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CONVENIENT ROUTE TO THIOCARBONATES FROM ALCOHOLS, THIOLS, AND TRIPHOSGENE

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An efficient and simple one-pot, three-component procedure has been introduced for the preparation of various thiocarbonates from thiols, alcohols, and triphosgene in dichloromethane.

Keywords: Alcohols; thiocarbonates; thiols; triphosgene

INTRODUCTION

Thiocarbonates have been used as protecting group for thiols,[1] synthetic intermediates in the preparation of other valuable substances,[2,3] heat stabilizers for polymers,[4] polymerization inhibitors,[5] bioactive compounds,[6] radiographic contrast agents,[7] precursors to polymercaptanes,[8] and as biological toxicants, particularly as mematocides.[9] The usual syntheses of thiocarbonates involve reactions of primary and benzyl alcohols with carbon dioxide, methanesulfonic anhydride, and thiols under basic conditions,[10] the treatment of thiols and disulfides with chloroformates,[7b] the reaction of β-nitroalcohols and 2,2,2-trihaloethanols with ethyl chlorothiolformate,[11] nucleophilic addition of potassium monothiocarbonates to epoxides or alkyl halides,[12] the rearrangement of diaryl thiocarbonates,[13] the reaction of aryloxide salts, carbonyl sulfide, and alkyl halides,[14] the reaction of trimethylsilyl enol ethers with phenyl thiofluoroformate in the presence of a naked fluoride ion catalyst,[15] selenium-catalyzed reaction of alcohols, carbon monoxide, sulfur, and alkyl halides,[16] and sulfur-assisted *O*-carbonylation of alcohols with carbon monoxide in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[17] However, most of the reported procedures suffer from serious drawbacks such as the use of poisonous phosgene and carbonyl sulfide, difficult-to-obtain reagents, poor yields, the use of moisture-sensitive chlorothioformate, preparation of certain thiocarbonate derivatives, and multistep procedures. Very recently, Nishiyama and coworkers[18] introduced a novel selenium-catalyzed reaction of alcohols with carbon monoxide and diaryl disulfides for synthesis of *S*-aryl-*O*-alkyl thiocarbonates.

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RESULTS AND DISCUSSION

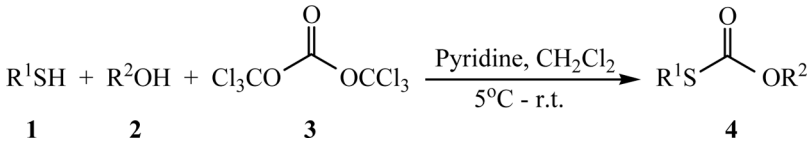
Bis(trichloromethyl)carbonate (BTC, triphosgene) is a phosgene substitute that combines the high reactivity of phosgene with the safety of a stable crystalline solid. The use of BTC as a synthetic auxiliary in the preparation of many important classes of organic compounds has been investigated in the past two decades.[19]

We report herein a simple method for the synthesis of various thiocarbonates via a one-pot multicomponent reaction (MCR) of alcohols/phenol and thiols with triphosgene in dry dichloromethane (Scheme 1).

In a typical general experimental procedure, a solution of thiols **1**, alcohols or phenol **2**, and pyridine in dry dichloromethane was cooled to 5 °C. This was followed by addition of triphosgene **3** to the solution at that temperature, which gave, after workup, the desired thiocarbonates **4**. We found that the reactants were converted readily to the corresponding thiocarbonate, with no other by-product, with a molar ratio of thiol/alcohol/triphosgene of 1:1:1. The structures of the products were confirmed from physical and spectroscopic [infrared (IR), ^{1}H and ^{13}C NMR] data.

A series of thiols and various alcohols (methyl, primary, secondary, tertiary, benzylic, and phenol) were reacted with triphosgene. The results summarized in Table 1 show that the reaction is amenable to the synthesis of various thiocarbonates. The reaction of aromatic thiols with methyl-, ethyl-, and benzyl alcohol are in general fast (10–30 min) and clean, and thiocarbonates are obtained as the sole product in good to excellent yields. In the case of secondary alcohols (entries 10 and 11, Table 1), longer reaction times are required, giving the products with lower yields. *S*-Phenyl-*O*-*tert*-butyl thiocarbonate was not obtained on the reaction of *tert*-butyl alcohol (entry 12, Table 1). In the case of phenol, the reaction proceeded efficiently, giving the corresponding *S*-aryl-*O*-phenyl thiocarbonate in good yields (entries 13 and 14, Table 1). Under the same reaction conditions, an experiment was also conducted with thiophenol, benzyl alcohol, and triphosgene in a molar ratio of 1:1:0.3; after 4 h, the isolated yield of the product was 27%. We assume that *S*,*S*-diaryl (dialkyl) dithiocarbonates are initially formed by nucleophilic attack of 2 equivalents of thiols to triphosgene at low temperature, followed by nucleophilic attack of an equivalent of alcohol or phenol to the dithiocarbonates at room temperature to afford the final product, thiocarbonates.

In summary, this method provides an efficient one-pot, three-component approach for the synthesis of various thiocarbonates. This reaction is versatile and also offers several advantages, such as good yields, shorter reaction times, and simple experimental and workup procedures.



Scheme 1.

Table 1. One-pot synthesis of thiocarbonates

Entry	R^1	R^2	Product	Time (min)	Yield (%)[a,b]
1	Ph	Et	PhSCOOEt	15	94[18]
2	4-ClC_6H_4	Et	4-$ClC_6H_4SCOOEt$	15	98[18]
3	4-MeC_6H_4	Et	4-$MeC_6H_4SCOOEt$	10	90[18]
4	4-$MeOC_6H_4$	Et	4-$MeOC_6H_4SCOOEt$	30	87[18]
5	4-BrC_6H_4	Et	4-$BrC_6H_4SCOOEt$	15	96[18]
6	Ph	$PhCH_2$	$PhSCOOCH_2Ph$	10	80[7b]
7	4-ClC_6H_4	$PhCH_2$	4-$ClC_6H_4SCOOCH_2Ph$	10	86[7b]
8	$PhCH_2$	$PhCH_2$	$PhCH_2SCOOCH_2Ph$	45	60[7b]
9	Ph	Me	PhSCOOMe	10	80[18]
10	Ph	Me_2CH	$PhSCOOCHMe_2$	50	46[18]
11	Ph	Ph_2CH	$PhSCOOCHPh_2$	120	18[7b]
12	Ph	Me_3C	$PhSCOOCMe_3$	60	Trace
13	Ph	Ph	PhSCOOPh	10	72[7b]
14	4-ClC_6H_4	Ph	4-$ClC_6H_4SCOOPh$	10	60[7b]

[a]Yields refer to those of pure isolated products characterized by IR, ^1H NMR, and ^{13}C NMR spectroscopy.
[b]References for known compounds.

EXPERIMENTAL

Chemicals were purchased from Merck and Aldrich chemical companies. Yields refer to isolated products. Melting points were determined by a Büchi B-540 apparatus. IR spectra were run on an ABB FTLA 2000 instrument. The ^1H NMR (300-MHz) and ^{13}C NMR (75-MHz) spectra were recorded on a Bruker AQS-300 Avance NMR spectrometer. The progress of the reaction was followed by thin-layer chromatography (TLC) using silica-gel SILG/UV 254 plates. Products were characterized by comparing their physical and spectral data with the authentic samples.[7b,18]

General Experimental Procedure

A stirred solution of thiol (1.0 mmol), alcohol/phenol (1.0 mmol), and pyridine (4.0 mmol) in dry CH_2Cl_2 (25 mL) was cooled to 5 °C, and triphosgene (1.0 mmol) was added in one portion. Then, the solution was allowed to stir for the appropriate time (Table 1) at room temperature (25 °C). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with water (2×20 mL); the combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by preparative TLC (silica gel, eluent, *n*-hexane/EtOAc = 15:1).

SUPPLEMENTARY DATA

O-Ethyl-*S*-(4-methylphenyl)thiocarbonate (T1-3)[18]

Colorless oil; IR (neat): $\nu_{max} = 1137, 1728\ cm^{-1}$; ^1H NMR ($CDCl_3$): $\delta = 1.35$ (t, $J = 7.2$ Hz, 3H), 2.41 (s, 3H), 4.33 (t, $J = 7.2$ Hz, 2H), 7.24 (d, $J = 8.3$ Hz, 2H), 7.46

(d, $J = 8.3$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.3$, 21.3, 63.9, 124.4, 130.0, 134.9, 139.8, 169.9 ppm.

O-Ethyl-*S*-(4-bromophenyl)thiocarbonate (T1-5)[18]

Colorless oil; IR (neat): $\nu_{max} = 1142$, 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.32$ (t, $J = 7.0$ Hz, 3H), 4.29 (q, $J = 7.0$ Hz, 2H), 7.38 (d, $J = 8.5$ Hz, 2H), 7.52 (d, $J = 8.5$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.3$, 64.3, 124.2, 127.0, 132.3, 136.2, 168.9 ppm.

O-Benzyl-*S*-(4-chlorophenyl)thiocarbonate (T1-7)[7b]

Colorless oil; IR (neat): $\nu_{max} = 1717$ cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 5.29$ (s, 2H), 7.37–7.42 (m, 7H), 7.49 (d, $J = 8.7$ Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 69.7$, 126.2, 128.6, 128.70, 128.73, 129.5, 129.7, 134.9, 136.1, 136.4, 169.2 ppm.

O-Methyl-*S*-phenyl Thiocarbonate (T1-9)[18]

Colorless oil; IR (neat): $\nu_{max} = 1726$ cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.89$ (s, 3H), 7.46–7.48 (m, 3H), 7.58–7.60 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 54.9$, 128.1, 129.7, 130.1, 135.3, 170.7 ppm.

O-(1,1-Diphenyl)methyl-*S*-phenyl Thiocarbonate (T1-11)[7b]

Colorless oil; IR (neat): $\nu_{max} = 1138$, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 5.47$ (s, 1H), 7.31–7.59 (m, 15H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 80.4$, 127.5, 127.7, 127.9, 128.8, 129.7, 130.6, 135.7, 142.6, 188.8 ppm.

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