

## Synthesis of Substituted Thioureas and Schiff Bases from Organic Isothiocyanates in Dimethyl Sulfoxide\*

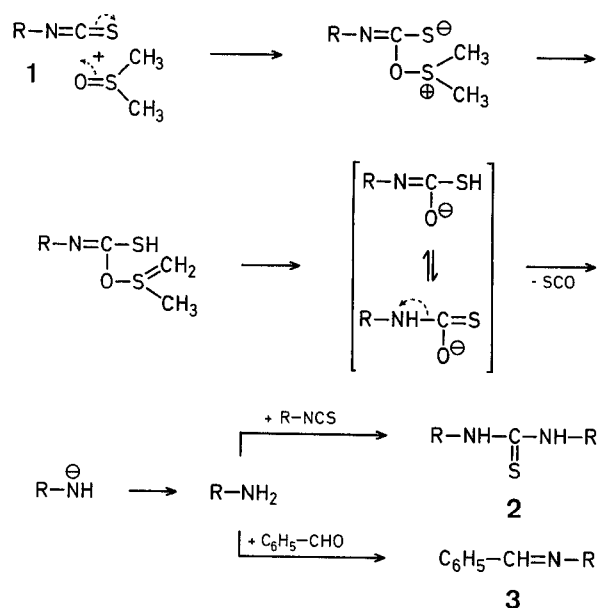
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Symmetrical *N,N'*-disubstituted thioureas have been prepared by the reaction of primary amines with carbon disulfide<sup>1</sup>, thiocarbonyl chloride<sup>2</sup>, organic isothiocyanates<sup>3</sup>, salts of trithiocarbamic acid<sup>4</sup>, and by the reaction of nitrosoarenes with aqueous solutions of salts of trithiocarbamic acid<sup>5</sup>. They can also be made from isothiocyanates and water in the presence of acidic or basic catalysts or under pressure at elevated temperature<sup>6</sup>. Normally, "isothiocyanates are so stable towards water that they may be purified by steam distillation"<sup>7</sup>.

In the present communication we wish to report an investigation of the reactions of organic isothiocyanates with dimethyl sulfoxide in the absence or presence of benzaldehyde. When a mixture of phenyl isothiocyanate (**1**, R = C<sub>6</sub>H<sub>5</sub>) and 3 equivalents of anhydrous dimethyl sulfoxide was heated on the steam bath, carbonyl sulfide was evolved and *N,N'*-diphenylthiourea (**2**, R = C<sub>6</sub>H<sub>5</sub>) was obtained in quantitative yield. The carbonyl sulfide was identified by conversion to potassium xanthate with ethanolic potassium hydroxide solution<sup>8</sup>. The above reaction using equimolar amounts of reactants gave only a 30% yield of *N,N'*-diphenylthiourea.

A reaction mechanism is proposed in the scheme. The proton transfer from dimethyl sulfoxide to the isothiocyanate has been substantiated by carrying out the reaction of **1** (R = C<sub>6</sub>H<sub>5</sub>) with DMSO-*d*<sub>6</sub> (isotopic purity: >98 atom % D); the resultant product was characterized as *N,N'*-diphenylthiourea-*N,N'*-*d*<sub>2</sub> (mass spectrum). The *O*-atom of dimethyl sulfoxide attacks the *C*-atom of the isothiocyanate group nucleophilically, followed by proton transfer; elimination of carbonyl sulfide leads to the formation of a primary amine, which in turn reacts with the isothiocyanate to give the *N,N'*-disubstituted thiourea (**2**). The fate of the dimethyl sulfoxide is not clear; a conversion product of dimethyl sulfoxide could not be isolated from the reaction mixture.



When a mixture of phenyl isothiocyanate (**1**, R = C<sub>6</sub>H<sub>5</sub>), dimethyl sulfoxide, and benzaldehyde (molar ratio 1:3:1)

was heated on the steam bath for 18 h, benzylideneaniline (3, R=C<sub>6</sub>H<sub>5</sub>; 65%) and *N,N'*-diphenylthiourea (2, R=C<sub>6</sub>H<sub>5</sub>; 30%) were obtained. This result is noteworthy since isothiocyanates, unlike isocyanates, do not react with aldehydes under usual reaction conditions, due to the low nucleophilicity of the N-atom of the isothiocyanate group (and the low electrophilicity of the C-atom). Related methods for the synthesis of Schiff bases are the reactions of aldehydes with isocyanates<sup>9</sup>, *N*-sulfinylamines<sup>10</sup>, sulfurdiamides<sup>11</sup>, and carbodiimides<sup>12</sup>.

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





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<sup>6</sup> E. E. Reid, *Organic Chemistry of Bivalent Sulphur*, Chemical Publishing Co. Inc., New York, 1963, Vol. VI, p. 70.

**Table.** Reaction of Organic Isothiocyanates (1) with Dimethyl Sulfoxide in the Absence or Presence of Benzaldehyde

R	Reaction of 1 with Dimethyl Sulfoxide			Reaction of 1 with Dimethyl Sulfoxide + Benzaldehyde			
	Products 2			Products 3			Products 2
	Yield <sup>a</sup> (%)	m.p.	Ref. <sup>1,3</sup> , m.p.	Yield (%)	m.p.	Ref. <sup>1,4</sup> , m.p.	Yield (%)
a 	93	152 <sup>b</sup>	152–153 <sup>c</sup>	65	46–48 <sup>c</sup>	48 <sup>c</sup>	30
b 	78	167 <sup>b</sup>	167 <sup>c</sup>	55	62 <sup>c</sup>	62 <sup>c</sup>	38
c 	92	176 <sup>c</sup>	176 <sup>c</sup>	62	119 <sup>c</sup>	120 <sup>c</sup>	29
d 	89	162 <sup>c</sup>	164 <sup>c</sup>	51	73 <sup>c</sup>	73 <sup>c</sup>	22
e 	82	174–175 <sup>b</sup>	174–175 <sup>c</sup>	43	(b.p. 318 <sup>c</sup> )	(b.p. 318 <sup>c</sup> )	47
f 	87	52 <sup>d</sup>	52 <sup>c</sup>	-	-	-	73

<sup>a</sup> Conversions were quantitative. Yields refer to isolated product.

<sup>b</sup> Recrystallized from benzene.

<sup>c</sup> Recrystallized from benzene/ethanol.

<sup>d</sup> Recrystallized from petroleum ether (b.p. 60–80°).

#### Preparation of Symmetrically Disubstituted Thioureas; General Procedure:

A mixture of the organic isothiocyanates (0.01 mol) and anhydrous dimethyl sulfoxide (0.03 mol) was heated on a steam bath for 18 h. The reaction mixture was then cooled and poured onto crushed ice (30–50 g). The solid that separated was collected, washed with cold water, and dried. It was crystallized from appropriate solvents as indicated in the Table.

#### Preparation of Schiff Bases from Isothiocyanates; General Procedure:

A mixture of the organic isothiocyanate (0.01 mol), benzaldehyde (0.01 mol), and anhydrous dimethyl sulfoxide (0.03 mol) was heated on steam bath for 18 h. The reaction mixture was then cooled and extracted with hexane (3 × 20 ml). The residual oil was poured onto crushed ice, the solid was collected by filtration, and characterized by conversion into the corresponding thioureas (comparison of m.p. and spectral properties with Lit. values). Removal of solvent from the hexane extract gave the benzylideneanilines which were purified by crystallization or distillation.

#### *N,N'*-Diphenylthiourea-*N,N'*-d<sub>2</sub>:

A mixture of phenyl isothiocyanate (0.3 ml, 0.0025 mol) and DMSO-*d*<sub>6</sub> (0.55 ml, 0.0075 mol; isotopic purity: >98% D) was heated on a steam bath for 18 h. The mixture was then cooled and the solid product was isolated by filtration; m.p. 55°.

C<sub>13</sub>H<sub>10</sub>D<sub>2</sub>S (230.3).

Mass Spectrum: *m/e* = 230 (M<sup>+</sup>).

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<sup>14</sup> *Dictionary of Organic Compounds*, ed. I. Heilbron, Eyre and Spottiswoode Publishers Ltd., London, 1965.