Synthesis of Symmetrical and Unsymmetrical *O,O*-Dialkyl Imidodicarbonothioates

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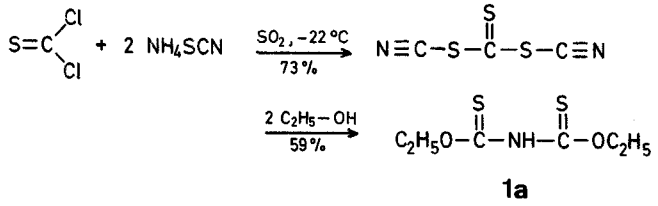
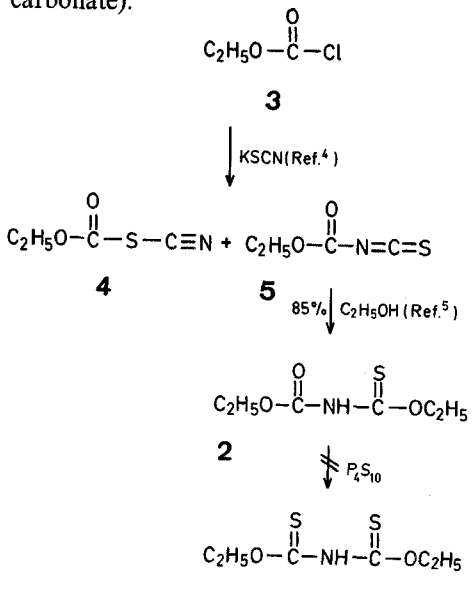
Symmetrical and unsymmetrical (with respect to the alkyl groups) *O,O*-dialkyl esters of imidodicarbonothioic acid are prepared by reaction of *O*-alkyl carbonochloridothioates with sodium thiocyanate and treatment of the resultant alkoxythiocarbonyl isothiocyanates with alcohols.

In connection with our interest in thiocarbamic acid derivatives we studied the synthesis of symmetrical and unsymmetrical imidodicarbonothioic *O*-esters (**1**; bis[alkoxythiocarbonyl]-imides, imino-bis-thiocarboxylic *O*-esters). The synthesis of some imidodicarbonothioic *O*-esters from thiophosgene, ammonium thiocyanate, and alcohols has been described[1], *O,O*-diethyl imidodicarbonothioate (**1a**) thus being obtained in 43% yield.



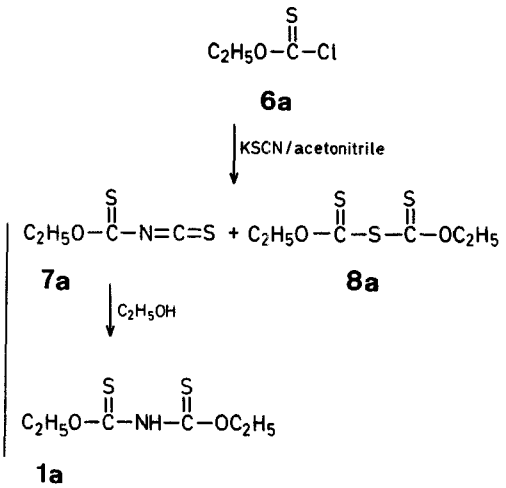
1a

We first attempted to use the known and synthetically useful[2,3] *O,O*-diethyl monothioimidodicarbonate (**2**) [obtained from ethyl carbonochloridate (**3**) via ethoxycarbonyl isothiocyanate (**5**, formed together with the isomeric thiocyanate **4**[4])] as starting material for the preparation of diester **1a**. However, with compound **2** the known *O/S* exchange reaction with phosphorus(V) sulfide[6] led only to a complex product mixture, independent of the conditions used (solvents: dioxan, pyridine, benzene, toluene, acetonitrile; catalysts: sodium sulfide, sodium carbonate, sodium hydrogen carbonate).



1a

An alternative access to diester **1a** might consist of the reaction of *O*-ethyl carbonochloridothioate[7] (**6a**) with potassium thiocyanate and treatment of ethoxythiocarbonyl isothiocyanate (**7a**) thus formed with ethanol. The reactivity of educt **6a**, which is greater than that of its oxygen analog **3**[8], should contribute to the formation of isothiocyanate **7a** at the expense of the corresponding thiocyanate (*cf.* formation of **4** + **5**) when **6a** is submitted to the reaction with the ambident nucleophile thiocyanate anion. However, we found that *O*-ethyl carbonochloridothioate (**6a**) reacts with potassium thiocyanate in acetonitrile to give the expected ethoxythiocarbonyl isothiocyanate (**7a**) together with *O,O*-diethyl trithiodicarbonate (**8a**) in only 3.4 and 4.5% yields (according to G.L.C. analysis), respectively. Product **7a** was characterized by conversion into **1a** with ethanol (product **1a** was compared with an authentic sample prepared according to Ref.[1]) and by its I.R. absorption[2,8] at $\nu = 1960\,cm^{-1}$.



1a

O,O-Diethyl trithiodicarbonate (**8a**) has also been detected in the products of other reactions of compound **6a**[9]. In the present procedure, it can be detected from the beginning of the reaction; it may be assumed to be produced from initially formed ethoxythiocarbonyl thiocyanate.

In order to optimize the conditions for the formation of isothiocyanate **7a** (and thereby of product **1a**) and to inhibit the formation of **8a**, we studied the effects of different solvents and catalysts on the reaction of *O*-ethyl carbonochloridothioate (**6a**) with potassium thiocyanate at room temperature, followed by addition of ethanol to the crude product mixture. With four different solvents, the following results were obtained:

Variation of Solvent:

Solvent	Yields [%] as determined by GLC analysis of the final solution	
	1a	**8a**
acetonitrile	1	9
acetone	1	3
dichlormethane	1	0
ethyl acetate	1	0
tetrachloromethane	2	0

On the basis of these results, the efficiencies of benzyltriethylammonium chloride, tetrabutylammonium bromide, and tributylhexadecylphosphonium bromide as possible solid/liquid phase-transfer catalysts in our reaction were tested in di- and tetrachloromethane; improvements could thereby not be achieved. Significantly better results were obtained when the reaction of *O*-ethyl carbonochloridothioate (**6a**) with finely powdered thiocyanates in tetrachlorometh-

Table. *O,O*-Dialkyl Imidodicarbonothioates (**1**) prepared

1	R^1	R^2	Yield[a] [%]	m.p.[b] [°C]	Molecular Formula[c]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
a	C_2H_5	C_2H_5	67	102–103°	$C_6H_{11}NO_2S_2$ (193.2)	3200, 1500, 1270, 1030, 920	1.45 (t, 3H, J = 7.2 Hz); 4.61 (q, 2H, J = 7.2 Hz); ~9.3 (br. s, NH)
b	C_2H_5	CH_3	74	52–53°	$C_5H_9NO_2S_2$ (179.2)	3190, 1530, 1280, 1050, 950	4.16 (s, 3H); 4.61 (q, 2H, J = 7.2 Hz); ~9.3 (br. s, NH)
c	C_2H_5	n-C_3H_7	75	44–46°	$C_7H_{13}NO_2S_2$ (207.3)	3200, 1510, 1270, 1030, 950	4.52 (t, 2H, J = 6.4 Hz); 4.61 (q, 2H, J = 7.2 Hz); ~9.4 (br. s, NH)
d	C_2H_5	i-C_3H_7	70	53–54°	$C_7H_{13}NO_2S_2$ (207.3)	3200, 1510, 1270, 1030, 930	4.57 (q, 2H, J = 7.1 Hz); 5.57 (m, 1H); ~9.2 (br. s, NH)
e	C_2H_5	n-C_4H_9	72	41–42°	$C_8H_{15}NO_2S_2$ (221.3)	3200, 1510, 1280, 1060, 940	4.54 (t, 2H, J = 6.2 Hz); 4.59 (q, 2H, J = 7.2 Hz); ~9.3 (br. s, NH)
	n-C_4H_9	C_2H_5	41				
f	C_2H_5	i-C_4H_9	71	27–28°	$C_8H_{15}NO_2S_2$ (221.3)	3200, 1500, 1270, 1050, 940	4.31 (d, 2H, J = 6.4 Hz); 4.61 (q, 2H, J = 7.1 Hz); ~9.4 (br. s, NH)
	i-C_4H_9	C_2H_5	45				
g	C_2H_5	c-C_6H_{11}	73	65–67°	$C_{10}H_{17}NO_2S_2$ (247.3)	3190, 1500, 1270, 1030, 940	4.59 (q, 2H, J = 7.2 Hz); 5.44 (m, 1H); ~9.3 (br. s, NH)
h	C_2H_5	C_6H_5—CH_2	48	75–76°	$C_{11}H_{13}NO_2S_2$ (255.3)	3190, 1510, 1270, 1030, 950	4.54 (q, 2H, J = 7.2 Hz); 5.58 (s, 2H); ~9.4 (br. s, NH)
i	i-C_4H_9	i-C_3H_7	85	51–52°	$C_9H_{17}NO_2S_2$ (235.2)	3200, 1500, 1270, 1030, 960	4.31 (d, 2H, J = 6.6 Hz); 5.60 (m, 1H); ~9.4 (br. s, NH)

[a] Isolated product. Calculated on **6**.
[b] Uncorrected.
[c] Satisfactory microanalyses obtained: C ± 0.18, H ± 0.11; N ± 0.14, S ± 0.23.

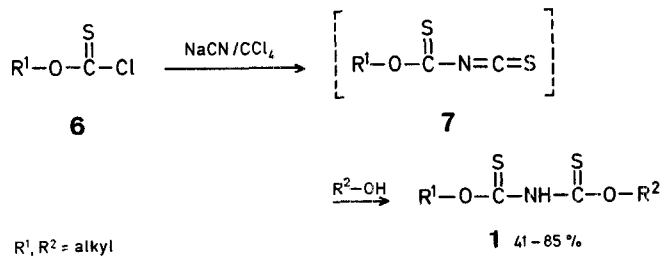
ane was performed in the presence of certain amines as catalysts at room temperature for 4 h, followed by treatment with ethanol. Under these conditions, the undesired product **8a** was not obtained and the yields of **1a** were satisfactory in most cases:

Variation of Thiocyanates and Effect of Amines as Catalysts

Thiocyanates	Amines	Yield [%] of **1a** as determined by G.L.C. analysis
sodium thiocyanate	imidazole	4
	nicotine	45
	pyridine	64
	4-methylpyridine	75
	3-methylpyridine	79
potassium thiocyanate	3-methylpyridine	64
ammonium thiocyanate	3-methylpyridine	40

It should be mentioned that some alkoxythiocarbonyl isothiocyanates have recently been prepared in 13–52% yields (isolated product) by the same method using pyridine as catalyst[10].

The best conditions for the synthesis of compound **1a** found (**6a** + NaSCN + 3-methylpyridine in tetrachloromethane) were applied to the preparation of other symmetrical and unsymmetrical (with regard to the alkyl groups) *O,O*-dialkyl imidodicarbonothioates **1**. The addition of the respective alcohols to the alkoxythiocarbonyl isothiocyanates **7** was performed without previous isolation of compounds **7** from the reaction mixtures of their preparation. In all cases, the I.R. spectra of these mixtures showed no absorption of the corresponding thiocyanate isomers. Because of the acidic character of compounds **1**, extraction with 5% sodium hydroxide was used for their purification. The fact that the same unsymmetric product **1** (e.g. **1e, 1f**) can be prepared from two different *O*-alkyl carbonochloridothioates (**6**) allows one to choose the easier accessible compound **6** as starting material.



O,O-Dialkyl Imidodicarbonothioates (1); General Procedure:
A mixture of powdered dry sodium thiocyanate (0.65 g, 8 mmol), tetrachloromethane (4 ml), the *O*-alkyl carbonochloridothioate (**6**; 4 mmol), and 3-methylpyridine (1 drop) is vigorously stirred for 4 h at room temperature under a nitrogen atmosphere. An excess of the respective anhydrous alcohol (5 ml) is added and the mixture is heated at reflux temperature for 1 h under nitrogen. The mixture is then shaken with water (10 ml) and extracted with chloroform (4 × 4 ml). The product **1** is extracted from the chloroform solution with 5% sodium hydroxide solution (10 ml), and then is precipitated by the addition of 5% hydrochloric acid. The suspension is extracted with chloroform (4 × 4 ml), the solvent evaporated, and the residue crystallized from ethanol or ethanol/water.

Conditions of G.L.C. Analysis of Compounds 1a and 8a:
The crude product, obtained from the reaction of educt **6a** with a thiocyanate in different solvents and further reaction with ethanol, is extracted with chloroform (6 ml). The extract is diluted to a volume of 10 ml with chloroform and this solution is analyzed by G.L.C.: Perkin-Elmer 900 instrument equipped with a flame-ionization detector and 1 m × 1/8 in stainless-steel column filled with 5% SE-30 on Chromosorb W at 140°C. Concentrations are determined by comparison with standard solutions of **1a**[1] and **8a**[11].

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