dimethylamine was added to 0.1 mole of sodium dithioacetate in about 150 ml. of water. The solution was stirred gently at room temperature for 3 hours. The amino ester separated as a red oil; at the end of 3 hours the color of the sodium dithioacetate had been almost completely discharged. The ester was taken up in benzene and then extracted from the benzene solution with 20-ml. portions of 5% hydrochloric acid. A slight excess of 5% sodium hydroxide was added to the aqueous solution of the ester hydrochloride, and the free ester was again extracted with benzene. The benzene solution was dried for 3 hours over anhydrous potassium carbonate and used in the preparation of the hydrochloride and the methiodide.

β-Dithioacetoxyethyldimethylammonium Chloride.—Cylinder hydrogen chloride was passed through concentrated sulfuric acid and a spray trap, and then bubbled into the dry benzene solution of the β-dimethylaminoethyl ester prepared from 0.1 mole of sodium dithioacetate. The hydrochloride precipitated as an amorphous yellow solid. Passage of hydrogen chloride through the solution was continued until the supernatant benzene was practically colorless. A yield of 15.2 g. of the hydrochloride (76%, calcd. from the sodium salt) was obtained. The hydrochloride was recrystallized twice from chlorobenzene as hygroscopic yellow plates melting at 130–132°.

Anal. Calcd. for $C_6H_{14}ClNS_2$: N, 7.01; S, 32.10. Found: N, 6.80; S, 32.35.

β-Dithioacetoxyethyltrimethylammonium Iodide (Dithioacetylcholine Iodide).—Eighty-five grams (0.6 mole) of methyl iodide was added to the dry benzene solution of the β-dimethylaminoethyl ester prepared from 0.1 mole of sodium dithioacetate. The mixture was allowed to stand for three days at room temperature. The methiodide precipitated as an amorphous greenish-yellow solid which was analyzed without recrystallization. A yield of 22.0 g. (72% from the sodium salt) was obtained; m.p. 172.5–173.5° (dec.), solubility in water 3.3 g. per 100 ml. at 28°.

Anal. Calcd. for $C_7H_{16}INS_2$: N, 4.59; S, 21.01. Found: N, 4.56; S, 21.00.

Summary

1. β-Dithioacetoxyethyldimethylammonium chloride and β-dithioacetoxyethyltrimethylammonium iodide (dithioacetylcholine iodide) have been prepared.

2. A new derivative, the *p*-bromophenacyl ester, of dithioacetic acid has been prepared.

CHAPEL HILL, NORTH CAROLINA RECEIVED MAY 4, 1950

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

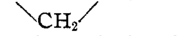
β-Dimethylaminoethyl Esters of Organic Dithio Acids. II. Esters of Aromatic Dithio Acids

BY R. W. BOST AND OTIS L. SHEALY[1]

The previous paper in this series[2] described a synthesis of the β-dimethylaminoethyl ester of dithioacetic acid. The analogous esters of a series of eleven aromatic dithio acids have now been prepared. Synthesis of these esters was accomplished by treating zinc or sodium salts of the acids with β-chloroethyldimethylamine.

With the exception of 4-methyldithiobenzoic acid, which was obtained by the action of carbon disulfide on *p*-tolylmagnesium bromide, the aromatic dithio acids were prepared by a modification of the method of Levi and Bruni.[3] Aromatic aldehydes, dissolved or suspended in alcohol, were heated with ammonium polysulfide of the approximate composition $(NH_4)_2S_2$. Acidification of the colored supernatant liquid gave "dithio acids."[3] However, it was found that yields of acid, in some cases the major part of the product, could also be obtained from the resinous material which precipitated on heating the aldehyde–ammonium polysulfide mixture. Digestion of this resinous material with saturated alcoholic potassium hydroxide, followed by acidification, gave an acid identical in all respects with that obtained from the supernatant liquid. In view of the well-known susceptibility of the dithio acids to oxidation by atmospheric oxygen, no attempt was made to isolate and purify the free acids. Instead, the acids were isolated as their sodium and zinc salts. The sodium salts were characterized by the formation of S-benzylpseudothiuronium salts or *p*-bromophenacyl esters.

In the initial work β-dimethylaminoethyl esters were synthesized by refluxing β-chloroethyldimethylamine with zinc salts of the acids in anhydrous organic solvents. The zinc chloride was filtered from the reaction mixture, and the highly colored solution of the ester was used directly in the formation of derivatives. Though this method was successful with dithiobenzoic, 4-methydithiobenzoic and 4-methoxydithiobenzoic acids, wider application was hindered by difficulty in finding suitable solvents for the zinc salts.

A more satisfactory synthesis of the esters involved reaction of sodium salts of the acids with β-chloroethyldimethylamine in aqueous solution. The reaction was carried out at room temperature; the dithio esters separated as water insoluble colored oils which were converted into hydrochlorides and methiodides. Formation of the esters in water solution probably involved the attack of the nucleophilic $ArCSS^-$ ion on an intermediate ethyleneimonium ion,  $\underset{\diagdown CH_2 \diagup}{CH_2\text{——}N^+(CH_3)_2}$. Bartlett, *et al.*,[4] have shown that the ethyleneimonium ion is an intermediate in cyclization and replacement reactions of β-halogenated trialkylamines. In this case the attack of the $ArCSS^-$ ion takes precedence over the dimeric quaternization of the amine, which normally goes to virtual completion in two to three hours in water solution.[5]

The dithio ester derivatives, such as hydrochlorides, citrates and methiodides, showed reactions typical of compounds containing thion sulfur. Addition of aqueous silver nitrate to the water solutions gave an immediate precipitate of silver sulfide. The derivatives were readily oxidized by 3% hydrogen peroxide or 3 *N* nitric acid;

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[1] du Pont Fellow in Chemistry, 1949–1950.

[2] Bost and Shealy, THIS JOURNAL, **73**, 24 (1951).

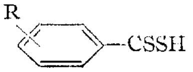
[3] Levi and Bruni, *Atti. Accad. Lincei*, **32**, i, 5 (1923).

[4] Bartlett, Ross and Swain, THIS JOURNAL, **69**, 2971 (1947).

[5] Knorr, *Ber.*, **37**, 3506 (1904).

Table I

Derivatives of Dithio Acids



Cpd.	R	Yield of acid,[a] %	Deriv. prepared[b]	Crystn. solv. for deriv.	Crys. form of deriv.[c]	M. p., °C.	Formula of deriv.	Analyses of derivs., %			
								Nitrogen		Sulfur	
								Calcd.	Found	Calcd.	Found
I	None	36	A	Water	o.-r. p.	101.5–102.5	$C_{15}H_{16}N_2S_3$	8.74	8.93	30.01	29.87
II	2-Chloro	22	A	Water	y. n.	87–88	$C_{15}H_{15}N_2S_3Cl$	7.89	7.98	27.10	26.87
III	4-Chloro	35	A	Water	o. p.	109–110	$C_{15}H_{15}N_2S_3Cl$	7.89	7.96	27.10	26.81
IV	2-Hydroxy	27	B	95% alc.	y. n.	122–123	$C_{15}H_{11}O_2S_2Br$			17.46	17.65
V	4-Hydroxy	45	A	Water	r. p.	75–76	$C_{15}H_{16}N_2OS_3$	8.33	8.31	28.58	28.38
VI	4-Methoxy	25	A	Water	o. p.	98–99	$C_{16}H_{18}N_2OS_3$	7.99	8.00	27.44	27.36
VII	4-Amino	16[d]	B	95% alc.	o. n.	174–175 (dec.)	$C_{15}H_{12}NOS_2Br$			17.50	17.39
VIII	4-Dimethylamino	37	A	Acetonitrile	o. n.	132.0–132.5	$C_{17}H_{21}N_3S_3$	11.56	11.52	26.46	26.29
IX	4-Methyl	24	A	Water	r. p.	107–108	$C_{16}H_{18}N_2S_3$	8.37	8.40	28.75	28.53
X	3,4-Methylenedioxy	23	A	Water	o. n.	92–93	$C_{16}H_{16}N_2O_2S_3$	7.68	7.62	26.39	26.41
XI	3-Methoxy-4-hydroxy	29	B	95% alc.	o.-y. n.	131–132	$C_{16}H_{13}O_3S_2Br$			16.14	16.12

[a] As the sodium salt. [b] A = S-benzylpseudothiuronium salt; B = *p*-bromophenacyl ester. [c] o. = orange, r. = red, y. = yellow; n. = needles, p. = plates. [d] Calculated from 4-nitrobenzaldehyde.

oxidation products included the oxygen acid corresponding to the dithio acid which had been esterified. Dilute aqueous solutions of the ester derivatives were reasonably stable; absorption spectra studies indicated no appreciable decomposition after one week at room temperature.

The hydrochlorides and citrates (Table II) of the dithio esters synthesized were of particular interest because of their analogy to the novocaine type esters. Since Einhorn and Uhlfelder[6] synthesized novocaine, a host of structural modifications have been made in the search for more effective local anesthetics with low toxicity. However, a complete study of the effect of substituting sulfur for oxygen in the ester linkage had not been made. Hansen and Fosdick[7,8] synthesized the thiol analog of novocaine, $p\text{-}H_2N\text{-}C_6H_4\text{-}CO\text{-}S\text{-}CH_2\text{-}CH_2\text{-}N\text{-}(C_2H_5)_2\cdot HCl$, and found it to be six times as active as novocaine but more toxic. Other thiol and thion analogs of the anesthetic esters have been prepared[9,10,11,12] and for the most part have shown promising activity. Since the hydrochlorides and citrates in Table II represent the hitherto unreported dithio analogs of the anesthetic esters, they were tested for activity as local anesthetics. Preliminary testing of six of the compounds was accomplished by the "goldfish test" of Adams and coworkers.[13] Compounds IIa, VIa and VIIIa showed a greater anesthetic potency than novocaine. However, Ia, Xa and XIa were found to have a marked toxicity for goldfish. More exhaustive corneal and infiltration tests were conducted by the Wm. S. Merrell Co. Results indicated that all of the compounds tested were too irritating to have practical value as topical or parenteral anesthetics.

Methiodides of the dithio esters (Table III) are analogs of acetylcholine iodide. In experiments conducted by the Wm. S. Merrell Co., the parasympathomimetic activity of the methiodides was evaluated by determining the increase in tonus which aqueous solutions produced in rabbit intestine. A positive activity was observed, but was in all cases much smaller and more evanescent than that produced by acetylcholine or prostigmine.

The vivid coloration of the amino-alkyl dithio esters indicated an experimental evaluation of their properties as dyestuffs. Compounds Ia and IVa were found to be direct dyes for wool, silk and acetate rayon. However, the colors produced showed a high fugitivity to light, water and mild oxidizing agents.

Absorption spectra studies of the dithio ester derivatives and related oxygen compounds will be reported in a subsequent paper.

Acknowledgment.—The authors are deeply grateful to the Wm. S. Merrell Co. of Cincinnati, Ohio, which—through the courtesy of Dr. Robert S. Shelton and Dr. M. G. Van Campen, Jr.—conducted a pharmacological study of a number of the compounds synthesized.

Experimental

Nitrogen was determined by the micro Dumas procedure. Sulfur was determined by the micro method of Hallett and Kuipers.[14] Melting points were obtained in an oil-bath with a calibrated thermometer. Samples were introduced about 10° below the recorded melting point and the temperature of the bath was raised 1° per minute. In most cases the melting point varied with the length and rate of heating of the sample.

Sodium Salts of Dithio Acids.—4-Methyldithiobenzoic acid was synthesized by the method of Bost and Mattox.[15] The remaining dithio acids were prepared by a modification of the method of Levi and Bruni.[3] General procedure: Sublimed sulfur (320 g.) was suspended in a mixture of 1530 ml. of ammonium hydroxide (sp. gr. 0.90) and 700 ml. of water, and 10 moles of hydrogen sulfide was bubbled slowly into the stirred solution. One mole of the required aromatic aldehyde (freshly purified) was dissolved or suspended in 300 ml. of 95% ethanol, heated to about 60°, stirred and 440

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(6) Einhorn and Uhlfelder, *Ann.*, **371**, 131 (1909).

(7) Hansen and Fosdick, This Journal, **55**, 2872 (1933).

(8) Hansen and Fosdick, *J. Pharmacol.*, **50**, 323 (1934).

(9) Karjala and McElvain, This Journal, **55**, 2966 (1933).

(10) Lischer and Jordan, *ibid.*, **59**, 1623 (1937).

(11) Fosdick and Barnes, *ibid.*, **67**, 335 (1945).

(12) Clinton and Salvador, *ibid.*, **68**, 2076 (1946).

(13) Adams, *et al.*, *ibid.*, **48**, 1758 (1926).

(14) Hallett and Kuipers, *Ind. Eng. Chem., Anal. Ed.*, **12**, 360 (1940).

(15) Bost and Mattox, This Journal, **52**, 332 (1930).

ml. of the ammonium polysulfide prepared as above was added slowly. The solution was boiled for 10 minutes. After cooling to room temperature, the reddish-black supernatant liquid was filtered, and the precipitated resinous material was warmed for 24 hours with 112 g. of potassium hydroxide dissolved in the minimum amount of 95% ethanol, and stirred frequently. After 24 hours the insoluble material was filtered off, and the filtrate combined with that from the original reaction mixture. The combined filtrates were covered with about 500 ml. of ether, and ice-cold 1:1 hydrochloric acid was added to free the dithio acid. The colored ether extract was washed several times with cold water, and was then extracted with 100-ml. portions of 1.25 *N* NaOH until the ether layer was practically colorless. The solution of the sodium salt was acidified with cold dilute hydrochloric acid, the dithio acid taken up in ether, and the extraction with 1.25 *N* NaOH repeated. The liberation of the acid and extraction with sodium hydroxide was repeated a third time. The volume of sodium hydroxide used in the final extraction procedure was noted, and the solution of the sodium salt was back-titrated with 1.50 *N* HCl until free dithio acid just began to separate. Yields of the sodium salts (Table I) were calculated from the volumes of sodium hydroxide and hydrochloric acid used. After back-titration, the solution of the sodium salt was extracted twice with 100-ml. portions of ether and stored in a tightly stoppered flask.

Aqueous solutions of the pure sodium salts of the dithio acids were stable for a period of one to three months. At the end of this time appreciable decomposition (precipitation of sludge or oil) was usually observed.

An attempted synthesis of *m*-nitrodithiobenzoic acid from *m*-nitrobenzaldehyde was unsuccessful due to a partial reduction of the nitro group. Derivatives prepared from the resulting sodium salt gave analyses intermediate between those calculated for the *m*-nitro and *m*-amino products.

In the synthesis of *p*-aminodithiobenzoic acid, *p*-nitrobenzaldehyde was reduced with a sodium bisulfite solution according to the method of Cohn and Springer.[16] The reaction product was insoluble in alcohol. However, on the addition of ammonium polysulfide to the hot alcoholic suspension, the formation of the dithio acid proceeded normally.

On the acidification of the sodium salt of *p*-dimethylaminodithiobenzoic acid, the free acid separated as an oily yellow solid insoluble in ether. The solid acid, however, concentrated in the ether layer, and the ether suspension could be washed with water and extracted with sodium hydroxide in the usual manner.

S-Benzylpseudothiuronium Salts of Dithio Acids (Table I).—Sodium salts of the dithio acids were characterized by the formation of the solid S-benzylpseudothiuronium salts. Two grams of S-benzylpseudothiuronium chloride was dissolved in 20 ml. of hot water, the solution stirred, and 0.01 mole of the sodium salt of the dithio acid in about 10 ml. of water was added slowly. The mixture was boiled gently for 3 to 4 minutes and allowed to cool to room temperature. The colored oily precipitates were filtered and recrystallized. In a few cases in which non-crystallizable oils were obtained, *p*-bromophenacyl esters were prepared.

***p*-Bromophenacyl Esters of Dithio Acids (Table I).**—*p*-Bromophenacyl bromide (2.8 g.) was dissolved in 25 ml. of hot 95% ethanol. The sodium salt of the dithio acid (0.01 mole) in about 10 ml. of water was added slowly with stirring. The mixture was boiled gently for 10 minutes and allowed to cool slowly to room temperature. The colored precipitates were separated and recrystallized.

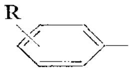
Zinc and Sodium Salts.—One-tenth mole of zinc acetate was dissolved in 500 ml. of water, acidified with 50 ml. of acetic acid, and 0.21 mole of the sodium salt of the dithio acid was added with constant stirring over a period of 3 to 4 hours. The colored amorphous precipitates were then filtered and dried. Near quantitative yields were obtained.

The crude zinc salts, which could not be crystallized without considerable decomposition, proved to be satisfactory for the synthesis of the dithio esters.

The crude zinc salts were more stable than aqueous solutions of the sodium salts, no apparent decomposition occurring after as long as one year. The zinc salts were thus used as a convenient "storage form" for the dithio acids. Reconversion to the sodium salts was accomplished by di-

TABLE II

SALTS OF β-DIMETHYLAMINOETHYL ESTERS OF DITHIO ACIDS—(ALL ESTERS SYNTHESIZED BY PROCEDURE B)



$—CSS—CH_2—CH_2—N(CH_3)_2·HA$

Cpd. no.	R	Phys. form of ester[a]	Solv. for ester	Salt prepared[b]	Yield,[c] %	Crystn. solv.	Crystn. form[d]	M. p., °C.	Formula	Analyses, % Nitrogen Calcd.	Nitrogen Found	Sulfur Calcd.	Sulfur Found
Ia	None	r. o.	Ether	Hyd.	75	CH_3NO_2	r. pr.	160–161	$C_{11}H_{16}NS_2Cl$	5.35	5.36	24.49	24.17
IIa	2-Chloro	y. s.	Ether	Hyd.	76	CH_3NO_2	y. pr.	171–172	$C_{11}H_{15}NS_2Cl_2$	4.73	4.65	21.64	21.32
IIIa	4-Chloro	r. o.	Ether	Citr.	58	Water	p. pl.	140.5–141.5 (dec.)	$C_{17}H_{23}NO_7S_2Cl$	3.09	3.16	14.16	14.06
IVa	2-Hydroxy	r. o.	$CHCl_3$	Citr.	60	Water	y. pr.	147–148 (dec.)	$C_{17}H_{23}NO_8S_2$	3.23	3.26	14.79	14.81
Va	*4-Hydroxy*	*y.-or. s.*	*Acetone*	*Hyd.*	40	CH_3NO_2	*o.* pr.	157.0–158.5	$C_{11}H_{16}NOS_2Cl$	5.04	5.10	23.08	22.66
VIa	4-Methoxy	r. o.	Ether	Hyd.	79	95% alc.	o pr.	194.0–194.5	$C_{12}H_{18}NOS_2Cl$	4.80	4.75	21.97	21.63
VIIa	4-Amino	r. o.	Ether	Mono-citr.	42	Water	y. c.	162.0–162.5 (dec.)	$C_{17}H_{24}N_2O_7S_2$	6.48	6.47	14.83	15.06
VIIIa	4-Dimethylamino	r.-b. s.	$CHCl_3$	Mono-hyd.	52	Alc.–water	y.-o. pl.	226 (dec.)	$C_{13}H_{21}N_2S_2Cl$	9.19	9.06	21.03	21.28
IXa	4-Methyl	r. o.	Ether	Citr.	55	Water	y. a.	128.5–130.0 (dec.)	$C_{18}H_{25}NO_7S_2$	3.25	3.21	14.86	15.04
Xa	3,4-Methylenedioxy	y.-b. s.	Ether	Hyd.	57	CH_3NO_2	r. n.	189–190	$C_{12}H_{16}NO_2S_2Cl$	4.58	4.59	20.96	20.77
XIa	3-Methoxy-4-hydroxy	y.-or. s.	Acetone	Hyd.	42	CH_3NO_2	y.-o. pr.	177–178	$C_{12}H_{18}NO_2S_2Cl$	4.55	4.44	20.83	20.52

[a] b. = brown, or. = orange, r. = red, y. = yellow; o. = oil, s. = solid. [b] Hyd. = hydrochloride, citr. = citrate. [c] Calculated from sodium salt of acid. [d] o. = orange, p. = pink, r. = red, y. = yellow; a. = amorphous, c. = cubes, n. = needles, pl. = plates, pr. = prisms.

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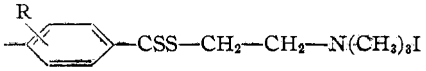
[16] Cohn and Springer, *Monatsh.*, **24**, 87 (1903).

TABLE III

METHIODIDES OF β-DIMETHYLAMINOETHYL ESTERS OF DITHIO ACIDS



Cpd.	R	Synthetic procedure for ester	Solv. for ester	Yield[a] methiodide, %	Crystn. solv.	Crystn. form[b]	M. p., °C.	Formula	Analysis, % sulfur Calcd.	Analysis, % sulfur Found
Ib	None	A	Benzene	45	Water	o.-y. n.	199–200 (dec.)	$C_{12}H_{18}NS_2I$	17.46	17.15
IIb	2-Chloro	B	Ether	80	Water	y. n.	158–159	$C_{12}H_{17}NS_2ClI$	15.96	15.92
IIIb	4-Chloro	B	Ether	60	95% alc.	o. pl.	209.5–210.0 (dec.)	$C_{12}H_{17}NS_2ClI$	15.96	16.23
IVb	2-Hydroxy	B	$CHCl_3$	65	95% alc.	y. n.	187.5	$C_{12}H_{18}NOS_2I$	16.73	16.96
Vb	4-Hydroxy	B	None	55	Water	y. pl.	194–195	$C_{12}H_{18}NOS_2I$	16.73	16.95
VIb	4-Methoxy	A	Xylene	31	Water	r. pr.	198.0–198.5 (dec.)	$C_{13}H_{20}NOS_2I$	16.14	16.26
		B	Ether	74						
VIIIb	4-Dimethylamino	B	$CHCl_3$	56	Water	y. pl.	202–203 (dec.)	$C_{14}H_{23}N_2S_2I$	15.62	15.81
IXb	4-Methyl	A	Benzene	53	Water	y. pl.	183.5–184.5	$C_{13}H_{20}NS_2I$	16.81	16.91
Xb	3,4-Methylenedioxy	B	Ether	59	Water	y. pl.	202.5–203.5 (dec.)	$C_{13}H_{18}NO_2S_2I$	15.59	15.61
XIb	3-Methoxy-4-hydroxy	B	None	71	Water	y. pl.	172–173	$C_{13}H_{20}NO_2S_2I$	15.51	15.63

[a] Calculated from metal salt of acid. [b] o. = orange, r. = red, y. = yellow; n. = needles, pl. = plates, pr. = prisms.

gesting the zinc salts for 24 hours with a 20% excess of 1.0 *M* sodium sulfide. The colored supernatant solution of the sodium salt was filtered and purified by a single liberation-extraction procedure as outlined in the synthesis of the dithio acids; yields 75–85%.

β-Chloroethyldimethylamine.—The free amine was prepared as described in ref. (2). Satisfactory storage was obtained by diluting the free base with an equal volume of dry xylene and storing in the refrigerator. The xylene solution of the amine was used directly in the preparation of dithio esters; the slight amount of the dimer which formed was filtered before use.

β-Dimethylaminoethyl Esters of Dithio Acids. Method A.—One-tenth mole of the crude zinc salt of the dithio acid was dissolved in the minimum volume of the boiling, anhydrous organic solvent indicated in Table III. Two-tenths mole (22 g.) of β-chloroethyldimethylamine was added and the mixture was refluxed for five hours, cooled, and the zinc chloride filtered. The highly colored solution of the ester was used immediately in the preparation of the methiodide.

Method B.—A mixture of 0.11 mole of β-chloroethyldimethylamine and 0.10 mole of the sodium salt of the dithio acid in 150 ml. of water was stirred at room temperature for 3 hours. The colored oily esters which precipitated were dissolved in the solvents indicated in Tables II and III and the solutions dried for 3 hours over anhydrous potassium carbonate.

Hydrochlorides and Citrates of the Dithio Esters (Table II).—The colored, amorphous hydrochlorides, prepared by passing dry gaseous hydrogen chloride through the anhydrous solutions of the esters until the solvent was virtually colorless, could usually be purified by repeated crystallization from nitromethane. In a few cases in which purification was particularly difficult, citrates were prepared by adding approximately twice the calculated amount of citric acid, dissolved in acetone, to a solution of the ester in ether or chloroform. The citrates which precipitated as colored oils, which solidified on standing in the refrigerator, were recrystallized from water.

All of the citrates synthesized showed a very low solubility in water (about 0.1 g. per 100 ml. at 28°). The hydrochlorides showed a greater water solubility ranging from 2 to 12 g. per 100 ml. at 28°.

Methiodides of the Dithio Esters (Table III).—Approximately six times the calculated amount of methyl iodide was added to solutions of the esters in the anhydrous solvents listed in Table III. After four days at room temperature the colored amorphous precipitates were recrystallized from water or ethanol. In a few cases (indicated in Table III) methiodides were prepared by adding eight times the calculated amount of methyl iodide to the solid esters.

All of the methiodides showed a low solubility in water, on the order of 0.1 to 1.0 g. per 100 ml. at 28°.

Summary

Eleven aromatic dithio acids have been prepared and characterized by the formation of S-benzylpseudothiuronium salts or *p*-bromophenacyl esters. β-Dimethylaminoethyl esters of the dithio acids were synthesized and isolated as the hydrochlorides (or citrates) and as the methiodides. The hydrochlorides and citrates were tested for local anesthetic activity and the methiodides for parasympathomimetic activity.

The dithio ester hydrochlorides and citrates were evaluated as dyestuffs.

CHAPEL HILL, N. C. RECEIVED MAY 4, 1950