Pergamon

Tetrahedron Letters 43 (2002) 3439–3441

TETRAHEDRON LETTERS

Efficient conversion of thiols to thiocyanates by in situ generated $Ph_3P(SCN)_2$†

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Received 5 December 2001; revised 18 February 2002; accepted 28 February 2002

Abstract—A new, novel, rapid and simple method is described for the one-pot conversion of thiols to thiocyanates by use of in situ generated $PPh_3(SCN)_2$ at room temperature.

Thiocyanates are considered as important and valuable sulfur-containing compounds for the synthesis of heterocycles and have traditionally been used as pesticides.[1,2] They are generally prepared via nucleophilic displacement of leaving groups by thiocyanate ion on a carbon atom preferably in the presence of phase transfer agents.[3–7]

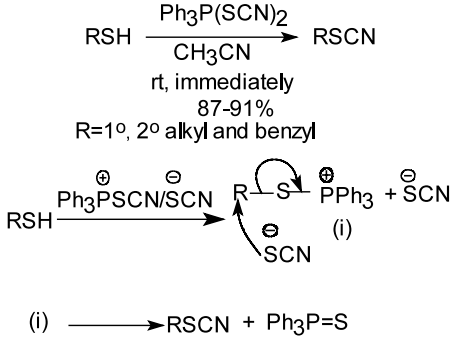
Mixed reagent systems of tertiary phosphines/halogens or tertiary phosphines/halogenated compounds have been widely used for the transformation of alcohols and also thiols to alkyl halides.[8–17] Due to the importance of the conversion of thiols to other functionalities, very recently we reported on the application of mixtures of Ph_3P and *N*-chloro-, *N*-bromo- and *N*-iodosuccinimide for the efficient conversion of thiols to different alkyl halides.[18]

In continuation of our work on the use of in situ generated $Ph_3P(SCN)_2$ for the preparation of thiocyanates from alcohols,[19] we wish to report on the use of this reagent for the efficient conversion of primary and secondary alkyl and benzyl thiols to their corresponding thiocyanates at room temperature (Scheme 1).

$Ph_3P(SCN)_2$ can be easily produced in situ from the reaction of Ph_3P, bromine and ammonium thiocyanate.[19] This compound has already been shown to be in equilibrium with Ph_3P^+SCN/SCN^-.[7b]

In order to optimize the reaction conditions, we first examined the effect of different ratios of triphenylphosphine/bromine/ammonium thiocyanate on the conversion of benzyl thiol to benzyl thiocyanate.

Similar to the reaction of benzyl alcohol, benzyl thiol reacted with $PPh_3(SCN)_2$ immediately at room temperature to give benzyl thiocyanate. In addition to benzyl thiocyanate, dibenzyl disulfide was formed as a side product in 20% yield when we used an equimolar ratio of 1/1/1/2 of benzyl thiol/Ph_3P/Br_2/NH_4SCN (entry 1, Table 1). In order to avoid the intermolecular coupling of thiols to disulfides by the electrophilic species[20] that are present in the reaction mixture, we decided to increase the stoichiometry of Ph_3P with respect to bromine. As shown in Table 1, when the stoichiometry of PPh_3 and ammonium thiocyanate are slightly more than that of bromine, the oxidation of thiol to disulfide is minimized and benzyl thiocyanate is obtained in excellent yield (entries 6 and 7, Table 1).



Scheme 1.

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† This paper is dedicated to our mentor Professor Ali Massoumi on the occasion of his 70th birthday.

0040-4039/02/$ - see front matter
PII: S0040-4039(02)00421-5

Table 1. Optimization of the ratio of benzyl thiol/Ph_3P/Br_2/NH_4SCN for preparation of benzyl thiocyanate at room temperature

$$PhCH_2SH \rightarrow \underset{A}{PhCH_2SCN} + \underset{B}{PhCH_2SSCH_2Ph}$$

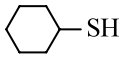
Entry	Sub/Ph_3P/Br_2/NH_4SCN ratio	GC Yield (%)[a]	
		A	B
1	1/1/1/2	75	20
2	1/1.1/1/2	86	12
3	1/1.2/1/2	91	9
4	1/1.2/1/2.2	95	5
5	1/1.2/1/2.3	96	4
6	1/1.3/1/2.5	100	0
7	1/1.5/1/3	100	0

[a] The reaction was completed immediately. Yields are based on GC analysis using *n*-heptane as internal standard.

We therefore used the stoichiometric ratio of thiol/Ph_3P/Br_2/NH_4SCN (1/1.3/1/2.5) for the conversion of thiols to their corresponding alkyl thiocyanates. The results are shown in Table 2. The results obtained show that this reagent is suitable for the immediate conversion of primary, secondary and benzyl thiols to their corresponding alkyl thiocyanates in excellent yields at room temperature.

Primary thiols produced exclusively the corresponding thiocyanates, but secondary thiols gave small amounts of isothiocyanates as side products (Table 1, entries 1–5). On treatment of 1-cyclohexanethiol with this reagent, 1-cyclohexyl thiocyanate was formed as the major product (96%) together with the formation of 1-cyclohexyl isothiocyanate (6%, Table 2, entry 6). The formation of thiocyanates or isothiocyanates can be easily detected in the reaction mixture by the characteristic ^{13}C absorption band of the -SCN and -NCS groups at $\sim$111 and $\sim$145 ppm, respectively.[22]

Table 2. One-pot conversion of thiols to thiocyanates with $Ph_3P(SCN)_2$ at room temperature

Entry	RSH	Yield (%)[a]	Percentage of the product[b]	
			RSCN	RNCS
1	$PhCH_2SH$	90	100	0
2	$CH_3(CH_2)_{11}SH$	91	100	0
3	$CH_3(CH_2)_7SH$	87	100	0
4	$CH_3(CH_2)_3SH$	89	100	0
5	$CH_3CH(SH)CH_3$	90	96	4
6		87	94	6

[a] Isolated yield. The products were identified by comparison of their physical data with those reported for known samples[6b,7b,22]

[b] The percentage of the products in the reaction mixture was determined by ^1H and ^{13}C NMR[22]

In order to observe the effect of temperature on the ratio of thiocyanate and isothiocyanate obtained from secondary thiols, we isolated the crude reaction mixture obtained from the reaction of 1-cyclohexanethiol with $Ph_3P(SCN)_2$ at 25°C. We then heated this mixture to 60°C for 15 min. Analysis of the mixture obtained did not show any change in the percentage of the products (RSCN, RNCS) in the reaction mixture. Thus, it can be concluded that isothiocyanates are not formed by the isomerization of the thiocyanates to isothiocyanates and their formation is due to the ambident nature of the NCS^- nucleophile. This result is in agreement with the reported data in the literature.[7b,21]

In summary, this method is the first report of the direct conversion of thiols into thiocyanates at room temperature. The use of in situ generated $PPh_3(SCN)_2$ provides the possibility of performing this transformation under very mild reaction conditions with excellent yield. The procedure is simple, rapid and the work up is clean and not time-consuming.

Experimental

The products were purified by column chromatography and the purity determinations of the products were accomplished by GLC on a Shimadzu model GC-10A instrument or by TLC on silica-gel polygram SIL G/UV 254 plates. Mass spectra were run on a Shimadzu GC MS-QP 1000EX at 75 eV. IR spectra were recorded on a Perkin–Elmer 781 spectrophotometer. The NMR spectra were recorded on a Bruker Avance DPX 250 MHz instrument.

General procedure for the synthesis of 1 and 2° thiocyanates from thiols

A three-necked flask equipped with a dropping funnel, stirrer, $CaCl_2$ drying tube and N_2 gas inlet was charged with Ph_3P (2.6 mmol) and dry CH_3CN (5 mL), then Br_2 (2.0 mmol) was added dropwise to the solution at room temperature under N_2 atmosphere. When the addition was complete, a solution of NH_4SCN (5.0 mmol) in CH_3CN (5 mL) was added dropwise. Upon addition of thiols (2.0 mmol) to the resulting mixture, spontaneous reactions occurred. To the resulting mixture, silica gel was added and the solvent was evaporated on a rotary evaporator. The resulting solid was applied on a silica gel column and washed with petroleum ether 60–80°C/EtOAc (9/1) to give the desired thiocyanate (Table 2).

Acknowledgements

The authors are grateful to Shiraz University Research Council for the partial support of this work.

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