

The Reaction of *S*-Methiodide Derivatives of Activated Thioureas with Hydroxylic Compounds. A Novel Synthesis of Mercaptans

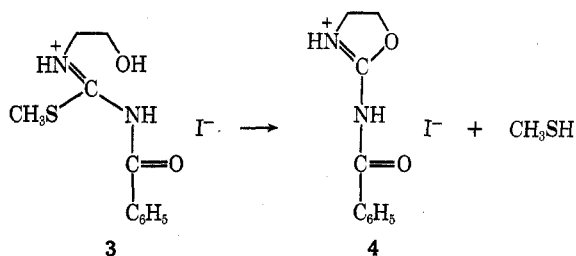
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2-Methyl-2-thiopseudourea hydriodides activated by electron-withdrawing groups undergo attack by alcohols and water to give several types of products whose formation is dependent on the nature of the hydroxylic reactant. When 1-benzoyl-2-methyl-2-thiopseudourea hydriodide (5) was heated with alcohols, methyl mercaptan was evolved and there was formed 1-benzoylurea (2) and the iodide corresponding to the alcohol. The yield of 2 was diminished and the formation of 1-benzoyl-2-thiourea (1) took on greater prominence in going from a primary to a tertiary alcohol. Methyl *N*-benzoylthiolcarbamate (6) and NH_4I were also formed when the more hindered alcohols were used and were essentially the only products obtained in the reaction of 5 with water. *S*-Methiodide derivatives of other activated thioureas, *i.e.*, 1-acetyl-2-methyl-2-thiopseudourea (9), 2-methyl-2-thiopseudobiuret (10), 2-methyl-2,4-dithiopseudobiuret (11), and 1-(4-nitrophenyl)-2-methyl-2-thiopseudourea (12) hydriodides, reacted with ethanol and water in a similar manner as 5. Thiols could be generated in moderate yields by the reaction of 1-acetyl-2-thiourea (14) with primary alkyl halides in ethanol.

In the course of a recent study,¹ it was necessary to prepare *S*-methiodide derivatives of numerous thioureas. This was accomplished by heating the thioureas with methyl iodide in ethyl alcohol, a solvent eminently suitable for this purpose.² When the formation of *S*-methyl derivatives of acylthioureas such as 1-benzoyl-2-thiourea (1) was attempted in ethyl alcohol, however, there was unexpectedly noted a copious evolution of methyl mercaptan and from the reaction mixture was isolated a high yield of 1-benzoylurea (2). Recently, we described³ a somewhat related reaction with 1-(2-hydroxyethyl)-3-benzoyl-2-methyl-2-thiopseudourea hydriodide (3) which cyclized *via* an intramolecular displacement of the methylthio group by the hydroxyl to give 2-benzamido-2-oxazoline hydriodide (4) with the concomitant evolution of methyl mercaptan.



The investigation of the reaction between 1-benzoyl-2-methyl-2-thiopseudourea hydriodide (5), chosen as a model acylthiourea derivative, and some representative hydroxylic compounds is reported here. In addition, the results obtained in the reaction of compounds structurally related to 5 with both ethyl alcohol and water are described.

Results

The desired 1-benzoyl-2-methyl-2-thiopseudourea hydriodide (5) could be readily prepared in a nonhydroxylic medium such as acetonitrile. The free base of 5⁴ was found to be virtually unaffected by boiling ethyl alcohol over a 24-hr period as evidenced by a negligible evolution of methyl mercaptan and recovery

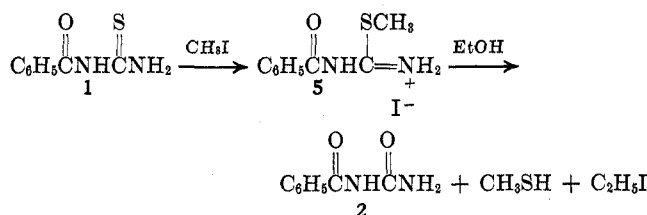
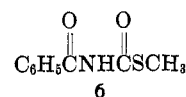


TABLE I

INTERACTION OF 1-BENZOYL-2-METHYL-2-THIOPSEUDOUREA HYDRIODIDE (5) WITH ALCOHOLS
5 + ROH → 1 + 2 + 6

R	Reflux time, hr	Yields, %			Other products (%)
		1	2	6	
CH ₃ -	3	94	<1		
CH ₃ CH ₂ -	3	90	1		
CH ₃ CH ₂ CH ₂ -	3	82	4		
	24	55			C ₆ H ₅ C(=O)NHC(=O)-OC ₂ H ₅ (31)
(CH ₃) ₂ CH-	16	28	61	7	C ₆ H ₅ C(=O)NHC(=O)-OCH(CH ₃) ₂ (4)
(CH ₃) ₃ C-	16	64	15	21	

of ~90% of the starting material. Compound 5 was heated under reflux with methyl and ethyl alcohols for 3 hr to give >90% yields of 2 (*cf.* Table I). A somewhat lower yield of 2 was obtained with *n*-propyl alcohol after an identical heating period and, in addition, methyl *N*-benzoylthiolcarbamate (6) was isolated as a minor product.



The decomposition of 5 in a secondary alcohol, *i.e.*, isopropyl alcohol, was considerably slower than had been seen with primary alcohols. After 3 hr, more than half of the starting material could be recovered and a 20% yield of the starting thiourea, 1, was obtained. When the reflux period was extended to 16 hr, the yield of 2 was 61%. In addition, a somewhat increased quantity of 1-benzoyl-2-thiourea (1) was isolated. Thiourea 1 was shown not to be the precursor of 2 in the above-described reactions by heating it for 24 hr with ethyl alcohol. Whereas extensive ethanolysis of the benzoyl group occurred, the formation of 2 or urea could not be detected.

(1) D. L. Klayman and R. J. Shine, *Anal. Chim. Acta*, **41**, 408 (1968).

(2) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. V, Chemical Publishing Co., New York, N. Y., 1963, p 28.

(3) D. L. Klayman, R. J. Shine, and A. E. Murray, Jr., *J. Pharm. Sci.*, **59**, 1515 (1970).

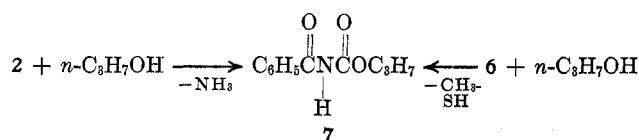
(4) G. Ito, *Chem. Pharm. Bull. (Tokyo)*, **9**, 245 (1961).

tert-Butyl alcohol also reacted much slower with **5** than did the primary alcohols. Most of the starting material could be recovered after a 3-hr reflux period; however, at the end of 16 hr there was obtained a 64% yield of the thiourea **1** and moderate quantities of **2** and **6**.

The components of the reaction mixtures obtained from the isopropyl and *tert*-butyl alcohols runs were extremely difficult to separate cleanly by crystallization methods. Column chromatography could not be used inasmuch as the products were insoluble in the solvents generally used with this technique. The most satisfactory method devised to quantitate the products was through the use of nmr spectroscopy in conjunction with sulfur microanalysis. This method gave the relative proportions of the products but not their absolute values.

Since the urea oxygen atom of **2** could only arise by transfer from the hydroxylic reactant, it was of interest to learn the fate of the alkyl moiety of the alcohol in this process. On distillation of the reaction mixtures from the ethyl, *n*-propyl, and isopropyl alcohol runs, the corresponding alkyl iodides were isolated and identified. The evolution of isobutylene, detected from the *tert*-butyl alcohol experiment, is ascribed to the breakdown of the thermally unstable *tert*-butyl iodide into the olefin and hydrogen iodide.⁵

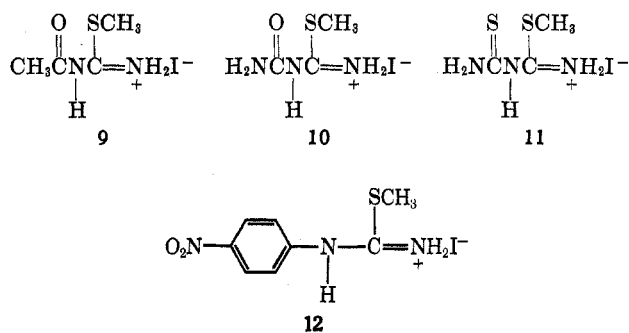
Secondary crystalline transformation products were observed in those mixtures which had been permitted to reflux >12 hr. It was demonstrated that *n*-propyl *N*-benzoylcarbamate (**7**), a constituent of the



mixture from the *n*-propyl alcohol experiment, arose from the interaction of the alcohol with either of the primary products of the reaction, *i.e.*, **2** or **6**. The conversion of ureas to carbamic esters has been reported by earlier workers.⁶ The related isopropyl *N*-benzoylcarbamate (**8**) was obtained in very low yield and *tert*-butyl *N*-benzoylcarbamate does not appear to have been formed at all.

The reaction of **5** with water resulted in its rapid and quantitative conversion to methyl *N*-benzoylthiolcarbamate (**6**) and ammonium iodide with only trace amounts of methyl mercaptan being evolved. Thus, the reaction course in water sharply contrasts with that which occurs in alcohols.

Compounds in which the benzoyl group of **5** was replaced by other electron-withdrawing groups, *i.e.*, acetyl, carbamoyl, thiocarbamoyl, and 4-nitrophenyl, were studied to determine if the resultant compounds would react similarly with hydroxylic nucleophiles. 1-Acetyl-2-methyl-2-thiopseudourea (**9**), 2-methyl-2-thiopseudobiuret (**10**), 2-methyl-2,4-dithiopseudobiuret (**11**), and 1-(4-nitrophenyl)-2-methyl-2-thiopseudourea (**12**) hydriodides were synthesized and each was heated under reflux with ethyl alcohol for 24 hr. In all instances the evolution of methyl mercaptan was

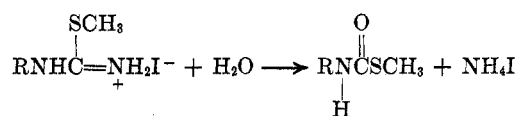


observed with the formation of acetylurea from **9**, biuret from **10** and **11**, and 1-(4-nitrophenyl)urea from **12**, respectively. The formation of biuret rather than thiobiuret from **11** was surprising and, therefore, it was necessary to confirm that thiobiuret is stable to boiling ethyl alcohol over a 24-hr period.

The essentiality of the 4-nitro group of **12** was dramatically demonstrated when the related 1-phenyl-2-methyl-2-thiopseudourea hydriodide was refluxed in ethyl alcohol for 24 hr. No methyl mercaptan evolution was detected and all the starting material was recovered unchanged. The *S*-methiodide derivative of 1-guanyl-2-thiourea was similarly unaffected.

When **9**–**12** were each heated in water, ammonium iodide was eliminated to give the corresponding methyl thiolcarbamate derivatives, generally in excellent yield (*cf.* Table II).

TABLE II
THE FORMATION OF METHYL THIOLCARBAMATES BY THE REACTION OF *S*-METHYLTHIOPSEUDOUREA HYDRIODIDES WITH WATER



R	Reflux time, hr	Yield, %	Mp, °C	Recrystn solvent	Molecular formula ^a
CH ₃ CO-	0.5	78	152–154 ^b	EtOH	C ₄ H ₇ NO ₂ S
C ₆ H ₅ CO-	1	96	162–164 ^c	CH ₃ CN	C ₉ H ₉ NO ₂ S
H ₂ NCO-	3	82	209–211 dec ^d	CH ₃ CN	C ₃ H ₆ N ₂ O ₂ S
H ₂ NCS-	3	95	171–172 dec	CH ₃ CN	C ₃ H ₆ N ₂ O ₂ S
<i>p</i> -NO ₂ C ₆ H ₄ -	13	75	200–204	CH ₃ CN- H ₂ O	C ₈ H ₆ N ₂ O ₃ S

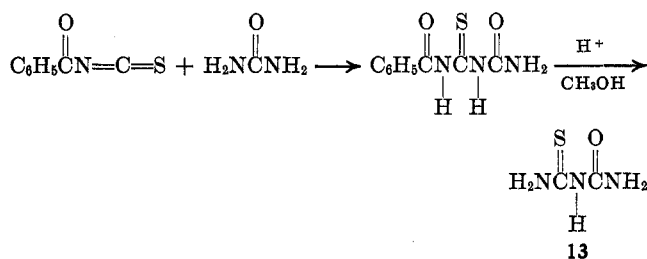
^a Satisfactory analytical data (±0.3% for C, H, N, S) were reported for all compounds listed in the table: Ed. Registry numbers are, respectively, 34277-65-1, 13996-86-6, 34277-67-3, 34277-68-4, and 34277-69-5. ^b Lit.²¹ mp 145.5–146°. ^c Lit.²¹ mp 152–153°. On recrystallization, the melting point is lowered and broadened with no change in ir or nmr spectra. ^d Heating above the melting point gives cyanuric acid.

A new synthesis of thiobiuret (**13**) was developed incidental to this investigation which is considerably simpler than the existing method⁷ which employs the reaction of hydrogen or ammonium sulfide with cyanourea. In our preparation, benzoyl isothiocyanate was condensed with urea to give 1-benzoyl-2-thiobiuret whose benzoyl group was easily removed by methanolysis to give thiobiuret in good yield.

(5) J. L. Jones and R. A. Ogg, Jr., *J. Amer. Chem. Soc.*, **59**, 1943 (1937).

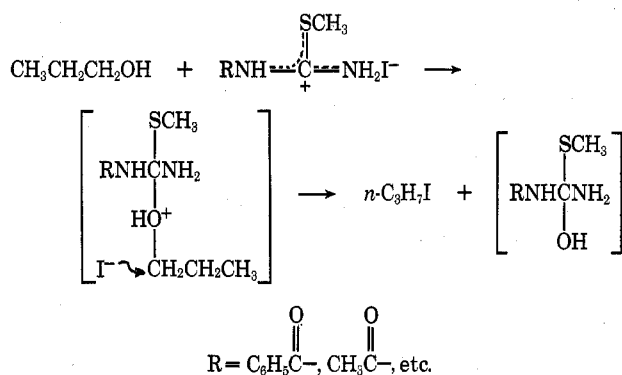
(6) R. A. Jacobson, *ibid.*, **60**, 1742 (1938), and references cited therein.

(7) A. Wunderlich, *Ber.*, **19**, 448 (1866); O. Hecht, *ibid.*, **25**, 749 (1892).



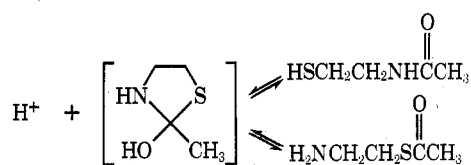
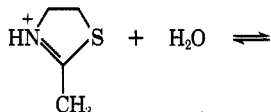
Discussion

An *S*-methiodide derivative of a thiourea which is *N*-substituted by an electron-withdrawing group undergoes addition by an alcohol, ordinarily a poor nucleophile, at the activated 2-carbon atom. This addition to the cationic substrate yields, in all probability, a



tetrahedral intermediate in the rate-determining step. The carbon adjacent to the protonated oxygen atom then is attacked by iodide ion under conditions which are highly favorable for ether cleavage, resulting in the formation of the alkyl iodide corresponding to the alcoholic reactant.

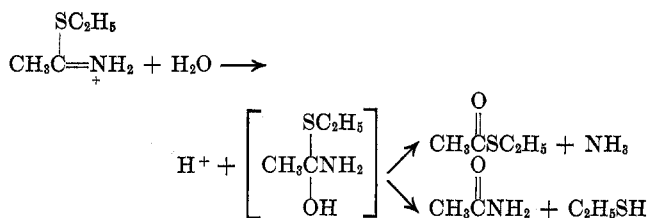
The uncharged carbinolamine intermediate, thus formed, closely resembles other tetrahedral intermediates possessing both a sulfur and a nitrogen atom about the central carbon whose mode of decomposition is highly dependent on the pH of the medium. For example, Martin, *et al.*,⁸ proposed a hydroxythiazolidine intermediate to explain the formation of *N*- and *S*-



acetyl-2-mercaptoethylamine in the course of the hydrolysis of 2-methyl-2-thiazoline. In studying the hydrolysis of thioimide esters, Schmir, *et al.*,⁹ found that, in general, C-N bond fission of the proposed tetrahedral intermediate occurs under acidic conditions to yield thiol esters and amines, whereas under neutral or alkaline conditions C-S fission takes place resulting in the formation of amides with the loss of

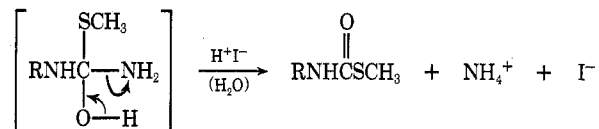
(8) R. B. Martin, S. Lowey, E. L. Elson, and J. T. Edsall, *J. Amer. Chem. Soc.*, **81**, 5089 (1959).

(9) R. K. Chaturvedi, A. E. MacMahon, and G. L. Schmir, *ibid.*, **89**, 6984 (1967); R. K. Chaturvedi and G. L. Schmir, *ibid.*, **91**, 737 (1969).



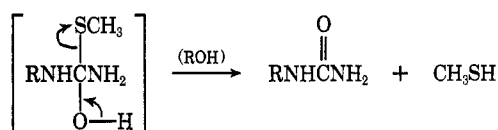
mercaptan. By adjusting the pH and buffer concentrations it was possible to obtain yields of the order of 90% of either the thiol ester or the amide. We have reported¹⁰ a similar reaction in which the attack of hydroselenide ion on certain *S*-methylthiopseudo-ureas, when conducted under acid conditions (pH 5-6), results in C-N bond cleavage and under basic conditions (pH 8-9) leads to C-S bond fission.

In the present case, the variables, in addition to hydrogen ion concentration, were the polarity and molecular configuration of the hydroxylic reactants. With water, the most polar reactant, the collapse of the tetrahedral intermediate proceeds at *ca.* pH 7 by the cleavage of the C-N bond to form an ionic by-product, ammonium iodide, and the thiolcarbamic ester (6). As part of each mechanism proposed for the hydrolysis of thiazolines,⁸ thioimide esters,⁹ imino-lactones,¹¹ and aliphatic Schiff bases¹² there is a step in which the positively charged carbinolamine intermediate loses a proton before conversion to the final product. Here too, there is little reason to believe that



another mechanism is operative since the reaction we have observed seems to possess the essential characteristics of the hydrolyses mentioned above.

Alcohols, being considerably less polar than water, favor the decomposition of the tetrahedral intermediate by a route leading to nonionic products *via* C-S



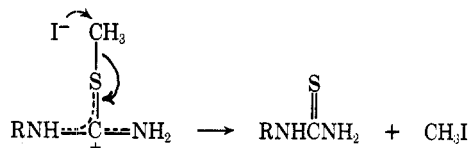
bond cleavage. Methyl mercaptan and acylurea formation takes place with methyl and ethyl alcohols with approximately equal ease, the slight steric disadvantage of the latter being apparently overcome by its higher boiling point. Reactivity of the alcohols used in this reaction than falls in the order *n*-propyl > isopropyl > *tert*-butyl as crowding increases about the carbinol carbon atom.

The competitive formation of the thiourea 1 as a minor but significant product in the reaction of 5 with isopropyl alcohol and as the major product in the reaction with *tert*-butyl alcohol probably does not involve the direct participation of the medium in intermediate formation. This decomposition follows the order of the thermal lability of the alkyl halides formed,

(10) D. L. Klayman and R. J. Shine, *J. Org. Chem.*, **34**, 3549 (1969).

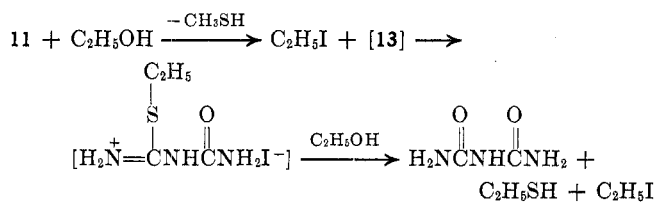
(11) G. L. Schmir and B. A. Cunningham, *J. Amer. Chem. Soc.*, **87**, 5692 (1965); B. A. Cunningham and G. L. Schmir, *ibid.*, **88**, 551 (1966).

(12) E. H. Cordes and W. P. Jencks, *ibid.*, **85**, 2343 (1963).

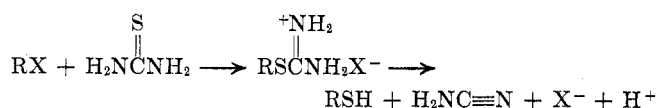


i.e., *tert*-butyl > isopropyl. Because iodide is not removed as a stable covalent compound, reaction mixtures from these alcohols have a more abundant quantity of ionic iodide to render the above reaction possible. It is interesting that, of the alcohols, only *tert*-butyl alcohol gives any significant amount of the thiocarbamic ester 6. This may also be a consequence of the increased acidity of the reaction medium due to the hydriodic acid formed in the decomposition of *tert*-butyl iodide.

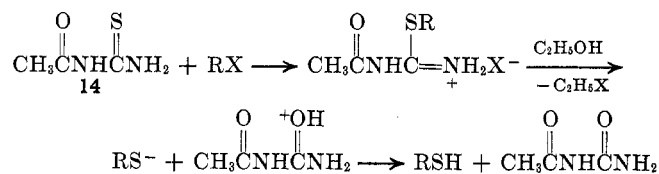
Compounds 9–12, possessing electron-withdrawing groups other than benzoyl, eliminated methyl mercaptan or ammonium iodide when heated with ethanol or water, respectively. The only unexpected result was the reaction of *S*-methylthiobiuret (11) with ethanol in which both sulfur atoms were separated from the molecule to give biuret. The loss of the second thiocarbonyl group can be hypothesized as occurring by the *S*-alkylation of thiobiuret (13) by ethyl iodide formed as a by-product of the first step, followed by reattack by an ethanol molecule.



Synthesis of Mercaptans.—The condensation of thiourea with alkyl halides to form thiopseudoureas, followed by their hydrolysis with aqueous alkali¹³ or amines¹⁴ is a well-known method for the production



of mercaptans. We have applied the above-described findings with activated thioureas to the synthesis of mercaptans. The procedure which was found most satisfactory consisted of heating alkyl halides (X = Br, I) with 1-acetyl-2-thiourea (14) in ethyl alcohol for



24 hr (*cf.* Table III). This method obviates the need for a separate hydrolysis step and may prove useful for the generation of thiols which are water or alkali sensitive. Acetyl- rather than benzoylthiourea was found preferable inasmuch as the partial ethanolysis of the amide function which occurs in the course of the reaction leads to the readily removable ethyl acetate

(13) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., New York, N. Y., 1958, p 32.

(14) B. C. Cossar, J. O. Fournier, D. L. Fields, and D. D. Reynolds, *J. Org. Chem.*, **27**, 93 (1962).

TABLE III

MERCAPTAN FORMATION FROM 1-ACETYL-2-THIOUREA (14) AND ALKYL HALIDES IN ETHANOL



RX	RSH, % yield
1-Bromooctane	53
1-Bromododecane	50
1-Iodododecane	52
1-Bromohexadecane	47
2-Bromooctane	12
α -Bromotoluene	76 ^a
2-Bromoethylbenzene	38
2-Iodoethylbenzene	44
<i>N</i> -(2-Bromoethyl)phthalimide ^b	21
2-Bromoethoxybenzene	37
1,5-Dibromopentane	36

^a Complete oxidation of the reaction product with iodine resulted in a 73% isolated yield of dibenzyl disulfide. ^b Owing to problems with solubility in petroleum ether, CH₂Cl₂ was used to elute the mercaptan from the column. Sulfur analysis of the chromatographed product was in good agreement with the value obtained by the iodine titration.

rather than ethyl benzoate (bp 211–213°). This competing reaction, which deactivates 14, prevents the quantitative formation of mercaptans regardless of how long the reflux time is extended beyond ~24 hr.

In comparison with thiourea, the thiocarbonyl group of 14 is deactivated as an *S* nucleophile owing to the electron-withdrawing effect of the *N*-acetyl group. Its diminished nucleophilicity could be demonstrated in its reaction with 2-bromooctane in acetonitrile. Whereas this secondary alkyl halide combined almost completely with thiourea in 24 hr, the reaction went to only ~20% completion with 14.

Also, the yields of mercaptans derived from primary halides and 14 were considerably higher than those obtained from secondary halides (*e.g.*, 53% from 1-bromooctane *vs.* 12% from 2-bromooctane). There was no observed mercaptan formation from *tert*-butyl bromide. The use of alkyl iodides in place of the bromides resulted in only a slight increase in the yields of the mercaptans.

Several alkyl halides containing additional functional groups did not give the desired mercaptans on reaction with 14 but instead led to products reported to be obtained with thiourea. For example, the reaction of 14 with 2-bromoethylamine hydrobromide in ethanol gave 2-amino-2-thiazoline hydrobromide.¹⁵ There was evidence that 2-acetamido-2-thiazoline was initially formed, with the acetyl group being lost by ethanolysis. Bromoacetic acid and 14 resulted in the formation of 2-amino-2-thiazolin-4-one hydrobromide.¹⁶

Experimental Section¹⁷

1-Benzoyl-2-thiourea (1).—To a solution of 89.2 g (1.1 mol) of sodium thiocyanate in 500 ml of warm acetone was slowly added 140 g (1 mol) of benzoyl chloride and the resulting mixture was

(15) D. G. Doherty, R. Shapira, and W. T. Burnett, Jr., *J. Amer. Chem. Soc.*, **79**, 5667 (1957).

(16) C. F. H. Allen and J. A. Allen, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 751.

(17) Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Mr. Joseph F. Alicino, New Hope, Pa. Ir spectra of solids were determined as KBr pellets on a Beckman IR-5 spectrometer. Nmr spectra were run on trifluoroacetic acid solutions using TMS as an internal standard on a Varian A-60 spectrometer. Mass spectra were measured either on an AEI MS-9 or a Varian EM-600 mass spectrometer at 70 eV.

heated (~10 min) until the odor of benzoyl chloride disappeared. Sodium chloride which precipitated as a fine powder was removed by filtration from the cooled mixture and to the filtrate was slowly added with agitation 150 ml of 28% aqueous ammonia. The mixture was evaporated to dryness and the residue was extracted with hot EtOH to give 87 g (48%) of 1-benzoyl-2-thiourea, mp 175° (lit.¹⁸ mp 169–170°). The analytical sample was recrystallized from EtOH.

Anal. Calcd for C₈H₉N₂OS: C, 53.30; H, 4.47; N, 15.55; S, 17.79. Found: C, 53.52; H, 4.57; N, 15.64; S, 17.77.

1-Benzoyl-2-methyl-2-thiopseudourea Hydriodide (5).—To a solution of 27.8 g (0.154 mol) of 1-benzoyl-2-thiourea in 400 ml of dry acetonitrile was added 28.5 g (0.21 mol) of methyl iodide. The solution was refluxed for 45 min and cooled and the crystals which formed were collected to give 45.7 g (92%) of **5**, mp 185–189°. The analytical sample (from CH₃CN) melted at 190–195° (lit.⁴ mp 186–190°).

Anal. Calcd for C₉H₁₁N₂OS: C, 33.53; H, 3.44; N, 8.70; S, 9.96. Found: C, 33.44; H, 3.60; N, 8.56; S, 10.17.

Reaction of 5 with Hydroxylic Compounds. A. Methyl Alcohol.—A solution of 3.22 g (0.01 mol) of **5** in 50 ml of MeOH was heated under reflux until methyl mercaptan was no longer evolved to any appreciable extent. MeSH could be detected by not only its distinctive odor, but also by the yellow lead mercaptide which formed on moistened lead acetate paper placed at the top of the reflux condenser, and was identified by its ir spectrum (3.82 μ, -SH).¹⁹ The solution was cooled giving white crystals of benzoylurea (**2**), the yield of which was increased by working up the mother liquors: mp 220–222° (lit. mp 215°, 20 214–215°²¹) on recrystallization from EtOH. The ir spectrum was identical with that of an authentic sample.

B. Ethyl Alcohol.—The reaction of **5** with EtOH was run and worked up as described above. The contents of the flask were distilled through a Vigreux column at atmospheric pressure. The first 0.5 ml of distillate, an azeotrope rich in ethyl iodide, was collected. It indicated it to be a mixture of ethyl iodide and ethyl alcohol; a mass spectrum of the mixture gave a parent ion at *m/e* 156 [C₂H₅I]⁺.

This procedure was also followed in the reaction of **5** with *n*-propyl and isopropyl alcohols. The *n*-propyl and isopropyl iodides collected gave the anticipated ir spectra and *m/e* 170 [C₃H₇I]⁺.

C. *n*-Propyl Alcohol.—When *n*-PrOH was heated with **5** as described above, there was isolated some starting material, much **2**, and a small quantity of methyl *N*-benzoylthiocarbamate (**6**) whose melting point and ir spectrum was identical with those of the material prepared by the reaction of **5** with water (cf. Table II).

The same reaction performed for an extended period of time gave, in addition, a moderate quantity of *n*-propyl *N*-benzoylcarbamate (**7**), mp 122–124°, whose ir spectrum was identical with that of **7** made from **6** by the method described below.

D. Isopropyl Alcohol.—A solution of 0.81 g (0.0025 mol) of **5** in 40 ml of *i*-PrOH was heated under reflux. The solvent was removed under reduced pressure and the residue was triturated with a minimum of cold water to remove the ammonium iodide present. Tlc of the dried water-insoluble residue (0.40 g) showed the presence of **1**, **2**, **6**, and **8**. The relative quantities of each component of this complex mixture was obtained by means of nmr and elemental analysis. Nmr integration gave the percentage of **6** by comparing the S-CH₃ peak area at δ 2.55 with that of the aromatic protons at 7.60–8.35. A further comparison of the *gem*-dimethyl peak areas of the isopropyl group at δ 1.48 with the aromatic proton area gave the percentage of **8**. Microanalysis gave the sulfur content of the mixture. Since sulfur is contained only in **1** and **6** and since the percentage of **6** was obtained by nmr, the percentage of **1** could be calculated by the following relationship: (% **1**)[% S₁] = % S_{found} - (% **6**)[% S₆]. (Percentages in brackets are calculated from empirical formulas.) Finally, the percentage of **2** was assumed to be the difference between 100% and the total of the percentages found for **1**, **6**, and **8**.

E. *tert*-Butyl Alcohol.—A solution of 0.81 g (0.0025 mol) of **5** in 50 ml of *tert*-BuOH was heated under reflux. After the solvent was removed and the residue was triturated with water,

three components were found by tlc. The relative amounts of these components (**1**, **2**, and **6**) were determined as described above for the reaction of **5** with *i*-PrOH. The percentage of **6** in the reaction product was found by means of nmr. By use of this quantity and the sulfur analysis, the percentage of **1** was determined. Finally, the percentage of **2**, which is the difference between 100% and the combined percentages of **1** and **6**, was calculated.

The effluent gases formed in the course of the reaction were passed through an aqueous solution of lead acetate to remove CH₃SH and into a solution of Br₂ in CHCl₃. The latter, decolorized by isobutylene, was evaporated to dryness leaving an oil whose ir was identical with that of an authentic sample of 1,2-dibromo-2-methylpropane and whose nmr was the same as the published spectrum²² of this compound.

F. Water. Formation of Methyl Thiocarbamates.—A solution of 0.01 mol of **5** in 20 ml of H₂O was heated near the reflux temperature during which time there was little evolution of methyl mercaptan detected. From the reaction mixture there was isolated **6** in excellent yield. Ammonium iodide was contained in the mother liquors.

Compounds **9**–**12** were treated with H₂O in a like manner to give methyl thiocarbamates (cf. Table II).

***n*-Propyl *N*-Benzoylcarbamate (7).**—A solution of 1.95 g (0.01 mol) of **6** in 30 ml of *n*-PrOH was heated under reflux for 24 hr. Methyl mercaptan was slowly evolved and from the solution, which contained some unreacted starting material, was isolated 0.64 g (31%) of *n*-propyl 1-benzoylcarbamate, mp 122–124° (from *n*-PrOH).

Anal. Calcd for C₁₁H₁₃NO₃: C, 63.75; H, 6.32; N, 6.76. Found: C, 64.08; H, 6.52; N, 6.80.

The ir spectrum was identical with that of the product, mp 122–124°, obtained by the reaction of benzoyl isocyanate with *n*-propyl alcohol.

Isopropyl *N*-Benzoylcarbamate (8).—An *i*-PrOH solution of **6** was heated for 48 hr as described above. After removal of several crops of starting material from the solution, 0.25 g (12%) of isopropyl *N*-benzoylcarbamate was obtained, mp 100–102° (lit.²³ mp 99–100°). The analytical sample was recrystallized from *i*-PrOH.

Anal. Calcd for C₁₁H₁₃NO₃: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.85; H, 6.09; N, 7.02.

1-Acetyl-2-methyl-2-thiopseudourea Hydriodide (9).—The title compound was synthesized in 81% yield from 1-acetyl-2-thiourea and methyl iodide as described above for the benzoyl derivative, **5**. Compound **9** melted at 161–164° (lit.²⁴ mp 148–149°) and was recrystallized from CH₃CN.

Anal. Calcd for C₈H₉IN₂OS: C, 18.47; H, 3.49; N, 10.77; S, 12.33. Found: C, 18.54; H, 3.58; N, 10.60; S, 12.50.

Reaction of 9 with Ethyl Alcohol.—A solution of 1-acetyl-2-methyl-2-thiopseudourea in EtOH was heated for 3 hr causing the evolution of methyl mercaptan. From the solution was isolated 83% acetylurea, mp 225–226° (lit.²⁵ mp 217°), whose ir was identical with that of an authentic sample.

1-Benzoyl-2-thiobiuret.—Benzoyl chloride (14.0 g, 0.1 mol) was slowly added to 9.7 g (0.12 mol) of sodium thiocyanate in 70 ml of warm acetone and the mixture was heated an additional 15 min. The benzoyl isothiocyanate solution was cooled to room temperature and the NaCl which formed was removed by suction with the assistance of a filter aid. The filtrate was then heated for 1 hr with 6.0 g (0.1 mol) of urea. The resultant solution was cooled and the product was collected and then recrystallized from CH₃CN to give 10.5 g (47%) of 1-benzoyl-2-thiobiuret as yellow crystals, mp 173–175°. The analytical sample was recrystallized from MeOH.

Anal. Calcd for C₉H₉N₃O₂S: C, 48.42; H, 4.06; N, 18.82; S, 14.37. Found: C, 48.17; H, 4.09; N, 18.87; S, 14.44.

Thiobiuret (13).—1-Benzoyl-2-thiobiuret (1.12 g, 0.005 mol) in 20 ml of MeOH containing 1 drop of concentrated HCl was heated under reflux for 24 hr. The solution was evaporated under reduced pressure to dryness and the residue was extracted with hexane to remove the methyl benzoate. The hexane-insoluble material was recrystallized from H₂O (charcoal) to

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give 0.44 g (75%) of **13** as white crystals, mp 189–193° (lit.⁷ mp 186°).

Anal. Calcd for C₂H₅N₃O₂S: C, 20.16; H, 4.23; N, 35.27; S, 26.92. Found: C, 20.31; H, 4.39; N, 34.97; S, 26.69.

2-Methyl-2-thiopseudobiuret Hydriodide (10).—To 5.95 g (0.05 mol) of thiobiuret suspended in 50 ml of CH₃CN was added 8.52 g (0.06 mol) of methyl iodide and the mixture was heated under reflux for 0.5 hr. The product, which separated as white shiny plates from the hot medium, was collected from the cooled mixture to give (11.3 g, 87%) of 2-methyl-2-thiopseudobiuret hydriodide, mp 181–183° (from CH₃CN).

Anal. Calcd for C₃H₇N₃O₂S: C, 13.80; H, 3.09; N, 16.09; S, 12.28. Found: C, 13.87; H, 2.96; N, 16.11; S, 12.20.

Reaction of 10 with Ethyl Alcohol.—A solution of 1.31 g (0.005 mol) of **10** in 25 ml of EtOH was heated under reflux for 24 hr during which time methyl mercaptan was evolved. The solution was then concentrated and cooled giving 0.44 g (85%) of biuret (from EtOH), mp 193–194° (lit.²⁸ mp 193°); its ir spectrum was identical with the spectrum of an authentic sample.

Reaction of 2-Methyl-2,4-dithiopseudobiuret Hydriodide (11) with Ethyl Alcohol.—A 25-ml EtOH solution of 2-methyl-2,4-dithiopseudobiuret hydriodide (**11**)¹⁰ was heated under reflux for 24 hr. From the concentrated solution was isolated 0.30 g (58%) of biuret.

1-(4-Nitrophenyl)-2-thiourea.—A suspension of 7.2 g (0.04 mol) of 4-nitrophenyl isothiocyanate in 35 ml of MeOH and 15 ml of 28% ammonium hydroxide was warmed on a steam bath for 20 min. The cooled mixture was filtered and the precipitate washed with MeOH to give 6.8 g (85%) 1-(4-nitrophenyl)-2-thiourea, mp 215–218° (lit.²⁷ mp 189–190°).

Anal. Calcd for C₇H₇N₃O₂S: C, 42.63; H, 3.58; N, 21.31; S, 16.26. Found: C, 42.31; H, 3.64; N, 21.31; S, 16.04.

2-Methyl-1-(4-nitrophenyl)-2-thiopseudourea Hydriodide (12).—A suspension of 1.06 g (0.0075 mol) of methyl iodide and 0.98 g (0.005 mol) of 1-(4-nitrophenyl)-2-thiourea in 10 ml of CH₃CN was heated under reflux for 2 hr. The cooled mixture was filtered and the solid was washed with CH₃CN to give 1.45

g (85%) of 2-methyl-1-(4-nitrophenyl)-2-thiopseudourea hydriodide, mp 188–190°.

Anal. Calcd for C₈H₁₀IN₃O₂S: C, 28.33; H, 2.97; N, 12.39; S, 9.45. Found: C, 28.10; H, 2.91; N, 12.37; S, 9.83.

Reaction of 12 with Ethyl Alcohol. Formation of 4-Nitrophenylurea.—A 17-ml EtOH solution containing 1.0 g (0.003 mol) of **12** was heated under reflux for 24 hr and cooled. From the solution was isolated 0.3 g (65%) of 4-nitrophenylurea, mp 228–230°, which resolidifies and then remelts at 328–330° (lit.²⁸ mp 237–238°). The analytical sample was recrystallized from (CH₃)₂CO–EtOH.

Anal. Calcd for C₇H₇N₃O₂: C, 46.41; H, 3.89; N, 23.20. Found: C, 46.59; H, 3.94; N, 22.94.

From the concentrated mother liquors was also isolated 120 mg (12%) of methyl *N*-(4-nitrophenyl)thiocarbamate whose ir spectrum was identical with that of the material which was synthesized by the reaction of **12** with H₂O (cf. Table II).

Mercaptan Synthesis from 1-Acetyl-2-thiourea (14) and Alkyl Halides.—Each of a series of alkyl halides (cf. Table III) was heated under reflux with 1.1 equiv of **14** in ethanol (~1000 ml/mol of halide). After 24 hr, the solvent was removed under reduced pressure and the residue containing the mercaptan, 1-acetylurea, and the unreacted starting materials was transferred to an alumina (activity II) chromatography column by means of petroleum ether (bp 30–60°). Elution of the column with this solvent permitted the passage of only the mercaptan and the unreacted alkyl halide. The yields of the mercaptans were determined iodometrically.

Registry No.—**1**, 614-23-3; **5**, 6966-84-3; **7**, 15146-42-6; **8**, 34277-73-1; **9**, 924-51-6; **10**, 34277-75-3; **12**, 34277-76-4; **13**, 23228-74-2; 1-benzoyl-2-thiobiuret, 34277-78-6; 1-(4-nitrophenyl)-2-thiourea, 3696-22-8; 4-nitrophenylurea, 556-10-5.

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Halomethyl Metal Compounds. LIII. Reactions of Phenyl(trihalomethyl)mercury Compounds with Thiocarbonyl Derivatives¹

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The reaction of phenyl(bromodichloromethyl)mercury with thiophosgene gave tetrachlorothirane in excellent yield. This product also was formed in the reaction of this mercury reagent with elemental sulfur; its thermolysis gave tetrachloroethylene and sulfur. Similar reactions of PhHgCCl₂Br, PhHgCClBr₂, and PhHgCBr₃ with thiobenzophenone gave 2,2-dichloro-, 2-bromo-2-chloro-, and 2,2-dibromo-3,3-diphenylthirane, respectively, in good yield. The first of these underwent extrusion of sulfur on thermolysis, but the second and third lost HBr on being heated to give 2-chloro-3-phenylbenzo[b]thiophene and 2-bromo-3-phenylbenzo[b]thiophene, respectively. The latter was converted to the Grignard reagent which was hydrolyzed and carboxylated.

The addition of CX₂ (X = halogen), either as the free carbene or *via* a carbenoid reagent, to the C=C and C=C bonds is well known.⁵ Some examples are known of such additions to the C=N bond⁶ and to the

C=O bond,⁷ but CX₂ addition to the C=S bond has been restricted to a few examples involving difluorocarbene derived from pyrolysis of perfluoropropylene oxide (eq 1).⁸ Addition of dichloro- or dibromocarbene, or of an appropriate "dihalocarbenoid," to any kind of C=S bond had not been reported.

Various diazoalkanes are known to react with thio-

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