Synthesis of *O*-Alkyl Carbonochloridothioates

Manuel A. Martínez

Departamento de Química, Facultad de Química, Universidad de Santiago de Chile, Casilla 5659, Santiago, Chile

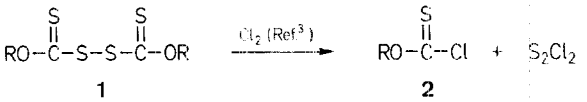
Juan C. Vega*

Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 6177, Santiago, Chile

The preparation of *O*-alkyl carbonochloridothioates (**2**) was improved by performing the reaction of thiophosgene with potassium alkoxides in the corresponding alcohol or in tetrahydrofuran at −65 °C for 1 hour. In all cases, the reaction yielded products **2**, *O,O*-dialkyl carbonothioates (**4**), and dialkyl carbonates (**5**) in varying distribution.

In our studies on the chemistry of thiocarbonates and derivatives we needed *O*-alkyl carbonochloridothioates (**2**), to be used as alkoxythiocarbonylating agents, since these allow, in principle, mild reaction conditions; moreover, the chloride leaving group shows less reactivity than leaving groups of other alkoxythiocarbonylating agents[1].

O-Alkyl carbonochloridothioates (**2**) have been prepared in low yields either by reaction of sodium alkoxides with thiophosgene[2], or by chlorolysis of bis[alkoxythiocarbonyl] disulfide[3] (**1**) according to the following formal equation[4].



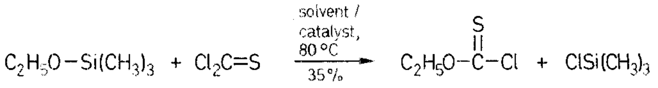
$$RO-\overset{\overset{S}{\|}}{C}-S-S-\overset{\overset{S}{\|}}{C}-OR \xrightarrow{Cl_2\ (Ref^3)} RO-\overset{\overset{S}{\|}}{C}-Cl + S_2Cl_2$$

1 **2**

According to our experience, this method is unsuitable. In fact, in the case of bis[ethoxycarbonyl] disulfide (**1**, R = C_2H_5), *O*-ethyl carbonochloridothioate (**2**, R = C_2H_5) was obtained in lower yields than published[3], and when pure reagents are required, the products are difficult to purify by fractional distillation[4,5]. On the other hand, *O*-aryl carbonochloridothioates have been obtained more readily by reaction of phenols with thiophosgene in alkaline media[6-9].

A promising alternative for the synthesis of compounds **2** should be the reaction of alkoxytrimethylsilanes with thiophosgene, since it would not require basic media; further, it would yield chlorotrimethylsilane which would easily be eliminated because of its volatility. Nevertheless, this alternative requires cleavage of the strong Si-O bond.

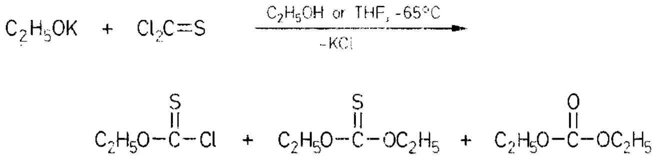
When the reaction of ethoxytrimethylsilane (**3**) with thiophosgene was performed under nitrogen at 80 °C, *O*-ethyl carbonochloridothioate (**2a**) was obtained in yields not higher than 35 %, in spite of the fact that several solvents (benzene, dioxan, tetrahydrofuran) and catalyst (hydrochloric acid, *p*-toluenesulfonic acid, Amberlite IRC-50, aluminium chloride, boron trifluoride) were used.



$$C_2H_5O-Si(CH_3)_3 + Cl_2C{=}S \xrightarrow[35\%]{\text{solvent / catalyst, } 80\,°C} C_2H_5O-\overset{\overset{S}{\|}}{C}-Cl + ClSi(CH_3)_3$$

3 **2a**

In view of these results, we reinvestigated the reaction of thiophosgene with equimolecular amounts of alkalimetal ethoxides[10]. In all cases, the reaction yielded compound **2a**, *O,O*-diethyl carbonothioate (**4a**), and diethyl carbonate (**5a**), which are identified by GLC, IR, and ^{1}H-NMR.

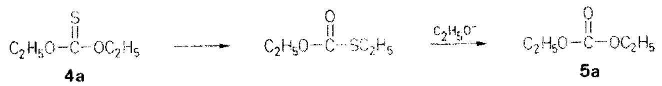


$$C_2H_5OK + Cl_2C{=}S \xrightarrow[-KCl]{C_2H_5OH \text{ or } THF,\ -65\,°C} C_2H_5O-\overset{\overset{S}{\|}}{C}-Cl + C_2H_5O-\overset{\overset{S}{\|}}{C}-OC_2H_5 + C_2H_5O-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

2a (81 or 50%) **4a** **5a**

In these experiments, thiophosgene was dissolved in chloroform or carbon tetrachloride, and the ethoxide of lithium, sodium, or potassium were used in ethanol or tetrahydrofuran. Thiophosgene was added to the ethoxide or the ethoxide to thiophosgene, at temperatures between −60° and 15 °C. The results show that the formation of **2a** is favored when potassium ethoxide is added to thiophosgene. A temperature of −60 °C and a reaction time not longer than 1 h increase the percentage of **2a** in the product. It could be observed that the yields of **4a** and **5a** increase at the expense of **2a**, the favored formation of which depends on particular conditions.

The presence of **5a** in the product can be explained by a thione-thiol rearrangement of **4a** due to the nucleophilicity of the C=S group, followed by substitution. This assumption is supported by the fact that treatment of **4a** with equimolecular amounts of potassium ethoxide in ethanol/carbon tetrachloride at −60 °C results in a gradually increasing percentage of **5a** (according to GLC analysis) at the expense of **4a**.



$$C_2H_5O-\overset{\overset{S}{\|}}{C}-OC_2H_5 \longrightarrow C_2H_5O-\overset{\overset{O}{\|}}{C}-SC_2H_5 \xrightarrow{C_2H_5O^-} C_2H_5O-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

4a **5a**

Under the conditions described in Ref. 2 there is a higher ethoxide concentration during the reaction which favors the conversion of **2a** into **4a** and **5a**.

On the basis of these results, other *O*-alkyl carbonochloridothioates **2** were prepared by adding a solution of the potassium alkoxide in the corresponding alcohol or in tetrahydrofuran (after elimination of excess alcohol) dropwise to a solution of thiophosgene in tetrahydrofuran at −65 °C. Temperatures below −65 °C are not recommended because of solubility problems. Preparation of the alkoxide and elimination of excess alcohol must be carried out under nitrogen. Washing the crude reaction product with water leaves compounds **2** pure enough for use as synthetic reagents.

Table. *O*-Alkyl Carbonochloridothioates (**2**) Prepared

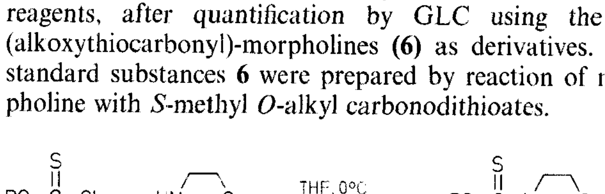
2	R	Yield[a] [%]		b.p. [°C]/torr		n_D (°C)	IR (KBr) $\nu_{C=S}$ [cm^{-1}]	^{1}H-NMR (CDCl$_3$) δ [ppm]
		in Alcohol	in THF	found	reported			
a	C_2H_5	81	50	46/33	52-5/40[3b]	1.4879 (18)	1270	4.60 (c, 2H)
b	n-C_3H_7	91	90	42/12	40-2/12[3b]	1.4885 (20)	1260	4.54 (t, 2H)
c	i-C_3H_7		88	34/10	35/4[4]		1280	5.56 (m, H)
d	n-C_4H_9	85	78	62/12	62/12[3b]	1.4815 (19)	1260	4.37 (t, 2H)
e[b]	i-C_4H_9	89	70	54/10		1.4776 (20)	1278	4.40 (d, 2H)

[a] Determined by conversion of the crude reaction product **2** into the 4-alkoxythiocarbonylmorpholine **6** and GLC analysis of an aliquot of the solution of **6**.

[b] The microanalyses were in good agreement with the calculated values: C +0.15, H −0.12.

The advantage of using tetrahydrofuran as solvent for alkoxide preparation is that most of it can be eliminated from the reaction mixtures by washing with water, whereas the solvent alcohols cannot be washed out with water and can thus contaminate the product.

Since the *O*-alkyl carbonochloridothioates **2** are thermally unstable and the reaction mixtures generate foam, compounds **2** are difficult to purify by distillation (at reduced pressure) in order to separate them from mixtures (~10%) of carbonothioates and carbonates which are present in all cases. For this reason, it is preferable to use products **2** directly; according to our experience, the mentioned impurities do not effect their behaviour in further reactions[11,12], whereas heating and long distillation times transform the carbonochloridothioates **2**. Once obtained and dried with magnesium sulfate, the carbonochloridothioates **2** can either be distilled, with 25–40% loss in yield, or used directly as reagents, after quantification by GLC using the *N*-(alkoxythiocarbonyl)-morpholines (**6**) as derivatives. The standard substances **6** were prepared by reaction of morpholine with *S*-methyl *O*-alkyl carbonodithioates.



O-Isopropyl carbonochloridothioate (**2c**) is unstable. On standing at room temperature for one day it decomposes to carbon oxide sulfide and 2-chloropropane (according to ^{1}H-NMR).

Careful study of the reaction of thiophosgene with potassium butoxide by GLC analysis showed that in addition to *O*-butyl carbonochloridothioate (**2d**), *O,O*-dibutyl carbonothioate (**4d**) and dibutyl carbonate (**5d**) are formed in relative amounts of 20% and 2%, respectively. Compound **4d** has hitherto not been described; its microanalysis (C, +0.28; H, −0.40) and its spectral properties were in accordance with its structure.

O-Alkyl Carbonochloridothioates (2a–e); General Procedure:

Potassium (3.9 g, 0.1 g-atom) is added in small pieces to the respective alcohol (50 ml) with stirring at 25°C under nitrogen. The resultant alkoxide solution can be directly used; otherwise, the excess of alcohol is eliminated under nitrogen in a rotatory evaporator and the residue dissolved in anhydrous tetrahydrofuran (20 ml). In a 3-neck flask are placed freshly distilled thiophosgene (11.5 g, 0.1 mol) and anhydrous tetrahydrofuran (20 ml). Under stirring, the flask is submerged into a cold bath at −65°C (dry ice in chloroform/butanol 2:1). Then, the solution of the alkoxide in alcohol or tetrahydrofuran is added dropwise over 60 min. Then, the mixture is immediately washed with distilled water (2 × 100 ml) at room temperature. The organic layer is dried with magnesium sulfate and the remaining solvent is distilled off at 30–36°C/180 torr. The crude, light-colored liquid product **2** is thus obtained; it can be used directly in further reactions.

If a purer product **2** is desired, the crude product **2** is distilled in a pear-shaped flask provided with a Vigreux column (20 cm long and 1 cm internal diameter) at 10–30 torr, with magnetic stirring, under nitrogen. Under these conditions, the froth that impairs the distillation is reduced.

Analysis of Compounds **2** after Conversion into *4-Alkoxythiocarbonylmorpholines* (**6**): After the solution of the crude product **2** has been washed with water, dried, and evaporated tetrahydrofuran is added to a total volume of 50 ml. To an aliquot (5 ml) of this solution, morpholine (2 ml) is slowly added and the mixture is stirred for 5 min. Then, 5% hydrochloric acid (20 ml) is quickly added and the mixture is extracted with chloroform (3 × 15 ml). The organic extract is dried with magnesium sulfate, filtered, and brought to a volume of 50 ml with chloroform. The analysis is performed with a Perkin Elmer 900 chromatograph equipped with a flame-ionization detector and a 1 m × 1/8 inch stainless-steel column filled with 5% SE-30 on Chromosorb W at 180°C. It is compared with a standard solution of the respective compound **6** of known concentration.

It should be noted that the reaction of stoichiometric amounts of morpholine and *O,O*-dibutyl carbonothioate in tetrahydrofuran at room temperature did not give 4-butoxythiocarbonylmorpholine after 3 h (according to GLC analysis).

The financial assistance of Dirección de Investigación de la Universidad Católica de Chile (DIUC), through project 17/83 is gratefully acknowledged.

Received: April 23, 1985
(Revised form: October 28, 1985)

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