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Synthesis of Stable Sulfines by Oxidation of Chlorodithioformates

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Summary. The oxidation of chlorodithioformates with *m*-chloroperoxybenzoic acid in dichloromethane at room temperature provides an efficient stereoselective synthesis of (*Z*)-sulfines. The expected (*Z*)-configuration was confirmed by an X-ray structure determination. The sulfines are reactive dienophiles and react with 2,3-dimethyl-1,3-butadiene to give the corresponding dihydrothiopyran-*S*-oxide.

Keywords. Sulfines; Chlorodithioformates; Oxidation; 1,3-Dienes; Dihydrothiopyran-*S*-oxides.

Introduction

Sulfines (thiocarbonyl-*S*-oxides) **1** constitute an interesting class of tetracoordinate sulfur containing cumulative double bonds. Their chemistry has developed rapidly during the past twenty years [1–9]. Sulfines undergo a multitude of interesting and synthetically useful reactions such as cycloadditions, rearrangements, and nucleophilic additions at carbon or sulfur atoms [9, 10]. In this context, chlorodithioformates **4** represent a special class of thiocarbonyl compounds and we have over the years developed a specific interest in these type of sulfur containing molecules [11–13]. The corresponding sulfines of **4** have been rather neglected and rarely appeared in literature despite their interesting non-linear heterocumulene structure and various practical applications. These compounds bear a leaving group at the sulfine carbon atom and are expected to be prone to nucleophilic displacement reactions with various reagents, with either retention or inversion of configuration at the sulfine moiety [14]. On the basis of this observation nucleophilic displacement reactions with sulfine carrying a good leaving group at the sulfine carbon atom would provide a potential method for the preparation of a variety of sulfines from substrates that already contain the sulfine unit. With the aim of further

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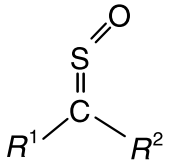
developing chlorodithioformates **4** as tools for organic synthesis, we became interested in the oxidation of **4** by *m*-chloroperoxybenzoic acid (*m-CPBA*). Another intriguing point to be addressed is the relative dienophilicity of the $>C{=}S$ double bonds of **4** and the corresponding sulfines **5** toward [4 + 2] cycloaddition reactions. The present work also quantifies the steric demands of the R^1S group of **4** and the competition for the diastereomerization in the resulting sulfines. In addition, we examined the intramolecular selective oxidation of the starting chlorodithioformates **4**, which contain two oxidizable sulfur atoms and extra functional groups such as *e.g.* the C=C double bond in chlorodithioformate **4c**.



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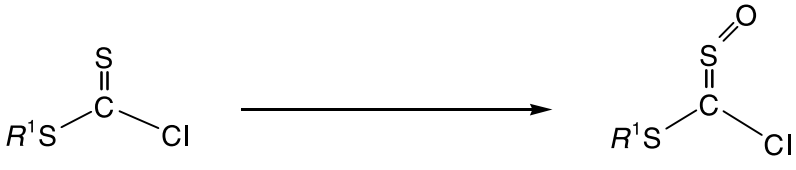
Results and Discussion

The starting chlorodithioformates **4a**–**4c** were prepared from the corresponding thiophenol **2** and thiophosgene **3** in chloroform in the presence of NaOH [15].

Oxidation of chlorodithioformates **4a**–**4c** with one equivalent of *m-CPBA* was achieved in dichloromethane at 0°C. The orange color of **4** changed to light yellow after 15 minutes and **4** quantitatively afforded the corresponding sulfines **5** (Scheme 1). To our delight, NMR spectra of the crude materials showed that the oxidation of the thiocarbonyl group was stereoselective and predominantly a single isomer was formed. No evidence for the oxidation of the other sulfur atom of **4** or the C=C double bond of **4c** was detected. It should be noted that the sulfines **5** are stable under aqueous conditions and this is in sharp contrast to other reported sulfines containing strong electron withdrawing substituents (*e.g.* SO_2R and Cl), which readily hydrolyse into the corresponding methylene compounds [16]. Consequently sulfines containing strong electron withdrawing substituents can not be prepared using the procedure described above, which



4a $R^1 = C_6Cl_5$
4b $R^1 = 2,4,5\text{-}Cl_3C_6H_2$
4c $R^1 = (C_6H_5)_2C{=}C(C_6H_5)$

5a $R^1 = C_6Cl_5$
5b $R^1 = 2,4,5\text{-}Cl_3C_6H_2$
5c $R^1 = (C_6H_5)_2C{=}C(C_6H_5)$

Scheme 1

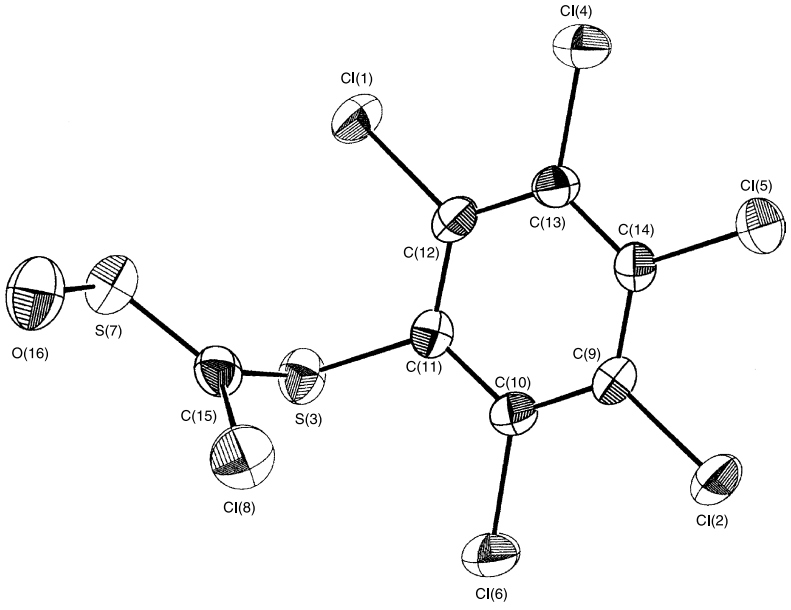


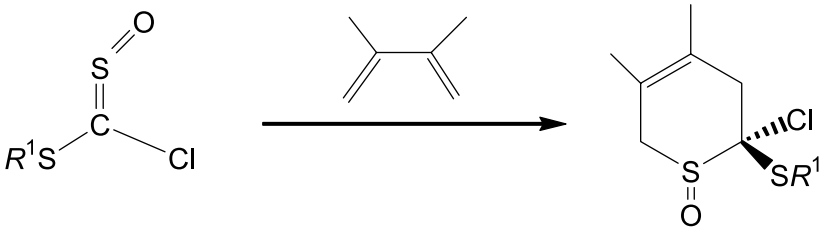
Fig. 1. The molecular structure of sulfine **5a** with 50% probability ellipsoids

involves an aqueous work up. Sulfines **5** can also be kept without deterioration for months at ambient temperature, and can be purified by column chromatography on silica gel or by recrystallization.

The crude sulfines **5** were analyzed by NMR. The quaternary ($>C{=}S{=}O$) carbon of the sulfines **5** resonates at 171.22 ppm for **5a**, 171.27 ppm for **5b**, and 173.69 ppm for **5c** in ^{13}C NMR, upfield from the corresponding ($>C{=}S$) group of the starting chlorodithioformates **4** (189.60 ppm for **4a**, 191.80 ppm for **4b**, and 193.72 ppm for **4c**). Furthermore, the strong IR absorptions at 1155 and 1035 cm^{-1} for **5a**, at 1150 and 1033 cm^{-1} for **5b**, and at 1145 and 1023 cm^{-1} for **5c** can be attributed to the ($>C{=}S{=}O$) group. Both ^{13}C NMR and IR spectra compared well with that reported for other sulfines [9].

An X-ray crystallographic analysis (Fig. 1) unambiguously confirmed the (*Z*)-geometry and the non-linearity of the $>C{=}S{=}O$ system of **5a**. The length of the $>C{=}S$ and $S{=}O$ bonds were found to be 1.63 and 1.46 Å, while the $>C{=}S{=}O$ angle was found to be 114.14°. The sulfine exhibits a non-planar arrangement with the oxygen atom located *trans* to the pentachlorophenylthio group. The dihedral angle between the planes of the sulfine group and the pentachlorophenylthio group is 99.42°, demonstrating a non-planar arrangement around the C(15)–S(3) bond. The sulfine moiety π-plane and the pentachlorophenylthio group are arranged perpendicular to each other, where the bulky pentachlorophenylthio group hinders the sulfine moiety to adopt a position in the same plane as the pentachlorophenythio moiety.

The (*Z*)-stereochemistry of the oxidation product is noteworthy. It is thermodynamically preferred and this preference has seldom been reported. In order to rationalize the observed selectivities we performed B3LYP/6-31G(d) calculations with the Jaguar program [17]. The results agreed well with the experiments. The energy difference between the (*Z*)- and (*E*)-isomers of **5a** is 3.3 kJ/mol at the B3LYP/6-31G(d) level favoring the (*Z*)-isomer. Absence of (*Z*)/(*E*)-isomerization



5a $R^1 = C_6Cl_5$ **6** $R^1 = C_6Cl_5$

Scheme 2

of **5a** was observed when subjected to thermolysis in toluene at 110°C. Interestingly, and to the best of our knowledge, this is the first confirmation of the configuration of a sulfine derived from **4**.

Despite the presence of a chlorine atom at the sulfine carbon atom, **5a** was sluggish in the reaction with 1,3-butadiene derivatives. This is probably due to the retarding effect exerted by the bulky pentachlorophenyl group. The hetero-*Diels-Alder* reaction between **5a** and 2,3-dimethyl-1,3-butadiene was carried out at room temperature in chloroform for 3 days, forming dihydrothiopyran-*S*-oxides **6** in only 50% yield (Scheme 2). Fortunately, by performing the reaction at 70°C the cycloaddition was completed in 4 h (96% isolated yield). The NMR and TLC analysis showed that a single diastereomer had been obtained. This implies that during the cycloaddition the initial stereochemistry present in the sulfine (*Z*) is retained in the adduct (*i.e.* the chlorine atom and sulfoxide oxygen are *cis* to each other).

It should be noted that while the hetero-*Diels-Alder* reactions of **5** with 1,3-diene derivatives gave the corresponding dihydrothiopyran-*S*-oxides, the reaction with **4** leads to the labile 2*H*-3,6-dihydrothiopyrans, which spontaneously eliminate hydrogen chloride to form the 2*H*-thiopyrans [13]. It may be suggested that the variable chemical behavior of **4** and their *S*-oxides **5** in [4 + 2] cycloaddition reactions is due to disruption of the aromatic character in the 2*H*-3,6-dihydrothiopyran product.

It may be concluded from the results described in this paper that the thiocarbonyl group in chlorodithioformates **4** is oxidised selectively, and neither sulfur nor the C=C double bonds reacted. The study also revealed the different reactivity of **4** and **5** as dienophiles in [4 + 2] cycloaddition reactions. The cycloaddition of sulfines with dienes proceeds stereospecifically to yield dihydrothiopyran-*S*-oxides, therefore these sulfines are interesting substrates in asymmetric cycloaddition reactions and the results presented here clearly stimulate further research of asymmetric reactions with sulfines.

Experimental

All ^{1}H and ^{13}C NMR experiments ($CDCl_3$) were carried out with a Varian Unity 400 MHz spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C). Chemical shifts are reported in ppm relative to *TMS* using appropriate solvent signals as internal standard. Mass spectra analyses were performed with Kratos 50 tc spectrometer, and melting points were recorded on a Büchi melting point apparatus. TLC was

done on Merck Kieselgel F_{254} precoated plates (Merck), the microanalysis was performed in the microanalysis lab. at Cairo University; these results agreed favourably with the calculated values. Single crystals suitable for X-ray studies from sulfine **5a** were grown in a mixture of CH_2Cl_2 and *n*-hexane (1/3), intensity data were measured at room temperature on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated Mo Kα radiation, wavelength: 0.71073 Å, cell measurement temperature: 298 K, crystal color: light yellow, crystal shape: prismatic, crystal system: triclinic, unit cell parameters: $a = 6.1559$ (3) Å, $b = 7.6979$ (4) Å, $c = 13.7443$ (7) Å, $\alpha = 100.678$ (3)°, $\beta = 98.165$ (3)°, $\gamma = 102.730$ (3)°, space group *P-1*, cell volume: 612.84 (5) Å^3, R_{all}: 0.029, cell formula units *Z*: 2, absorption coefficient: 0.65 mm^{-1}, *F*(000): 266. X-ray data were deposited at the Cambridge Crystallographic Data Center under No. CCDC 224948, copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code +44-1223-336033, E-mail: deposit@ccdc.cam.ac.uk]. Chlorodithioformates **4** were prepared according to literature procedures [15].

Chloro(pentachlorophenylthio) sulfine (**5a**, $C_7Cl_6OS_2$)

To a stirred solution of 300 mg of **4a** (0.83 mmol) in 10 cm^3 of CH_2Cl_2 at 0°C, 179 mg of *m*-chloroperoxybenzoic acid (1.04 mmol, 80%) dissolved in 5 cm^3 of CH_2Cl_2 were added within 10 min. After 15 min the orange color changed to light yellow, the solution was washed successively with saturated aqueous $NaHCO_3$ (3×10 cm^3) and saturated brine (30 cm^3). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure to leave **5a** as a single isomer. Recrystallisation from CH_2Cl_2/*n*-hexane (1/3) furnished pale yellow crystals (288 mg, 92%), mp 140–143°C; IR (KBr): $\bar{\nu} = 1155$, 1035 ($\nu_{C=S=O}$) cm^{-1}; ^{13}C NMR ($CDCl_3$): $\delta = 126.85$, 133.15, 137.52, 139.10, 171.22 (>*C*=*S*=*O*) ppm; MS: m/z (%) = 374 (7, M^+).

Chloro(2,4,5-trichlorophenylthio) sulfine (**5b**, $C_7H_2Cl_4OS_2$)

The procedure as given for **5a** was followed starting from 200 mg of **4b** (0.68 mmol) and 147 mg of *m-CPBA* (0.85 mmol, 80%). The sulfine was purified by crystallization from CH_2Cl_2/*n*-hexane (1/3) to give pale yellow crystals (190 mg, 90%), mp 99–102°C; IR (KBr): $\bar{\nu} = 1150$, 1033 cm^{-1} ($\nu_{C=S=O}$), ^{1}H NMR ($CDCl_3$): $\delta = 7.47$ (s, 1H), 7.57 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 129.18$, 131.53, 131.62, 132.39, 134.03, 137.47, 171.27 (>*C*=*S*=*O*) ppm; MS: m/z (%) = 306 (16, M^+).

Chloro(1,2,2-triphenylethenylthio) sulfine (**5c**, $C_{21}H_{15}ClOS_2$)

The procedure given for **5a** was followed with 300 mg of **4c** (0.82 mmol) and 147 mg of *m-CPBA* (0.85 mmol, 80%). After usual work-up, the corresponding sulfine was formed as a yellow solid. Further crystallization from CH_2Cl_2/*n*-hexane (1/3) afford analytically pure yellow crystals of **5c**. Yield 279 mg (89%), mp 177–179°C; IR (KBr): $\bar{\nu} = 1145$, 1023 cm^{-1} ($\nu_{C=S=O}$); ^{1}H NMR ($CDCl_3$): $\delta = 6.95$–7.45 (m, 15H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 127.60$, 127.83, 128.16, 128.36, 128.52, 129.99, 130.36, 130.74, 136.52, 140.06, 141.51, 149.92, 173.78 (>*C*=*S*=*O*) ppm; MS: m/z (%) = 382 (28, M^+).

3,6-Dihydro-4,5-dimethyl-2-(chloro)-2-(pentachlorophenylthio)-2H-thiopyran-S-oxide (**6**, $C_{13}H_{10}Cl_6OS_2$)

To a solution of 200 mg of **5a** (0.66 mmol) in 5 cm^3 of $CHCl_3$ was added an excess of 2,3-dimethyl-1,3-butadiene (3 cm^3). After stirring for 4 h at 80°C the volatiles were evaporated *in vacuo* and crude **6** was crystallized from CH_2Cl_2/*n*-hexane (1/3) giving analytically pure **6** as colorless crystals (293 mg,

96%); mp 168–170°C; IR (KBr): $\bar{\nu} = 1073$ ($\nu_{S=O}$) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 1.75$ (s, 3H), 1.77 (s, 3H), 2.84 and 3:54 (AB_q, $J = 17.60$ Hz, 2H), 3.37 and 4.06 (AB_q, $J = 17.18$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 19.15$, 20.11, 40.92, 52.85, 89.24, 118.10, 124.98, 129.67, 132.51, 137.10, 141.44, MS: m/z (%) = 456 (4, M^+).

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