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Preparation of Symmetrical Diaryl Disulfides Containing Side Chains Terminated by Halogen or by Tertiary Amino Functions

ARTHUR H. WEINSTEIN, ROBERT M. PIERSON, BERNARD WARGOTZ, AND TEH FU YEN

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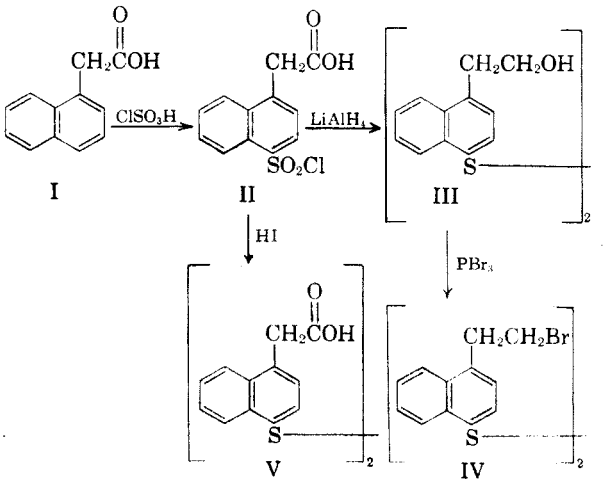
Various methods of preparation for a number of new symmetrically substituted diaryl disulfides containing (*a*) such side chain halogen or pseudo halogen-containing functions as ω-haloalkyl-, ω-haloacyl-, and ω-tosyloxyalkyl-, *e.g.*, bis(4-β-bromoethyl-1-naphthyl) disulfide, bis(4-γ-chloropropoxy-1-naphthyl) disulfide, bis(2-chloroacetamidophenyl) disulfide, bis(4-β-tosyloxyethoxy-1-naphthyl) disulfide, and bis(2-chloroacetophenyl) disulfide, and (*b*) such side chain tertiary amino functions as the isonicotinoyl-, ω-4-pyridylalkyl-, or ω-dimethylaminoalkyl, *e.g.*, bis(2-isonicotinamidophenyl) disulfide, bis[2-β-(2′,4′-pyridylethylthio)propionamidophenyl] disulfide, and bis(4-β-dimethylaminoethoxycarbonyl-2,6-xylyl) disulfide, are described. Chain transfer constant values of a number of these diaryl disulfides (as determined for bulk styrene polymerization at 50°) as well as other physical properties and data relating to the preparation of these disulfides and their intermediates are recorded.

It has been well established that linear polystyrene molecules containing one arylthio (ArS-) group at each chain end, can be prepared by a bulk polymerization process in which a diaryl disulfide modifier as well as an initiator is included in the polymerization recipe.[1] In previous papers, syntheses for a number of symmetrical, substituted diaryl disulfides which have proven to be chain transfer agents for bulk styrene polymerization systems, and sometimes for emulsion diene-containing polymerization systems have been reported.[1-4] This known group of substituted diaryl disulfides included two bis(haloalkylaryl) disulfides, namely bis(2-chloromethylphenyl) and bis-(2-bromomethyl-phenyl) disulfides.[1] One of the prime objectives of the present work was the expansion of the field of symmetrical, side-chain-halogen-substituted diaryl disulfides to include compounds with varying degree of halogen activity, and with chain transfer activity in a range suitable for efficient modification (molecular weight control by chain transfer reaction) of bulk and emulsion polymerization systems. This objective has been attained. A series of symmetrical, haloacyl-, haloalkyl-, and tosyloxylalkyl-substituted diaryl disulfides with fairly high modifier activity [with a range of transfer constant (*C*) values of 0.7 – 2.7[5]] whose halide functions have a wide range of activity toward alcoholic silver nitrate, solutions of sodium iodide in acetone, or tertiary amines, has been prepared.

Four methods for introduction of ω-haloalkyl groups (with alkyl carbon chain longer than one carbon atom) into diaryl disulfide systems have proven successful. Only one of these methods involves direct substitution of the haloalkyl group on the aromatic nucleus. Synthesis of a compound so substituted, bis-(4-β-bromoethyl-1-naphthyl) disulfide (IV), is indicated schematically:



1-Naphthalene acetic acid (I) was chlorosulfonated to the 4-sulfonyl chloride[6] II. This compound was

(1) R. M. Pierson, A. J. Costanza, and A. H. Weinstein, *J. Polymer Sci.*, **17**, 221 (1955).

(2) A. J. Costanza, R. J. Coleman, R. M. Pierson, C. S. Marvel, and C. King, *J. Polymer Sci.*, **17**, 319 (1955).

(3) E. J. Quinn, G. P. Scott, C. King, and C. S. Marvel, "Sterically Hindered Aromatic Disulfides," Copolymer Report No. 3757 to Office of Synthetic Rubber, F.F.C., 1955. [See reference (30) concerning availability of this publication.]

(4) C. S. Marvel, T. H. Shepherd, C. King, J. Economy, and E. D. Vessel, *J. Org. Chem.*, **21**, 1173 (1956).

(5) The *C* values, obtained by measurement of parameters in bulk styrene polymerizations run at 50°, using azoisobutyronitrile as initiator, in accordance with the method of F. R. Mayo, *J. Am. Chem. Soc.*, **65**, 2324 (1943), were determined by Mr. Albert J. Costanza under conditions fully described in (1).

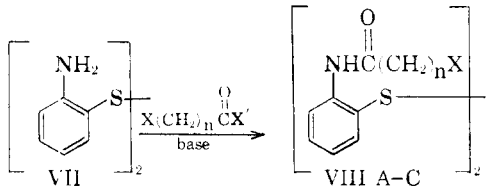
(6) Although indisputable evidence for assignment of the position of the sulfur atom in II at the para position is not presented, known facts about the orientation of the chlorosulfonyl groups of related compounds prepared under similar conditions would indicate that our assumption is well founded: (*a*) The 1-alkoxynaphthalenes chlorosulfonate almost quantitatively at the 4-position.[7] (*b*) Treatment of 1-benzylnaphthalene with chlorosulfonic acid in nitrobenzene yielded the 4-sulfonic acid as the sole product.[8] (*c*) Treatment of 1-methylnaphthalene with chlorosulfonic acid at low temperature yielded the 4-sulfonic acid as the predominant product as well as a small amount of isomeric sulfonic

reduced with lithium aluminum hydride. The reduction product, upon hydrolysis, proved to be bis(4-β-hydroxyethyl-1-naphthyl) disulfide (III) rather than the expected hydroxyethyl thiol.[11a] Compound III was converted to the dibromide IV. The sulfonyl chloride II was selectively reduced to bis(4-carboxymethyl-1-naphthyl) disulfide (V)[11b] with hydriodic acid.

Although bis(4-β-hydroxyethylphenyl) disulfide (VI) was successfully prepared from β-4-aminophenyl-ethanol by the Leuckart xanthate method,[12] a pure dibromide could not be isolated from the reaction mixture of this diol with phosphorus tribromide.

Three methods, other than that already described, leading to syntheses of bis (ω-haloalkylated) diaryl disulfides were developed, all leading to better over-all yields of desired dihalides. However, none of these routes led to synthesis of compounds containing haloalkyl groups directly substituted on aromatic rings, but rather to compounds containing haloalkyl groups linked to aromatic rings *via* oxygen or nitrogen bridges.

A simple example of such a synthesis involving a nitrogen bridge is as follows:



VIII A, n = 1, X = Cl, X′ = Cl
VIII B, n = 1, X = Br, X′ = Br
VIII C, n = 2, X = Br, X′ = Cl

Upon treatment of bis(2-aminophenyl) disulfide (VII) with chloroacetyl chloride in the presence of glacial acetic acid and aqueous sodium acetate[13] at 25°, an 87% yield of bis(2-chloroacetamidophenyl) disulfide (VIII A) was obtained. In a similar manner, the bis(2-bromoacetamido) analog VIII B was prepared. Compound VIII A was also prepared, in poor yield of pure compound, by treatment of VII with chloroacetyl chloride in anhydrous benzene-pyridine system. In this case, the reaction product proved to be a sharp melting, difficultly separable mixture of VIII A with a compound (IX) having the empirical formula $C_{16}H_{13}Cl_3N_2O_2S_2$. Compound IX, isolated by many fold fractional crystallizations of the reaction product with ethanol, was believed to be the unsymmetrical compound, N-chloroacetyl, *N′*-dichloroacetylbis(2-aminophenyl) disulfide. It is believed that presence of IX in the reaction product was caused by presence of dichloracetyl chloride in the chloracetyl chloride reagent. Nevertheless, the yield of bis(2-β-bromopropionamidophenyl) disulfide (VIII C) obtained by haloacylating VII in the benzene-pyridine system was much better than that obtained by the use of the buffered acetate system.

Another member of this family of bis(haloacylamidoaryl) disulfides, namely bis(4-chloroacetamido-1-naphthyl) disulfide (X), was prepared by a more circuitous route. α-Naphthylamine was chloroacetylated to α-chloracetnaphthalide (XI),[14] which was chlorosulfonated to the 4-sulfonyl chloride (XII).[15] By reduction of this sulfonyl chloride with 50% hydriodic acid,[16] the desired disulfide X was obtained.

Data pertaining to the synthesis, physical properties, and polymerization transfer constants of these bis(haloacylamidoaryl) disulfides may be found in Table I.

Attempts to replace the chlorine atoms of VIII A with either the methylthio or *n*-butylthio function, or with the amino function, all resulted in formation of the same non-halogen containing

acids.[9] (*d*) Stewart[10] proved that the only sulfonyl chloride obtained by treatment of cinnamic acid with this reagent was 4-chlorosulfonylcinnamic acid and felt certain that the sulfonyl chloride he obtained from phenylacetic acid was also a para-sulfonyl chloride.

(7) E. H. Huntress and F. H. Carten, *J. Am. Chem. Soc.*, **62**, 511 (1940).

(8) K. Dziewonski and S. Dziecelewski, *Bull. intern. acad. Polonsci.*, 1927A, 273; *cf. Chem. Abstr.*, 22, 2164 (1928).

(9) V. Vesely, F. Stursa, H. Olejnicek and E. Rein, *Collection Czechoslov. Chem. Commun.*, **1**, 493 (1929); *cf. Chem. Abstr.*, **24**, 611 (1930).

(10) J. Stewart, *J. Chem. Soc.*, **121**, 2555 (1922).

(11) (a) Similar experiences were observed when (i) the compound obtained upon acidification of the alkaline hydrolysis product of the (4-β-hydroxyethylphenyl) ester of ethylxanthic acid proved to be bis(4-β-hydroxyethyl phenyl) disulfide (VI) rather than the mercaptan, and when (ii) the hydrolysis product obtained from the reaction of 1-naphthylmagnesium bromide with an atom equivalent of sulfur contained a 70:30 ratio of mercaptan to disulfide. Evidently, the $LiAl^{+4}$ and $MgBr^{+1}$ mercaptides of aryl thiols as well as their alkali and ammonium mercaptides are sensitive to air oxidation; (b) Bis(4-carboxymethoxy-1-naphthyl) disulfide, m.p. 215.0–215.9° in white flakes from aq. HOAc, with (*C*) value of 1.79, was prepared (49%) similarly (Calcd. for $(C_{12}H_9O_3S)_2$: S, 13.74; N.E., 233. Found: C, 13.5, 13.6; N.E. 237) from the intermediate, 4-carboxymethoxy-1-naphthalene sulfonyl chloride, m.p. 177.7–178.7°, in white crystals from 15:1 benzene-nitrobenzene, prepared in turn (69%) by chlorosulfonating 1-naphthoxyacetic acid by the general method of Huntress,[7] at 0°, using 3 moles $ClSO_3H$ per mole of carboxylic acid. Calcd. for $C_{12}H_9ClO_5S$: Cl, 11.79; S, 10.66. Found: Cl, 11.7, 11.7; S, 10.5, 10.7.

(12) (a) R. Leuckart, *J. prakt. Chem.*, [2] 41, 189 (1890); (b) D. S. Tarbell and D. K. Fukushima, *Org. Syntheses*, **Coll. Vol. III**, 809 (1955).

(13) A reagent combination used effectively by W. A. Jacobs and M. Heidelberger, *J. Am. Chem. Soc.*, 41, 1450 (1919), in chloroacetylating various anisidines and phenetidines.

(14) D. Tommasi, *Bull. soc. chim.*, [2] 20, 19 (1873).

(15) This compound was prepared under essentially the same conditions used by L. N. Goldyrev and I. Ya. Postovskii, *J. Appl. Chem. U.S.S.R.*, 11, 316 (1938) for preparation of 4-chlorosulfonyl-1-acetnaphthalide.

(16) A method developed by A. Ekbom, *Ber.*, 24, 335 (1891) for preparation of aryl disulfides from sulfonyl chlorides, and modified by L. Bauer, and J. Cymerman, *J. Chem. Soc.*, 3434 (1949) who developed a homogeneous reaction system by utilization of glacial acetic acid solvent.

TABLE I

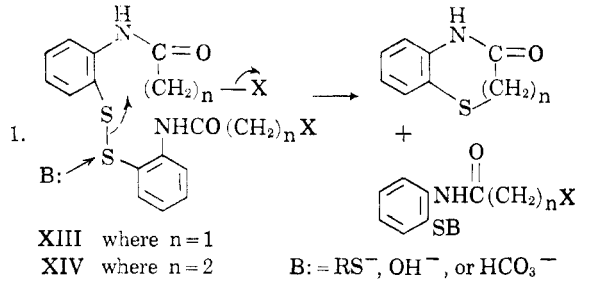
BIS(ω-HALOACYLAMIDOARYL) DISULFIDES

Bis-disulfide[a]	Crude Yield,[b] %	M.P.,[c] °C.	Halogen, % Calcd.	Halogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found	Transfer Constant (C)
2-Chloroacetamidophenyl (VIII A)	87	133.2–133.7[d]	17.79	17.67 17.77	6.98	7.14 7.07	15.97	16.13 16.09	5.3
2-Bromoacetamidophenyl (VIII B)[e]	74	157.4–157.7[f]	32.61	31.43 31.44			13.08	13.10 12.83	3.8
2-β-Bromopropionamidophenyl (VIII C)	79	155.1[f]	30.83	30.90 30.75	5.40	5.50 5.64	12.37	12.57 12.51	7.3
4-Chloroacetamido-1-naphthyl (X)	68	203.5[g]					12.79	12.29 12.39	0.0[h]

[a] All disulfides are white crystalline products. [b] Yields are based on product of less than 3° melting range. [c] Corrected melting points of analytical samples. [d] 85% Aq. ethanol. [e] Calcd. for carbon and hydrogen, %: 39.20; 2.88. Found: 39.05; 39.40; 2.91, 3.04. [f] Absolute ethanol. [g] Dioxane-chlorobenzene. [h] Compound so insoluble in styrene and in most solvents suitable for use in transfer constant determination that it did effect a reduction of molecular weight of polystyrene obtained from a bulk styrene polymerization below that obtained in the control polymerization.

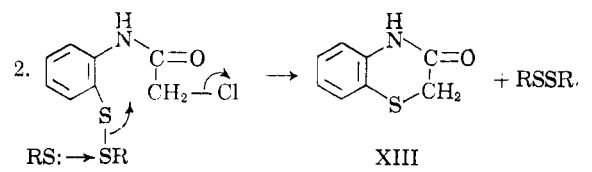
compound of empirical formula C_8H_7NOS, believed to be identical with 3-keto-2,3-dihydro-1,4-benzothiazine (XIII)[17] previously prepared by Unger.[18]

An attempt to hydrolyze the halide functions of VIII C resulted in formation of another non-halogen-containing compound believed to be the known bicyclic fused six-seven membered compound 2,3-dihydrobenzothiazepin-4(5)-one (XIV).[19] A suggested mechanism for cyclization of VIII A and VIII C to the bicyclic compounds XIII and XIV in the presence of various bases is illustrated.



XIII where n = 1
XIV where n = 2

B: = RS^-, OH^-, or HCO_3^-



XIII

In view of the fact that formation of XIII from VIII A was almost quantitative when sodium methyl- or sodium butyl-mercaptides were used, step 2, which like step 1 involves a pair of S_N2 reactions, is suggested to account for a theoretical yield based upon 100% rather than upon 50% cyclization of substituted arylthio units.

A method of preparation of bis(ω-haloalkylated) diaryl disulfides in which the haloalkyl function is joined to the aromatic ring by an ether linkage was developed. The second and third steps of this method are identical to that used for preparation of X. First, a phenol or naphthol is converted to the ω-haloalkyl aryl ether by treatment of the phenolic compound with the appropriate α, ω-dihaloalkane in presence of aqueous alcoholic alkali by an adaptation of the Williamson method.[20] The resultant haloethers were chlorosulfonated by the method of Huntress.[7] The chlorosulfonyl derivatives of the naphthyl haloalkyl ethers were assumed to have the same orientation of chlorosulfonyl groups as those assigned to the chlorosulfonation products of the analogous methoxy- and ethoxy-naphthalenes by Huntress, *i.e.*, the 1-naphthyl haloalkyl ethers were considered to chlorosulfonate at the 4-position, the 2-naphthyl haloalkyl ethers at the 1-position at 0°. The chlorosulfonyl group of a product obtained by chlorosulfonation of 5-β-bromoethoxy-1,3-xylene was assigned to the 2-position (*para* to the ether function) analogous to the assignment given to a chlorosulfonation product by Marvel *et al.*[4] obtained similarly from ethyl 3,5-dimethylphenoxyacetate (5-carbethoxymethoxy-1,3-xylene). The ω-haloalkoxy aromatic sulfonyl chlorides were reduced selectively to the respective bis(ω-haloalkoxyaryl) disulfides by means of the previously mentioned hydriodic acid reduction method.[16]

In a similar manner, 1-β-tosyloxyethoxynaphthalene (XV), prepared by tosylation of 2-α-naphthoxyethanol, was chlorosulfonated, and the 4-sulfonyl chloride reduced to bis(4-β-tosyloxyethoxy-1-naphthyl) disulfide (XXX). Data pertinent to the preparation and properties of the ω-haloalkyl or β-tosyloxyethyl aryl ethers, the ω-haloalkoxy- or β-tosyloxyethoxy- aromatic sulfonyl chlorides, and the bis(ω-haloalkoxy- or β-

(17) See A. M. Patterson and L. T. Capell, *The Ring Index*, Rheinhold Publishing Corp., New York, 1940, Nos. 955 and 956.

(18) O. Unger, *Ber.*, **30**, 607 (1887), prepared this compound from 2-mercaptoaniline and bromoacetic acid.

(19) (a) F. Mayer and C. Horst, *Ber.*, **56B**, 1415 (1923); (b) W. H. Mills and J. B. Whitworth, *J. Chem. Soc.*, 2738 (1927).

(20) C. S. Marvel and A. L. Tanenbaum, *Org. Syntheses*, Coll. Vol. I., 435 (1941).

TABLE II

ω-HALOALKYL OR β-TOSYLOXYETHYLARYL ETHERS

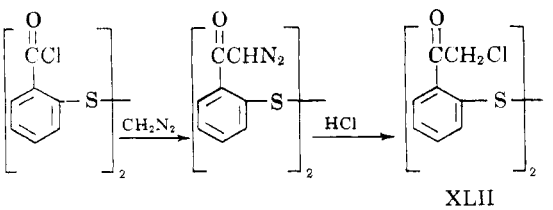
Ether	Crude Yield, %	B.P., °C./Mm.	n_D^{25}	M.P.,[a] °C.	Recryst. Solvent	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
1-β-Tosyloxyethoxynaphthalene (XV)	52			98.7–99.2	EtOH	66.65	66.56 66.47	5.30	5.18 5.13			9.36	9.03 9.02
1-β-Bromoethoxynaphthalene (XVI)[b]	50	167–170/3.2	1.6286	34.0–35.0	n-C_6H_{14}	57.39	57.68 57.75	4.42	4.49 4.41	31.83	31.79 31.88		
2-β-Bromoethoxynaphthalene (XVII)[c]	62			94.8–96.0	EtOH								
1-β-Chloroethoxynaphthalene (XVIII)[d]				37.0–38.0	EtOH	69.71	69.40 69.25	5.37	5.27 5.20	17.16	16.32 16.39		
2-β-Chloroethoxynaphthalene (XIX)[i]				82.7–83.3	95% EtOH (2B)	69.71	69.35 69.25	5.37	5.29 5.27	17.16	16.77 16.37		
1-γ-Chloropropoxynaphthalene (XX)[e]	49	153.4–156.0/1.0	1.5997							16.07	15.56 15.80		
5-β-Bromoethoxy-1,3-xylene (XXI)[f]	41	124–132/15											
5-β-Bromoethoxy-3-ethyltoluene (XXII)	35	106.7–108.1/0.8	1.5359							32.86	31.32 31.08		

[a] Corrected melting points of analytical samples. [b] Prepared by W. A. Jacobs and M. Heidelberger, *J. Biol. Chem.*, **21**, 441 (1915), as a solid m.p. 25°, b.p. 154–156°/0.8 mm. [c] A. Wohl and E. Berthold, *Ber.*, **43**, 2179 (1910), obtained 40% yield of this compound, recryst. to m.p. 96° from absolute ethanol. [d] Prepared by treating a mixture of 1- and 2-β-hydroxyethoxynaphthalenes with thionyl chloride and pyridine, fractionally distilling, and fractionally recrystallizing the mixture of chlorides. W. R. Kirner and G. H. Richter *J. Am. Chem. Soc.*, **51**, 3409 (1929), and G. R. Clemo and W. H. Perkins, Jr. *J. Chem. Soc.*, **121**, 646 (1922), prepared these chlorides previously. C. and P. report the melting points for the 1-β- and 2-β-isomers as 28° and 83°, respectively. [e] W. R. Kirner and G. H. Richter (see reference d) obtained this chloride in 54% yield of yellow oil b.p. 167–181°/1 mm., n_D^{20} 1.6025. [f] W. S. Gump and E. J. Nikawitz, *J. Am. Chem. Soc.*, **72**, 3847 (1950), report this bromide as an oil b.p. 120–121°/5 mm., n_D^{20} 1.5405; P. Hey, *Brit. J. Pharm.*, **7**, 117 (1952), reports it as an oil b.p. 99°/1 mm., n_D^{20} 1.5426.

tosyloxyethoxyaryl) disulfides is given in Tables II, III, and IV, respectively.

Although the crude yields of the bis(haloalkoxynaphthyl) disulfides approached theoretical values, on basis of the yields of iodine formed during the hydriodic acid reduction process (as determined roughly by back titrating with sodium thiosulfate), presence of impurities in the reaction products made them very tacky and difficult to purify by fractional crystallization.

Only one of the several schemes devised for synthesis of a bis(haloketoaryl) disulfide proved completely successful. Bis(2-chloroformylphenyl) disulfide was prepared by the following indirect route:



XLII

Bis(2-chloroformylphenyl) disulfide,[21] was converted to the bis(diazoketo) compound by treatment with diazomethane. The latter compound was treated *in situ* with hydrogen chloride gas to form the bis chloroketone (XLII).

Several previous attempts to prepare bis(chloroacetaryl) disulfides by a more direct route, namely by treatment of symmetrical, alkyl-substituted diphenyl disulfides with chloroacetyl chloride under Friedel-Craft conditions, were only partially successful. For example, a crude chloroacetylated di-2,6-xylyl disulfide (XXXIX), obtained as a viscous sirup, and which appeared to contain a 73:27 ratio of dichloroacetylated to monochloroacetylated product, was obtained under very mild chloracetylation conditions (reaction at 25°). The product could not be separated into pure crystalline fractions by elution chromatography using a 1:1 mixture of activated silicic acid/Hi-Flow Supercell. In addition to the complications introduced by formation of dissymmetrical haloacetylation products and positional isomers, the tendency of the diaryl disulfides to undergo a reductive S-haloacylation even under mild conditions made the problem insurmountable. In several instances, pure thiol haloesters such as phenylthiol chloro-

(21) R. List and M. Stein, *Ber.*, **31**, 1669 (1898).

TABLE III

ω-HALOALKOXY- OR β-TOSYLOXYETHOXYAROMATIC SULFONYL CHLORIDES

Sulfonyl chloride[a]	Crude Yield,[b] %	M.P.,[c] °C.	Recryst. Solvent	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
4-β-Tosyloxyethoxy-1-naphthalene (XXIII)	58	109.6-110.2	$CHCl_3$/ n-C_6H_{14}							14.54	14.44 14.67
4-β-Bromoethoxy-1-naphthalene (XXIV)	81	120.8	Ditto or gl. HOAc	41.21	41.60 41.75	2.89	3.01 2.92			9.17	9.03 8.93
4-β-Chloroethoxy-1-naphthalene (XXV)	85	102.3-103.3	80% aq. HOAc					23.24	23.15 23.13		
4-γ-Chloropropoxy-1-naphthalene (XXVI)	78	127.0 128.0	n-C_7H_{16}/ C_6H_6					22.22	21.95 22.03	10.04	9.95 10.16
2-β-Bromoethoxy-1-naphthalene (XXVI)	14	120.9-121.9	gl. HOAc					33.00	32.38[d] 32.52[d]	9.17	9.30 9.27
2-β-Chloroethoxy-1-naphthalene (XXVIII)	17	122.7 123.9	i-PrOH					23.24	23.14	10.50	10.58
4-β-Bromoethoxy-2,6-xylene (XXIX)	51	70-71	n-C_6H_{14}	36.70	36.30	3.68	4.09			9.80	9.91
4-γ-Bromo-n-propoxy 1-naphthylene (L)	33	132.3-133.6	gl. HOAc or n-C_7H_{16}/ C_6H_6					31.73	30.50[d] 30.62[d]	8.81	9.06 9.20

[a] All sulfonyl chlorides are white crystals, except XXIV and XXVI which are yellowish white crystals, and XXIX and L which are yellow crystalline compounds. [b] Yields are based on products of less than 3° melting range. [c] Corrected melting point of analytical sample. [d] Assuming that a 1:1 atomic ratio of Br:Cl is present.

acetate (XL),[22] and a product believed to be 4-chloroacetomesitylthiol chloroacetate (XLI), were isolated as sharp-melting crystalline products from haloacylation reaction products of diphenyl disulfide[23] and dimesityl disulfide,[24] respectively.

An attempt to couple diazotized p-amino-α-chloroacetophenone with sodium disulfide led only to formation of an organic solvent-insoluble substance.

Various attempts to prepare ω-haloesters of symmetrical hydroxy-substituted diaryl disulfides proved unsuccessful. The chloroacetate of 1-naphthol (XXXVIII) could not be chlorosulfonated by the method of Huntress.[7]

Attempts to haloacylate 4,4′-dithio-1-naphthol[26] with chloroacetyl chloride, bromoacetyl bromide or β-bromopropionyl chloride, either in the presence or absence of such catalysts as pyridine or phosphorus oxychloride, did not lead to pure crystalline products.

An attempt to prepare a bis haloester from bis(2-hydroxymethylphenyl) disulfide[1,2] by treatment of this diol with chloroacetyl chloride in benzene solution, resulted in formation of a crude uncrystallizable product containing an average of 2.2 chloroacetyl groups per disulfide molecule. (It may be that some S-chloroacylation as well as the desired O-chloroacylation occurred.)

The novel methods of preparation of diaryl disulfides containing substituents introduced by electrophilic substitution, developed by Kharasch and Swidler,[27] and by Tarbell and Herz,[28] could not be applied directly to preparation of diaryl disul-

(22) C. E. Dalgliesh and F. G. Mann, *J. Chem. Soc.*, 559 (1947), prepared this compound as a solid, m.p. 45°, by chloroacetylating thiophenol.

(23) A. H. Herz and D. S. Tarbell, *J. Am. Chem. Soc.*, **75**, 4657 (1953) observed a similar cleavage of diphenyl disulfide by acetyl chloride in presence of aluminum bromide with isolation of phenylthiol acetate as the major product as well as a very low yield of p-bromophenylthiol acetate. The crude product XXXIX did give the transfer constant 0.72 (a value close to that of di-2,6-xylyl disulfide itself—0.69[1]) although XL has absolutely no modifier activity, and was considered to be essentially a nuclearly acylated diaryl disulfide.

(24) A sample of dimesityl disulfide was prepared for us, under the supervision of Professor C. S. Marvel at the University of Illinois, Urbana, Ill., by a method indicated in reference (2). Since that time, Prof. Marvel's group has prepared this compound by two somewhat different methods as indicated in reference (3).

(25) An adaptation of a method used by D. S. Tarbell and A. H. Herz, *J. Am. Chem. Soc.*, **75**, 1668 (1953) to prepare bis(4-acetophenyl) disulfide.

(26) Prepared by the method of T. Zincke and J. Ruppersberg, *Ber.*, **48**, 129 (1915).

(27) N. Karasch and R. Swidler, *J. Org. Chem.*, **19**, 1704 (1954).

TABLE IV
BIS(ω-HALOALKOXY- OR β-TOSYLOXYETHOXYARYL) DISULFIDES

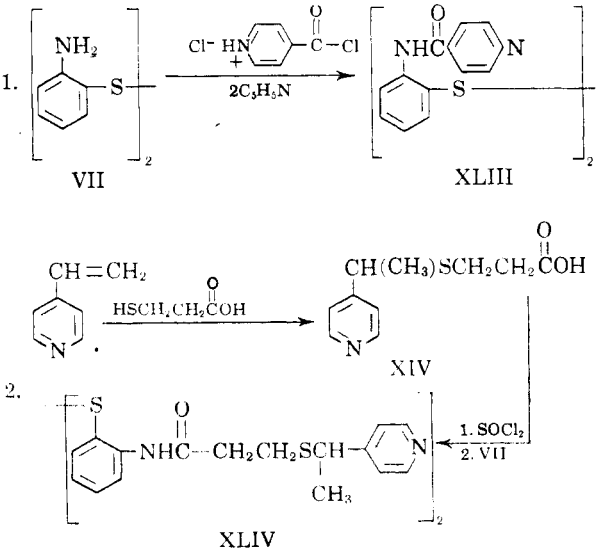
Bis-disulfide[a]	Crude Yield,[b] %	M.P.,[c] °C.	Recryst. Solvent	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found	Sulfur, % Calcd.	Sulfur, % Found	Transfer Constant (C)
4-β-Tosyloxyethoxy-1-naphthyl (XXX)	75	141.2-142.6	*i*-PrOH or gl. HOAc	61.10	60.80 60.65	4.59	4.43 4.38			17.17	17.42 17.16	1.81
4-β-Bromoethoxy-1-naphthyl (XXXI)	41	99.2-100.2	*i*-PrOH					28.32	28.52 28.49	11.36	11.56 11.50	1.46
4-β-Chloroethoxy-1-naphthyl (XXXII)	68	90.5-91.3	EtOH/*i*-PrOH					14.92	14.68 14.82	13.49	13.50 13.51	1.57
4-γ-Chloropropoxy-1-naphthyl (XXXIII)	60	100.1-100.9	*i*-PrOH					14.09	13.93 13.82	12.74	12.70 12.66	1.40
2-β-Bromoethoxy-1-naphthyl (XXXIV)	88	144.6	Cyclohexane or gl. HOAc					28.32	27.66 27.71	11.36	10.93 11.17	2.88
2-β-Chloroethoxy-1-naphthyl (XXXV)	83	155.4-156.4	EtOH/*i*-PrOH					14.92	14.81 14.77	13.49	13.74 14.07	2.60
4-β-Bromoethoxy-2,6-xylyl (XXXVI)	82	104.8-106.5	*n*-C_6H_{14}	46.15	46.15	4.65	4.64					0.73
4-γ-Bromo-*n*-propoxy-1-naphthyl (LI)	53	104.5-105.5	*i*-PrOH					26.98	26.6 26.9	10.82	10.57 10.78	1.42

[a] Above disulfides are all bright yellow crystalline compounds when in purest form, XXXIV and XXXV being needlelike crystals, and compounds, XXXI, XXXV, and XXXVI being more of a lemon shade as compared with a plain yellow color for the others. [b] Yields are based on products of 5° melting range or better. [c] Corrected melting point of analytical sample.

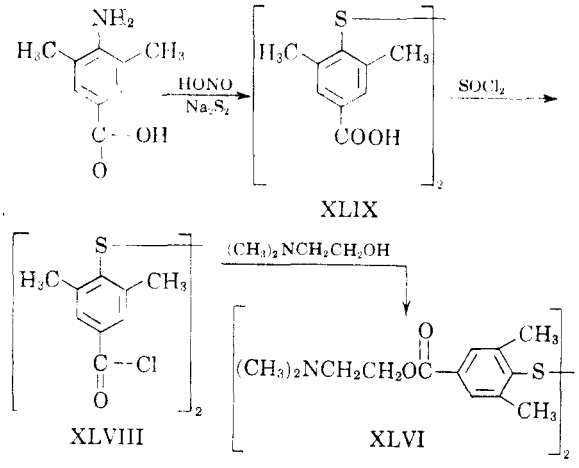
fides containing labile halogen because of the fact that both methods involve cleavage of mixed aryl sulfide intermediates by strong bases.

A second objective of this project was the preparation of symmetrical, substituted diaryl disulfides containing tertiary amino groups. Three such compounds were prepared as follows. Bis(2-isonicotinamidophenyl) disulfide (XLIII) was prepared by acylating VII with isonicotinyl chloride hydrochloride.[28]

Bis[2 - β - (α′ - 4′ - pyridylethyl)propionamido phenyl] disulfide (XLIV), a sirup with theoretical amine content (on basis of perchloric acid titration), was prepared by treating VII with an acid chloride obtained from the addition product of 4-vinylpyridine with β-mercaptopropionic acid. The intermediate carboxylic acid was assigned the configuration β[-(α′-4′-vinyl)ethylthio]propionic acid (XLV) on basis of a prominent band in the infrared absorption spectrum at 1734 cm.$^{-1}$,[29] indicating presence of a terminal methyl group (indicating that mercaptan addition was in accordance with Markownikoff's rule). The third and last bis(tertiary-amino-substituted) diaryl disulfide, bis(4-β-dimethylaminoethoxycarbonyl-2,-6-xylyl) disulfide (XLVI), was prepared by treating bis(4-chloroformyl-2,6-xylyl) disulfide (XLVIII), prepared in turn from the new diacid, bis(4-carboxy-2,6-xylyl) disulfide (XLIX), by treatment with β-dimethylaminoethanol:



(28) E. Späth, *Ber.*, **59**, 1429 (1926).
(29) Determined by Mr. Dexter E. Woodford at this laboratory.



EXPERIMENTAL[30]

4-Chlorosulfonyl-1-naphthalene acetic acid (II). To 583 g. (5.0 moles) of chlorosulfonic acid (Eastman Kodak pract. grade), kept at 0–5°, was added slowly 186 g. (1.00 mole) of 1-naphthaleneacetic acid (Matheson, Coleman and Bell Co.). As the reaction proceeded, hydrogen chloride gas was evolved. After 6 hr. at 0°, followed by 12 hr. at room temperature, reaction mixture was warmed to 40–45° for 4 hr. The dark, viscous sirup was poured onto ice and 107 g. of yellow-brown precipitate collected. This solid was recrystallized twice from benzene to 91 g. (32%) of white needles, m.p. 174–175°.

Anal. Calcd. for $C_{12}H_9ClO_4S$: Cl, 12.45; S, 11.26. Found: Cl, 12.40, 12.64; S, 11.37, 11.26.

Bis(4-β-hydroxyethyl-1-naphthyl) disulfide (III). To a stirred suspension of 7.6 g. (0.20 mole) of lithium aluminum hydride (Metal Hydrides Inc.) in 600 ml. of anhydrous ethyl ether (dried over sodium), a solution of 25.2 g. (0.0877 mole) of II in 400 ml. of this ether was introduced dropwise. After addition of all reagent, the system was refluxed for another 8 hr. The reaction mixture was carefully hydrolyzed with water and then with dilute acid. By extracting the yellow solid, m.p. 101–110°, so obtained with ether, and recrystallizing the solid so isolated from benzene/*n*-hexane mixture, 3.8 g. (21%) of fine yellow crystals, m.p. 115–117°, containing 95% of theoretical disulfide,[37] having *C* value 1.95, was obtained.

Anal. Calcd. for $(C_{12}H_{11}OS)_2$: C, 66.33; H, 4.17; S, 14.75. Found: C, 65.60, 65.50; H, 4.28, 4.23; S, 14.84, 14.99.

Bis(4-β-bromoethyl-1-naphthyl) disulfide (IV). To a mixture of 600 mg. (0.0015 mole) of IV in 50 ml. benzene (C.P.) at 10°, was added a solution of 140 mg. phosphorus tribromide in 20 ml. of this benzene, dropwise, with stirring. The reaction mixture was allowed to stand for 3 hr. at 10°, then warmed to 40°. Upon removal of benzene *in vacuo*, the sirup residue was dissolved in a minimum of ethanol. The dibromide crystallized from this solution upon standing overnight, in 90 mg. (13%) quantity of white crystals, m.p. 113–115°.

Anal. Calcd. for $(C_{12}H_{10}BrS)_2$: Br, 30.02. Found: Br, 28.87, 28.99.

Bis(4-carboxymethyl-1-naphthyl) disulfide (V). To 7.0 g. (0.025 mole) of II was added 90 ml. glacial acetic acid and 30 ml. of 50% hydriodic acid. The mixture was well shaken, and allowed to stand for 24 hr. at room temperature. To the darkened reaction mixture was added 300 ml. of ice cold 10% sodium thiosulfate solution. By extracting the resultant yellow precipitate with hot benzene 2.05 g. (38%) of yellow fluffy powder, m.p. 187–189°, with *C* value 2.24, was obtained.

Anal. Calcd. for $(C_{12}H_9O_2S)_2$: C, 70.90; H, 5.45; S, 15.77. Found: C, 69.45; H, 5.60; S, 15.02.

Bis(4-β-hydroxyethylphenyl) disulfide (VI). A 24.0 g. (0.175 mole) quantity of 4-β-hydroxyethylaniline, m.p. 110–111°, (isolated from a mixture of *o*- and *p*-β-hydroxyethyl-anilines obtained from Eastman Kodak Co. by fractional crystallization) was diazotized, the diazonium solution treated with potassium ethyl xanthate, and the xanthate ester hydrolyzed in accordance with the mercaptan synthesis procedure of Tarbell and Fukushima.[12b] Upon acidifying the alkaline hydrolysis system with 6*N* sulfuric acid, and cooling the system to 0°, an orange solid was obtained. This solid, when recrystallized from a hot absolute ethanol/*n*-hexane solution by cooling to −78°, yielded 5.46 g. (20.5%) of pale yellow platelets, m.p. 86–96°. By recrystallizing this product from 725 ml. of aqueous 40% ethanol, 3.83 g. of flaky white crystals (14.4%), m.p. 94.8–95.2°, was obtained. Although this compound did not dissolve in concentrated ammonium hydroxide, nor dilute sodium hydroxide, and would not form a silver or lead mercaptide, it could be reduced with sodium sulfite solution to a compound which did react with silver nitrate to form a mercaptide. The *C* value of VI was 0.09. On basis of titration for disulfide content,[37] 94.4% of theoretical disulfide was accounted for.

Anal. Calcd. for $(C_8H_9OS)_2$: C, 62.71; H, 5.92; S, 20.93. Found: C, 62.45, 62.70; H, 6.12, 6.13; S, 20.48, 20.31.

Bis(2-haloacylamidophenyl) disulfides (VIII A-C). VIII A. To a solution of 20.0 g. bis(2-aminophenyl) disulfide (VII) (0.0806 mole of American Cyanamid Co. product) in 450 ml. glacial acetic acid was added 100 ml. of saturated sodium acetate solution. The solution was cooled to 0°, and treated with 16.0 ml. of chloroacetyl chloride (Eastman Kodak white label), dropwise with stirring over a 20-min. period. The system, now containing a voluminous white precipitate, was diluted with one volume of cold water, and the precipitate collected, washed, and dried on a clay plate. The 34.7 g. (87%) of crude product, m.p. 126.5–129°, was recrystallized from 85% ethanol to white needles, m.p. 130.2–130.9°, (77%), and this product recrystallized for analysis to m.p. 133.2–133.7°.

VIII B. By treating VII with bromoacetyl bromide in the same manner, a 74% yield of greenish white bis(2-bromoacetamidophenyl) disulfide (VIII B), m.p. 140.5–143.5, was obtained. By recrystallizing this product twice from absolute ethanol a white, needle-like product, m.p. 157.4–157.7°, was obtained.

VIII C. A 57% yield of VIII C was obtained by treating VII with β-bromopropionyl chloride (Matheson, Coleman and Bell Co.) in this manner. However, if VII was treated with two mole equivalents of this acyl chloride in a benzene solution containing two mole equivalents of pyridine, a 79% yield of VIII C was obtained.

Isolation of IX. By treating a mixture of 60 g. of VII in benzene solution, two equivalents of chloroacetyl chloride (Eastman Kodak pract. grade), and two equivalents of solid sodium bicarbonate at reflux for 2 hr., cooling the system, and washing it with water, hydrochloric acid, water, bicarbonate solution, water, drying the benzene solution, and removing benzene *in vacuo*, 87.5 g. of a mixture of VIII A and IX was obtained. By recrystallizing from hot absolute ethanol, 32.8% of orange colored needles, m.p. 144.7–146.2°, was obtained. By repeatedly recrystallizing the most insoluble fraction six more times from ethanol, a 100-mg. crop of white needles, m.p. 151.7–152.8°, was obtained.

Anal. Calcd. for $C_{16}H_{12}Cl_2N_2O_2S_2$: C, 44.13; H, 3.01; Cl,

(30) Melting points of all compounds reported herein are corrected. Element analyses were determined by Messrs. Wellman W. Dietz and William C. Hukari of this laboratory or by Clark Microanalytical Laboratory, Urbana, Ill. Amine content of compounds XLIII, XLV, and XLVI was determined by titrating benzene solutions of these compounds with perchloric acid in acetic acid to a methyl violet end point. Disulfide content was determined by a sodium sulfite–silver nitrate titration method. (See reference 37).

24.42; N, 6.43; S, 14.71. Found: C, 44.25, 44.24; H, 2.83, 3.09; Cl, 24.27, 24.08; N, 6.55, 6.36; S, 14.84, 14.94.

4-Chloracetamido-1-naphthalenesulfonyl chloride (XII). By treating 1-naphthylamine (Du Pont tech. grade) in benzene solution with a mole equivalent each of chloroacetyl chloride and pyridine at reflux, and working up the product an 85% yield of crude α-chloroacetnaphthalide (XI), m.p. 153–159°, was obtained. This product was recrystallized from absolute ethanol to a 58% yield of pure XI, as white needles m.p. 163.6–166.8°, (recrystallized for analysis to m.p. 166.4° as compared with m.p. 161° reported for XI by Tommasi[14]).

Anal. Calcd. for $C_{12}H_{10}ClNO$; Cl, 16.14; N, 6.38. Found: Cl, 15.95, 16.01; N, 6.41, 6.25.

To a flask containing 200 ml. of chlorosulfonic acid maintained at 0°, was added 38.7 g. of XI, m.p. 166.1–166.4°, in small portions, with stirring, over a 20-min. period. This solution was warmed to 60°, and maintained at this temperature for 1 hr. to complete hydrogen chloride evolution. The solution, after being cooled, was poured onto ice water, and the resultant precipitate collected, washed, and dried. The 53.3 g. (95.3%) of product was recrystallized from 600 ml. hot chlorobenzene to 23.1 g. (41.3%) of tan needles, m.p. 180–182°. An analytical sample, recrystallized to tiny yellow needles, m.p. 184–185°, had an equivalent weight (on basis of halogen hydrolyzed with piperidine and titrated potentiometrically with silver nitrate solution) of 157 (theoretical eq. wt. is 159).

Anal. Calcd. for $C_{12}H_9Cl_2NO_3S$: Cl, 22.29; S, 10.08. Found: Cl, 22.33, 22.53; S, 10.25, 10.06.

Bis(4-chloroacetamido-1-naphthyl) disulfide (X). To 9.55 g. of XII, (0.0302 mole) m.p. 184–185°, was added 180 ml. of glacial acetic acid, and 30 ml. of 50% hydriodic acid. This slurry formed a gel upon standing 1 hr. at room temperature. The gel was mixed thoroughly, and allowed to react at this temperature for another 23 hr. Upon addition of 300 ml. of a 10% solution of hydrated sodium thiosulfate in water, the resultant precipitate was collected, washed, and dried. The 6.5 g. of product was separated into a 1.76 g. fraction, m.p. 195–198, and 1.57 g. of less soluble fraction, m.p. 204–205°, by recrystallizing from hot glacial acetic acid. By recrystallizing both fractions separately from dioxane/chlorobenzene solutions, and combining fractions, 1.67 g. of solid, m.p. 203.0–203.5°, (0.00334 mole or 22.1%) was obtained. This compound contained 100% of theoretical disulfide on the basis of the sodium sulfite/silver nitrate titration method. The product was insoluble in most organic solvents, and only slightly soluble in hot glacial acetic acid, hot chlorobenzene, or hot dioxane.

Anal. Calcd. for $(C_{12}H_9ClNOS)_2$: S, 12.79. Found: S, 12.29, 12.39.

Treatment of VIII A *with sodium alkyl mercaptides and with ammonium hydroxide.*

A. By treating 10.0 g. (0.0250 mole) VIII A with a solution of 4.51 g. (0.0500 mole) butyl mercaptan in 200 ml. methanol to which 1.15 g. (0.0500 g. atom) sodium has been added, at reflux for 1.5 hr., and pouring reaction mixture into one volume of cold water, 8.2 g. of white crystals, m.p. 181.2°, was obtained (8.25 g. is theoretical yield for 0.0500 mole of 3-keto-2,3-dihydro-1,4-benzothiazine (XIII) whose m.p. has been reported as 179°[18]). The compound gave a negative Beilstein test, and negative tests for mercaptan or disulfide functions.

B. By treating another 0.0250 mole of VIII A similarly with 0.0500 mole of sodium methyl mercaptide, 7.88 g. (95.5% yield on basis of XIII as a product) of white flaky crystals, m.p. 178.2–180.2°, was obtained as in A.

C. By treating 20.1 g. (0.0500 mole) VIII A with 400 ml. of 29% ammonium hydroxide (d = 0.90), in an autoclave for 4 hr. at average temperature of 90°, 8.5 g. of gray crystals, m.p. 180.0–181.2°, was isolated (52% yield on basis of XIII as product). This product, when recrystallized twice from aqueous ethanol, gave white needles, m.p. 181.3–181.5°, whose melting point was undepressed upon admixture with product obtained in A.

Analysis of product A. Calcd. for C_8H_7NOS: C, 58.16; H, 4.27; S, 19.41. Found: C, 58.75, 58.80; H, 4.46, 4.57; S, 19.14.

Treatment of VIII C *with aqueous sodium bicarbonate.* To 1.90 g. (0.00375 mole) of VIII C was added an aqueous solution of 0.61 g. (0.0073 mole) of sodium bicarbonate dissolved in 20 ml. of water. After refluxing the mixture for 40 min., and adding 10 ml. absolute ethanol, the mixture was refluxed for an additional 2 hr. Upon cooling, 0.40 g. (25% based on XIV) of white flaky crystals was formed. By recrystallizing this product from 8 ml. of absolute ethanol, 0.19 g. of white flakes, m.p. 213–214°, was obtained. This product also gave a negative Beilstein test, and contained neither mercaptan nor disulfide [compare with melting point reported for 2,3-dihydro-1,5-benzothiazepin-4(5)-one (XIV)—215–216°[19]].

Anal. Calcd. for C_9H_9NOS: C, 60.32; H, 5.06; N, 7.82. Found: C, 60.30, 60.42; H, 5.33, 5.21; N, 7.42.

1-β-Tosyloxyethoxynaphthalene (XV). This compound was prepared by tosylating 1-β-hydroxyethoxy-naphthalene according to one of the methods described by Tipson.[31]

A 17.1-g. quantity (0.0910 mole) of 1-β-hydroxyethoxy-naphthalene, m.p. 40–43°, (obtained from reaction of 1-sodionaphtholate with ethylene bromohydrin) was added in small portions to a stirred solution of tosyl chloride (Eastman Kodak pract. grade) in 72 ml. of dry pyridine precooled to −10°, in brine. When addition was completed, the reaction mixture was allowed to stand for 20 min. at −10°. A solution of 210 ml. of 5*N* sulfuric acid, cooled to 0°, was added to it. By rubbing the oil, which now separated from the system, against the flask wall with a glass rod, a white crystalline solid was obtained. The washed, dried solid weighed 22.4 g., had m.p. 77–87°. By recrystallizing this product from 340 ml. of hot methanol, 13.9 g. (40.7%) of white platelets, m.p. 98.7–99.2°, was obtained.

4-β-Bromethoxy-1-naphthalenesulfonyl chloride (XXIV). This compound, as well as the other ω-haloalkoxy aromatic sulfonyl chlorides, and 4-β-tosyloxyethoxy-1-naphthalene sulfonyl chloride, whose preparations are indicated in Table III, was prepared by chlorosulfonation of the respective haloether or tosyloxy ether by an adaptation of the method of Huntress[7] as follows: A solution of 24.0 g. (0.096 mole) of 1-β-bromethoxynaphthalene (XVI), m.p. 33.9–35.1°, in 90 ml. of chloroform solution, was cooled in an ice salt bath. To it was added, dropwise, with stirring, 22.2 g. (2.00 equivalents) chlorosulfonic acid. During this time, a white precipitate of sulfonic acid formed, and redissolved. The mixture was allowed to warm to room temperature, and stand at this temperature, with stirring, for 20 min. The reaction mixture was poured onto 400 g. of cracked ice. After addition of more chloroform and some brine to the system, it was filtered free of 3.6 g. of the sulfonic acid precipitate. After separating liquid phases of the filtrate, washing, and drying the chloroform phase, and removing chloroform, 27.1 g. (80.7%) of sulfonyl chloride, m.p. 118.7–120.7°, was isolated as light yellow crystals. By recrystallizing from either hot glacial acetic acid or hot isopropanol, large yellow needles, m.p. 120.2–120.7°, were obtained.

Bis(4-β-bromethoxy-1-naphthyl) disulfide (XXXI). The general procedure of Bauer and Cymerman[16] was followed in reducing the aromatic sulfonyl chlorides listed in Table III to the corresponding disulfides with this exception. Since the substituted naphthalenesulfonyl chlorides were not soluble in a glacial acetic acid/50% hydriodic acid mixture, enough benzene was added to this mixture to make a homogeneous ternary system in which these sulfonyl chlorides were soluble. Only 4-β-bromethoxy-2,6-xylnesulfonyl chloride (XXXVI) did not require benzene as a component of the reduction system.

A solution of 49.4 g. (0.142 mole) XXIV, m.p. 119.7–

(31) R. S. Tipson, *J. Org. Chem.*, 9, 235 (1944).

120.7°, in 420 ml. benzene, was treated with 1085 ml. of glacial acetic acid and 189 g. of 47.7% hydriodic acid (a fresh, yellow colored Eastman Kodak white label grade solution or 5.00 mole equivalents of hydriodic acid per mole of XXIV). The reaction mixture, which turned brown immediately, was shaken, and allowed to stand at room temperature for 23 hr. To this was added 1170 ml. of an aqueous solution containing 123 g. of sodium thiosulfate pentahydrate (enough thiosulfate to decolorize all iodine). The layers were separated, the aqueous layer extracted with more benzene, and the washed, dried benzene extract distilled *in vacuo*, leaving 40.6 g. of residual golden sirup. An extract of 39.4 g. of this sirup in 1170 ml. hot isopropyl alcohol dissolved all product except 4.2 g. of gummy residue. The decantate, upon cooling, yielded a mixed crop of waxy rosettes, and very fine yellow crystals. The precipitate, when collected, crushed, rinsed with cold isopropanol, *n*-hexane, and desiccated, weighed 22.3 g. (56.1%), of m.p. 89–93°. By recrystallizing this product from 240 ml. of hot isopropanol, 16.3 g. (40.9%) of lemon yellow crystals, m.p. 99.2–100.2°, was obtained. The equivalent weight of disulfide (on basis of disulfide titration method) was 565. (Theoretical eq. wt. is 564.4). The product can be recrystallized from hot glacial acetic acid also.

Ethyl 4-γ-chloropropoxy-1-naphthalene sulfonate (XLVII). In attempting to recrystallize 4-γ-chloropropoxy-1-naphthalenesulfonyl chloride (XXVI), m.p. 124.1–125.6, from 16 parts of hot absolute ethanol, the melting of the product was lowered to 92–98°. By recrystallizing this crystallizate from ethanol several times more, a crop of long, coarse, white needles, m.p. 102.2–103.3, of the ethyl sulfonate (XLVII) was obtained. Since it is known that the β-chloroethoxynaphthalenes XVIII and XIX can be recrystallized from hot ethanol without solvolysis, it is considered very unlikely that an ethyl ether rather than an ethyl ester was obtained from XXVI.

Anal. Calcd. for $C_{15}H_{17}ClO_4S$: Cl, 10.78; S, 9.75. Found: Cl, 10.51, 10.15; S, 9.79, 9.76.

Reaction of diphenyl disulfide with chloroacetyl chloride. A. A solution of 34.4 g. (0.158 mole) of diphenyl disulfide (Eastman Kodak white label) in 100 ml. of dry carbon disulfide was added dropwise, over a 20-min. period to a mixture of 44.0 g. (0.330 mole) anhydrous aluminum chloride (Merck Co.) and 39.3 g. (0.348 mole) chloroacetyl chloride, precooled to 0°. After the addition was complete, the system was removed from the ice bath, and allowed to react for an additional 40 min. The mixture was poured onto 500 g. of crushed ice, containing 50 ml. of concentrated hydrochloric acid. The gummy product which appeared was extracted with chloroform, and the extract washed, and dried. Upon removal of solvent at below 27° *in vacuo*, 39.09 g. of brown gum was isolated (indicating that a maximum of 16.6% of dichloracetylated product was present). By dissolving the gum in 38 ml. acetone, adding nine volumes of isopropanol, and cooling to −78°, a 1.0-g. fraction of white crystalline phenyl thiol chloroacetate (XL), having m.p. 43.0–43.5°, (compare with m.p. 45° by Dalgliesh and Mann[22]) was obtained.

Anal. Calcd. for C_8H_7ClOS: Cl, 18.99; S, 17.17. Found: Cl, 19.09, 19.11; S, 17.17, 17.01.

B. By combining the same ratio of reagents used in A in a different manner, *i.e.*, by adding the aluminum chloride and then the chloracetyl chloride to the solution of disulfide, allowing the mixture to warm to 46°, and to react at reflux for 2.25 hr., and distilling the gum isolated from the hydrolyzate, an oil, b.p. 127–145°/9 mm., was obtained. Upon cooling the distillate, white crystals of m.p. 43° were formed (27%).

Preparation of 3-chloroacetomesitylenethiol chloroacetate (XLI). A solution of 2.195 g. dimesityl disulfide[24] in 3 ml. of dry carbon disulfide was added, dropwise, with stirring, to a mixture containing 4.4 mole equivalents of anhydrous aluminum chloride, and 4.0 mole equivalents of chloroacetyl chloride in 10 ml. of dry carbon disulfide, cooled in an ice bath. There was no evolution of hydrogen chloride gas at 0°. The reaction mixture was refluxed for 20 min. at 46°, causing considerable evolution of hydrogen chloride. By cooling the mixture, hydrolyzing the product, and working it up in the usual manner, 3.0 g. (91% of dichloroacetylated product on a weight basis) of viscous brown oil was obtained. By triturating this product with much petroleum ether, 1.045 g. (32%) of white crystalline product, m.p. 112–114.5° was obtained. By recrystallizing the product from 2:3 chloroform/*n*-hexane white crystals, m.p. 118.5–119.5°, were obtained. The product was not a mercaptan, and had no activity as a polymerization modifier.

Anal. Calcd. for $C_{13}H_{13}Cl_2O_2S$: Cl, 23.31; S, 10.53. Found: Cl, 23.58; S, 10.34.

Bis(2-chloroacetophenyl) disulfide (XLII). An ethereal solution of diazomethane was prepared from 2.5 g. of *p*-tolylsulfonyl methyl nitrosoamide by the method of DeBoer and Backer[32] by treatment with caustic potash solution. To the ethereal diazomethane solution, was added, slowly, a solution of 1.00 g. of bis(2-chloroformylphenyl) disulfide,[18] m.p. 153–155°, in warm dry benzene. After the initial vigorous reaction had subsided, the mixture was allowed to stand for 1 hr. After excess diazomethane and some solvent was removed *in vacuo*, 20 ml. of benzene was added to the concentrated bisdiazoketone solution. Upon introduction of hydrogen chloride gas to the system, white crystals of bischloroketone formed. The product, weighing 0.46 g. (43%), had m.p. 183–185°, and was recrystallized to m.p. 184–185°. This compound had a *C* value of 0.14.

Anal. Calcd. for $(C_8H_6ClOS)_2$: C, 52.00; H, 3.26. Found: C, 52.00, 52.25; H, 3.36, 3.31.

Bis(2-isonicotinamidophenyl) disulfide (XLIII). To 17.8 g. (0.100 mole) of isonicotinyl chloride hydrochloride, prepared by the method of Späth[28] from isonicotinic acid (Reilly, Tar and Chem. Co.), was added 50 ml. of dry benzene, and 8.0 g. (0.10 mole) of dry pyridine. To this system was added, dropwise, with stirring, a solution of 12.4 g. (0.0500 mole) VII in 150 ml. of benzene, over a 0.5-hr. period. The mixture was refluxed for 0.5 hr., cooled, poured into ice water, and the yellow precipitate collected. The solid was washed successively with sodium bicarbonate solution, water, dilute hydrochloric acid, more water, more bicarbonate, and more water, and dried on a clay plate. A diamide sample weighing 16.0 g. (70.0%) of compound, m.p. 185.0–186.5°, was obtained. By recrystallizing the product from absolute ethanol, white crystals, m.p. 185.5–186.5°, were obtained. The equivalent weight of product (on basis of amine titration) was 228 (theoretical eq. wt. is 229.2). This compound had a *C* value of 3.6.

By preparing the compound by the method used by Hook to prepare bis(2-nicotinamidophenyl)disulfide,[33] a 35% yield of product, m.p. 185° was obtained.

Anal. Calcd. for $(C_{12}H_9N_2SO)_2$: C, 62.84; H, 3.95; N, 12.21; S, 13.97. Found: C, 62.40; 62.55; H, 3.99, 3.96; N, 12.23, 11.89; S, 24.11, 24.01.

4-[α-(β'-Carboxyethylthio)ethyl]pyridine (XLV). Upon mixing 34.4 g. (0.328 mole) of 4-vinylpyridine (Reilly Tar and Chem. Co. product stabilized with *p-t*-butyl-catechol) and 38.7 g. (0.328 mole) of 90% β-mercaptopropionic acid (B. F. Goodrich Co.), great evolution of heat was observed, and the reaction mixture solidified. After washing the solid with water, then benzene, and drying it on a clay plate, 53.4 g. (73.1%) of white crystals, m.p. 154.0–155.0, was obtained. The melting point of a sample recrystallized for analysis was 154.0–154.5°.

Anal. Calcd. for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; S, 15.17. Found: C, 56.55, 56.45; H, 6.13, 6.12; S, 15.10, 15.15.

Bis[2-β-(α'-4'-pyridylethylthio)propionamidophenyl] disulfide (XLIV). To 5.00 g. (0.0474 mole) of XLV, m.p. 154.0–155.0°, was added 50 ml. of chloroform followed by 5.64 g.

(32) T. J. DeBoer and H. J. Backer, *Rec. trav. chim.*, **73**, 229 (1954).

(33) E. O. Hook, U. S. Patent **2,502,150** (1950).

(0.0474 mole) of thionyl chloride. After refluxing the mixture for 15 min. on a hot water bath, excess thionyl chloride and chloroform were removed by distillation *in vacuo*. To the oily residue was added a solution of 2.94 g. of VII in 70 ml. of chloroform, and 7.77 g. (0.948 mole) of anhydrous sodium acetate. The mixture was refluxed on a hot water bath for 1 hr., washed twice each with sodium bicarbonate solution and water, and the chloroform extract dried, and evaporated to dryness. The residue was a brown sirup weighing 7.12 g. (61%), giving an equivalent weight of 314 (on basis of titration of amine function, indicating that 99% of theoretical amine was present). The *C* value of this compound was 5.0.

Bis(4-carboxy-2,6-xylyl) disulfide (XLIX). A 2.54 g. (0.0154 mole) quantity of 4-aminomesitylenic acid, m.p. 249–254°, (prepared by a series of reactions from mesitylene, *via* nitromesitylene,[34] 4-nitromesitylenic acid,[3,35] and 4-amino-mesitylenic acid[36]) was treated with 3.08 ml. of concentrated hydrochloric acid and 50 ml. of water. The slurry was cooled to 0°, and diazotized by addition of an ice cold solution of 1.06 g. sodium nitrite in 10 ml. of water (to a starch-iodide paper end point), in small portions. The diazonium solution was decanted from 0.32 g. of unreacted amino acid, and added, dropwise, to a solution containing 4.9 g. of sodium disulfide nonahydrate, 0.52 g. sulfur, 0.61 g. sodium hydroxide, and 8 ml. water, kept at 5°. After addition of diazonium-salt was complete, the system was allowed to warm to room temperature, and to stand at this temperature for 2 hr. The system was acidified with 2.8 ml. of concentrated hydrochloric acid, and the precipitate filtered. The crude solid was extracted with aqueous sodium carbonate, and the extract reacidified. By recrystallizing the product from hot 85% ethanol, 1.40 g. (50%) of very fine yellow crystals, m.p. 286.5–287.5°, was obtained. A sample, recrystallized for analysis from absolute ethanol at −78°, was a white power of m.p. 281–282°. The compound was insoluble in cold *n*-hexane or cold benzene, but soluble in cold ethanol or hot chloroform. The compound, which gave negative tests for mercaptan, had a *C* value of 2.11.

Anal. Calcd. for $(C_9H_9O_2S)_2$: C, 59.64; H, 5.02; S, 17.69. Found: C, 59.95, 59.80; H, 5.10, 5.17; S, 17.60.

Bis(4-chloroformyl-2,6-xylyl) disulfide (XLVIII). By treating 1.23 g. of XLIX, m.p. 288–290°, with 40 ml. of thionyl chloride at reflux for 3 hr., removing excess thionyl chloride and some benzene, a sirup was obtained. By adding a few ml. of benzene followed by addition of some *n*-hexane, a yellow precipitate was obtained. When collected, rinsed with hexane, and desiccated, the product, weighing 0.37 g. (27%), m.p. 162.9–164.4°, having a sweet sharp odor, was obtained.

Bis(4-β-dimethylaminoethoxycarbonyl-2,6-xylyl) disulfide (XLVI). By treating 0.98 g. (0.0027 mole) of XLIX with thionyl chloride just as in the previously described preparation of XLVIII, a crude sirupy form of XLVIII was obtained. This sirup was dissolved in 20 ml. of dry benzene. To this was added a solution of 0.48 g. (0.0054 mole) β-dimethylaminoethanol (Eastman Kodak white label) in benzene. After refluxing the mixture for 1 hr., during which time a hydrochloride precipitated, the benzene was removed, *in vacuo*, and the residue dissolved in water. Solid potassium carbonate was added to this solution until maximum coagulation of gum had been achieved. The gum was extracted with ether, the extract washed twice with brine, dried over anhydrous sodium sulfate, and the ether removed. The residual 0.50 g. of brown sirup (37%), having an equivalent weight of 262 (on basis of amine content, indicating 96% of theoretical amine content, theoretical eq. wt. being 252), gave a *C* value of 2.2.

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(34) G. Powell and F. R. Johnson, *Org. Syntheses*, **Coll. Vol. II**, 449 (1943).

(35) Emerson, *Am. Chem. J.*, **8**, 269 (1868).

(36) H. L. Wheeler and C. Hoffman, *Am. Chem. J.*, **44**, 119 (1910).

(37) This disulfide assay method, as reported by G. E. Meyer, R. J. Coleman, and R. M. Pierson, "Behavior of Some Bis-Type Modifiers in Emulsion Butadiene Polymerization," Copolymer Report No. 3635 to Office of Synthetic Rubber, F.F.C., 1954, (a publication distributed by the Dept. of Commerce, Office of Technical Services as indicated in Public Bulletin 118310s, and available from the Library of Congress, Photoduplication Service, Publication Board Project, Washington, D.C.), is based upon the newly discovered fact that diaryl disulfides are cleaved quantitatively by treatment with sodium sulfite, generally to one mole of sodium mercaptide and one mole of Bunte salt, and in special cases to two moles of sodium mercaptide. The mercaptide content is then determined by potentiometric titration with standardized silver nitrate solution by a modification of the method of M. W. Tamale, L. B. Ryland and V. C. Irvine, *Ind. Eng. Chem. Anal. Ed.*, **13**, 618 (1941), substituting a silver electrode sensitized by treatment with ammoniacal, alcoholic dodecyl mercaptan for the prescribed silver sulfide electrode.