392, 1368, 1248, 1096, 1026, 1000, 879, 834, 770, 688, 643, 615 cm^{-1}. ^1H NMR: δ = 1.35 (t, ^3J = 7.0 Hz, 6 H, 2 CH_3), 4.35 (q, ^3J = 7.0 Hz, 4 H, 2 CH_2), 7.25−8.10 (m, 5 H, ArH) ppm. ^{13}C NMR: δ = 13.9 (2 CH_3), 63.9 (2 CH_2), C-2 signal not observed, 127.6 (C-2, C-6), 127.8 (C-3, C5), 129.9 (C-1), 131.4 (C-4), 164.0 (2 COO), 189.5 (COS) ppm. MS (CI): *m*/*z* (%) = 380 (28) [M + NH_4^+], 263 (10) [M + H^+], 105 (100) [C_7H_5O]. $C_{14}H_{15}ClO_5S_2$ (362.85): calcd. C 46.34, H 4.17, S 17.67; found C 45.70, H 4.19, S 17.74.

Diethyl 2-Chloro-2-(phenyldithio)propanedioate (5bc): Colorless crystals, m.p. 69.5−70.0 °C. IR: $\tilde{\nu}$ = 3030 (arom. CH), 2983 (aliph. CH), 1742 (C=O), 1576, 1477, 1440, 1368, 1251, 1095, 1024, 895, 857, 788, 743, 688, 668 cm^{-1}. ^1H NMR: δ = 1.35 (t, ^3J = 7.0 Hz, 6 H, 2 CH_3), 4.35 (q, ^3J = 7.0 Hz, 4 H, 2 CH_2), 7.50 −7.95 (m, 5 H, ArH) ppm. ^{13}C NMR: δ = 13.9 (2 CH_3), 63.9 (2 CH_2), C-2 signal not observed, 127.8 (C-2, C-6), 127.9 (C-3, C5), 129.6 (C-1), 131.4 (C-4), 164.0 (2 CO) ppm. MS (EI): *m*/*z* (%) = 334 (16) [M], 261 (1) [$C_{10}H_{10}ClO_2S_2$], 218 (18) [$C_{12}H_{10}S_2$], 197 (7), 141 (100)

$[C_6H_5S_2]$, 109 (57) $[C_6H_5S]$, 77 (20) $[C_6H_5]$, 65 (20), 45 (14), 29 (21). $C_{13}H_{15}ClO_4S_2$ (334.84): calcd. C 46.63, H 4.52, S 19.15; found C 46.50, H 4.47, S 19.95.

Reactions of 2e with Mercapto Compounds: When **2e** was treated with thioacetic acid, thiobenzoic acid, or thiophenol under the above-mentioned conditions the only isolated propanedioic acid derivative was **1e**[13] in 94%, 61%, and 75% yield, respectively. In the second case the co-product was dibenzoyl trisulfide,[15] in the third case diphenyl disulfide.[16]

Substitution/Reduction of 2. a) With *p*-Toluenesulfinate Ions: A general procedure[17] was followed. A two-phase mixture of sodium *p*-toluenesulfinate dihydrate (2.20 g, 10 mmol), **2** (10 mmol), tetrabutylammonium hydrogen sulfate (0.20 g), 25 mL water, and 25 mL benzene was stirred at room temperature until TLC showed that the reaction was complete (5 h). The benzene phase was washed three times with water and dried over anhydrous calcium chloride. After evaporation in vacuo the residue was column chromatographed. The following products (in the order of elution) were obtained: from **2a**: **12a** (1.40 g, 40%), **11a** (0.30 g, 17%), **9a**, m.p. 57.0−58.5 °C (0.55 g, 28%); from **2e**: **11e** (1.80 g, 65%)**, 9e** (0.60 g, 23%).

Dimethyl 2-Chloro-2-(*p*-tolylsulfonylthio)propanedioate (12a): Colorless crystals, m.p. 89.5−90.5 °C. IR: $\tilde{\nu}$ = 3040 (arom. CH), 2995 (aliph. CH), 1744 (C=O), 1593, 1429, 1339, 1267, 1147, 1079, 1013, 946, 848, 817, 764, 700, 653, 587, 519 cm^{-1}. ^1H NMR: δ = 2.55 (s, 3 H, CH_3), 3.95 (s, 6 H, 2 CH_3), 7.35 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.85 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR: δ = 21.8 (CH_3Ar), 54.2 (2 CH_3), C-2 signal not observed, 128.3 (C-3, C-5), 129.9 (C-2, C-6), 141.5 (C-1), 146.1 (C-4), 163.3 (2 C=O) ppm. MS (EI): *m*/*z* (%) = 352 (0.2) [M], 293 (0.2) $[C_{10}H_{10}ClO_4S_2)]$, 265 (2), 254 (0.3), 229 (2), 221 (0.2), 162 (45) $[C_5H_6O_4S]$, 155 (38) $[C_7H_7O_2S]$, 139 (10) $[C_7H_7OS]$, 103 (18), 91 (100) $[C_7H_7]$, 65 (26), 59 (46) $[C_2H_3O_2]$, 45 (15), 39 (8), 29 (2). $C_{12}H_{13}ClO_6S_2$ (352.20): calcd. C 40.85, H 3.71, S 18.18; found C 41.09, H 3.62, S 18.31.

***N,N,N′,N′*-Tetra-*tert*-butyl-1,2,4-trithiolane-3,3,5,5-tetracarboxamide (9e):** Colorless crystals, m.p. 76.5−77.5 °C. IR: $\tilde{\nu}$ = 3304 (NH), 2967 (aliph. CH), 1688 (C=O), 1652, 1527, 1458, 1393, 1366, 1273, 1221, 825, 623, 476 cm^{-1}. ^1H NMR: δ = 1.35 (s, 36 H, 12 CH_3), 7.55 (br. s, 4 H, 4 NH) ppm. ^{13}C NMR: δ = 28.4 (12 CH_3), 52.6 (4 C_t), C-3, C-5 signals not observed, 164.2 (4 CO) ppm. MS (CI): *m*/*z* (%) = 521 (22) [M + H^+], 229 (100). $C_{22}H_{40}N_4O_4S_3$ (520.78): calcd. C 50.74, H 7.74, N 10.76, S 18.47; found C 50.94, H 7.70, N 10.58, S 18.14. A single crystal structure determination was performed (vide supra).

b) With Potassium Iodide, Triphenylphosphane,[18] Sodium Azide, Tin(II) Chloride,[19] or Magnesium: The sulfenyl chlorides **2** were cleanly and in good yields reduced to the disulfides **11** by potassium iodide in acetonitrile, by triphenylphosphane in toluene, by sodium azide in DMF, by tin(II) chloride in dichloromethane/37% HCl, and by magnesium turnings in ether.

c) Electrochemical Reduction: Compound **2a** (1.00 g, 4.29 mmol) was reduced in an H cell at a platinum net electrode in 30 mL of an argon deaerated 0.1 M solution of tetrabutylammonium tetrafluoroborate in *N,N*-dimethylformamide.[20] A graphite electrode was used as anode. The potential was fixed at 0 V vs. Ag/AgI, 0.1 M I in DMF, and the temperature of the cell kept at ambient temperature (22 °C) by means of a water bath. After the consumption of 837 C (calculated 831 C, *n* = 2) the current stopped and the catholyte solution was poured into 1000 mL water and extracted with 250 mL ether. The ether phase was washed twice with 100 mL water and finally dried over anhydrous magnesium sulfate. Filtration and subsequent evaporation of the ether yielded 0.75 g (88%) of tetramethyl 1,4-dichloro-2,3-dithiabutane-1,1,4,4-tetracarboxylate (**11a**), m.p. 72.0−72.5 °C (vide supra).

When **2b** (1.00 g, 3.85 mmol) was reduced as above the yield of **11b** was 0.80 g (81%), m.p. 52.5−53.0 °C (ref.[13] m.p. 51.5−52.0 °C). Current consumption 749 C, calculated for a 2-electron process 742 C.

d) With Sodium Trithiocarbonate: A general procedure was followed.[21] Sodium trithiocarbonate[21] (1.50 g, 10 mmol) was dissolved in 10 mL water and **2** (10 mmol), dissolved in 20 mL dichloromethane, was added, with stirring, at 0 °C. When the red color of the aqueous phase had disappeared the organic layer was separated, washed with water, and dried overnight over anhydrous calcium chloride and charcoal. The products were isolated by evaporation in vacuo and subsequent column chromatography. We obtained **10a**, m.p. 165.0−166.5 °C (ref.[13] m.p. 164.5−165.5 °C) (from **2a**, yield 86%), **10b** (from **2b**, yield 71%), and **9e** (from **2e**, yield 56%).

Chlorination of 11: Sulfuryl chloride (1.00 mL, 10 mmol) was added dropwise to a stirred solution of **11** (10 mmol) in 30 mL tetrachloromethane. When TLC showed that the reaction was complete (3 h) the reaction solvents were evaporated in vacuo and the residue column chromatographed. We thus obtained **2a** (from **11a**, yield 93%), **2b** (from **11b**,[13] yield 89%), as well as (in the order of elution) **2e** and **14e** (from **11e**, yields 29% and 69%, respectively).

***N,N′*-Di-*tert*-butyl-2,2-dichloropropanediamide (14e):** Colorless crystals, m.p. 98.0−99.0 °C. IR: $\tilde{\nu}$ = 3310 (NH), 2983 (aliph. CH), 1690 (C=O), 1521, 1455, 1363, 1265, 1217, 943, 868, 836, 597 cm^{-1}. ^1H NMR: δ = 1.40 (s, 18 H, 6 CH_3), 6.9 (br. s, 2 H, 2 NH) ppm. ^{13}C NMR: δ = 28.0 (6 CH_3), 52.8 (C_t), 80.8 (C-2), 161.9 (2 C=O) ppm. MS (CI): *m*/*z* (%) = 283 (100) [M + H^+]. $C_{11}H_{20}Cl_2N_2O_2$ (283.20): calcd. C 46.65, H 7.12, N 9.89; found C 46.08, H 7.26, N 9.86.

Chlorination of 9: Sulfuryl chloride (2.00 mL, 20 mmol) was added dropwise to a stirred solution of **9** (10 mmol) in 30 mL tetrachloromethane at room temperature. The mixture was stirred until TLC showed that the reaction was complete (3 h). After evaporation in vacuo the residue was column chromatographed. The following products (in the order of elution) were obtained: from **9a**: **2a** (1.10 g, 47%) and dimethyl 2,2-bis(chlorothio)propanedioate (**15a**)[22] (1.30 g, 49%); from **9e**: **2e** (0.80 g, 26%) and **14e** (1.60 g, 57%).

Reaction of 2 with Sulfur: Compound **2** (10 mmol) and elemental sulfur (0.32 g, 10 mmol) were fused together at 190 °C under a reflux condenser until TLC showed that the reaction was complete (6 h), then evaporated to dryness and the residue column chromatographed. The following products (in the order of elution) were obtained: from **2a**: **9a** (0.35 g, 20%), **11a** (0.30 g, 15%) and **12a** (1.10 g, 52%); from **2b**: **11b**[13] (1.70 g, 76%); from **2e**: **9e** (0.70 g, 27%), **11e** (1.10 g, 39%) and **14e** (0.70 g, 25%).

Reaction of 5ab with Morpholine: Compound **5ab** (6.70 g, 20 mmol) was dissolved in 50 mL diethyl ether, cooled in an ice bath, and treated, with stirring, with morpholine (10.4 mL, 120 mmol), dissolved in 25 mL diethyl ether. The rate of the addition was adjusted so as to prevent any appreciable rise in the temperature of the reaction mixture. The reaction mixture was extracted three times with water, the organic phase dried over anhydrous calcium chloride, filtered, and the solvents evaporated in vacuo. The remaining crude product was column chromatographed. The following products (in

the order of elution) were obtained: tetramethyl 1,2,4-trithiolane-3,3,5,5-tetracarboxylate (**9a**) (0.50 g, 28%), tetramethyl 1,2,4,5-tetrathiane-3,3,6,6-tetracarboxylate (**10a**) (0.50 g, 26%), tetramethyl 1,4-dichloro-2,3-dithiabutane-1,1,4,4-tetracarboxylate (**11a**) (0.65 g, 33%).

X-ray Crystal Structure Determination of 11a: Data were collected at 296 K on a SMART diffractometer using Mo-K_α radiation. The crystal-to-detector distance was 4.5 cm. The structures were solved by direct methods (SHELXTL) and refined with a full-matrix least-squares technique. All hydrogen atoms were at calculated positions using a riding model with C−H = 0.96−0.97 and fixed thermal parameters [U(H) = 1.2 times U for attached CM; see Table 2 for the crystallographic data].

CCDC-183065 (**11a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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