[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SYRACUSE UNIVERSITY]

The Condensation of Thiophenols with Secondary Amines and Formaldehyde

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In the condensation of formaldehyde and secondary amines with thiophenols aryl dialkylaminomethyl sulfides and not the expected Mannich bases were obtained. Picrates of these sulfides are described. *p*-Nitrobenzoyl chloride forms stable compounds, presumed to be sulfonium salts, with the sulfides obtained from *p*-thiocresol and the thionaphthols, whereas from the other sulfides only the *p*-nitrobenzoate of the original thiophenol could be isolated.

TABLE I

CONDENSATION PRODUCTS

Thiophenol	Amine[a]	M.p. or b.p., °C.[b]	Yield, %	Formula	Analyses, %	
					Calcd.	Found
Thiophenol	P[c]	138–141 (5–6)	67	$C_{12}H_{17}NS$	S, 15.46	15.31, 15.75
	M[d]	146–149 (5–6)	33	$C_{11}H_{15}ONS$	S, 15.32	15.48, 15.31
	D[e]	110–112 (5–6)	71	$C_{11}H_{17}NS$	S, 16.42	16.25, 16.61
o-Thiocresol	P	133–135 (2–3)	45	$C_{13}H_{19}NS$	S, 14.48	14.55, 14.45
	M	138–140 (2–3)	54	$C_{12}H_{17}ONS$	S, 14.36	14.35, 14.61
	D	115–117 (2–3)	67	$C_{12}H_{19}NS$	S, 15.32	15.47, 15.10
m-Thiocresol	P	141–142 (2–3)	64	$C_{13}H_{19}NS$	S, 14.48	14.86, 14.86
	M	133–137 (2–3)	79	$C_{12}H_{17}ONS$	S, 14.36	14.28, 14.54
	D	114–117 (2–3)	55	$C_{12}H_{19}NS$	S, 15.32	15.47, 15.45
2-Thionaphthol	P	48–49	89	$C_{16}H_{19}NS$	S, 12.46	12.48, 12.52
	M	47–48	96	$C_{15}H_{17}ONS$	S, 12.36	12.48, 12.60
1-Thionaphthol	P	136–137	89	$C_{16}H_{19}NS$	S, 12.46	12.34, 12.30
	M	73–74	88	$C_{15}H_{17}ONS$	S, 12.36	12.30, 12.30
p-Nitro-	P	90–93	59	$C_{12}H_{26}N_2O_2S$	S, 12.70	12.66, 12.88
	M	79–81	70	$C_{11}H_{14}N_2O_3S$	S, 12.61	12.76, 12.91
p-Chloro-	P	47–49	43	$C_{12}H_{16}NSCl$	Cl, 14.68	14.68, 14.88
	M	60–61	79	$C_{11}H_{14}ONSCl$	Cl, 14.55	14.69, 14.57
	D	135–138 (2–3)	43	$C_{11}H_{16}NSCl$	Cl, 15.44	15.45, 15.57
p-Bromo-	P	54–55	44	$C_{12}H_{16}NSBr$	Br, 27.93	27.73, 27.54
	M	66–66.5	69	$C_{11}H_{14}ONSBr$	Br, 27.73	27.84, 27.61
	D	110–115 (2–3)	38	$C_{11}H_{16}NSBr$	Br, 29.15	29.62, 30.35
2,5-Dibromo-	P	39–40	47	$C_{12}H_{15}NSBr_2$	Br, 43.80	44.69, 43.77
	M	84–85	61	$C_{11}H_{13}ONSBr_2$	Br, 43.56	43.77, 43.87
	D	122–124 (4–5)	31	$C_{11}H_{15}NSBr_2$	Br, 45.29	45.93, 46.01
p-Methoxy-	P	127–131 (4–5)	38	$C_{13}H_{19}NOS$	S, 13.52	13.46, 13.36
	M	50–51	73	$C_{12}H_{17}O_2NS$	S, 13.41	13.37, 13.27
	D	107–110 (4–5)	40	$C_{12}H_{19}NOS$	S, 14.25	14.09, 14.07
p-Thiocresol	P	32–32.5	76	$C_{13}H_{19}NS$	S, 14.48	14.28, 14.41
	M	38–38.5	96	$C_{12}H_{17}ONS$	S, 14.36	14.23, 14.32
	D[f]	113–114 (2–3)	58	$C_{12}H_{19}NS$	S, 15.32	15.36, 15.45
2,4,6-Trimethyl	P[g]	46–47	22	$C_{15}H_{23}NS$	S, 12.85	12.75
					N, 5.43	5.61
	M[g]	60–62	26	$C_{14}H_{21}ONS$	S, 12.75	13.16
					C, 66.87	66.97
					H, 8.42	7.97
					N, 5.60	5.59
	D	138–140 (3–4)	40	$C_{14}H_{23}NS$	S, 13.5	13.7
					C, 70.8	71.1
					H, 9.76	9.28
					N, 5.90	5.65

[a] P = piperidine, M = morpholine, D = diethylamine. [b] Numbers in parentheses are pressures in mm.; other values are melting points. [c] Constants of product: n_D 1.5789 (25°), d^{30}_4 1.0520. [d] Constants of product: n_D 1.5809 (25°), d^{30}_4 1.1251. [e] Constants of product: n_D 1.5500 (25°), d^{30}_4 0.9878. [f] Constants of product: n_D 1.5481 (20°), d^{30}_4 0.9804; viscosity in dynes/cm. = 33.60. [g] Analyses performed by Drs. Strauss and Weiler, 164 Banbury Road, Oxford, England.

An investigation of the reactions of thiophenols with secondary amines and formaldehyde indicates that, in general, aryl dialkylaminomethyl sulfides are formed.

$$ArSH + R_2NH + CH_2O = ArSCH_2NR_2 + H_2O$$

Thiophenols therefore behave like aliphatic mercaptans[1] and not like phenols which undergo Mannich reactions.

The reactions of formaldehyde and either piperidine, morpholine or diethylamine with *o*-, *m*- and

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(1) C. M. McLeod and G. M. Robinson, *J. Chem. Soc.*, **119**, 1470 (1921); R. R. Renshaw and D. E. Searle, THIS JOURNAL, **59**, 2056 (1937).

TABLE II

p-NITROBENZOYL CHLORIDE REACTION PRODUCTS[a]

Thiophenol	Amine[b]	M.p., °C.	Yield, %	Formula	Analyses, %	
					Calcd.	Found
p-Thiocresol	P	108–109		$C_{20}H_{23}O_3N_2SCl$	S, 7.88	8.10, 8.19
					Cl, 8.71	8.50, 8.53
	M	155–155.5		$C_{19}H_{21}O_4N_2SCl$	S, 7.84	7.88, 7.99
					Cl, 8.67	8.65, 8.65
	D	193–194		$C_{19}H_{23}O_3N_2SCl$	S, 8.12	8.21, 8.24
					Cl, 8.99	9.06, 9.13
2-Thionaphthol	P	159–160		$C_{23}H_{23}O_3N_2SCl$	S, 7.24	7.54, 7.54
					Cl, 8.01	7.90, 8.12
	M	176–178		$C_{22}H_{21}O_4N_2SCl$	S, 7.21	7.48, 7.58
					Cl, 7.97	7.50, 7.81
1-Thionaphthol	P	198–200		$C_{23}H_{23}O_3N_2SCl$	S, 7.24	6.90, 6.99
					Cl, 8.01	7.81, 8.20
	M	180–182		$C_{22}H_{21}O_4N_2SCl$	S, 7.21	6.99, 7.17
					Cl, 7.97	7.68, 7.70
p-Chloro-	[c]	144–145	57	$C_{13}H_8O_3NSCl$	Cl, 12.10	12.13, 12.20
p-Bromo-	[c]	179–179.5	54	$C_{13}H_8O_3NSBr$	Br, 23.70	23.48, 23.44
2,5-Dibromo	[c]	146–147	49	$C_{13}H_7O_3NSBr_2$	Br, 38.34	38.50, 38.33
p-Nitro-	[c]	150–153		$C_{13}H_8N_2O_6S$	S, 10.53	10.44, 10.65
p-Methoxy	[c]	120–121	63	$C_{14}H_{11}O_4NS$	S, 11.09	11.11, 11.10
2,4,6-Trimethyl-	[d,c]	94–96	55	$C_{16}H_{15}O_3NS$	S, 10.63	10.33
					N, 4.65	4.65

[a] The first seven substances are addition products, assumed to be sulfonium salts; the remainder are *p*-nitrobenzoates of the thiophenols. [b] P = piperidine, M = morpholine, D = diethylamine. [c] The same product was obtained with the thiophenol or with any one of its dialkylaminomethyl sulfides. [d] Analyses performed by Drs. Strauss and Weiler, 164 Banbury Road, Oxford, England.

p-thiocresol, *p*-chloro-, *p*-bromo-, *p*-nitro-, *p*-methoxy-, 2,4,6-trimethyl- and 2,5-dibromothiophenol, and 1- and 2-thionaphthol have been studied. Dialkylaminomethyl sulfides were obtained except in the reaction of diethylamine with *p*-nitrothiophenol, which gave *p*-nitrophenyl sulfide and *p*-nitrophenyl disulfide, and in the case of diethylamine and the thionaphthols from which no products could be isolated.

Evidence for the sulfide structure of the condensation products includes their instability in dilute acids, in which they resemble the aliphatic sulfides,[1] the successful introduction of only one dialkylaminomethyl group, the typical condensation of 2,4,6-trimethylthiophenol in which the *ortho* and *para* positions are blocked, the absorption peak at 3.72 to 3.90 μ for the spectrum of the unassociated SH group,[2] this peak being absent in the piperidinomethyl derivatives of thiophenol, *p*-thiocresol and 2,4,6-trimethylthiophenol.[3]

Based on their reactions with *p*-nitrobenzoyl chloride, the dialkylaminomethyl sulfides can be divided into three groups. The sulfides of *p*-thiocresol and the thionaphthols combined with *p*-nitrobenzoyl chloride in a one-to-one molar ratio, giving products which appear to be sulfonium salts. The sulfides of *o*-thiocresol and 2,4,6-trimethylthiophenol apparently react with *p*-nitrobenzoyl chloride, but pure products could not be isolated. The sulfides of *m*-thiocresol, *p*-chloro-, *p*-bromo-, *p*-nitro- and *p*-methoxythiophenol combined with *p*-nitrobenzoyl chloride to give the *p*-nitrobenzoate esters of the thiophenols.

Finally, the synthesis of the picrates of the sulfides is reported.

Experimental

Synthesis of the Thiophenols.—*p*-Chloro-, *p*-bromo-, *p*-methoxy-, 2,5-dibromo- and 2,4,6-trimethylbenzenesulfonyl chloride were prepared by the method described for benzenesulfonyl chloride[4] and their properties agreed with those reported in the literature.[5] The sulfonyl chlorides were reduced by zinc[6] to give the corresponding thiophenols. 2,5-Dibromothiophenol, melting at 39–40°, was obtained in 50% yield.

Anal. Calcd. for $C_6H_4SBr_2$: Br, 59.63. Found: Br, 59.73, 59.71.

The properties of the other thiophenols agreed with those reported in the literature.[7] *p*-Nitrothiophenol was prepared by the method of Price and Steacy.[8] The source of 1-thionaphthol is described in an earlier paper.[9]

Condensation of Thiophenols with Formaldehyde and Secondary Amines.—The secondary amine was added dropwise to an equimolar quantity of the thiophenol, maintaining the temperature below 20°. In most cases a precipitate of the addition product appeared.[10] To this mixture was added an equimolar quantity of formalin (37% formaldehyde), the temperature was raised to 80° over a one-hour period and then maintained at 80° for two hours. Upon cooling, some of the mixtures gave solid products, others gave oils. The solids obtained from *p*-nitrothiophenol and piperidine or morpholine were recrystallized from ligroin, the others from alcohol. The oils were extracted with ether, the ether solutions dried over magnesium sulfate, the volatile materials removed at about 20 mm. pressure and a

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(2) F. Bell, *Ber.*, **61B**, 1918 (1928).

(3) The infrared spectra of these compounds were determined by Samuel P. Sadtler and Son, Inc., Philadelphia 3, Pa. They also determined the infrared spectrum of a sample of diethylaminomethyl isopropyl sulfide, finding no peak at 3.72 to 3.90 μ.

(4) A. H. Blatt, Editor, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1946, p. 85.

(5) F. Kraft and A. Roos, *Ber.*, **25**, 2260 (1892); M. S. Morgan and L. H. Cretcher, THIS JOURNAL, **70**, 375 (1948); E. H. Huntress and F. H. Carten, *ibid.*, **62**, 511 (1940); A. Holtmeyer, *Z. Chem.*, 686 (1867).

(6) Reference 4, p. 504.

(7) R. Otto, *Ann.*, **143**, 109 (1867); H. Hübner and J. Alsberg, *ibid.*, **156**, 327 (1870); F. Taboury, *Bull. soc. chim.*, [3] **33**, 837 (1892); A. Holtmeyer, *Z. Chem.*, 686 (1867).

(8) C. C. Price and G. W. Steacy, THIS JOURNAL, **68**, 498 (1946).

(9) G. F. Grillot, *et al.*, *ibid.*, **72**, 1863 (1950).

(10) G. F. Grillot and T. J. Brooks, *ibid.*, **72**, 4281 (1950).

TABLE III

PICRATES OF CONDENSATION PRODUCTS

				Analyses, %	
Thiophenol	Amine[a]	M.p., °C.	Formula	Calcd.	Found
Thiophenol	P	142–143	$C_{18}H_{20}O_7SN_4$	S, 7.54	7.51, 7.41
	M	132–133	$C_{17}H_{18}O_8SN_4$	S, 4.80(di)	4.48, 5.09
	D	87.5–89	$C_{17}H_{20}O_7SN_4$	S, 7.35	7.33, 7.30
o-Thiocresol	P	149–151	$C_{19}H_{22}O_7SN_4$	S, 7.13	7.28, 7.24
	M	159–160	$C_{18}H_{20}O_8SN_4$	S, 7.10	7.36, 7.13
	D	108–110	$C_{18}H_{22}O_8SN_4$	S, 7.32	7.36, 7.10
m-Thiocresol	P	133–134	$C_{19}H_{20}O_7SN_4$	N, 12.42	11.8
	M	145–147	$C_{18}H_{20}O_8SN_4$	N, 12.35	12.8
	D	87–89	$C_{18}H_{22}O_7SN_4$	N, 12.78	13.2
p-Chlorothiophenol	P	160–161	$C_{18}H_{19}O_7SN_4Cl$	Cl, 7.54	7.69, 7.64
	M	172–173	$C_{17}H_{17}O_8SN_4Cl$	Cl, 7.50	7.69, 7.69
	D	124–125	$C_{17}H_{19}O_7SN_4Cl$	Cl, 7.77	7.81, 7.86
p-Bromothiophenol	P	162–163	$C_{18}H_{19}O_7SN_4Br$	Br, 15.59	15.39, 15.46
	M	172–174	$C_{17}H_{17}O_8SN_4Br$	Br, 15.50	15.10, 15.10
	D	127–128	$C_{17}H_{19}O_7SN_4Br$	Br, 15.90	16.10, 16.05
2,5-Dibromothiophenol	P	157–158	$C_{18}H_{18}O_7SN_4Br_2$	Br, 26.91	26.62, 26.73
	M	174–175	$C_{17}H_{16}O_8SN_4Br_2$	Br, 26.82	27.01, 27.19
	D	112–113	$C_{17}H_{18}O_7SN_4Br_2$	Br, 27.46	27.12, 26.98
p-Methoxythiophenol	P	145–146	$C_{19}H_{22}O_8SN_4$	S, 6.88	6.94, 6.95
	M	158–159	$C_{18}H_{20}O_9SN_4$	S, 6.85	6 66, 6.72
	D	110–111	$C_{18}H_{22}O_8SN_4$	S, 7 06	6.91, 6.88
2,4,6-Trimethylthiophenol[b]	P	179–181	$C_{21}H_{26}O_7SN_4$	S, 6.70	6.48
				N, 11.7	11.55
	M	174–175	$C_{20}H_{24}O_8SN_4$	S, 6.67	6.51
				N, 11.7	11.5
	D	149–150	$C_{20}H_{26}O_7SN_4$	S, 6.87	7.08
				N, 12.0	12.1

[a] P = piperidine, M = morpholine, D = diethylamine. [b] Analysis performed by Drs. Strauss and Weiler, 164 Banbury Road, Oxford, England.

temperature of about 50°, and the oily products finally distilled at 1 to 5 mm. pressure. In the case of the compounds obtained from 2,4,6-trimethylthiophenol and piperidine or morpholine, however, the products crystallized upon removal of the ether.

Table I summarized the data concerning these products.

Reaction of the Condensation Products with *p*-Nitrobenzoyl Chloride.—Fifty milliliters of a freshly prepared and filtered solution of 11 g. of *p*-nitrobenzoyl chloride in dry toluene was added to a boiling solution of 15 g. of the condensation product in 100 ml. of dry toluene, and the mixture was refluxed for two hours.

The products resulting from the addition of *p*-nitrobenzoyl chloride (assumed to be sulfonium salts) precipitated when the toluene solution was cooled. These were filtered and recrystallized, the product of 1-naphthyl morpholinomethyl sulfide from dioxane–alcohol (60–40), the product of 1-naphthyl piperidinomethyl sulfide from dioxane–alcohol (50–50) by adding water, and the remaining addition products from 95% alcohol, after which they were washed with ether and dried in a vacuum desiccator.

In the other cases, *p*-nitrobenzoates of the thiophenols were formed and did not separate from the cooled toluene solution. These solutions were concentrated until the esters crystallized. The *p*-nitrobenzoates were also independently synthesized from *p*-nitrobenzoyl chloride and the thiophenols[9] in yields of 50–60%. The *p*-nitrobenzoate of 2,4,6-trimethylthiophenol was prepared by dissolving the thiophenol in a 10% sodium hydroxide solution, adding a slight excess of *p*-nitrobenzoyl chloride and shaking the mixture for two hours. The yellow solid product was recrystallized from 95% alcohol.

Table II summarizes the data concerning the *p*-nitrobenzoyl chloride products.

Picrates of the condensation products were prepared by the usual methods. Analytical data and physical constants for these picrates are listed in Table III.

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