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Reaction of Thiolates with Carbon Monoxide

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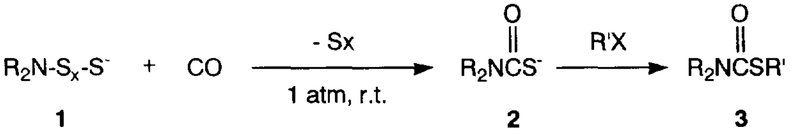
Abstract : Thiolates generated from elemental sulfur with amines or lithium amides, easily reacted with carbon monoxide to form thiocarbamates in good yields. Furthermore, the reaction of diaminodisulfide with carbon monoxide in the presence of DBU proceeded similarly to give thiocarbamates.

Elemental sulfur is readily subject to fission of S-S bond by the reaction with nucleophiles such as an ammonia or phosphines to form thiolates **1**. The formation of **1** from elemental sulfur by nucleophilic attack of primary or secondary amines is also well known.[1,2] Indeed, piperidinethiols prepared from piperidines with elemental sulfur were isolated.[6] However, reactivities of **1** for carbon monoxide have been entirely unexplored. Therefore, we now wish to report novel reaction of **1** with carbon monoxide under the mild conditions (1 atm, r.t.) to convert the corresponding thiocarbamates **2** efficiently (Eq. 1).



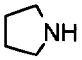
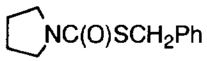
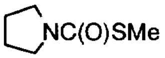
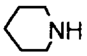
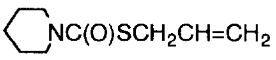
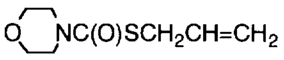
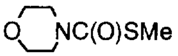
$$\underset{\mathbf{1}}{R_2N\text{-}S_x\text{-}S^-} \quad + \quad CO \xrightarrow[\text{1 atm, r.t.}]{\text{- Sx}} \underset{\mathbf{2}}{R_2N\overset{\overset{O}{\|}}{C}S^-} \xrightarrow{R'X} \underset{\mathbf{3}}{R_2N\overset{\overset{O}{\|}}{C}SR'} \qquad (1)$$

The reaction of thiolates **1** with carbon monoxide was examined according to the two methods.

Method A : Into a benzene solution (20 mL) containing amine (22 mmol) was added elemental sulfur (0.32 g, 10 mmol), and the solution was refluxed for 4 h with stirring to generate thiolate **1**, as described in the literature.[6a] Then, the resulting solution of **1** was cooled and was vigorously stirred under carbon monoxide (1 atm) for 20 h at 20 °C. Quenching the reaction mixture by alkyl halide (25 mmol) afforded the corresponding *S*-alkyl thiocarbamate **3** after purification using short-column chromatography.

Method B : To a THF solution (20 mL) of primary or secondary amine (10 mmol) was added slowly 10 %w/v hexane solution of butyl lithium (6.4 mL, 10 mmol) at -78 °C, and the solution was gradually warmed to -20 °C with stirring. Then, the resulting solution of lithium amide was cooled to -78 °C and elemental sulfur (0.32 g, 10 mmol) was added to form lithium thiolate **1**. This solution of **1** was gradually warmed up to 20 °C and the carbonylation was subsequently performed at 20 °C with carbon monoxide (1 atm) for 2 h followed by alkylation with alkyl halide (12 mmol) to give the corresponding **3**.

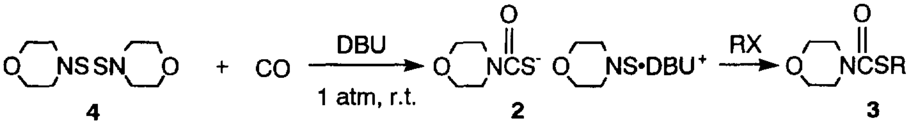
Table 1. Synthesis of *S*-Alkyl Thiocarbamates **3**

amine	alkyl halide	method	product **3**	yield, %[a]
	$PhCH_2Br$	A		80
	MeI	A		77
	$CH_2{=}CHCH_2Br$	A		56
	$CH_2{=}CHCH_2Br$	A		0
	MeI	B		39
Et_2NH	$PhCH_2Br$	B	$Et_2NC(O)SCH_2Ph$	65
	$CH_2{=}CHCH_2Br$	B	$Et_2NC(O)SCH_2CH{=}CH_2$	53
Pr_2NH	$CH_2{=}CHCH_2Br$	A	$Pr_2NC(O)SCH_2CH{=}CH_2$	0
	$CH_2{=}CHCH_2Br$	B	$Pr_2NC(O)SCH_2CH{=}CH_2$	45
	MeI	B	$Pr_2NC(O)SMe$	77
i-Pr_2NH	$CH_2{=}CHCH_2Br$	B	i-$Pr_2NC(O)SCH_2CH{=}CH_2$	57
PhMeNH	MeI	B	PhMeNC(O)SMe	0
$PhCH_2NH_2$	MeI	B	$PhCH_2NHC(O)SMe$	0

a) Isolated yields based on elemental sulfur used. Products were identified by IR, ^{1}H-NMR, MS, and exact MS spectra.

The results are summarized in Table 1. Thiolates **1** starting from pyrrolidine or piperidine were smoothly reacted with carbon monoxide to give the corresponding *S*-alkyl thiocarbamates **3** in good yields (method A).[7] But, reaction of **1** from other amines with carbon monoxide did not occur using method A. Therefore, to promote the formation of **1**, lithium amides derived from the reaction of amines with butyl lithium were used (method B). In these cases, lithium thiolates **1** prepared from lithium amides and elemental sulfur, generally reacted with carbon monoxide to give the corresponding *S*-alkyl thiocarbamates **3** in reasonable yields. However, use of aromatic or primary amines did not proceed under the similar conditions.

Furthermore, the carbonylation of diaminodisulfide **4** with carbon monoxide was also performed to examine the similar reactivity as thiolates **1**. Dimorpholinedisulfide **4** easily reacted with carbon monoxide in the presence of DBU[9] to form the thiocarbamate **2** under the ordinary pressure at 20 °C. The alkylation of **2** gave *S*-alkyl thiocarbamates **3** in good yields (Eq. 2).

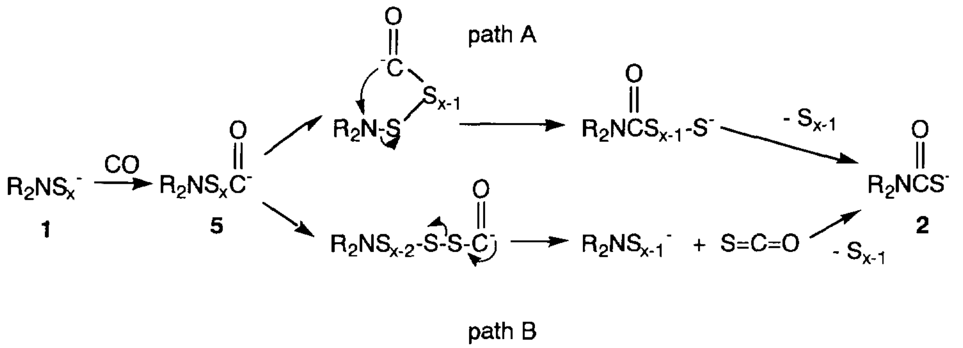


(2)

RX : $CH_2=CHCH_2Br$, 64%
$PhCH_2Br$, 56%

The following scheme shows a plausible pathway for conversion of thiolates **1** into thiocarbamates **2** under the mild conditions (Scheme 1). The nucleophilic attack of an amine to elemental sulfur gives the thiolate **1** which reacts with carbon monoxide to form the carbonylated species **5**. Through an intramolecular rearrangement of **5** (path A) or elimination of carbonyl sulfide from **5** (path B), the thiocarbamate **2** was generated.

Scheme 1



In summary, thiolates **1** from the reaction of elemental sulfur with amines or lithium amides, reacted with carbon monoxide under the ordinary pressure at 20 °C to form thiocarbamates **2** in good yields. Also, the reaction of diaminodisulfide **4** with carbon monoxide brought about efficient formation of **2** in a similar manner. This facile conversion of **1** into **2** may suggest the reaction pathway of sulfur-assisted carbonylation of amines with carbon monoxide.

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References and Notes

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2. The carbonylation of amines with carbon monoxide assisted by elemental sulfur to form urea derivatives was reported.[3-5] In these cases, thiolates **1** were postulated to generate *in situ* as the intermediates.
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7. Because of high basicities of pyrrolidine and piperidine, the correponding thiolates **1** might be generated efficiently (pyrrolidine : pKb = 2.9, piperidine : pKb = 2.8, morpholine : pKb = 5.6).[8]
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9. DBU was suitable for this reaction as a base. Et_3N and K_2CO_3 were ineffective, and BuLi gave complex miture of products.

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