

N-Nitroso Compounds. IV.¹⁾ Reaction of N-Nitrosourea with Thiol. A New Synthesis of Thiocarbamic S-Esters

Kitarō YOSHIDA,* Masayoshi ISOBE, Kazuyuki YANO, and Kazuo NAGAMATSU

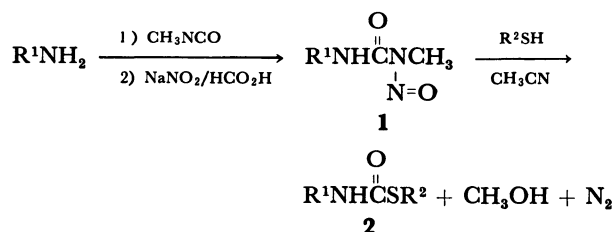
Department of Chemistry, Saitama Medical School, 981 Kawakado, Moroyama, Iruma-gun, Saitama 350-04

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Synopsis. Thirteen thiocarbamic S-esters have been synthesized in good yield by the reaction of thiol with substituted N-methyl-N-nitrosourea in anhydrous acetonitrile.

Although several methods have been reported on the preparation of thiocarbamic S-esters, the most commonly used ones are those from alkylcarbamoyle chlorides with sodium alkanethiolates,^{2a)} alkyl thiocyanates with alcohols,^{2b)} or those using carbonyl sulfide with base,^{2a)} or carbon monoxide with selenium as a catalyst.^{2c)} Since the preparation of herbicidal thiocarbamic S-esters is of commercial importance, it is significant to explore an alternative route to this class of compounds.

Recently, we have shown that N'-substituted N-methyl-N-nitrosourea readily reacts with aliphatic amines to give "transaminated" urea in substantial yield.¹⁾ Similar S_N2 reactions have also been reported for N-alkyl-N-nitroso amides with aliphatic primary amines in refluxing dichloromethane.³⁾ Furthermore, Challis and his co-workers observed a nucleophilic rather than a general base catalysis of imidazole in the hydrolyses of N-nitroso-2-pyrrolidone and related compounds in aqueous buffer solution.⁴⁾ All of these results are undoubtedly related to an enhanced leaving property of the N-nitrosoamino moiety of the substrates. Thus a facile reaction is also expected to occur with other nucleophiles. We have now found that N-nitrosourea **1** reacts with various thiols under mild conditions to give the corresponding thiocarbamic S-esters **2** in good yields as shown in Scheme 1.



Scheme 1.

We wish to report here a convenient method of the preparation of **2** from primary amines by the use of **1** as a key compound.

Results and Discussion

N-Methylurea (R¹NHCONHCH₃) was obtained conventionally⁵⁾ through the carbamoylation of starting amine with methyl isocyanate. On treatment of the urea with sodium nitrite in formic acid, an N-nitrosated urea **1** was produced exclusively; this was the product from the mononitrosation at the less hindered N-position.⁶⁾ The crude product **1** was treated with 2 equiv of thiol in anhydrous acetonitrile at 60 °C. Because of the limited solubility and to avoid the hydrolysis of **1**,⁷⁾ the use of organic solvent may be of significance. As the reaction proceeded, gas evolution was observed and in most cases, almost all quantity of **1** was consumed within several hours. However, under the same

TABLE 1. YIELDS, MELTING POINTS, AND IR DATA OF **2**

Run	R ¹ (Amine)	R ² (Thiol)	Reaction conditions		2		
			Temp/°C	Time/h	Overall Yield/% ^{a)}	Mp(θ _m /°C)	IR(C=O)/cm ⁻¹
1	n-C ₄ H ₉	Ph	reflux	18	39	oil	1660
2	cyclo-C ₆ H ₁₁	n-C ₄ H ₉	60	21	77	65—66 ^{b)}	1650
3	1-Adamantyl	n-C ₄ H ₉	60	2	99	62—64	1670
4	Ph	C ₂ H ₅	60	1	73	69.5—70.0	1680
5	Ph	n-C ₄ H ₉	60	1	83	68—70	1670
6	Ph	i-C ₄ H ₉	60	0.5	73	105—107	1670
7	Ph	t-C ₄ H ₉	60	0.5	12 ^{c)}	142—143	1670
8	Ph	CH ₂ CH=CH ₂	60	1	91	69—70	1680
9	Ph	CH ₂ CH ₂ OH	60	0.5	71	72.5—73.5	1660
10	Ph	cyclo-C ₆ H ₁₁	60	0.5	86	115.0—115.5	1660
11	Ph	n-C ₁₀ H ₂₁	r.t.	72	69	62.5—64.0	1680
12	Ph	Ph	reflux	16	89	120—121 ^{d)}	1670
13	Ph	p-CH ₃ C ₆ H ₄	reflux	16	88	130.0—130.5 ^{e)}	1670

a) Isolated Yield. b) 68 °C, Ref. 2b). c) Ref. 8). d) 122—124 °C, Ref. 9). e) 130—132 °C, Ref. 9).

conditions, aromatic thiol did not react with **1** even after a prolonged reaction period, so that an elevated temperature was required. After work up, the thiocarbamic S-ester **2** was obtained in the yields of 42–100% (39–99% based on the amine used).⁸ The results are summarized in Table I.

For synthetic purposes, the present method has some advantages in that (i) the direct reaction of **1** with alkanethiol (not sodium alkanethiolates) occurs spontaneously under rather mild conditions; (ii) by-products such as methanol and nitrogen arising from the *N*-methyl-*N*-nitrosoamino fragment can readily be eliminated, so that no tedious work up is necessary (see Experimental); (iii) in addition to the current availability of aromatic amines, it becomes possible to utilize aromatic thiols as well. Thus the present study provides an efficient new route to thiocarbamic S-esters.

Experimental

Mps are uncorrected. IR spectra were taken in chloroform solution by a Shimadzu IR-400 spectrophotometer. All the reagents were of commercial grade and used without further purification.

Reaction of 1 with Thiol. An *N'*-substituted *N*-methylurea was prepared in a usual fashion.⁹ The urea (10 mmol) was treated by sodium nitrite (20 mmol) in formic acid (10 ml) at 0–5 °C for 1 h. The mixture was poured onto ice-water, and the precipitate formed was collected, washed with cold water, and dried under reduced pressure to yield exclusively *N*-nitrosated urea **1** (77–100% from the amine). The crude product **1** and an excess of thiol (20 mmol) were dissolved in anhydrous acetonitrile (20 ml) and the mixture was stirred at 60 °C with monitoring the reaction by TLC analysis. After **1** was

consumed, evaporation of the solvent and the excess thiol under reduced pressure gave **2** in almost pure solid. When a thiol of high boiling point was used, isolation by column chromatography (silica gel, CHCl₃–hexane or ether–hexane) was carried out. The IR and ¹H NMR spectra of the crude solid **2** were consistent with the assigned structure. In most cases, the analytical sample was obtained by recrystallization to give a satisfactory elemental analysis within ±0.4% for C, H, N, and S. The yields and some of the physical data of **2** are summarized in Table I.

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