and poured into 15 ml. of ice water. The white solid that precipitated was removed by filtration and dried at 60° *in vacuo* over phosphorus pentoxide; yield, 430 mg. (64%); m.p., 83.5°. λ_{max} in mμ ($\epsilon \times 10^{-3}$): *p*H 1—238, 298 (15.9, 14.3); *p*H 7—288 (17.9); *p*H 13—288 (17.9).

Anal. Calcd. for $C_9H_{11}ClN_4S$: C, 44.50; H, 4.51; Cl, 14.59. Found: C, 44.46; H, 4.50; Cl, 14.52.

Acknowledgment. The authors are indebted to Dr. W. J. Barrett and the members of the Analytical Section of Southern Research Institute who performed the spectral and most of the microanalytical determinations reported, and to Mr. C. L. Kussner for technical assistance. Some of the analyses reported were performed by the Galbraith Microanalytical Laboratories, Knoxville, Tenn.

BIRMINGHAM, ALA.

[CONTRIBUTION FROM ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

Preparation and Some Reactions of Thiobis-*N*-(trifluoromethyl)amines[1]

TRAVIS E. STEVENS

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The fluorination of aryl and alkyl isothiocyanates with iodine pentafluoride in pyridine solution has been found to produce thiobis-*N*-substituted *N*-(trifluoromethyl)amines. The preparation and some of the reactions of these novel compounds are discussed. A unique rearrangement of a thiobisamine to a diphenyl sulfide is reported.

Although iodine pentafluoride is a mild fluorinating agent,[2] very few fluorinations of organic compounds have been explored with this reagent.[3] During the course of an investigation of the reactions of iodine pentafluoride and organic compounds it was found that aryl and alkyl isothiocyanates were converted cleanly to thiobis-*N*-(trifluoromethyl)amines[4] (I) by iodine pentafluoride in pyridine solution.

$$R{-}N{=}C{=}S + IF_5 \longrightarrow R{-}\overset{CF_3}{\overset{|}{N}}{-}S{-}\overset{CF_3}{\overset{|}{N}}{-}R$$

I

Formulation of these products as thiobis amines is based on the analytical data given in Table I, the NMR spectra, and the other experiments discussed below.

Preparation. Fluorination of aromatic isothiocyanates[5] occurred much more readily than did fluorination of their alkyl counterparts, although this is not obvious from the yields reported in Table I. In all the aromatic cases, fluorination was complete after a few minutes at 75–90° and a product free of isothiocyanate was isolated in almost quantitative yield. However, recrystallization of these products from ethanol or hexane was necessary to obtain the melting points reported in Table I. Since the infrared spectrum of the crude product essentially was identical with that of the purified thiobis amine, the material removed by recrystallization may have been the dithiobis-*N*-(trifluoromethyl)amine.[6]

Iodination of the ring of the aromatic isothiocyanates was observed only with phenyl isothiocyanate. Some of the *N*-(*p*-iodophenyl)thiobisamine was isolated in most experiments. If any unsymmetrical thioamine formed it was not isolated.

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(1) This research was carried out under Army Ordnance Contract DA-01-021-ORD-5135.

(2) M. C. Sneed, J. L. Maynard, and R. C. Brasted, *Comprehensive Inorganic Chemistry, Vol. III, The Halogens*, Van Nostrand, New York, 1954, pp. 210–213, General Chemical Division, Allied Chemical and Dye Corporation, Technical Bulletin TA-8532-2, *Chlorine Trifluoride and Other Halogen Fluorides*.

(3) Fluorinations utilizing iodine pentafluoride that have been reported to lead to a trifluoromethyl group include the conversion of ICN to $CF_3—N=N—CF_3$ [O. Ruff and W. Willenberg, *Ber.*, **73**, 724 (1940)] and the formation of trifluoromethyl disulfide from carbon disulfide [R. N. Haszeldine and J. M. Kidd, *J. Chem. Soc.*, 3219 (1953)].

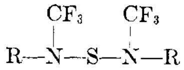
(4) In a preliminary report of this work [T. E. Stevens, Tetrahedron Letters, **17**, 16 (1959)] these compounds were called bis-*N*-(trifluoromethyl)amino sulfides. The name bisamino sulfide is used in E. E. Reid, *Organic Chemistry of Bivalent Sulfur*, Chemical Publishing Co., New York, Vol. II, to denote the symmetrical alkyl sulfides containing amine functions. A section on p. 296 of this volume discusses thioamines.

(5) In an earlier communication[4] it was reported that the fluorination of *p*-nitrophenyl, *p*-acetylphenyl and *p*-dimethylaminophenyl isothiocyanates did not yield thiobisamines. Since then the conversion of the first two compounds to the desired product has been accomplished. The initial failure with the *p*-nitrophenyl isothiocyanate can be attributed to an impure sample; the lack of success with the *p*-acetyl member was due to too stringent reaction conditions (see Experimental). However, several attempts to fluorinate *p*-dimethylaminophenyl isothiocyanate led only to intractable tars.

(6) It generally was observed that attempts to concentrate the mother liquors from the recrystallization of the thiobisamines led to oily products, the infrared spectra of which were indistinguishable from those of the purified products or of the crude products. An oily residue from the *p*-chlorophenyl isothiocyanate reaction contained 10.6% sulfur. The related thiobisamine contains 7.6% sulfur, the dithiobisamine, 14.1% sulfur.

TABLE I

THIOBIS-*N*-(TRIFLUOROMETHYL)AMINES



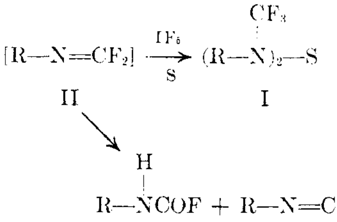
$$R{-}N(CF_3){-}S{-}N(CF_3){-}R$$

R	M.P. (b.p.)	Yield, %	Calcd.			Found			F^{19}NMR,[a] C.p.s.
			C	H	N	C	H	N	
Phenyl	54	26[b]	47.73	2.86	7.95	47.87	3.05	7.81	
p-Fluorophenyl	33	34	43.30	2.08	7.22	43.41	2.30	7.52	−885[c]
p-Chlorophenyl	56	59	39.92	1.91	6.65	39.88	2.00	6.99	−993
p-Bromophenyl[d]	70	69	32.96	1.58	5.49	32.68	1.76	5.46	−927
p-Iodophenyl	104	47	27.83	1.33	4.64	27.96	1.54	4.82	
p-Tolyl[e]	59	40	50.52	3.71	7.37	50.52	3.83	7.60	−932
m-Bromophenyl	(125/0.5 mm.)	90	32.96	1.58	5.49	32.78	1.92	5.47	
p-Nitrophenyl[f]	122	55	38.01	1.82	12.67	37.09	1.95	12.75	
p-Acetylphenyl[g]	92	55	49.54	3.23	6.42	48.65	3.24	6.56	
Ethyl[h]	(44/30 mm.)	48	28.12	3.92	10.94	28.54	4.36	11.34	−761
Butyl[i]	(80/12 mm.)	72	38.45	5.81	8.97	38.71	5.95	8.58	−763
Heptyl[j]	(91/0.5 mm.)	59	48.47	7.63	7.07	47.98	7.51	7.25	−777
Dodecyl	[k]	*ca.* 80	58.18	9.39	5.22	58.62	9.23	5.47	
Cyclohexyl[l]	(93/0.3 mm.)	29	46.14	6.09	7.69	45.83	5.99	6.89	
1-Phenylethyl	(128/0.4 mm.)	25	52.93	4.44	6.86	52.97	4.45	7.27	

[a] Relative to external trifluoroacetic acid, 40 mc. probe. [b] The crude product was a mixture of this and iodophenylthiobisamines. [c] Resonance at +1412 c.p.s. due to aromatic C-F. [d] Also found: F, 22.0; S, 6.59. Calcd.: F, 22.35; S, 6.29. [e] Also found: F, 29.6; Calcd.: 30.0. [f] Also found: F, 25.9; Calcd.: 25.8. [g] Also found: F, 26.0; Calcd.: 26.1. [h] n_D^{20} 1.3632. [i] n_D^{20} 1.3880; Also found: F, 36.4; Calcd.: F, 36.50. [j] n_D^{20} 1.4115. Also found: S, 7.69. Calcd.: S, 8.09. [k] Sample not distilled. [l] n_D^{20} 1.4548.

As Table I indicates, the reaction was less successful with secondary alkyl isothiocyanates. Also, only a small amount of thiobisamine could be obtained from a tertiary alkyl isothiocyanate such as *t*-octyl, and the separation of this from the other products (isocyanate and carbamyl fluoride[7]) of the reaction was not successful. Apparently some stage of the reaction is subject to steric hindrance.

The manner of formation of the thiobisamines I from isothiocyanates in pyridine solution is not obvious.[8] It is conceivable that a carbonimidyl fluoride such as II is an intermediate in this reaction. It is well known that aromatic isothiocyanates[9] and aromatic and aliphatic isonitriles[10] react with chlorine to produce carbonimidyl chlorides. The isolation of *N*-trifluoromethyl secondary amines from the reaction of hydrogen fluoride and carbonimidyl chlorides also was reported recently.[11]



$$[R{-}N{=}CF_2] \xrightarrow[S]{IF_5} (R{-}N(CF_3))_2{-}S \qquad II \rightarrow R{-}N(H)COF + R{-}N{=}C{=}O$$

Rationalization of the results obtained, particularly with the aliphatic isothicyanates,[7] is reasonably straightforward if it is assumed that the carbonimidyl fluoride, as a reactive intermediate, can be converted to the thiobisamine by the sulfur-iodine fluoride-pyridine mixture, or to the carbamyl fluoride and isocyanate by hydrolysis during work-up.[12] Steric hindrance in the intermediate II probably accounts for the lack of success in converting secondary and tertiary alkyl isothiocyanates to thiobis amines.

Preparation of the thiobis-*N*-(trifluoromethyl)-amines from iodine pentafluoride, sulfur and isoni-

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(7) The infrared spectra of these crude reaction mixtures from the fluorination of all the alkyl isothiocyanates possessed absorption at about 4.5 μ due to the isocyanate and at 5.5 to 5.6 μ due to carbamyl fluoride. The *p*-chlorophenylcarbamyl fluoride characterized in the experimental section exhibited carbonyl absorption at 5.6 μ. From the ethyl isothiocyanate–iodine pentafluoride reaction was obtained a fraction, b.p. 40° (65 mm.), which possessed the infrared spectrum expected for I, R = ethyl, (strong absorption, 7.8–8.8 μ) contaminated by material absorbing at 5.6, 6.5 and 10.5 μ. Chromatography on silica gel removed the latter compound. The *N*-ethylformamide-iodine pentafluoride reaction afforded a compound having the same 5.6 6.5 and 10.5 μ absorption bands in the infrared. This material was converted to *N*,*N*,-diethylurea, m.p. 111°, on reaction with ethylamine in benzene.

(8) Iodine pentafluoride and pyridine appear to undergo no reaction at temperatures up to 115° other than an apparent complex formation. Addition of iodine pentafluoride to pyridine results in an exothermic reaction, and on cooling, a white solid is observed. No attempt was made to characterize this complex. A dioxane–iodine pentafluoride complex has been reported by A. F. Scott and J. F. Bunnett, *J. Am. Chem. Soc.*, **64,** 2727 (1942), and iodine pentafluoride and dimethylformamide also appear to complex (T. E. Stevens, *Chem. & Ind.*, 1090 (1958)).

(9) G. M. Dyson and T. Harrington, *J. Chem. Soc.*, 191 (1940), 150 (1942). R. S. Bly, G. A. Perkins, and W. C. Lewis, *J. Am. Chem. Soc.*, **44,** 1896 (1922).

(10) J. U. Nef, *Ann.*, **270,** 267 (1892). R. A. Smith and N. W. Kalenda, *J. Org. Chem.* **23,** 1599 (1958).

(11) K. A. Petrov and A. A. Neimysleva, *J. Gen. Chem. USSR*, **29,** 2131 (1959) (Engl. trans.).

(12) The hydrolysis of $CF_3N{=}CF_2$ to CF_3NCO has been reported, J. H. Young, S. N. Tsoukalas, and R. D. Dresdner, *J. Am. Chem. Soc.*, **80,** 3604 (1958).

triles, formamides, and isocyanates[13] also was explored. Thiobis-*N*-(*n*-butyl)-*N*-(trifluoromethyl)amine was obtained from both *n*-butylisonitrile (43%) and *N*-*n*-butylformamide (21%), but there was no evidence for thiobisamine formation in the *n*-butyl isocyanate-iodine pentafluoride-sulfur reaction. Although *p*-bromophenylisonitrile could be converted to thiobis-*N*-(*p*-bromophenyl)-*N*-(trifluoromethyl)amine in low yield (18%), this preparation was not successful with either *p*-bromophenyl isocyanate or *p*-bromophenylformamide.

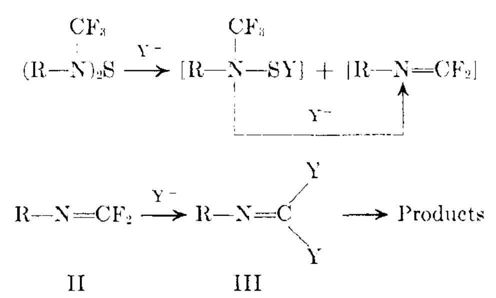
$$R-\overset{+}{N}=\overset{-}{C} + S + IF_5 \longrightarrow I$$

Since the isonitrile-sulfur mixture is known to lead to isothiocyanates[14] this preparation of the thiobisamines cannot be taken as evidence for the direct formation of a carbonimidyl fluoride, although it is probable that such an intermediate is produced initially.[15] Dehydration of *n*-butylformamide to *n*-butylisonitrile probably accounts for the formation of the thiobisamine from this substrate.[16]

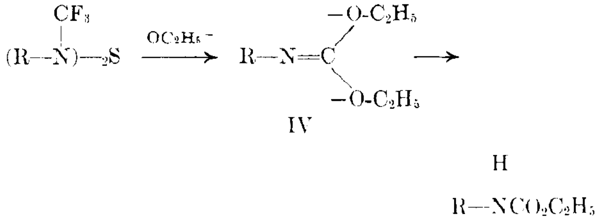
Degradation by basic reagents. During the analysis of these thiobisamines, quantitative liberation of fluoride ion was observed on treatment of the trifluoromethyl compound with aqueous ethanolic sodium hydroxide[17]; all the fluorine analyses reported in Table I were obtained in this fashion. Examination of the organic products of this hydrolysis, conducted in 75% aqueous ethanol containing an excess of sodium hydroxide, revealed that both the thiobis-*N*-(*p*-chlorophenyl)-*N*-(trifluoromethyl)amine and the thiobis-*N*-(*p*-bromophenyl)-*N*-(trifluoromethyl)amine were converted to a mixture of the corresponding aromatic amine and urethan. When the thiobisamines were exposed to an ethanol-water-hydrochloric acid mixture, the same products were isolated.

The *N*-*p*-chlorophenyl- and *N*-*p*-bromophenylthiobisamines also were exposed to an aqueous sodium hydroxide-acetonitrile mixture. Both were hydrolyzed readily and the respective ureas were obtained.

The results of these cleavage reactions indicated a carbon-sulfur bond was not present in the thiobisamines, and pointed to the following pathway for the basic degradation.



It was possible to obtain the diethyl *N*-substituted imidocarbonates (IV) cleanly from the reaction of the thiobisamines and excess sodium ethoxide in ethanol. The isolation of two aromatic imidocarbonates (IV, R = phenyl and *p*-chlorophenyl) and two alkyl imidocarbonates (IV, R = *n*-butyl and *n*-heptyl) is detailed in the Experimental section.



Chromatography on a silica gel column caused the imidocarbonates to hydrolyze to urethans.

The formation of diethyl *N*-phenylimidocarbonate (IV, R = phenyl) from the interaction of sodium ethoxide and *N*-phenylcarbonimidyl dichloride (III, R = phenyl, Y = Cl) has been reported,[18] and provides an analogy for the suggestion of the substituted carbonimidyl difluorides II as intermediates in these degradations.

Reactions with acidic reagents. In addition to the hydrolyses of the thiobisamines by aqueous hydrochloric acid mentioned above, other acid-catalyzed reactions were explored. Cleavage of the N—S bond in several of the aromatic derivatives of I, with the formation of an *N*-(trifluoromethyl)acetamide, was accomplished with acetic anhydride or acetyl chloride containing sulfuric acid. The *N*-

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[13] Several isocyanate (*n*-butyl, *p*-bromophenyl, phenyl)-iodine pentafluoride reactions were conducted, there was no evidence for the formation of any oxobis-*N*-(trifluoromethyl)amines. At higher temperatures (115°) intractable mixtures were formed. Under milder conditions the main product isolated was the urea formed during hydrolysis of the reaction mixture.

[14] J. Houben, *Die Methoden der Organischen Chemie*, Georg Thieme Verlag, Leipzig, Germany (1941), Vol. 4, p. 31.

[15] The results obtained from several isonitrile-iodine pentafluoride reactions can be explained on the basis of a carbonimidyl fluoride intermediate. *t*-Octylisonitrile, after the usual hydrolysis of the reaction mixture,

$$R-\overset{+}{N}=\overset{-}{C} + IF_5 \longrightarrow [R-N=CF_2] \xrightarrow{H_2O} R-\overset{H}{\overset{|}{N}}COF + RNCO$$

was converted cleanly to *t*-octyl isocyanate[12], only a trace of carbamyl fluoride was indicated by the infrared spectrum of the crude product. However, cyclohexylcarbamyl fluoride was the initial product of the cyclohexyl isonitrile-iodine pentafluoride reaction, but this fluoride decomposed to isocyanate during distillation.

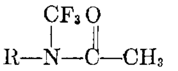
[16] The iodine pentafluoride-pyridine dehydration of formamide to isonitriles is not surprising in view of other means of accomplishing the same results, see W. R. Hertler and E. J. Corey, *J. Org. Chem.*, **23**, 1221 (1958), I. Ugi and R. Meyer, *Ber.*, **93**, 239 (1960). Of course, the complications introduced by iodine pentafluoride prevent this method from being a route to isonitriles.

[17] Analyses and method by Mr. R. Donald Strahm.

[18] L. Smith, *Am. Chem. J.*, **16**, 390 (1894).

TABLE II

N-TRIFLUOROMETHYLACETAMIDES

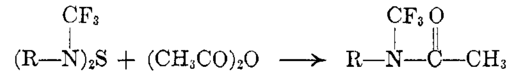


$$R-N(CF_3)-C(=O)-CH_3$$

	M.P.	C	H	N	C	H	N
p-Fluorophenyl	[a]	48.88	3.19	6.33	49.21	3.81	6.35
p-Bromophenyl[b]	52	38.32	2.50	4.96	38.38	2.43	4.64
p-Iodophenyl[c]	59	32.85	2.15	4.25	33.29	2.27	4.20
p-Tolyl	34	55.30	4.64	6.45	54.44	4.77	6.35
p-Chlorophenyl	43	45.49	2.97	5.89	45.30	3.23	5.68

[a] n_D^{20} 1.4482. F^{19} NMR, resonance at −875 cps ($-CF_3$) and at +1332 cps (aromatic C—F). [b] F: Calcd., 20.21; Found: 20.29; [c] F: Calcd., 17.32; Found: 16.53.

(trifluoromethyl)acetamides (V) prepared in this fashion are listed in Table II.

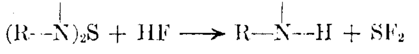


$$(R-N(CF_3))_2S + (CH_3CO)_2O \longrightarrow \underset{V}{R-N(CF_3)-C(=O)-CH_3}$$

The acetamide V, R = phenyl, also was prepared, but was not obtained analytically pure. Crude samples of V, R = *n*-butyl and R = *n*-heptyl were obtained (as evidenced by infrared spectra).

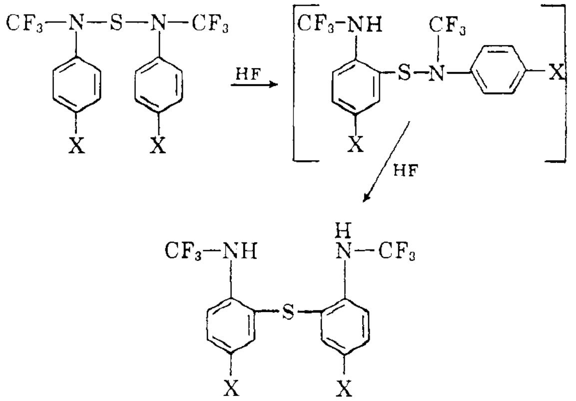
On treatment with ethanolic sodium ethoxide, V, R = *p*-chlorophenyl, was converted to diethyl *N*-(*p*-chlorophenyl) imidocarbonate, undoubtedly *via* the same intermediates as postulated for the ethanolysis of I.

Acid catalysis of acylation may be due either to protonation of the acylating agents or to acid-catalyzed cleavage of the thiobisamines prior to acylation. The latter possibility suggested an attempt to prepare the trifluoromethylamines[11] by cleavage of the thiobisamines with hydrogen fluoride, i.e.,



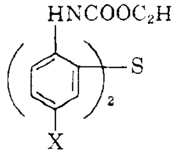
$$(R-N(CF_3))_2S + HF \longrightarrow R-N(CF_3)-H + SF_2$$

Treatment of aromatic thiobisamines with hydrogen fluoride either gave intractable products or new products having compositions indicating that they were *isomers* of the starting materials. Infrared spectra of the new compounds showed N—H frequencies at 2.93 μ and had lost the absorption in the 7.8-9.0 μ region which is characteristic of thiobisamines. The F^{19} NMR spectra contains doublets near −900 cps with a small splitting, indicating the presence of $-NH-CF_3$ groups (see Table I). The results indicate that rearrangements have occurred in such a way as to generate an N-H group and retain both the sulfur and the $N-CF_3$ linkages. Since *para* substituents (CH_3, Br and Cl) were retained, it seems likely that the rearrangement involves migration of sulfur from nitrogen to an *ortho* position.



VI

Treatment of the products with sodium ethoxide gives urethans having compositions corresponding to VII.



VII

The urethan, VII, with X = CH_3 has been reported previously.[19] Rearrangement of thiobis-*N*-trifluoromethyl-*p*-toluidine (I, R = *p*-tolyl) and degradation of the product with sodium ethoxide gave a small amount of a urethan melting at 110°, 3° lower than the literature value. Since the yield was low it would probably be advisable to base a rigorous structure proof on one of the other series of compounds.

The rearrangement would be analogous to Fries rearrangements and the acid-catalyzed rearrangements of *N*-haloanilides. We have no real evidence as to whether the reaction is intramolecular or intermolecular. However, several observations indicate that para positions may become involved. The *N*-phenylthiobisamine gave an intractable mixture of products; the *N*-(*p*-iodophenyl) compound evolved iodine when treated with hydrofluoric acid; and the *p*-bromo compound gave a mixture which, on treatment with sodium ethoxide, gave *p*-bromophenylurethan and 2,4-dibromophenylurethan in addition to the expected product (VII, X = Br). The latter two results suggest that electrophilic displacement of positive iodine and positive bromine occur.

EXPERIMENTAL

Melting points and boiling points are uncorrected. Iodine pentafluoride was obtained from the Matheson Co.; it was pumped *in vacuo* from the cylinder, trapped in a Kel-F test tube at −78°, and allowed to melt in a stream of dry nitrogen. The test tube then was detached from the vacuum line and the iodine pentafluoride was withdrawn and measured in a glass pipet. The isothiocyanates used were obtained

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(19) M. T. Bogert and M. R. Mandelbaum, *J. Am. Chem. Soc.*, **45**, 3045 (1923).

from commercial sources or prepared by standard methods.[20]

The procedures used for the preparation of the thiobisamines listed in Table I are illustrated by the examples given below.

Reaction of p-chlorophenyl isothiocyanate and iodine pentafluoride in pyridine. A mixture of 35 ml. of pyridine and 8.86 g. (0.052 mole) of *p*-chlorophenyl isothiocyanate was warmed to 65° and the dropwise addition of iodine pentafluoride (4.0 ml., 0.057 mole) was carried out so as to maintain a reaction temperature of 75–80°. The solution gradually darkened, and when about one-half of the iodine pentafluoride had been added a more exothermic reaction occurred; the solution then was only slightly discolored. After the iodine pentafluoride had been added the solution was stirred at 80° for 10 min. The mixture was then poured over crushed ice and extracted with methylene chloride. When the methylene chloride solution had been washed with water, 10% hydrochloric acid and 15% sodium thiosulfate solution, it was dried (magnesium sulfate) and concentrated to 30 ml. This methylene chloride solution was placed on a 1 × 6 in. silica gel column and eluted with 250 ml. of pentane-methylene chloride (1:1). The solid residue obtained on evaporation of this solvent, 10.3 g. (94%), was recrystallized from ethanol-water to give thiobis-*N*-(*p*-chlorophenyl)-*N*-(trifluoromethyl)amine, 6.52 g., m.p. 55–56°. The infrared spectrum (Nujol mull) had only a very weak peak at 6.3 μ in the 3.5 to 6.7 μ region. Strong absorption at 7.80, 8.26, 8.46 and 8.85 μ was observed.

Preparation of thiobis-N-(p-acetylphenyl)-N-(trifluoromethyl)amine. The temperature of a solution of 2.0 g. of *p*-acetylphenyl isothiocyanate in 10 ml. of pyridine was maintained at 60–65° while 1.0 ml. of iodine pentafluoride was added dropwise. The mixture was stirred at 60° for 15 min., and then was poured over crushed ice. The residue obtained from the methylene chloride extraction of the hydrolysis product was extracted with hot hexane. Upon chilling, this extract deposited thiobis-*N*-(*p*-acetylphenyl)-*N*-(trifluoromethyl)amine, 1.36 g. (55%), m.p. 85–87°. The sample was recrystallized from hexane, m.p. 92–93°.

Reaction of butyl isothiocyanate and iodine pentafluoride. A mixture of 8.1 g. (0.070 mole) of *n*-butyl isothiocyanate and 40 ml. of pyridine was stirred at 85–95° while 5.0 ml. (0.071 mole) of iodine pentafluoride was added slowly. The solution was heated at 115° for 4 hr., cooled and poured on ice. The methylene chloride extract of the hydrolysate was concentrated to 25 ml., passed through a short silica gel column with methylene chloride-pentane (1:1) and distilled in the Holzmann column. There was obtained thiobis-*N*-(*n*-butyl)-*N*-(trifluoromethyl)amine, 7.85 g. (72%), b.p. 80° (12 mm.), n_D^{20} 1.3880, d_4^{25} 1.1725.

Reaction of p-bromophenylisonitrile, sulfur and iodine pentafluoride in pyridine. A mixture of 2.55 g. (0.014 mole) of *p*-bromophenylisonitrile, 0.20 g. (0.007 mole) of sulfur and 12 ml. of pyridine was warmed to 65° and 2.0 ml. (0.028 mole) of iodine pentafluoride was added dropwise. An exothermic reaction, controlled by external cooling and the rate of addition of iodine pentafluoride, occurred. The mixture was stirred at 80° for 15 min. after the addition. The product was isolated as described above. The residue from the methylene chloride solution was extracted with pentane: a considerable insoluble residue was discarded. Evaporation of the pentane left a residue which was crystallized from ethanol. Initially a gum separated and was discarded. The ethanol solution then deposited 0.53 g. of thiobis-*N*-(*p*-bromophenyl)-*N*-(trifluoromethyl)amine, m.p. 61–63°, mixed m.p. with an authentic specimen (m.p. 68–69°) 67–69°. The infrared spectrum was identical with that of an authentic specimen.

Sulfur, N-n-butylformamide and iodine pentafluoride. A mixture of 40 ml. of pyridine, 0.73 g. (0.023 mole) of sulfur, and 6.0 ml. (0.084 mole) of iodine pentafluoride was stirred at 85–95° while 4.7 g. (0.047 mole) of *n*-butylformamide in 5 ml. of pyridine was added dropwise. After 1 hr. at 115° the solution was cooled, hydrolyzed, extracted and chromatographed as usual. Distillation gave thiobis-*N*-(*n*-butyl)-*N*-(trifluoromethyl)amine, 1.50 g. (21%) n_D^{20} 1.3892, infrared spectrum identical with that of material prepared from isothiocyanate.

n-Butylisonitrile, sulfur and iodine pentafluoride. The procedure outlined for *n*-butylformamide was followed using 3.9 g. (0.047 mole) of *n*-butylisonitrile, 0.057 mole of iodine pentafluoride and 0.024 mole of sulfur. After the addition of the isonitrile the solution was stirred at 93° (steam bath) for 30 min., then processed as usual. In this manner was obtained thiobis-*N*-(*n*-butyl)-*N*-(trifluoromethyl)amine, 3.13 g. (43%), b.p. 83° (13 mm.), n_D^{20} 1.3880, infrared spectrum identical with that of samples prepared previously.

Hydrolysis of thiobis-N-(p-bromophenyl)-N-(trifluoromethyl)amine. (A) *With ethanolic sodium hydroxide.* To a stirred solution of 1.00 g. of the *p*-bromophenylthiobisamine in 40 ml. of 95% ethanol was added 10 ml. of 20% aqueous sodium hydroxide. The mixture was stirred at 30–40° for 3 hr., then poured into water (150 ml.), acidified with dilute hydrochloric acid and extracted with methylene chloride. The semi-solid obtained upon evaporation of the methylene chloride was chromatographed on a silica gel column. The fraction eluted by 10% ethyl acetate in methylene chloride, 0.314 g. m.p. 82–83° (after hexane recrystallization) was identified as *p*-bromophenylurethan by infrared spectrum and ultimate analysis; reported[21] m.p. 85°. The acidic aqueous layer was basified and re-extracted. From the extract there was obtained *p*-bromoaniline, 0.35 g., m.p. 61–63°, mixed m.p. 63–64°, infrared spectrum identical with that of an authentic specimen.

(B) *Ethanolic hydrogen chloride.* A mixture of 40 ml. of 95% ethanol, 2.0 ml. of concd. hydrochloric acid and 1.00 g. of the *p*-bromophenylthiobisamine was refluxed for 3 hr., then evaporated to dryness under reduced pressure. The residue was shaken with a methylene chloride–water mixture. Separation of the methylene chloride and evaporation to dryness gave 0.55 g. (57.5%) of *p*-bromophenylurethan. The aqueous washes were made basic and extracted with methylene chloride to yield 0.22 g. (33%) of *p*-bromoaniline. Both compounds were identified as described above.

(C) *With aqueous sodium hydroxide in acetonitrile.* A solution containing 20 ml. of acetonitrile, 1.0 g. of the *p*-bromophenylthiobisamine, 2 ml. of water and 3 ml. of 20% aqueous sodium hydroxide was stirred at 35° for 2 hrs. The mixture then was poured into water (150 ml.) and the resulting precipitate was filtered and washed with water. This solid, m.p. >240°; 0.43 g. (59%) was *N,N'-bis-p*-bromophenylurea, reported m.p.[22] 330. The infrared spectrum was identical with that of an authentic sample prepared from *p*-bromophenyl isocyanate and *p*-bromoaniline.

Alkaline degradation of thiobis-N-(p-chlorophenyl)-N-(trifluoromethyl)amine. (A) *Ethanolic aqueous potassium hydroxide.* A solution containing 1.0 g. of the *p*-chlorophenylthiobisamine and 0.0029 mole of potassium hydroxide in 30 ml. of 80% ethanol was stirred for 3 hr. at 30–35°. The reaction mixture was diluted with water, acidified, and processed as described above for the similar hydrolysis of the *p*-bromophenyl compound. There was obtained 0.216 g. (23%) of *p*-chlorophenylurethan, m.p. 65–66°, reported[23] m.p. 68°, and 0.31 g. (51%) of *p*-chloroaniline, m.p. 70–71°, identified by mixture m.p. and infrared spectrum.

(B) *Aqueous sodium hydroxide in acetonitrile.* A solution of 1.0 g. of the *p*-chlorophenylthiobisamine in 20 ml. of acetonitrile containing 2 ml. of water and 3 ml. of 20% sodium

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(20) L. Doub, *et al.*, *J. Am. Chem. Soc.*, **80**, 2205 (1958), F. B. Dains, R. Q. Brewster, and C. P. Olander, *Org. Syntheses*, Coll. Vol. I, 448 (1941).

(21) S. Basterfield, E. L. Woods, and H. N. Wright, *J. Am. Chem. Soc.*, **48**, 2371 (1926).

(22) Beilstein's *Handbuch der Organischen Chemie*, Julius Springer Verlag, Berlin, Germany, 1929, Vol. 12, p. 645.

(23) Ref. 22, p. 614.

hydroxide was stirred at 35° for 2 hr. When this solution was poured into water, *N,N'-bis-p*-chlorophenylurea 0.46 g., precipitated. The sample did not melt at 255°; reported[24] m.p. 306°. The infrared spectrum was consistent with the urea structure.

Anal. Calcd. for $C_{13}H_{10}Cl_2N_2O$: N, 9.97. Found: N, 10.00.

(C) *Sodium ethoxide in ethanol.* A solution of 2.10 g. (5-mmoles) of the *p*-chlorophenylthiobisamine in 10 ml. of ethanol was added dropwise to 25 ml. of ethanol containing 40 mmoles of sodium ethoxide at 20°. The mixture was stirred at 35–40° for 3 hr., then poured into water and extracted with methylene chloride. The residue from the methylene chloride possessed an infrared spectrum identical with that of the sample of diethyl *N*-(*p*-chlorophenyl)imidocarbonate prepared from sodium ethoxide and *N*-(trifluoromethyl)-*N*-(*p*-chlorophenyl)acetamide. This residue was chromatographed on a 1 × 12'' silica gel column; eluents were pentane–methylene chloride (1:1), methylene chloride, and methylene chloride–ethyl acetate (9:1). Methylene chloride eluted 1.80 g. (90%) of *p*-chlorophenylurethan, m.p. 68–69° after one recrystallization from hexane, reported[23] m.p. 68°.

Reaction of thiobis-N-phenyl-N-(trifluoromethyl)amine and sodium ethoxide. A solution of 2.0 g. (5.7 mmoles) of the *N*-phenylthiobisamine in 10 ml. of ethanol was added dropwise to a solution of 46 mmoles of sodium ethoxide in 25 ml. of ethanol at 20°. After stirring at 40–45° for 3 hr. the solution was poured into water and extracted with methylene chloride. The residue from the methylene chloride, diethyl *N*-phenylimidocarbonate, 2.11 g. (96%), was flash distilled at 100° (5 mm.) to give a colorless liquid, n_D^{20} 1.5140, reported[10] b.p. 122° (12 mm.)

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.36; H, 7.83; N, 7.25. Found: C, 68.02; H, 7.38; N, 7.48.

A 1.00-g. sample of this liquid was chromatographed on silica gel as described above. From the methylene chloride eluates, phenylurethan was obtained, 0.80 g. (94%), m.p. 49–50° after recrystallization from hexane. A mixed m.p. with an authentic sample of the same m.p. was 49–50°; the infrared spectra of the two samples were identical.

Reaction of thiobis-N-(n-butyl)-N-(trifluoromethyl)amine and sodium ethoxide. To 40 ml. of ethanol containing 70 mmoles of sodium ethoxide was added a solution of 3.125 g. (10 mmoles) of the *N-n*-butylthiobisamine in 10 ml. of ethanol. The solution was refluxed for 3 hrs., then poured into 300 ml. of distilled water in which sodium chloride had been dissolved. The aqueous mixture was extracted with methylene chloride, and the methylene chloride extract was washed three times with portions of distilled water. The aqueous extracts were combined; they were found to contain 1.137 g. of fluoride ion (99.7% recovery). The methylene chloride extracts were evaporated at reduced pressure and the dark residue was distilled in the Holzmann column. Distillation gave diethyl *N*-(*n*-butyl)imidocarbonate, 2.77 g. (80%) as a colorless liquid, n_D^{20} 1.4217.

Anal. Calcd. for $C_9H_{19}NO_2$: C, 62.39; H, 11.06; N, 8.09. Found: C, 62.04; H, 10.87; N, 8.39.

Reaction of sodium ethoxide and thiobis-N-(n-heptyl)-N-(trifluoromethyl)amine. The procedure outlined for the sodium ethoxide-*n*-butylthiobisamine reaction was followed using 3.97 g. (10 mmoles) of the *n*-heptylthiobisamine and 70 mmoles of sodium ethoxide. Distillation of the residue from the organic extract gave 3.63 g. (84%) of diethyl *N*-(*n*-heptyl)imidocarbonate, n_D^{20} 1.4311.

Anal. Calcd. for $C_{12}H_{25}NO_2$: N, 6.50. Found: 6.85.

The *N*-(trifluoromethyl)acetamides listed in Table III were prepared by the following procedures.

(A) *Reaction of acetic anhydride and thiobis-N-(p-chlorophenyl)-N-(trifluoromethyl)amine.* A mixture of 5.0 g. of the *p*-chlorophenylthiobisamine, 25 ml. of acetic anhydride and 2.0 ml. of concd. sulfuric acid was swirled and allowed to stand at ambient temperature for 2 hr. The mixture then was poured into 200 ml. of water and stirred 1 hr. The aqueous mixture was extracted with methylene chloride; these organic extracts were washed with 10% aqueous sodium bicarbonate and with water and dried over magnesium sulfate. Evaporation of the methylene chloride left 5.21 g. (93%) of *N*-(trifluoromethyl)-*N*-(*p*-chlorophenyl)-acetamide as an oil. This oil was recrystallized from hexane to give the solid acetamide, 3.73 g., m.p. 42–43°.

(B) *Reaction of acetyl chloride and thiobis-N-(p-chlorophenyl)-N-(trifluoromethyl)amine.* A mixture of 1.0 g. of the *p*-chlorophenylthiobisamine, 5.0 ml. of acetyl chloride and 0.25 ml. of concd. sulfuric acid was allowed to stand at ambient temperature for 2 hr. The mixture was poured on ice and then was extracted with methylene chloride. Evaporation of the methylene chloride left 1.07 g. of *N*-(trifluoromethyl)-*N*-(*p*-chlorophenyl)acetamide, m.p. 42–43° after recrystallization from hexane.

Reaction of sodium ethoxide and N-(p-chlorophenyl)-N-(trifluoromethyl)acetamide. A solution of 2.38 g. (10 mmoles) of the above acetamide in 10 ml. of ethanol was added dropwise to 25 ml. of ethanol containing 40 mmoles of sodium ethoxide. The mixture was stirred at 40–45° for 3 hr., poured into water, and the aqueous mixture was extracted with methylene chloride. The residue obtained on evaporation of the methylene chloride at reduced pressure left diethyl *N*-(*p*-chlorophenyl)imidocarbonate, 2.03 g. (89%) as a viscous oil. The sample was flash distilled at 0.01 mm. prior to analysis.

Anal. Calcd. for $C_{11}H_{14}NO_2Cl$: C, 58.02; H, 6.20; N, 6.15. Found: C, 57.71; H, 5.85; N, 6.30.

Hydrolysis of diethyl N-(p-chlorophenyl)imidocarbonate. A solution consisting of 0.51 g. of diethyl *N*-(*p*-chlorophenyl)-imidocarbonate, 1.0 ml. of concd. hydrochloric acid and 10 ml. of 70% ethanol was warmed on the steam bath for 30 min., then poured into 100 ml. of water and extracted with methylene chloride. Evaporation of the methylene chloride left 0.08 g. of diethyl carbonate, identified by infrared spectrum. The aqueous solution remaining was made basic with aqueous potassium hydroxide and extracted with methylene chloride. Evaporation of the methylene chloride left *p*-chloroaniline, 0.21 g., m.p. 64–66°, identified by mixed m.p. and infrared spectrum.

Oxidation of thiobis-N-(p-bromophenyl)-N-(trifluoromethyl)amine. A mixture containing 1.0 g. of the *p*-bromophenylthiobisamine, 2.6 ml. of 30% hydrogen peroxide and 15 ml. of acetic acid was refluxed for 1 hr., then allowed to stand at ambient temperature for 2 days. This solution was poured into water (50 ml.); a solid separated and was removed by filtration. A total of 0.44 g. of *p*-nitrobromobenzene, m.p. 118–120°, reported[25] m.p. 125°, was collected. The infrared spectrum was identical with that of an authentic specimen.

Reaction of hydrogen fluoride and thiobis-N-(p-chlorophenyl)-N-(trifluoromethyl)amine. A solution of 5.0 g. of the *p*-chlorophenylthiobisamine in 200 ml. of methylene chloride in a polyethylene bottle was stirred magnetically and cooled to −20° while 5 ml. of anhydrous hydrogen fluoride was swept into the mixture by a nitrogen stream. After the addition of the hydrogen fluoride, the nitrogen stream was continued and the cooling bath was removed and the solution was allowed to warm to 20° over 1 hr. The mixture then was stirred 30 min. at 35–40°. The methylene chloride was removed at reduced pressure, and the residue was taken up in warm hexane (35 ml.). The hexane solution was filtered and then evaporated under reduced pressure to leave 4.81 g. of solid residue. The infrared spectrum of this residue had strong absorption at 2.93 μ; very weak bands near 5.5μ (carbamyl fluoride) and 9.83 μ (unchanged starting material) were present. Absorption bands at 7.80 (strong), 8.10 (medium), 8.55 (medium) and 9.05 μ (strong) formed a characteristic pattern different from that of the starting thiobis amine. The residue was recrystallized (0°) from 16 ml. of hexane. In this manner 3,3'-dichloro-6,6'-

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[24] Ref. 25, p. 615.

[25] Ref. 22, Vol. 5, p. 248.

bis[*N*-(trifluoromethyl)amino]diphenyl sulfide, 2.45 g., m.p. 69–71° was isolated. An additional 0.80 g. of product, m.p. 64–67°, was obtained by chilling the filtrate to −80°, and then recrystallizing the solid from hexane. The sample melted at 74–75° after additional recrystallization from hexane.

Anal. Calcd. for $C_{14}H_{18}N_2F_6Cl_2S$: C, 39.93; H, 1.91; N, 6.65; F, 27.07; S, 7.61. Found: C, 40.07, 40.14; H, 2.06, 2.27; N, 6.59, 6.94; F, 26.72, 27.04; S, 8.27.

The *p*-chlorophenylcarbamoyl fluoride formed in the reaction was less soluble in hexane than the diphenyl sulfide and was removed as the first crop of crystals formed during recrystallization from hexane. It melted at 114–115°.

Anal. Calcd. for C_7H_5ClNOF: N, 8.07; F, 10.95. Found: N, 8.06; F, 11.23.

The *p*-chlorophenylcarbamyl fluoride, 40 mg., was dissolved in 5 ml. of absolute ethanol containing a trace of pyridine. The solution was warmed to 60°, then stripped to dryness at reduced pressure. The residue consisted of *p*-chlorophenylurethan, 42 mg. (91%), m.p. 65–66°. The infrared spectrum was identical with that of samples prepared previously, and a mixed m.p. with a sample of m.p. 68–69° was 67–68°.

Reaction of hydrogen fluoride and thiobis-N-(p-fluorophenyl)-N-(trifluoromethyl)amine. A solution of 2.0 g. of the crude *p*-fluorophenylthiobisamine obtained directly from the *p*-fluorophenyl isothiocyanate-iodine pentafluoride reaction in 80 ml. of methylene chloride was treated with 2 ml. of anhydrous hydrogen fluoride in the manner described above. A total of 1.73 g. of the residue obtained on evaporation of the methylene chloride was hexane souble. The infrared spectrum indicated a small amount of isocyanate and a considerable amount of carbamyl fluoride was present. The sample was recrystallized from hexane (initial crops of the carbamyl fluoride were not characterized) to give 3,3′-difluoro-6,6′-bis-[*N*-(trifluoromethyl)amino]diphenyl sulfide, m.p. 65–66°.

Anal. Calcd. for $C_{14}H_8N_2F_8S$: C, 43.30; H, 2.08; N, 7.22; S. 8.3. Found: C, 44.31; H, 2.47; N, 7.52; S, 7.7.

The analysis and the infrared spectrum pointed to a slight contamination of the sample by *p*-fluorophenylcarbamyl fluoride.

Hydrogen fluoride and thiobis-N-p-tolyl-N-(trifluoromethyl)amine. The procedure outlined above was followed utilizing 2.00 g. of the *p*-tolylthiobisamine, 80 ml. of methylene chloride and about 2 ml. of hydrogen fluoride. The infrared spectrum of the hexane-soluble product (1.57 g.) showed that the desired reaction had occurred; absorption at 4.4 and 5.54 μ revealed the presence of a trace of isocyanate and a small amount of carbamyl fluoride. This residue was recrystallized twice from hexane to give 3,3′-dimethyl-6,6′-bis[*N*-(trifluoromethyl)amino]diphenylsulfide as a waxy solid, m.p. 54–56° after drying 16 hr. at 1 mm. and 25°.

Anal. Calcd. for $C_{16}H_{14}N_2F_6S$: C, 50.52; H, 3.71; N, 7.37; S, 8.43. Found: C, 50.38; H, 3.63; N, 7.23; S, 7.91.

Ethanolic potassium hydroxide and 3,3′-dichloro-6,6′-bis-[N-(trifluoromethyl)amino]diphenyl sulfide. To a solution of 0.200 g. of the above diphenyl sulfide in 10 ml. of ethanol was added 0.22 g. of potassium hydroxide dissolved in 95% ethanol. The solution was stirred at 50° for 2 hr., then poured into water and extracted with methylene chloride. The 0.216 g. of residue obtained on evaporation of the methylene chloride was chromatographed on silica gel in the usual manner. The first fraction eluted appeared, from its infrared spectrum, to be the unchanged diethyl imidocarbonate. Methylene chloride eluted 3,3′-dichloro-6,6′-biscarbethoxyaminodiphenyl sulfide, 0.098 g., m.p. 210–212° (from hexane).

Anal. Calcd. for $C_{18}H_{18}Cl_2N_2O_4S$: C, 50.36; H, 4.23; N, 6.53; S, 7.45. Found: C, 50.34; H, 4.54; N, 6.77; S, 7.38.

Hydrolysis of the reaction product of hydrogen fluoride and thiobis-N-(p-bromophenyl)-N-(trifluoromethyl)amine. A 4.0-g. portion of the *p*-bromophenylthiobisamine in 160 ml. of methylene chloride was treated with about 5 ml. of hydrogen fluoride as described for the *p*-chlorophenylthiobisamine. The mixture was processed as usual to give 3.05 g. of hexane-soluble residue. Attempts to recrystallize this material from hexane were not successful. A 1.9-g. portion of this oily product was added to 25 ml. of ethanol containing 1.7 g. of potassium hydroxide. The ethanolic solution was stirred at 50–60 for 2 hrs., then cooled and poured into water (200 ml.). The aqueous mixture was extracted with methylene chloride. Evaporation of the methylene chloride left 1.5 g. of non-volatile residue. This residue was chromatographed on silica gel as usual. The first fraction eluted was 2,4-dibromophenylurethan, 0.234 g. of m.p. 103–104°, reported[29] m.p. 101°.

Anal. Calcd. for $C_9H_9NO_2Br_2$: C, 33.46; H, 2.81; N, 4.34; Br, 49.5. Found: C, 33.44; H, 2.92; N, 4.24; Br, 49.5.

The second fraction eluted was *p*-bromophenylurethan, 0.154 g. of m.p. 82–83°, mixed m.p. 82–83°, infrared spectrum identical with that of an authentic specimen. The last fraction eluted was presumably 3,3′-dibromo-6,6′-bis(carbethoxyamino)diphenyl sulfide, 0.210 g. of m.p. 215–217°. A sample recrystallized from hexane-chloroform melted at 219–220°.

Anal. Calcd. for $C_{18}H_{18}N_2O_4BrS$: C, 41.71; H, 3.50; N, 5.41; S, 6.19. Found: C, 41.61; H, 3.50; N, 5.98; S, 5.69.

Hydrolysis of 3,3′-dimethyl-6,6′-bis[N-(trifluoromethyl)amino]diphenyl sulfide. A solution of 0.768 g. of the semisolid product from the reaction of the *p*-tolylthiobisamine and hydrogen fluoride in 10 ml. of absolute ethanol was added dropwise to 1.06 g. of potassium hydroxide in 30 ml. of ethanol. The mixture was stirred 3 hr. at 50–60°, and then was poured into water. The aqueous mixture was extracted with methylene chloride. The residue obtained upon evaporation of the methylene chloride was chromatographed on a silica gel column as usual. A syrupy fraction, 0.527 g., was eluted by methylene chloride–ethyl acetate (9:1). On recrystallization from hexane, this fraction initially deposited oily material, then white crystals, m.p. 91–95°, formed. These crops were combined and chromatographed on neutral alumina, activity grade III; fractionation of the mixture was not accomplished. The material then was chromatographed on a silicic acid–Celite column (3:2 by weight) packed in hexane. The column was eluted with hexane containing increasing amounts of ether (3%, 6%, 9%, 15%, 25%, 50% ether by volume). A total of 0.459 g. of material was eluted from the column; a 0.125-g. portion of this, eluted by 15% ether, melted at 107–108°. This was chromatographed again on a similar silicic acid–Celite column. The material eluted by 15% ether was recrystallized (hexane) to give what was presumed to be 3,3′-dimethyl-6,6′-bis(carbethoxyamino)diphenyl sulfide, m.p. 109.5–110.5°, reported[19] 113°.

Anal. Calcd. for $C_{20}H_{24}N_2O_4S$: C, 61.83; H, 6.23; N, 7.12; S, 8.25. Found: C, 61.93; H, 6.27; N, 7.21; S, 8.12.

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(29) Ref. 22, Vol. 12, Suppl. I. p. 328.