[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Studies in Thiophenol Chemistry. I. A Condensation Reaction between Thiophenols and Condensed Aldehyde-Ammonias[1]

BY GREGG DOUGHERTY AND WENDELL H. TAYLOR[2]

In connection with a study of the condensation of thiophenol and formaldehyde under a variety of conditions, it was found that this mercaptan readily condenses with hexamethylenetetramine and several other hydramides, ammonia being evolved. This work has already been mentioned in a brief communication[3] and it is now desired to present a more detailed account of the several reactions and their products.

Hexamethylenetetramine and Thiophenols.—It has long been known that hexamethylenetetramine reacts with certain weakly acidic compounds according to the general equation

$$(CH_2)_6N_4 + 6HR \longrightarrow 2N(CH_2R)_3 + 2NH_3 \qquad (1)$$

where, for example, R may be $-CN$,[4] C_6H_5CONH-,[5] or $CH_3N(NO_2)-$.[6] Stronger acids generally cause complete decomposition of the base, and phenols, which first form addition compounds, finally yield resinous substances[7] when heated with hexamethylenetetramine.

It is therefore interesting that thiophenol and various substituted thiophenols should yield condensation products exactly of the type $N(CH_2R)_3$. Thus, in reaction (1), R may be $—SC_6H_5$, $—SC_6H_4Br$, $—SC_6H_4NO_2$, $—SC_6H_4CH_3$ (the last three para substituted) or even $—SCH_2C_6H_5$.

The reaction is easily brought about by refluxing the reactants in an inert solvent such as 1,4-dioxane, and its course may be followed by determining the amount of ammonia evolved. By this means the reaction in the case of hexamethylenetetramine and thiophenol has been shown to be

$$(CH_2)_6N_4 + 6C_6H_5SH \longrightarrow 2N(CH_2SC_6H_5)_3 + 2NH_3 \qquad (2)$$

The triphenylmercaptomethylamine structure of the product is substantiated by analyses and molecular weight determinations, and by quantitative hydrolysis experiments in which the following reaction takes place

$$N(CH_2SC_6H_5)_3 + 3HOH \xrightarrow{HCl} NH_3 + 3C_6H_5SH + 3HCHO \qquad (3)$$

The intermediate formation of $N(CH_2OH)_3$ may be presumed; the final

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(1) The material of this paper is from the dissertation of Wendell H. Taylor, presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy at Princeton University, 1933.

(2) Charlotte Elizabeth Procter Fellow, 1931–1932.

(3) Dougherty and Taylor, THIS JOURNAL, **55**, 1294 (1933).

(4) Eschweiler, *Ann.*, **278**, 230 (1894).

(5) Descudé, *Ann. chim. phys.*, [7] **29**, 541 (1903).

(6) Franchimont, *Rec. trav. chim.*, **29**, 355 (1910).

(7) Redman, Weith and Brock, *Ind. Eng. Chem.*, **6**, 3 (1914). Scheiber and Sändig, "Artificial Resins," Pitman, London, 1931, p. 302.

products weighed are ammonium chloride and formaldehyde-diphenylmercaptal.[8]

It may be pointed out in passing that the reaction postulated here (2) is much more readily explained on the basis of a symmetrical hexamethylenetetramine molecule containing four equivalent nitrogen atoms than upon the assumption of the Lösekann formula, $N(CH_2N{=}CH_2)_3$, still occasionally advocated.[9] x-Ray analysis of the hexamethylenetetramine crystal[10] so strongly indicates the tetrahedral structure of the molecule that only the most positive chemical evidence may now be considered admissible in favor of the old formula.

Hydrobenzamide and Thiophenols.—Hydrobenzamide, $(C_6H_5CH{=}N)_2CHC_6H_5$, more properly named tribenzylidenediamine, is a condensed aldehyde-ammonia or "hydramide." Whether it is regarded merely as a secondary condensation product of benzaldehyde and ammonia, or as an aldehyde of the "ammonia system,"[11] its close relationship to hexamethylenetetramine is evident.

The ready hydrolysis of hydrobenzamide by acids into benzaldehyde and ammonia is a characteristic reaction, but its stepwise decomposition by weak acids, as in the case of hexamethylenetetramine, has not hitherto been known. It has been found that thiophenol and various substituted thiophenols, as well as benzyl mercaptan, cause such a partial decomposition, which may be looked upon as the formation of a half-mercaptal. Thus

$$2(C_6H_5CH{=}N)_2CHC_6H_5 + 3RSH \longrightarrow 3C_6H_5CH{=}NCH(SR)C_6H_5 + NH_3 \quad (4)$$

It may well be that the first stage in the reaction is the formation of benzylidene-imine, a substance recently found[11] to be capable of existence in the free state.

$$(C_6H_5CH{=}N)_2CHC_6H_5 + RSH \longrightarrow C_6H_5CH{=}NCH(SR)C_6H_5 + C_6H_5CH{=}NH \quad (5)$$

Two molecules of benzylidene-imine formed in this way might then react with the third molecule of mercaptan, giving ammonia and the third molecule of the half-mercaptal

$$RSH + 2C_6H_5CH{=}NH \longrightarrow C_6H_5CH{=}NCH(SR)C_6H_5 + NH_3 \quad (6)$$

In any case, the stoichiometric equation for the reaction may be represented by (4). This has been established by quantitative estimation of the evolved ammonia, and by analyses and molecular weight determinations on the products. The latter are well-crystallized, colorless solids, obtained in nearly quantitative yield when the condensation is carried out in boiling 1,4-dioxane solution. The half-mercaptal structure assigned to them appears to be confirmed by the results of quantitative hydrolysis experiments; thus

$$C_6H_5CH{=}NCH(SC_6H_5)C_6H_5 + HOH \longrightarrow 2C_6H_5CHO + C_6H_5SH + NH_3 \quad (7)$$

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(8) Formed from the thiophenol and excess formaldehyde in the presence of dry hydrogen chloride.

(9) Marotta and Alessandrini, *Gazz. chim. ital.*, **59**, 942 (1929); **61**, 977 (1931).

(10) Dickinson and Raymond, THIS JOURNAL, **45**, 23 (1923).

(11) Strain, *ibid.*, **49**, 1558 (1927).

The benzaldehyde may be weighed as the phenylhydrazone; the thiophenol as lead phenyl mercaptide; the ammonia as ammonium chloride.

Extension to Other Hydramides and Mercaptans.—The same type of condensation has been found to take place with such substituted hydrobenzamides as 3,3′,3″-trinitrohydrobenzamide and hydro-*p*-toluamide, and with hydrofurfuramide; in these cases only the reaction with thiophenol was investigated. Preliminary work has shown that it may be possible to extend this reaction to the simple aliphatic mercaptans. *n*-Amyl mercaptan—the only one studied thus far—undergoes slow reaction with both hexamethylenetetramine and hydrobenzamide, ammonia being evolved. In neither case, however, has a crystalline product yet been obtained.

General Nature of the Products.—The products from all these reactions are very similar in physical and chemical properties. They are nearly all colorless, odorless, crystalline[12] solids of fairly low melting point; they are readily soluble in most organic solvents but only sparingly so in cold alcohol and in petroleum ether.

In alcohol solution they give no immediate precipitate when alcoholic lead acetate is added, but on warming, or on addition of a little acid, a mercaptide precipitate soon forms. They are much less easily hydrolyzed by alkalies than are the substituted trimethylamines obtained from hexamethylenetetramine and hydrogen cyanide.

The solid members of this group melt sharply without decomposition, but may not be distilled, even under greatly reduced pressure. Thus, triphenylmercaptomethylamine gives large amounts of diphenyl disulfide upon attempted distillation at 1 mm. pressure; the nature of any other pyrolytic products has not been determined.

Attempts to prepare simple derivatives, such as sulfones, have not been successful. Because of the ease with which these compounds are hydrolyzed by acids, neutral or alkaline oxidizing agents must be employed. However, dilute alkaline potassium permanganate may be boiled for several hours with benzalphenylmercaptobenzylamine, $C_6H_5CH{=}NCH(SC_6H_5)$-C_6H_5, with little effect; while 30% hydrogen peroxide in glacial acetic acid solution brings about complete decomposition, with formation of benzoic acid. Bromine in dilute ether solution is rapidly decolorized by benzalphenylmercaptobenzylamine but the molecule is completely broken up and diphenyl disulfide can be isolated from the solution as the chief product.

Experimental Part

Materials Used.—Thiophenol, *p*-thiocresol, thio-β-naphthol, benzyl mercaptan and *n*-amyl mercaptan were obtained from the Eastman Kodak Company. *p*-Bromothiophenol was prepared by reduction with zinc and hydrochloric acid of 4,4′-dibromodi-

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[12] The only products not obtained crystalline are those from hexamethylenetetramine with thiophenol or thio-β-naphthol.

phenyl disulfide, the latter being obtained by direct bromination[13] of diphenyl disulfide. *p*-Nitrothiophenol was made by the action of alcoholic potassium hydrosulfide upon *p*-nitrochlorobenzene.[14]

The hexamethylenetetramine used was Merck U. S. P. "Formin." Hydrobenzamide was prepared by shaking strong aqueous ammonia with pure benzaldehyde. The product was always recrystallized before use. 3,3′,3″-Trinitrohydrobenzamide was made by the method of Fürth,[15] while hydro-*p*-toluamide and hydrofurfuramide were obtained by direct condensation of aqueous alcoholic ammonia with *p*-tolualdehyde and furfuraldehyde, respectively.

Commercial dioxane was twice treated with sodium wire and redistilled, the fraction boiling at 101–102° (760 mm.) being retained. Removal of chlorinated compounds is essential, since in their presence hexamethylenetetramine hydrochloride is sometimes formed; oxidation of certain thiophenols to disulfides has also been observed in dioxane containing chlorine compounds.

Apparatus.—The condensations of thiophenols with the various hydramides were carried out in a 150-cc. side-neck Erlenmeyer flask provided with a long vertical spiral condenser. A slow current of dry air (in some runs, nitrogen) was passed into the side-neck of the flask while the dioxane solution of the reactants was gently refluxed; this carried the evolved ammonia through the condenser into a receiver containing an excess of standard hydrochloric acid. By determining the acid left in the receiver after ammonia was no longer given off,[16] the course and nature of the reaction could be studied.

Analyses for carbon, hydrogen and nitrogen were carried out by the micro methods of F. Pregl; halogens and sulfur were determined by a semi-micro method using the micro-balance and small fritted glass filter crucibles, following in general the usual Carius technique.

Molecular weights were determined either by the familiar freezing point method of Beckmann, or with the very convenient boiling point apparatus designed by Rieche.[17] The solvents used are designated later.

Hexamethylenetetramine and Thiophenol.—One and four-tenths grams (0.01 mole) of hexamethylenetetramine and 3.24 g. (nearly 0.03 mole) of thiophenol were mixed with 20 cc. of 1,4-dioxane and refluxed for twenty-three hours in the apparatus described above. The evolved ammonia was determined by back titration of the excess acid. Evaporation of the dioxane solution at room temperature gave a thick, pale yellow oil which, after several extractions with dry ether, permitted the weighing of the residue of unchanged hexamethylenetetramine. Four experiments of this kind were run, all of which yielded amounts of ammonia corresponding to 95–97% of the calculated amount.

The combined ether extracts were dried with anhydrous sodium carbonate and evaporated, yielding a light yellow oil that could not be made to crystallize, and which decomposed on attempted distillation at 1 mm. pressure. This material was extremely soluble in all common solvents except cold 95% alcohol, and could not easily be purified. That it was triphenylmercaptomethylamine was indicated by its analysis, molecular weight and hydrolytic products.

Hydrolysis of Triphenylmercaptomethylamine.—Four and two hundred thirty-five thousandths grams of the condensation product from hexamethylenetetramine and

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(13) Bourgeois and Abraham, *Rec. trav. chim.*, **30**, 421 (1911).

(14) Mayer, *Ber.*, **42**, 3050 (1909).

(15) Fürth, *Monatsh.*, **27**, 844 (1906).

(16) A piece of litmus paper placed in the upper end of the condenser served to indicate when all of the ammonia had been driven over.

(17) Rieche, *Ber.*, **59**, 2181 (1926).

thiophenol was placed in a 125-cc. Erlenmeyer flask and dissolved in 30 cc. of glacial acetic acid. The solution was gently refluxed under a vertical condenser for two hours while dry hydrogen chloride was passed in through a capillary tube. The product was then transferred to a Claisen flask and the acetic acid distilled off at 25–35° (15–20 mm.) leaving a dark brown residue. This was repeatedly extracted with 10-cc. portions of boiling anhydrous ether and finally with small portions of boiling benzene until no more soluble material could be removed. The ether–benzene extract gave on evaporation 3.520 g. of a light yellow oil which crystallized on standing, and then melted at 36°, evidently formaldehyde-diphenylmercaptal. The dark brown residue in the flask was repeatedly extracted with hot water, giving a yellow solution which, after decolorizing with charcoal, gave on evaporation 0.610 g. of ammonium chloride. The latter was identified by the usual qualitative tests.

Assuming the original material to be $(C_6H_5SCH_2)_3N$, theory requires 3.830 g. of mercaptal and 0.590 g. of ammonium chloride as products of this conversion by dry hydrogen chloride. These figures check reasonably well with those obtained in the experiment.

Hydrobenzamide and Thiophenol.—From 5.96 g. of hydrobenzamide (0.02) mole and 3.34 g. of thiophenol (0.03 mole) refluxed for ten hours in 30 cc. of 1,4-dioxane, 0.178 g. of ammonia was evolved, as determined by back titration of excess standard acid with sodium hydroxide. Calcd., 0.170 g. The reaction product, isolated by evaporation of the dioxane solution at room temperature, was a crystalline mass weighing 9 g. This was twice recrystallized from 95% alcohol giving a colorless, odorless product melting at 79.5°, presumably benzalphenylmercaptobenzylamine.

Various other runs of this condensation gave amounts of ammonia corresponding to 97–104% of the theoretical.

Hydrolysis of Benzalphenylmercaptobenzylamine.—0.303 g. (0.001 mole) of the crystalline product from the condensation of hydrobenzamide and thiophenol was placed in a 50-cc. distilling flask and the side-neck of the latter connected to a vertical descending spiral condenser. Ten cc. of approximately 1 normal sulfuric acid was added and the mixture gently boiled for fifteen minutes, at the end of which about half the liquid had distilled over. To the milky liquid in the receiver was added 50 cc. of 95% alcohol, rinsed down through the condenser; 0.19 g. of lead acetate dissolved in 20 cc. of water was then added and the yellow precipitate which formed was stirred to promote crystallization. After a few minutes it was filtered off, washed with a small quantity of 50% aqueous alcohol, and dried at 100°.

The clear filtrate, which gave a negative test for thiophenol, was then treated with a solution of 0.22 g. of pure colorless phenylhydrazine in 20 cc. of 10% acetic acid. The white precipitate of the phenylhydrazone was stirred for a few minutes and then filtered off. It was washed once on the filter with 20% aqueous alcohol and then dried in the oven at 100°.

In this way, 0.210 g. of lead phenyl mercaptide was obtained, its identity being established by analysis (see below); calcd., 0.212 g. The weight of benzaldehyde phenylhydrazone (m. p. 156°) obtained was 0.360 g., whereas theory requires 0.392 g. However, the solubility of the hydrazone in cold dilute alcohol easily explains this discrepancy.

Analysis of Lead Phenyl Mercaptide.—0.205 g. of the mercaptide obtained above was slowly heated in a porcelain crucible until no more diphenyl sulfide was given off. At constant weight, 0.115 g. of lead sulfide remained, equivalent to 48.54% Pb. Calcd. for $Pb(SC_6H_5)_2$: Pb, 48.71.

Condensations of Other Hydramides and Mercaptans.—Numerous other condensations were carried out in the manner just described. In Table I are collected physical and analytical data concerning all of the reaction products thus far obtained.

TABLE I

PRODUCTS FROM THE CONDENSATION OF HYDRAMIDES WITH THIOPHENOLS OR MERCAPTANS

Hydramide	Product, amine	Crystal form, C = colorless	M. p., °C.
Hexamine[a]	Tri-phenylmercaptomethyl-	...	Oil
Hexamine	Tri-*p*-bromophenylmercaptomethyl-	C. glittering prisms[c]	135
Hexamine	Tri-*p*-nitrophenylmercaptomethyl-	Yellow needles[e]	146
Hexamine	Tri-*p*-cresylmercaptomethyl-	C. glittering prisms[g]	52
Hexamine	Tri-benzylmercaptomethyl-	C. needles[h]	46
Hydrobenzamide	Benzal-phenyl-mercaptobenzyl-	C. prisms[h]	79.5
Hydrobenzamide	Benzal-*p*-cresylmercaptobenzyl-	C. needles[h]	74
Hydrobenzamide	Benzal-benzylmercaptobenzyl-	C. needles[h]	67
3,3',3"-Trinitrohydrobenzamide	3-Nitrobenzalphenylmercapto-3'-nitrobenzyl-	Pale yellow needles[h]	122
Hydro-*p*-toluamide	Methylbenzalphenylmercaptotolyl-	C. microcryst. powder[h]	71
Hydrofurfuramide	Furfural-phenylmercaptofurfuryl-	Small glittering prisms[k]	49

Formula	Molecular weight Calcd.	Molecular weight Found	Analyses, % Calcd.		Analyses, % Found			
$C_{21}H_{21}NS_3$	383	358, 369[b]	C, 65.79	H, 5.47	65.15	65.13	5.40	5.47
			N, 3.65	S, 25.09	4.16	4.28	25.73	
$C_{21}H_{18}NBr_3S_3$	620	597[d]	Br, 38.70		39.03			
$C_{21}H_{18}O_6N_4S_3$	528	520, 569[f]	S, 18.18		18.08			
$C_{24}H_{27}NS_3$	425		C, 67.76	H, 6.35	67.79	67.77	5.91	6.06
$C_{24}H_{27}NS_3$	425	417[b]	C, 67.76	H, 6.35	67.57	67.88	6.04	6.11
			N, 3.30	S, 22.60	3.52	3.60	22.30	
$C_{20}H_{17}NS$	303	285[b]	C, 79.16	H, 5.65	79.41	79.42	5.91	5.25
			N, 4.62	S, 10.57	5.05		9.98	
$C_{21}H_{19}NS$	317	303[d]	C, 79.49	H, 5.99	79.44		5.58	
			N, 4.41		4.72			
$C_{21}H_{19}NS$	317	293, 309[b]	C, 79.49	H, 5.99	78.60[j]		5.77	
$C_{20}H_{15}O_4N_3S$	393	401[d]	C, 61.07	H, 3.81	61.06		4.03	
$C_{22}H_{21}NS$	331		C, 79.75	H, 6.34	79.69		5.90	
$C_{16}H_{13}O_2NS$	283		C, 67.84	H, 4.55	67.88		4.63	

[a] Hexamethylenetetramine. [b] In freezing benzene. [c] From benzene. [d] In boiling, 1,4-dioxane. [e] From acetic acid. [f] In boiling benzene. [g] From 1:1 alcohol–ether. [h] From alcohol. [j] This compound burned only with great difficulty. [k] From ligroin (b. p. 70°); slowly turns brown on standing.

Summary

1. It has been shown that hexamethylenetetramine is decomposed by thiophenol when boiled with it in 1,4-dioxane solution. Two atoms of nitrogen per molecule of hexamethylenetetramine are eliminated as ammonia, the other product being $N(CH_2SC_6H_5)_3$.

2. Numerous other thiophenols and mercaptans have been shown to cause analogous decompositions of hexamethylenetetramine.

3. It has been shown that hydrobenzamide, hydrofurfuramide and other hydramides are partially decomposed by thiophenols when boiled in 1,4-dioxane solution. These reactions are of the same type, yielding the typical product $RCH{=}NCH(SR')R$, as well as ammonia.

4. Evidence for the stoichiometry of these reactions has been presented, as well as data concerning products from eleven of them.

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