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Studies of Organosulfur Compounds. VI. The Preparation of Carbamoyl Esters of Aromatic Dithio Acids and Their Spectral Properties

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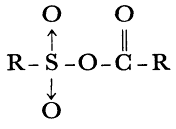
It was found that aromatic dithio acids readily reacted with aryl isocyanate at room temperature to give the corresponding mixed thioanhydrides with the general formula of (ArCS·S·CONHAr) in excellent yields as stable crystals. The mixed thioanhydrides reacted with primary amines at room temperature to give the corresponding thioamides and asymmetric ureas, while the reaction with secondary amines gave the corresponging amine salts and asymmetric ureas in good yields. The spectral properties of the mixed thioanhydrides were discussed.

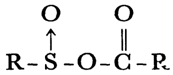
Although a few studies of the preparation of the mixed anhydrides (I[1], II[1e], *etc.*) and asymmetric thioanhydrides (III)[2] have been reported, there has been no report on the preparation of the mixed thioanhydrides of Structure (IV) except for the unsuccessful attempt by Houben and Schultze[3] to prepare



$$R-\underset{\underset{O}{\downarrow}}{\overset{\overset{O}{\uparrow}}{S}}-O-\overset{\overset{O}{\|}}{C}-R$$

I

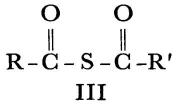
R: Alkyl
Aryl



$$R-\overset{\overset{O}{\uparrow}}{S}-O-\overset{\overset{O}{\|}}{C}-R$$

II

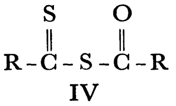
R: Alkyl
Aryl



$$R-\overset{\overset{O}{\|}}{C}-S-\overset{\overset{O}{\|}}{C}-R'$$

III

R: Alkyl
R': Aryl



$$R-\overset{\overset{S}{\|}}{C}-S-\overset{\overset{O}{\|}}{C}-R$$

IV

R: Alkyl
Aryl

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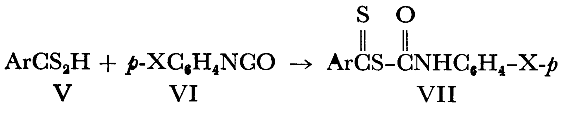
[1] a) A. Fahlberg, *Ber.*, **22**, 758 (1889). b) A. Baroni, *Atti Accad. Naz. Lincei*, **17**, 1081 (1933). c) C. G. Overberger and E. Sarlo, *J. Amer. Chem. Soc.*, **85**, 2446 (1963). d) G. A. Olah and S. J. Kuhn, *J. Org. Chem.*, **27**, 2667 (1962). e) H. Böhme and K. H. Meyer-Dulheuer, *Ann.*, **688**, 78 (1965). f) M. H. Karger and Y. Mazur, *J. Amer. Chem. Soc.*, **90**, 3878 (1968). M. H. Karger and Y. Mazur, *J. Org. Chem.*, **36**, 528 (1971).

[2] Q. Minagoia, *Gazz. Chem. Ital.*, **55**, 713 (1925).

[3] J. Houben and K. M. L. Schultze, *Ber.*, **43**, 2481 (1910).

the anhydrides (IV, Ar; C_6H_5, R′; C_6H_5, CH_3) of dithio and carboxylic acid from magnesium halogenide salts of aromatic dithio acids and acid chlorides or anhydrides. Dithio acids in general are stronger acids[4] than the corresponding carboxylic acid or thio acid, and it is expected that dithio acids react with heterocumulenes (isocyanates, ketenes, *etc.*) to give the corresponding mixed thioanhydrides. In a previous work,[5] it was found that bis(thioacyl)disulfide was readily reacted with secondary amines to give their amine salts in good yields, and the use of the amine salts for the purification of aromatic dithio acids was more effective than that of the metal salts. In this paper, we will describe the preparation of the mixed thioanhydride with the general formula of VII from aromatic dithio acids and aryl isocyanates (Eq. (1)) and an investigation of some aspect of their chemistry.



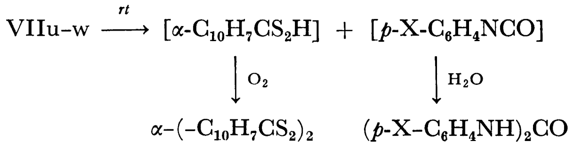
$$\underset{\mathrm{V}}{\mathrm{ArCS_2H}} + \underset{\mathrm{VI}}{p\text{-}\mathrm{XC_6H_4NCO}} \rightarrow \underset{\mathrm{VII}}{\mathrm{Ar}\overset{\overset{\mathrm{S}}{\|}}{\mathrm{C}}\mathrm{S}\text{-}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHC_6H_4}\text{-}\mathrm{X}\text{-}p} \qquad (1)$$

Ar: Aromatic X: Substituents

Results and Discussion

When p-methyldithiobenzoic acid in an ethyl acetate–ether (1 : 1) mixture was treated with an equimolar amount of phenyl isocyanate, phenylcarbamoyl p-methyldithiobenzoate (VIIg) was easily obtained in an 86% yield as reddish yellow crystals. The structure VIIg was identified by means of elemental analysis and by studying the spectral data. In the IR spectrum, very intensive absorption bands at 1708 cm^{-1} due to carbonyl stretching and at 1540 cm^{-1} due to amide II band stretching were observed. The NMR spectrum showed peaks at τ 7.70 (CH_3, s, 3H), 2.00—2.90 (aromatic, 9H), and −2.31 (NH, s, 1H). On the other hand, the absorption band at 499 mμ (ε 113) due to the $n\rightarrow\pi^*$ transition of the thiocarbonyl group was observed in the visible region. By an analogous treatment of other aromatic dithio acids with *para*-substituted phenyl isocyanates, the corresponding mixed thioanhydrides (VII) were prepared in good yields. The results are summarized in Table 1.

The mixed thioanhydrides (VII) thus obtained, except for VIIu, VIIv, and VIIw, were fairly stable crystals, and did not change in atmosphere for over two months. However, the heating of VII over their melting points decomposed VII to give the corresponding isocyanates, together with dark brown, intractable oil. Similar formations of the isocyanates on the heating of alkyl thiocarbamates have been described in German Patents.[6,7] On the other hand, the carbamoyl α-dithionaphthoates (VIIu, VIIv, and VIIw), except for VIIx which contains a p-nitro substituted carbamoyl group, were dark brown oil and gradually decomposed on standing in the atmosphere or in a solution (ethyl acetate or dichloromethane) at room temperature to give bis(α-thionaphthoyl)disulfide and the corresponding ureas in almost quantitative yields. These formations can be explained by the following scheme 1:[8]



Scheme 1.

One of the interesting points about in the mixed thioanhydrides is their reaction with nucleophilic reagents because of their multi-reaction center, shown with the arrows a, b, and c, in Fig. 1. When the mixed thioanhydride was treated with a two-molar amount of p-toluidine in dichloromethane at room temperature, N-p-tolylthiobenzamide (VIII) and phenyl-p-tolylurea (IX) were obtained in 94 and 95% yields, and also hydrogen sulfide evolved (Eq. (2)). Unlike p-toluidine, a similar treatment of VIIi with piperidine afforded piperidinium dithiobenzoate (X)[9] and the asymmetric urea (XI) in quantitative yields, and no evolution of hydrogen sulfide was observed (Eq. 3).

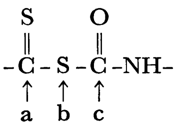
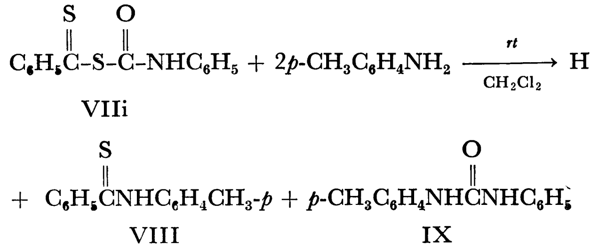
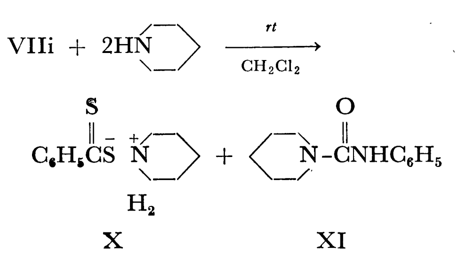


Fig. 1.



$$\underset{\mathrm{VIIi}}{\mathrm{C_6H_5}\overset{\overset{\mathrm{S}}{\|}}{\mathrm{C}}\text{-}\mathrm{S}\text{-}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\mathrm{NHC_6H_5}} + 2p\text{-}\mathrm{CH_3C_6H_4NH_2} \xrightarrow[\mathrm{CH_2Cl_2}]{rt} \mathrm{H_2S} + \underset{\mathrm{VIII}}{\mathrm{C_6H_5}\overset{\overset{\mathrm{S}}{\|}}{\mathrm{C}}\mathrm{NHC_6H_4CH_3}\text{-}p} + \underset{\mathrm{IX}}{p\text{-}\mathrm{CH_3C_6H_4NH}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NHC_6H_5}} \qquad (2)$$



(3)

Furthermore, the competitive reactions of an equimolar mixture of VIIi and dithiobenzoic acid with an equimolar amount of p-toluidine or piperidine in the same

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[4] M. J. Jansen, "The Chemistry of Carboxylic Acids and Esters" ed. by S. Patai, Interscience-Publisher, New York (1969), p. 717.

[5] S. Kato and M. Mizuta, *Int. J. Sulfur Chem. A*, **2** (No.4), 27 (1972).

[6] H. Pelster, E. Muelbauer, and D. Delfs, Ger. 1176127 (1964).

[7] H. Pelster, E. Muehlbauer, and D. Delfs, Ger. 1171421 (1964).

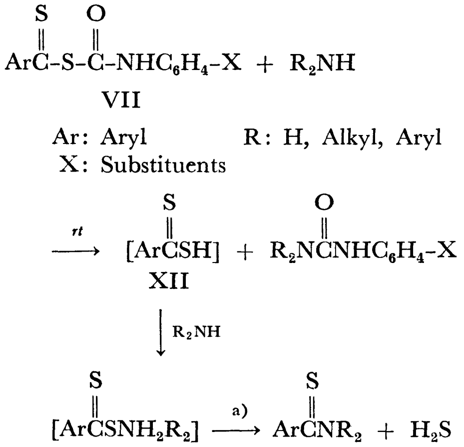
[8] α-Dithiohaphthoic acid was readily oxidized with oxygen to give bis(α-thiohaphthoyl)disulfide in a quantitative yield: J. Houben, *Ber.*, **39**, 3219 (1906).

[9] An analogous formation of the amine salts from bis(thioaroyl) disulfide and secondary amines was observed: S. Kato and M. Mizuta, This Bulletin, **45**, 3492 (1972).

Table 1. Physical properties and elemental analysis of arylcarbamoyl dithioaroylates

Compd	ArCS·S·OC-NHC$_6$H$_4$-X-p Ar	X	Yield %	Mp °C	IR (cm^{-1}), KBr νC=O	δN-H[a)]	νC=S	UV, mμ, CH$_2$Cl$_2$ λ_{max} (ε)			Formula	Found (Calcd), % C	H	Br	Cl	N	S
VIIa	p-CH$_3$OC$_6$H$_4$	CH$_3$O	94	103—104	1680	1540	1234	249 (4.36)	365 (4.27)	473 (2.09)	C$_{16}$H$_{15}$NO$_3$S$_2$	57.55 (57.65)	4.48 (4.50)			4.19 (4.20)	19.88 (19.21)
b		CH$_3$	88	120—121	1707	1540	1245		365 (4.17)	484 (2.06)	C$_{16}$H$_{15}$NO$_2$S$_2$	60.93 (60.56)	4.62 (4.73)			3.38 (4.42)	20.68 (20.19)
c		H	92	94— 95	1700	1545	1230	288	365 (4.22)	486 (2.03)	C$_{15}$H$_{13}$NO$_2$S$_2$	60.21 (59.41)	4.22 (4.29)			4.76 (4.62)	20.55 (21.12)
d		NO$_2$	89	129—130	1715	1552	1258		294 (4.25)	477 (2.07)	C$_{15}$H$_{13}$N$_2$O$_4$S$_2$	52.03 (51.57)	3.68 (3.72)			8.03 (8.02)	18.63 (18.34)
e	p-CH$_3$C$_6$H$_4$	CH$_3$O	74	95.0—96.5	1690	1534	1236	245 (4.31)	327 (4.18)	486 (2.05)	C$_{16}$H$_{15}$NO$_2$S$_2$	61.11 (60.57)	4.77 (4.73)			4.44 (4.42)	20.55 (20.19)
f		CH$_3$	91	122—123	1700	1530	1240		320 (4.19)	497 (2.06)	C$_{16}$H$_{15}$NOS$_2$	63.70 (63.79)	4.87 (4.87)			4.66 (4.65)	21.28 (21.26)
g		H	86	92.0—93.8	1708	1540	1252		323 (4.21)	498 (2.05)	C$_{15}$H$_{13}$NOS$_2$	62.09 (62.72)	4.51 (4.53)			4.90 (4.88)	22.36 (22.30)
h		NO$_2$	90	110.5—112.0	1695	1549	1250		330 (4.38)	488 (2.07)	C$_{15}$H$_{13}$N$_2$O$_3$S$_2$	54.88 (54.22)	3.99 (3.92)			8.51 (8.43)	19.23 (19.28)
i	C$_6$H$_5$	CH$_3$O	83	84.0—85.0	1688	1542	1250	246 (4.21)	311 (4.20)	490 (2.05)	C$_{15}$H$_{13}$NO$_2$S$_2$	59.32 (59.41)	4.33 (4.29)			4.58 (4.62)	21.65 (21.12)
j		CH$_3$	32	oil	1710	1525	1240				C$_{15}$H$_{13}$NOS$_2$	63.00 (62.72)	4.49 (4.53)			4.83 (4.88)	22.46 (22.30)
k		H	90	63.5—65.5	1697	1546	1250		324 (4.19)	506 (2.05)	C$_{14}$H$_{11}$NOS$_2$	62.03 (61.54)	4.12 (4.03)			5.26 (5.13)	23.48 (23.44)
l		NO$_2$	90	109.0—109.5	1696	1556	1256		314 (4.41)	485 (2.05)	C$_{14}$H$_{11}$N$_2$O$_3$S$_2$	52.88 (52.83)	3.49 (3.46)			8.92 (8.81)	20.54 (20.13)
m	p-ClC$_6$H$_4$	CH$_3$O	83	82.0—83.0	1690	1540	1245	245 (4.16)	319 (4.24)	478 (2.09)	C$_{15}$H$_{12}$ClNO$_2$S$_2$	53.00 (53.33)	3.55 (3.56)		11.02 (10.52)	4.21 (4.15)	18.83 (18.96)
n		CH$_3$	46	oil	1735	1555	1245				C$_{15}$H$_{12}$ClNOS$_2$	56.09 (55.99)	3.68 (3.73)		11.33 (11.04)	4.36 (4.35)	19.32 (19.91)
o		H	90	71.0—72.0	1693	1527	1250		330 (4.22)	493 (2.11)	C$_{14}$H$_{10}$ClNOS$_2$	54.48 (54.63)	3.23 (3.25)		12.05 (11.54)	4.44 (4.55)	21.05 (20.81)
p		NO$_2$	88	106—108	1714	1552	1256		323 (4.35)	4.85 (2.08)	C$_{14}$H$_{10}$ClN$_2$O$_3$S$_2$	47.34 (47.66)	2.69 (2.84)		9.93 (10.07)	7.88 (7.94)	18.44 (18.16)
q	p-BrC$_6$H$_4$	CH$_3$O	75	109—110	1685	1528	1240	245 (4.11)	316 (4.32)	500 (2.06)	C$_{15}$H$_{12}$BrNO$_2$S$_2$	47.28 (47.12)	3.21 (3.14)	20.65 (20.94)		3.68 (3.66)	17.02 (16.75)
r		CH$_3$	28	93— 94	1685	1528	1240		325 (4.30)	501 (2.09)	C$_{15}$H$_{12}$BrNOS$_2$	50.00 (49.18)	3.22 (3.28)	20.99 (21.86)		3.88 (3.83)	17.77 (17.49)
s		H	67	90— 91	1700	1538	1245		322 (4.12)	494 (2.02)	C$_{14}$H$_{10}$BrNOS$_2$	48.79 (48.72)	2.82 (2.84)	22.76 (22.73)		3.87 (3.98)	18.18 (18.18)
t		NO$_2$	88	132—133	1708	1546	1252		328 (4.34)	488 (2.06)	C$_{14}$H$_{10}$N$_2$O$_3$S$_2$	42.44 (42.42)	2.65 (2.53)	20.12 (20.20)		3.45 (3.54)	16.58 (16.16)
u	α-C$_{10}$H$_7$	CH$_3$O	39	oil	1690	1545	1242				C$_{19}$H$_{15}$NO$_2$S$_2$	65.43 (64.59)	4.16 (4.25)			3.94 (3.97)	18.63 (18.13)
v		CH$_3$	42	oil	1710	1520	1245				C$_{19}$H$_{15}$NOS$_2$	68.01 (67.66)	4.38 (4.45)			4.07 (4.15)	19.94 (19.99)
w		H	44	oil	1700	1520	1245				C$_{18}$H$_{13}$NOS$_2$	66.66 (66.87)	4.01 (4.02)			4.32 (4.33)	19.32 (19.81)
x		NO$_2$	91	129—130	1695	1510	1255		323 (4.32)	504 (2.03)	C$_{18}$H$_{13}$N$_2$O$_3$S$_2$	58.37 (58.70)	3.55 (3.53)			3.81 (3.80)	17.41 (17.39)

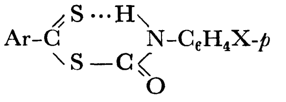
conditions gave the asymmetric ureas (IX or XI) in yields of over 60%. These results indicate the possibility of the nucleophilic attack of amines on the carbonyl carbon of the mixed thioanhydrides and the formation of the corresponding dithio acid (XII) as an intermediate (Scheme 2).



a) in the case of primary amines.

Scheme 2.

Spectral Data. *a) IR Spectra*: The IR spectra of all these anhydrides, without any exception, surprisingly showed no N–H stretching absorption band in the expected range (3100—3400 cm^{-1}); instead, we observed new absorption bands near 2900 cm^{-1} considered to be due to the N–H stretching band. Such an unusual shift in νN–H suggests a structure (XIII) containing an intramolecular hydrogen bond between sulfur and hydrogen. The NMR spectrum (NH near -2.30τ) further supported the XIII structure.



XIII

Ar: Aryl X: Substituents

The location of C=S group frequencies in organosulfur compounds has been a matter of considerable discussion. Bak *et al.*[10] reported that the two frequencies (ν C=S and C–S) obtained by a simplified force-constant calculation must be looked for in the vicinity of 1200 cm^{-1} (C=S) and 700 cm^{-1} (C–S), and the locations of the C=S in a series of twenty-one carboxymethyl dithio esters were observed between 1190 and 1225 cm^{-1}. Lately, Bellamy and Rogasch[11] have confirmed those results using solvent effects, and also suggested in a recent review[12] that ν C=S lies between 1225 and 1190 cm^{-1} in the dithio esters. The arylcarbamoyl dithio esters obtained, almost without exceptions, showed two fairly intensive absorption bands at near 1250 and 1050 cm^{-1}. However, it is difficult to assign the lower-frequency band to the C=S because that of amine salts of aromatic dithio acids was observed between 990 and 1020 cm^{-1}. Therefore, it seemed reasonable that the intensive absorption bands at near 1250 cm^{-1} are due to the C=S stretching bands in arylcarbamoyl dithioesters (VII). This also fits well with the assignment given by Bak *et al.*[10] and Bellamy.[11]

b) UV and Visible Spectra: Table 1 lists the absorption maxima in mμ and the molecular extinction coefficients at each maximum. As is shown in Table 1, all the mixed anhydrides (VII), showed two characteristic maximum absorption bands near 300 mμ (ε 15000—25000) and 500 mμ (ε 100—130). It may be considered that the former absorption bands are due to $\pi\rightarrow\pi^*$, and the latter, to the $n\rightarrow\pi^*$ transition of the thiocarbonyl group. The location of $n\rightarrow\pi^*$ fits well with the assignment given by Fabian *et al.*[13] for the methyl esters of aromatic dithio acids.

Experimental[14]

Materials. The aromatic dithio acids were prepared by the method described in a previous report[5], using THF as the solvent. Phenyl isocyanate was of a commercial grade and was distilled before use. The other aryl isocyanates were prepared, following the directions of the literature,[15] from the corresponding amines and phosgen; *p*-methoxyphenyl isocyanate, bp 105—106°C/8 mmHg *p*-tolyl isocyanate, bp 52—53°C/5 mmHg; *p*-nitrophenyl isocyanate: mp 55—57°C. The *p*-toluidine and piperidine were of a commercial grade and were purified by distillation or recrystallization before use. The solvents were dried and distilled.

Reactions were carried out under nitrogen. Some typical procedures will be described below, while the detailed data are summarized in Table 1.

Reaction of p-Methyldithiobenzoic Acid with Phenyl Isocyanate. An equimolar amount of phenyl isocyanate was added to a solution of *p*-methyldithiobenzoic acid (1.68 g, 0.01 mol) in 10-m*l* of ether-ethyl acetate (1 : 1), and the mixture was stirred for 30 min, at room temperature. The evaporation of the solvent from the reaction mixture below 20°C *in vacuo*, the recrystallization of the residue from ethyl acetate-petroleum ether (bp below 50°C, 1 : 3) gave 2.45 g of phenylcarbamoyl *p*-methyldithiobenzoate (VIIg).

Thermolysis of Phenylcarbamoyl Dithiobenzoate (VIIk). Phenylcarbamoyl dithiobenzoate (VIIk), 5.30 g, 0.02 mol) in a glass ampoule under nitrogen was heated for 30 min at 120°C. The distillation of the decomposition mixture gave 1.5 g (63%, based on the VIIk used) of phenyl isocyanate.

Decomposition of Phenylcarbamoyl α-Dithionaphthoate (VIIv) on Standing in an Atmosphere. A solution of 1.6 g (0.005 mol) of VIIv in ethyl acetate (20 m*l*) was allowed to stand in the atmosphere at room temperature. After 7 days, the color of the solution completely changed from dark brown to pink, and the precipitates appeared. After the removal of the solvent, the fractional crystallization of the residue from di-

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[10] B. Bak, L. Hansen-Nygaard, and C. Pedersen, *Acta Chem. Scand.*, **12**, 1451 (1958).

[11] L. J. Bellamy and P. E. Rogasch, *J. Chem. Soc.*, **1960**, 2218.

[12] L. J. Bellamy, "Advances in Infrared Group Frequencies" Methuem & Co. Ltd., London (1968), p. 213.

[13] J. Fabian, St. Scheithauer, and R. Mayer, *J. Prakt. Chem.*. **311**, 45 (1969).

[14] All melting points were not corrected. The IR spectra were measured on a JASCO Grating Infrared Spectrophotometer IR-G. The UV spectra were recorded on Hitachi 124 Spectrophotometer. The NMR spectra were taken on a JEOL H-60 apparatus.

[15] R. J. Slocombe, E. E. Hardy, T. H. Saunder, and R. L. Jenkins, *J. Amer. Chem. Soc.*, **72**, 1888 (1950).

chloromethane-ether gave 0.82 g (80%) of bis(α-thionaphthoyl)disulfide (mp 169—170°C[16] and 0.55 g (91%) of diphenylurea (mp 60—70°C), which were identified by a comparision of their melting points and IR spectrum with those of an authentic sample.

Reaction of Phenylcarbamoyl Dithiobenzoate (VIIk) with p-*Toluidine or Piperidine.* *a*): *p*-Toluidine (1.07 g, 0.01 mol) was added to a solution of 1.36 g (0.005 mol) of VIIk in dichloromethane (10 m*l*) and stirred for 8 hr at room temperature. After the vacuum evaporation of the solvent from the reaction mixture, the residue was extracted with a small portion of ether. After the evaporation of the ether from the extracts, the recrystallization of the residue gave 1.2 g of *N*-*p*-tolylthiobenzamide (mp 126—127°C). On the other hand, the recrystallization of the ether-insoluble parts from dichloromethane gave 1.05 g of phenyl-*p*-tolylurea (mp (196—197°C). The thiobenzamide and the urea were identified by a comparision of the melting points and IR spectrum with those of authentic samples.[17]

b): The reaction of VIIk (0.05 mol) and piperidine (0.01 mol) under the same conditions as in a) gave 1.08 g (86%) of piperidinium dithiobenzoate (mp 112—114°C) and 0.97 g (96%) of phenylpiperidylurea (mp 165—166°C). The melting points and the IR spectra of the amine salts and the urea coincided exactly with those of authentic samples.

c) Competitive Reaction: A similar treatment of a mixture of dithiobenzoic acid (0.01 mol) and VIIk (0.01 mol) in dichloromethane (15 m*l*) with 0.01 mol of *p*-toluidine gave 1.43 g (63%, based on the *p*-toluidine used) of *N*-*p*-tolylphenylurea and 0.59 g (26%, based on the *p*-toluidine used) of *N*-*p*-tolylthiobenzamide.

d): A similar treatment of a mixture of dithiobenzoic acid (0.01 mol) and VIIk (0.01 mol) in dichloromethane (15 m*l*) with piperidine (0.01 mol) gave 1.47 g (72%, based on the piperidine used) of phenylpiperidylurea and 0.37 g (13%, based on the piperidine used) of piperidinium dithiobenzoate.

The authors wish to thank Professor Yoshio Hirabayashi and Mr. Hideharu Ishihara for their discussions.

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16) For bis(α-thionaphthoyl)disulfide: J. Houben, *Ber.*, **39**, 3219 (1906).

17) a) For *p*-tolylthiobenzamide: S. Kato, and M. Mizuta, This Bulletin, submitted for. b) *p*-Tolylphenylurea was prepared from phenyl isocyanate and *p*-toluidine.

18) a) For piperidinium dithiobenzoate: see Ref. 5. b) Phenylpiperidylurea was prepared from phenyl isocyanate and piperidine.