### A General, Facile, and Safe Procedure for the Preparation of S-Methyl N-Alkylthiocarbamates by Methylthiocarbonylation of Primary Aliphatic Amines with S,S-Dimethyl Dithiocarbonate

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**Abstract:** A general procedure is reported for the selective preparation of *S*-methyl *N*-alkylthiocarbamates by methylthiocarbonylation of primary aliphatic amines, employing *S*,*S*-dimethyl dithiocarbonate as a phosgene substitute. The reactions are carried out in water at room temperature (20–25 °C), with *S*,*S*-dimethyl dithiocarbonate/amine ratios varying between 1:1.2 and 1:2, and with quantitative recovery of the excess amine. The target products are obtained in exceptionally high yields (generally >95%) and with very high purity (generally >99.5%). Also to be noted is the complete chemoselectivity of the reactions, which can be carried out in the presence of hydroxy or aminophenyl groups.

Key words: thiocarbamates, thiocarbonylation, dithiocarbonates, amines, chemoselectivity

S-Alkyl N-alkylthiocarbamates constitute an important class of compounds that are of notable interest in various fields of 'fine chemicals'.<sup>2-7</sup> Indeed, such compounds are widely used as agrochemicals (fungicides, bactericides, nematocides, and, above all, herbicides), as pharmaceuticals (analgesics, anesthetics, and antivirals), and as intermediates and starting materials in organic synthesis. Given the importance of S-alkyl N-alkylthiocarbamates, various procedures have been proposed for their preparation.<sup>2,3,5-11</sup> Among these, the most widely used procedures, which are also of practical interest for industrial production, employ the following reactions: (1) reaction of primary aliphatic amines with S-alkyl chlorothioformates; (2) reaction of thiols with carbamoyl chlorides in the presence of a base; (3) condensation of thiols with alkyl isocyanates; (4) reaction of alkyl halides with S-alkali or S-ammonium N-alkylthiocarbamates, prepared by the reaction of an amine with alkali and carbonyl sulfide or with carbon monoxide and sulfur in the presence or absence of a base and, in some cases, of a catalyst; (5) intramolecular rearrangements of O-alkyl N-alkylthiocarbamates. Methods 1-3 are closely related, as, in the vast majority of cases, carbamoyl chlorides and isocyanates are obtained by phosgenation of amines, while S-alkyl chlorothioformates are obtained by phosgenation of thiols. The disadvantage common to these three methods is the use of phosgene; it is a highly toxic reagent that is haz-

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DOI: 10.1055/s-2007-965943; Art ID: Z25906SS © Georg Thieme Verlag Stuttgart · New York ardous to handle, especially for large-scale preparations.<sup>12</sup> Hence, while methods 1–3 may circumvent the use of phosgene, overall its use is not avoided. Furthermore, the isocyanates used in method 3 are extremely toxic, particularly those of low molecular weight. Recently,<sup>5,6</sup> the alkylthiocarbonylation of primary aliphatic amines (method 1) was realized with *S*-alkyl trichlorothioacetates, obtained, in turn, by the reaction of thiols with trichloroacetyl chloride. This new procedure has the advantage of avoiding the use of phosgene entirely. Method 4 is the method most widely used for secondary amines, but it is much less frequently used for primary amines.<sup>10</sup> Method 5 has many reported examples, but yields of *S*-alkyl *N*-alkylthiocarbamates are not always good.<sup>11</sup>

The present paper reports a general, facile, and safe procedure for the preparation of *S*-methyl *N*-alkylthiocarbamates **3** using *S*,*S*-dimethyl dithiocarbonate (**1**) as a reagent for the methylthiocarbonylation of primary aliphatic amines **2** (Scheme 1).

MeS		SMe +	RNH <sub>2</sub> 2	H <sub>2</sub> O 20–25 °C	MeS NHR +	MeSH 4
		2,3	R	2,3	R	
		а	Me	g	CH <sub>2</sub> =CHCH <sub>2</sub>	
	b		Et	h	Bn	
		с	Pr	i	HOCH <sub>2</sub> CH <sub>2</sub>	
	d		Bu	j	HOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
	е		<i>i</i> -Bu	k	HOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	
		f	<i>c</i> -Hex	I	$4-H_2NC_6H_4CH_2$	

#### Scheme 1

*S*,*S*-Dimethyl dithiocarbonate (1) is a nontoxic reagent that can be handled and stored in complete safety.<sup>13–15</sup> It can be obtained easily in high yield by rearrangement of the corresponding inexpensive *O*,*S*-dimethyl dithiocarbonate,<sup>16</sup> and it is produced industrially according to this procedure.<sup>17</sup> The following positive features of *S*,*S*-dimethyl dithiocarbonate (1, DMDTC) make it an excellent reagent for use on both a laboratory and an industrial scale: (i) it is a liquid compound (bp 168 °C) and can therefore be measured and handled without difficulty;

(ii) it is a stable compound and it is not evil-smelling; and finally, (iii) under appropriate reaction conditions (e.g. PTC conditions in the presence of KOH) it can be hydrolyzed in situ to give quantitatively methanethiol, which can be used in subsequent reactions, and potassium carbonate as the sole byproduct. In previous work we proposed *S*,*S*-dimethyl dithiocarbonate (1) as the thiomethylating reagent for the preparation of organic sulfides,<sup>18</sup> including triazine derivatives,<sup>20</sup>

Furthermore, S,S-dimethyl dithiocarbonate (1) has already been proposed as a phosgene substitute for the preparation of S-methyl N-alkylthiocarbamates<sup>13,21</sup> and symmetrical and asymmetrical N,N'-dialkylureas<sup>13</sup> starting from aliphatic amines. The most recent work,<sup>13</sup> which was published in 1996, states that reaction of S,S-dimethyl dithiocarbonate (1) (even in excess) and primary aliphatic amines in methanol at 60 °C, cannot be stopped at the S-methyl N-alkylthiocarbamate stage, and that successive reaction of S-methyl N-alkylthiocarbamates to give symmetrical N,N'-dialkylureas, proceeds even more rapidly. To overcome this drawback, and thus stop the reaction at the S-methyl N-alkylthiocarbamate stage, the reaction of an equimolar mixture of S,S-dimethyl dithiocarbonate (1) and primary aliphatic amines was carried out under basic conditions (LDA) and a nitrogen atmosphere, initially at -78 °C and then at room temperature (20 h). Under such conditions the resulting S-methyl Nalkylthiocarbamates were deprotonated immediately on formation to give the corresponding N-anions, which were relatively stable toward nucleophilic substitution and did not react further to give N, N'-dialkylureas. Subsequent treatment of the N-anions with an acid afforded Smethyl *N*-alkylthiocarbamates. Using this procedure only two compounds were prepared: S-methyl N-benzylthiocarbamate (62% yield) and S-methyl N,N'-(p-xylylene)bis(thiocarbamate) (yield not reported). Therefore this work, which has repeatedly been cited in the literature,<sup>14,15,22</sup> asserts that the reaction between *S*,*S*-dimethyl dithiocarbonate (1) and primary aliphatic amines cannot be stopped at the initial stage to give S-methyl N-alkylthiocarbamates. An earlier work,<sup>21</sup> that was patented in 1965 and to our knowledge has never been cited, instead gave the opposite result. In this patent<sup>21</sup> the reaction of an equimolar mixture of S,S-dimethyl dithiocarbonate (1) and a variety of primary aliphatic amines under vacuum (12-100 Torr) in a solvent-free system with continuous removal of methanethiol at 0 °C or 10-15 °C (preferably 0 °C) for from 5–6 hours to 3–4 days gave S-methyl thiocarbamates in high yields. However, the use of a vacuum presents two marked drawbacks: (i) the procedure is not suitable for the methylthiocarbonylation of low-molecular-weight amines  $(C_1-C_3)$ ; (ii) the use of complex equipment is required, so the operative management of the procedure is more difficult. Nevertheless, this work demonstrates that, given the appropriate conditions, the reaction between S.S-dimethyl dithiocarbonate (1) and primary aliphatic amines can be stopped at the S-methyl thiocarbamate stage.

In order to identify suitable conditions for the formation of S-methyl thiocarbamates, we examined the reaction between S,S-dimethyl dithiocarbonate (1) and benzylamine (2h) under various conditions as a trial reaction (Table 1). Initially we followed the literature protocol,<sup>13</sup> i.e. molar ratio 1/2h 1.6:1 or 1:2 in methanol at 60 °C for 24 hours, monitoring the progress of the reaction by GC and GC-MS analyses. For the first set of conditions the literature<sup>13</sup> reports the formation of a mixture of S-methyl N-benzylthiocarbamate (3h) and N, N'-dibenzylurea (6) in a ratio of 1:30 (yield was not reported), and for the second reaction the exclusive formation of 6 in 85% yield. In our hands, the first reaction (entry 1) failed to reach completion (~20% of unreacted benzylamine) and afforded the two products **3h** and **6** in 78% overall yield and ratio of products by weight varied in repeated trial reactions from 1:4.6 to 1:5.1. The second reaction (entry 2) went almost to completion (unreacted 1: 1%) and afforded the urea 6 in 72% maximum yield together with two byproducts, i.e. S-methyl N-benzylthiocarbamate (3h; 7%) and methyl Nbenzylcarbamate (5%). The latter was formed by reaction of the thiocarbamate 3h with methanol. The same reaction was then carried out at a lower temperature, 20-25 °C, for 24 and 48 hours (entries 3 and 4). Both reactions afforded only one product, S-methyl N-benzylthiocarbamate (3h) in modest yields (43% and 51%), but neither went to completion (unreacted 1: 30% and 14%), despite the excess of amine. The merit of these reactions performed in methanol at low temperatures is that they give exclusively the monosubstitution product **3h**; their drawback is that they are extremely slow and provide **3h** in only modest yields. However, when the reaction was carried out in water with an equimolar ratio 1/2h at temperatures ranging from room temperature (20-25 °C) to 80 °C and for prolonged reaction times to 24 hours (entries 5, 7-11) and up to 48 hours (entry 6), the results demonstrated that the possibility of stopping the reaction at the monosubstitution depends upon the temperature. Indeed, the reaction leads exclusively to S-methyl N-benzylthiocarbamate (3h) in 70% yield when it was performed at 20–25 °C (entry 5); **3h** was also formed exclusively in 84% yield when the reaction time was prolonged to 48 hours (entry 6). When the reaction was performed at 30 °C (entry 7) or at higher temperatures (entries 8-11) both the thiocarbamate 3h and N,N'-dibenzylurea (6) were formed, the latter prevailing at higher temperatures (entries 10, 11).

Scheme 2 shows a possible pathway for the reaction between *S*,*S*-dimethyl dithiocarbonate (1) and benzylamine (2h). It can be hypothesized that the replacement of the first methylthio group occurs on *S*,*S*-dimethyl dithiocarbonate (1) with a tetrahedral mechanism, which gives rise to the selective formation of the monosubstitution product, i.e. *S*-methyl *N*-benzylthiocarbamate (3h). The replacement of the second methylthio group could then proceed on 3h by an elimination–addition mechanism, i.e. elimination of methanethiol from 3h with formation of benzyl isocyanate (5), which immediately undergoes addition of benzylamine (2h) to give *N*,*N*'-dibenzylurea (6). When the reaction was performed at 20–25 °C, nucleo-



#### Scheme 2

philic substitution on *S*,*S*-dimethyl dithiocarbonate (1) took place exclusively (Table 1, entries 5, 6). At 30 °C or higher, subsequent substitution on the thiocarbamate **3h** (entries 7–11) became possible, and this reaction prevailed at temperatures higher than 50 °C (entries 10, 11). On the basis of well-consolidated knowledge,<sup>14,15,23</sup> the formation of *N*,*N'*-dibenzylurea (6) by nucleophilic substitution with a tetrahedral mechanism on the thiocarbamate **3h** can be excluded. This interpretation, based on the results in Table 1, entries 1–11, clarifies the apparent contradictions that appear in the literature<sup>13,21</sup> related to the possibility of stopping the reaction between *S*,*S*-dimethyl

dithiocarbonate (1) and primary aliphatic amines 2 at the monosubstitution stage.

After this preliminary examination, the conditions for the synthesis of *S*-methyl *N*-benzylthiocarbamate (**3h**) were optimized (Table 1, entries 12–14). Use of an excess of benzylamine (**2h**) in water at 20–25 °C for a shortened reaction time gave **3h** in almost quantitative yield (Table 1, entry 12 compare with entries 5 and 6). It is noteworthy that the excess **2h** can be quantitatively recovered at the end of the reaction.

Using reaction conditions similar to those for Table 1, entry 12, *S*,*S*-dimethyl dithiocarbonate (1) was reacted with

Entry	Molar ratio	Solvent	Temp (°C)	Time (h)	GC ratio	Yield <sup>a</sup> (%	<b>b</b> )	Unreacted <sup>b</sup> 1 (%)
	1/2				3h/6	3h	6	
1	1.6:1	MeOH	60	24	1:4.6 <sup>c</sup>	10	68	
2	1:2	MeOH	60	24	1:11	7 <sup>d</sup>	72 <sup>d</sup>	1
3	1:2	MeOH	20–25	24		43	-	30
4	1:2	MeOH	20–25	48		51	_	14
5	1:1	$H_2O$	20–25	24		70	-	8
6	1:1	$H_2O$	20–25	48		84	-	5
7	1:1	$H_2O$	30	24	1:0.05	77	6	6
8	1:1	$H_2O$	40	24	1:0.26	65	26	8
9	1:1	$H_2O$	50	24	1:0.64	49	47	9
10	1:1	$H_2O$	60	24	1:1.30	33	65	14
11	1:1	$H_2O$	80	24	1:6.06	10	90	36
12	1:1.5	$H_2O$	20–25	17		98 <sup>e</sup>	-	_
13	1:2	H <sub>2</sub> O	20–25	15		98 <sup>e</sup>	-	_
14	1.5:1	$H_2O$	20–25	24		80	-	

 Table 1
 Trial Reactions between S,S-Dimethyl Dithiocarbonate (1) and Benzylamine (2h)

<sup>a</sup> Unless otherwise noted yields refer to pure products isolated by column chromatography (elution of **3h**: petroleum ether– $Et_2O$ , 7:3; elution of **6**:  $Et_2O$ –MeOH, 1:1). Yields reported in entries 1 and 14 are based on **2h**, while those in entries 2–13 are based on **1**.

<sup>b</sup> Determined by GC analysis on completion of the reaction.

<sup>c</sup> In repeated trial reactions the GC ratios varied from 1:4.6 to 1:5.1 and the unreacted benzylamine (2h) was ~20%.

<sup>d</sup> Methyl *N*-benzylcarbamate was also isolated in 5% yield. Colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 3.67 (s, 3 H, CH<sub>3</sub>), 4.37 (d, *J* = 5.2 Hz, 2 H, CH<sub>2</sub>), 5.04 (m, 1 H, NH), 7.23–7.40 (m, 5 H, C<sub>6</sub>H<sub>5</sub>).

<sup>e</sup> Purity of the crude product was 99.7% (determined by GC analysis).

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a variety of primary aliphatic amines **2a–g,i–l** (Table 2). The best conditions were as follows: amine 2 in an aqueous solution (concentrations varying between 40 and 70%) was added very slowly with stirring to S,S-dimethyl dithiocarbonate (1); the temperature of the mixture was maintained at 20-25 °C with an ice-water bath. The only exception was the reaction with 2-aminoethanol (entry 16), which was performed in a solvent-free system at 0 °C to limit the cyclization of the formed S-methyl N-(2-hydroxyethyl)thiocarbamate (3i) to oxazolidin-2-one; the latter was the sole product when the reaction was performed under the usual conditions, i.e. in water at 20-25 °C (entry 15). When the amine was not water soluble, it was added neat to a suspension of S,S-dimethyl dithiocarbonate (1) in water. The molar ratio 1/2 varied from 1:1.2 to 1:2 and the course of the reaction was monitored by GC and GC-MS analyses until the disappearance of S,S-dimethyl dithiocarbonate (1). As the S-methyl N-alkylthiocarbamates 3 formed they separated out from the reac-

 Table 2
 S-Methyl N-Alkylthiocarbamates 3a-I

tion mixtures as oily or solid substances. The majority of the reactions went to completion in 5-10 hours; a large excess of the amine (1/2 = 1:2) shortened the reaction time (e.g., Table 2 entry 2 vs entry 1 or entry 9 vs entry 8). Generally the thiocarbamates 3 were extracted with dichloromethane and the organic solutions were washed with aqueous 5% hydrochloric acid to separate the excess amine, which was quantitatively recovered as the chloride. After evaporation of the solvent, the crude thiocarbamates 3 were obtained in yields that, in most cases, were between 97% and 100% and with a purity greater than 99.5% (GC and <sup>1</sup>H NMR analyses). Only S-methyl N-(2-hydroxyethyl)thiocarbamate (3i) required purification by column chromatography (Table 2, entry 16). During the reaction a mole of methanethiol (4) formed, and this could be collected in an aqueous solution of sodium hydroxide and recovered as sodium methanethiolate in yields higher than 95%.<sup>24</sup> It is also noteworthy the complete chemoselectivity of these reactions (entries 16-19)

Entry <sup>a</sup>	R	Ratio 1/2	Time (h)	Product	Yield <sup>b</sup> (%)	GC purity <sup>c</sup> (%)
1	Me	1:1.2	5	<b>3</b> a	99.6	99.8
2		1:2.0	15 min	<b>3</b> a	100	99.8
3	Et	1:1.5	5	3b	98.8	99.8
4		1:2.0	2	3b	97	99.9
5	Pr	1:1.5	6	3c	95	99.5
6	Bu	1:1.5	5	3d	97	99.8
7		1:2.0	2	3d	100	100
8	<i>i</i> -Bu	1:1.5	10	3e	96	99.4
9		1:2.0	4.5	3e	98.6	99.5
10	c-Hex	1:2.0	24	3f	95	99.0
11	CH <sub>2</sub> CH=CH <sub>2</sub>	1:1.5	16	3g	95	99.8
12		1:2	6.5	3g	90.4	99.8
13	Bn	1:1.5	17	3h	97.7	99.7
14		1:2	15	3h	98	99.7
15	CH <sub>2</sub> CH <sub>2</sub> OH	1:2	15	3i	d	
16		1:2	7 <sup>e</sup>	3i	81 <sup>f</sup>	
17	CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH	1:2	7	3ј	93 <sup>g</sup>	100
18	CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OH	1:2	3	3k	97 <sup>g</sup>	99.5
19	$4-H_2NC_6H_4CH_2$	1:2	16	31	93	100

 $^{\rm a}$  Unless otherwise noted, all the reactions were performed at r.t. (20–25 °C) in H\_2O.

<sup>b</sup> Unless otherwise noted, yields refer to the crude isolated products.

° Purities refer to the crude isolated products.

<sup>d</sup> Oxazolidin-2-one was the sole reaction product isolated in 97% yield (see experimental).

<sup>e</sup> The reaction was carried out at 0 °C in a solvent-free system.

<sup>f</sup> Yield refers to the product isolated by column chromatography ( $Et_2O$ –EtOAc, 1:1). The other isolated product was oxazolidin-2-one (10% yield).

<sup>g</sup> Yield refers to the product obtained after filtration of the mixture on a short silica gel column (3j: Et<sub>2</sub>O-EtOAc, 1:1; 3k: CHCl<sub>3</sub>-MeOH, 4:1).

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which can be carried out in the presence of other groups like hydroxy and aminophenyl.

In conclusion, the present research has set up a general procedure for the preparation of S-methyl N-alkylthiocarbamates 3 by the methylthiocarbonylation of primary aliphatic amines using S,S-dimethyl dithiocarbonate as a phosgene substitute. The synthetic advantages of the new procedure, with respect to many of the known ones, can be summarized as follows: (i) substitution of phosgene, an extremely toxic reagent hazardous to handle, by S,S-dimethyl dithiocarbonate (1), a readily available, low-cost, low-risk reagent that is easy to handle; (ii) substitution of a gaseous reagent (COCl<sub>2</sub>, bp 8.2 °C) by a liquid reagent (1, bp 168 °C), with evident simplification with regard to measurement, storage, and equipment; (iii) mild reaction conditions that are easily performed; (iv) exclusive formation of the monosubstitution products, S-methyl N-alkylthiocarbamates 3, in exceptionally high yields and very high purities, usually > 95% and >99.5%; (v) complete chemoselectivity in the presence of hydroxy and aminophenyl groups; (vi) formation of one mole of methanethiol, which can be recovered, for each mole of S,Sdimethyl dithiocarbonate (1). Thus, this new procedure, especially given its simplicity and economic advantages, is suitable for work on both the laboratory scale and much larger scales.

Column chromatography and TLC were performed on Merck silica gel 60 (70–230 mesh ASTM) and GF 254, respectively. Petroleum ether was bp 40–60 °C. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance 200 spectrometer at 200 MHz and 50 MHz, respectively, in CDCl<sub>3</sub>, unless otherwise noted. MS spectra were recorded on an AT 5973N mass selective detector connected to an AT 6890N GC, cross-linked methyl silicone capillary column. Details for the reactions and yields for the pure (GC, GC-MS, TLC, <sup>1</sup>H NMR) products are listed in Tables 1 and 2. Structure of all the products were confirmed by comparison of their physical (mp or bp) and spectral data (MS, <sup>1</sup>H NMR) with those reported in the literature. All amines were purchased from Aldrich and used without further purification. *S*,*S*-Dimethyl dithiocarbonate (1) was supplied from Oxon Italia S.p.A. (Italy).

#### S-Methyl N-Benzylthiocarbamate (3h): Typical Procedure

An aq 40% soln of benzylamine (2h, 1.61 g, 15 mmol) in  $H_2O$  (4.03 mL) was added dropwise over a period of 5-10 min to S,S-dimethyl dithiocarbonate (1, 1.22 g, 10 mmol) with stirring. The reaction was mildly exothermic, and during the addition the temperature of the mixture was maintained at 20-25 °C with an ice-water bath. The progress of the reaction was monitored by GC and GC-MS analyses. During the reaction the product **3h** separated out from the mixture as a white solid substance. Stirring at r.t. (20-25 °C) was maintained until disappearance of 1 (17 h). When the reaction was complete, the mixture was treated with CH<sub>2</sub>Cl<sub>2</sub>-H<sub>2</sub>O (2:1, 150 mL). The aqueous soln was separated and extracted with  $CH_2Cl_2$  (2 × 50 mL). The combined organic extracts were washed with aq 5% HCl (50 mL) and then with H<sub>2</sub>O (50 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated under reduced pressure. The crude residue was the title compound 3h; yield: 1.77 g (98%); 99.7% purity (GC analysis); mp 80.3-80.9 °C (Et<sub>2</sub>O-pentane) (Lit.<sup>25</sup> 79-80 °C).

<sup>1</sup>H NMR:  $\delta$  = 2.38 (s, 3 H, CH<sub>3</sub>), 4.48 (d, *J* = 5.7 Hz, 2 H, CH<sub>2</sub>), 5.71 (m, 1 H, NH), 7.24–7.32 (m, 5 H, C<sub>6</sub>H<sub>5</sub>); similar to that previously reported.<sup>11e</sup>

MS (EI, 70 eV): m/z (%) = 181 (24) [M<sup>+</sup>], 133 (46) [M<sup>+</sup> – CH<sub>3</sub>SH], 91 (100) [C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>].

The aqueous layers were collected and evaporated under reduced pressure. The residue was benzylammonium chloride that was treated with 5% aq NaOH to afford pure (GC and GC-MS analyses) benzylamine (**2h**). Yield of the recovered benzylamine, based on the excess of **2h**, was 97% (0.52 g).

S-Methyl N-alkylthiocarbamates 3a-g,j-l were also prepared according to the above procedure. The only exception was S-methyl N-(2-hydroxyethyl)thiocarbamate (3i), which was prepared at 0 °C in a solvent-free system.

Yields and GC purities of the crude compounds **3a–g,h–l** are reported in Table 2; physical and spectral data are reported below.

### S-Methyl N-Methylthiocarbamate (3a)

Colorless oil; bp 50 °C/40 Torr (Lit.  $^{11e}$  81–82 °C/45 Torr).

<sup>1</sup>H NMR:  $\delta = 2.23$  (s, 3 H, SCH<sub>3</sub>), 2.76 (d, J = 4.8 Hz, 3 H, NH*CH*<sub>3</sub>), 6.28 (m, 1 H, NH); similar to that previously reported.<sup>11e</sup>

MS (EI, 70 eV): m/z (%) = 105 (85) [M<sup>+</sup>], 75 (14) [M<sup>+</sup> – NHCH<sub>3</sub>], 58 (100) [M<sup>+</sup> – SCH<sub>3</sub>].

#### S-Methyl N-Ethylthiocarbamate (3b)

Colorless oil; bp 60 °C/45 Torr (Lit.<sup>11e</sup> 82-84 °C/50 Torr).

<sup>1</sup>H NMR:  $\delta = 1.14$  (t, J = 7.3 Hz, 3 H, CH<sub>2</sub>CH<sub>3</sub>), 2.32 (s, 3 H, SCH<sub>3</sub>), 3.24–3.38 (app quint, 2 H, CH<sub>2</sub>), 5.62 (m, 1 H, NH); similar to that previously reported.<sup>11e</sup>

$$\begin{split} \text{MS (EI, 70 eV): } m/z\,(\%) &= 119\,(100)\,[\text{M}^+], 75\,(31)\,[\text{M}^+ - \text{NHC}_2\text{H}_5], \\ 72\,(98)\,[\text{M}^+ - \text{SCH}_3], 29\,(30)\,[\text{C}_2\text{H}_5]. \end{split}$$

#### S-Methyl N-Propylthiocarbamate (3c)

Colorless oil; bp 54–55 °C/50 Torr (Lit.<sup>11a</sup> oil).

<sup>1</sup>H NMR:  $\delta$  = 0.88 (t, *J* = 7.3 Hz, 3 H, CH<sub>2</sub>CH<sub>3</sub>), 1.41–1.56 (app sext, 2 H, CH<sub>2</sub>CH<sub>3</sub>), 2.30 (s, 3 H, SCH<sub>3</sub>), 3.21 (app q, *J* = 6.6 Hz, 2 H, NHCH<sub>2</sub>), 5.81 (m, 1 H, NH); similar to that previously reported.<sup>11a</sup>

MS (EI, 70 eV): m/z (%) = 133 (97) [M<sup>+</sup>], 86 (100) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (53) [M<sup>+</sup> – NHC<sub>3</sub>H<sub>7</sub>], 43 (92) [C<sub>3</sub>H<sub>7</sub>].

#### S-Methyl N-Butylthiocarbamate (3d)

White crystals; mp 37.2–37.5 °C (pentane) (Lit.<sup>11e</sup> 34.8–35.4 °C).

<sup>1</sup>H NMR:  $\delta$  = 0.91 (t, *J* = 7.2 Hz, 3 H, CH<sub>2</sub>CH<sub>3</sub>), 1.24–1.40 (m, 2 H, CH<sub>2</sub>CH<sub>3</sub>), 1.42–1.57 (m, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.33 (s, 3 H, SCH<sub>3</sub>), 3.23–3.33 (m, 2 H, NHCH<sub>2</sub>), 5.61 (m, 1 H, NH); similar to that previously reported.<sup>11e</sup>

MS (EI, 70 eV): m/z (%) = 147 (28) [M<sup>+</sup>], 100 (100) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (37) [M<sup>+</sup> – NHC<sub>4</sub>H<sub>9</sub>], 57 (98) [C<sub>4</sub>H<sub>9</sub>].

#### S-Methyl N-Isobutylthiocarbamate (3e)

White crystals; mp 28.0–28.9 °C (pentane).

<sup>1</sup>H NMR:  $\delta$  = 0.90 (d, *J* = 6.6 Hz, 6 H, 2 CH<sub>3</sub>), 1.71–1.84 (m, 1 H, CH), 2.33 (s, 3 H, SCH<sub>3</sub>), 3.11 (app t, *J* = 6.4 Hz, 2 H, NHC*H*<sub>2</sub>), 5.61 (m, 1 H, NH).

<sup>13</sup>C NMR: δ = 13.80 (SCH<sub>3</sub>), 21.40 (2 CH<sub>3</sub>), 30.17 (CH), 50.20 (NHCH<sub>2</sub>), 169.11 (CO).

MS (EI, 70 eV): m/z (%) = 147 (12) [M<sup>+</sup>], 100 (21) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (16) [M<sup>+</sup> – NHC<sub>4</sub>H<sub>9</sub>], 43 (100) [(CH<sub>3</sub>)<sub>2</sub>CH].

Anal. Calcd for  $C_6H_{13}NOS$ : C, 48.94; H, 8.90; N, 9.51; S, 21.78. Found: C, 48.88; H, 8.85; N, 9.46; S, 21.72.

#### S-Methyl N-Cyclohexylthiocarbamate (3f)

White crystals; mp 113.2–113.8 °C (EtOH–pentane) (Lit.<sup>11e</sup> 111.0–111.3 °C).

<sup>1</sup>H NMR:  $\delta$  = 0.96–2.09 (m, 10 H, 5 CH<sub>2</sub>), 2.31 (s, 3 H, SCH<sub>3</sub>), 3.39–3.99 (m, 1 H, CH), 5.52 (m, 1 H, NH); identical to that previously reported.<sup>11e</sup>

MS (EI, 70 eV): m/z (%) = 173 (33) [M<sup>+</sup>], 126 (57) [M<sup>+</sup> – SCH<sub>3</sub>], 83 (100) [c- $C_6H_{11}$ ], 75 (16) [M<sup>+</sup> – NHC<sub>6</sub>H<sub>11</sub>].

#### S-Methyl N-Allylthiocarbamate (3g)

White crystals; mp 43.4–43.8 °C (pentane). This is a known compound,<sup>26</sup> but physical and spectroscopic data were not reported.

<sup>1</sup>H NMR:  $\delta$  = 2.36 (s, 3 H, SCH<sub>3</sub>), 3.92 (app t, *J* = 5.7 Hz, 2 H, NHC*H*<sub>2</sub>), 5.13–5.18, 5.24–5.26 (2 m, 1:1, 2 H, =CH<sub>2</sub>), 5.53 (m, 1 H, NH), 5.74–5.94 (m, 1 H, CH=).

<sup>13</sup>C NMR: δ = 13.78 (SCH<sub>3</sub>), 45.19 (NHCH<sub>2</sub>), 118.18 (=CH<sub>2</sub>), 135.20 (CH), 169.32 (CO).

MS (EI, 70 eV): m/z (%) = 131 (7) [M<sup>+</sup>], 83 (21) [M<sup>+</sup> – CH<sub>3</sub>SH], 75 (7) [M<sup>+</sup> – NHCH<sub>2</sub>CH=CH<sub>2</sub>], 56 (100) [M<sup>+</sup> – CH<sub>3</sub>SCO].

Anal. Calcd for  $C_5H_9NOS$ : C, 45.77; H, 6.91; N, 10.68; S, 24.44. Found: C, 45.70; H, 6.95; N, 10.73; S, 24.50.

#### S-Methyl N-(3-Hydroxypropyl)thiocarbamate (3j)

The mixture was directly mixed with silica gel and filtered through a short column (EtOAc) to eliminate the excess 3-aminopropanol (**2j**).

White crystals; mp 34.1-35.0 °C (Et<sub>2</sub>O). This is a known compound,<sup>21</sup> but physical and spectroscopic data were not reported.

<sup>1</sup>H NMR:  $\delta$  = 1.66–1.78 (app quint, 2 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.33 (s, 3 H, SCH<sub>3</sub>), 2.90 (br s, 1 H, OH), 3.44 (app q, *J* = 6.1 Hz, 2 H, NHCH<sub>2</sub>), 3.68 (br t, *J* = 5.7 Hz, 2 H, CH<sub>2</sub>OH), 6.15 (m, 1 H, NH).

 $^{13}\text{C}$  NMR:  $\delta$  = 13.82 (SCH\_3), 33.50 (CH\_2CH\_2CH\_2), 39.90 (NHCH\_2), 61.23 (CH\_2OH), 170.43 (CO).

MS (EI, 70 eV): m/z (%) = 149 (3) [M<sup>+</sup>], 102 (100) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (23) [M<sup>+</sup> – NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH].

Anal. Calcd for  $C_5H_{11}NO_2S$ : C, 40.25; H, 7.43; N, 9.39; S, 21.49. Found: C, 40.19; H, 7.40; N, 9.33; S, 21.54.

#### S-Methyl N-(4-Hydroxybutyl)thiocarbamate (3k)

The mixture was directly mixed with silica gel and filtered through a short column (CHCl<sub>3</sub>–MeOH, 4:1) to eliminate the excess 4-aminobutanol (2k).

White crystals; mp 79.8-80.7 °C (EtOAc).

<sup>1</sup>H NMR:  $\delta$  = 1.54–1.63 (m, 4 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.03 (br s, 1 H, OH), 2.34 (s, 3 H, SCH<sub>3</sub>), 3.32 (app t, *J* = 6.6 Hz, 2 H, NHCH<sub>2</sub>), 3.66 (app t, *J* = 5.9 Hz, 2 H, CH<sub>2</sub>OH), 5.78 (m, 1 H, NH).

<sup>13</sup>C NMR: δ = 13.76 (SCH<sub>3</sub>), 27.74 (NHCH<sub>2</sub>CH<sub>2</sub>), 31.03 (CH<sub>2</sub>CH<sub>2</sub>OH), 42.69 (NHCH<sub>2</sub>), 63.74 (CH<sub>2</sub>OH), 169.66 (CO).

MS (EI, 70 eV): m/z (%) = 163 (2) [M<sup>+</sup>], 116 (100) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (39) [M<sup>+</sup> – NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH].

Anal. Calcd for C<sub>6</sub>H<sub>13</sub>NO<sub>2</sub>S: C, 44.15; H, 8.03; N, 8.58; S, 19.64. Found: C, 44.20; H, 8.05; N, 8.57; S, 19.60.

## *S*-Methyl *N*-(4-Aminobenzyl)thiocarbamate (3l) White crystals; mp 134.6–135.5 °C (EtOH).

<sup>1</sup>H NMR:  $\delta$  = 2.37 (s, 3 H, SCH<sub>3</sub>), 4.35 (d, *J* = 5.3 Hz, 2 H, CH<sub>2</sub>), 5.57 (m, 1 H, NH), 6.63 (br s, 2 H, NH<sub>2</sub>), 6.65 (d, *J* = 8.2 Hz, 2 H, H3, H5), 7.08 (d, *J* = 8.2 Hz, 2 H, H2, H6).

<sup>13</sup>C NMR: δ = 13.82 (SCH<sub>3</sub>), 46.60 (CH<sub>2</sub>), 116.64 (C3, C5), 128.87 (C1), 130.58 (C2, C6), 147.46 (C4), 168.98 (CO).

MS (EI, 70 eV): m/z (%) = 196 (6) [M<sup>+</sup>], 148 (36) [M<sup>+</sup> – CH<sub>3</sub>SH], 106 (100) [4-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>].

Anal. Calcd for C<sub>9</sub>H<sub>12</sub>N<sub>2</sub>OS: C, 55.08; H, 6.16; N, 14.27; S, 16.34.

Found: C, 55.13; H, 6.19; N, 14.28; S, 16.30.

#### S-Methyl N-(2-Hydroxyethyl)thiocarbamate (3i) and Oxazolidin-2-one

*Reaction 1, Table 2, entry 15*: The reaction was carried out according to the typical procedure for the preparation of thiocarbamates **3a–h,j–l**. During the reaction *N*-(2-hydroxyethyl)thiocarbamate (**3i**) formed and it immediately cyclized to oxazolidin-2-one. The reaction was complete after 7 h [disappearance of *S*,*S*-dimethyl thiocarbonate (**1**)] and GC analysis of the mixture showed the presence of **3i** and oxazolidin-2-one in an 8:92 ratio; the latter was the sole product after 15 h. The mixture was mixed directly with silica gel and filtered through a short column (CHCl<sub>3</sub>–MeOH, 9:1) to eliminate the excess 2-aminoethanol (**2i**). Oxazolidin-2-one was obtained as white crystals; yield 0.84 g (97%); mp 88.0–88.9 °C (CH<sub>2</sub>Cl<sub>2</sub>–petroleum ether); identical to that of a commercially available sample (Aldrich) of analytical purity.

#### Oxazolidin-2-one

<sup>1</sup>H NMR:  $\delta$  = 3.65 (t, *J* = 8.1 Hz, 2 H, NHC*H*<sub>2</sub>), 4.46 (t, *J* = 8.1 Hz, 2 H, OCH<sub>2</sub>), 6.12 (m, 1 H, NH); identical to that of a commercially available sample (Aldrich) of analytical purity.

MS (EI, 70 eV): m/z (%) = 87 (100) [M<sup>+</sup>], 59 (40) [M<sup>+</sup> – CO].

*Reaction 2, Table 2, entry 16*: The reaction was carried out at 0 °C in a solvent-free system and monitored by GC analysis. Two products were always present: oxazolidin-2-one and *S*-methyl *N*-(2-hydroxyethyl)thiocarbamate (**3i**), the latter was the major product. When the reaction was complete (disappearance of **1**; 7 h), the mixture was immediately mixed with silica gel and column chromatographed to eliminate the excess 2-aminoethanol (**2i**). Elution with Et<sub>2</sub>O–EtOAc (1:1) afforded *S*-methyl *N*-(2-hydroxyethyl)thiocarbamate (**3i**) (1.09 g, 81%) and then oxazolidin-2-one (0.09 g, 10%). When isolated, compound **3i** was stable. In contrast, when the reaction mixture was left at r.t. in the presence of the excess 2-aminoethanol (**2i**), compound **3i** cyclized rapidly and thus the amount of the cyclic carbamate increased.

#### *N*-(2-Hydroxyethyl)thiocarbamate (3i)

White crystals; mp 21.5–22.7 °C (Et<sub>2</sub>O). This is a known compound,<sup>21</sup> but physical and spectroscopic data were not reported.

<sup>1</sup>H NMR:  $\delta$  = 2.35 (s, 3 H, SCH<sub>3</sub>), 2.67 (br s, 1 H, OH), 3.46 (br t, *J* = 5.0 Hz, 2 H, NHCH<sub>2</sub>), 3.74 (br t, *J* = 5.0 Hz, 2 H, CH<sub>2</sub>OH), 6.11 (m, 1 H, NH).

<sup>13</sup>C NMR:  $\delta$  = 13.83 (SCH<sub>3</sub>), 45.25 (NHCH<sub>2</sub>), 63.17 (CH<sub>2</sub>OH), 170.52 (CO).

MS (EI, 70 eV): m/z (%) = 135 (11) [M<sup>+</sup>], 88 (100) [M<sup>+</sup> – SCH<sub>3</sub>], 75 (35) [M<sup>+</sup> – NHCH<sub>2</sub>CH<sub>2</sub>OH].

Anal. Calcd for  $C_4H_9NO_2S$ : C, 35.54; H, 6.71; N, 10.36; S, 23.72. Found: C, 35.50; H, 6.66; N, 10.30; S, 23.75.

*Reaction 3*: Other proofs were carried out: (A) solvent-free system, r.t. (B) solvent-free system, 10 °C; (C) toluene, r.t. Reactions A and C were complete after 5 h and afforded oxazolidin-2-one as the sole product in 0.84 g (97%) and 0.83 g (95%) yields, respectively. Reaction B was complete after 3 h and afforded oxazolidin-2-one (0.19 g, 22%) and thiocarbamate **3i** (0.90 g, 67%).

# Trial Reactions between *S*,*S*-Dimethyl Thiocarbonate (1) and Benzylamine (2h); Typical Procedure

An aq 40% soln of benzylamine (**2h**; 1.07 g, 10 mmol) in H<sub>2</sub>O (2.67 mL) was added dropwise over a period of 5–10 min to *S*,*S*-dimethyl dithiocarbonate (**1**, 1.22 g, 10 mmol), under stirring, and the mixture was heated at 60 °C with an oil bath. After 24 h, GC analysis showed the presence of *S*-methyl *N*-benzylthiocarbamate (**3h**), MS: m/z = 181 [M<sup>+</sup>], and *N*,*N*'-dibenzylurea (**6**), MS: m/z = 240 [M<sup>+</sup>], in a 1:1.30 ratio. The reaction was incomplete and about 14% of unre-

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acted **1** was present. The mixture was extracted with  $CH_2Cl_2(2 \times 80 \text{ mL})$ , dried ( $Na_2SO_4$ ), and evaporated under reduced pressure. The crude residue was then column chromatographed. Elution with petroleum ether–Et<sub>2</sub>O (7:3) afforded thiocarbamate **3h** (0.60 g, 33%); elution with Et<sub>2</sub>O–MeOH (1:1) afforded urea **6** (0.78 g, 65%), based on benzylamine (**2h**).

#### N,N'-Dibenzylurea (6)

Mp 171.0-171.7 °C (CHCl<sub>3</sub>) (Lit.<sup>27</sup> 172-173 °C).

<sup>1</sup>H NMR:  $\delta = 4.33$  (s, 4 H, 2 CH<sub>2</sub>), 7.22–7.30 (m, 10 H, 2 C<sub>6</sub>H<sub>5</sub>).

Conditions for the other trial reactions (entries 1-9, 11-14) and yields for the two products **3h** and **6** are reported in Table 1.

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