quantitative accord with predictions based on the Debye–Brönsted limiting theory at ionic strengths less than 0.01 *M*.

The ethanolysis of the ethyl bromide produced in the main reaction was shown to proceed at a comparable rate at 54.95° and was considered in the kinetic analysis. The specific rate of ethanolysis of ethyl bromide was measured in independent experiments and found to be quite insensitive to changes in the ionic strength of the medium.

LOS ANGELES 24, CALIF. RECEIVED APRIL 3, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Some Basically Substituted Diaryl Sulfides and Sulfones

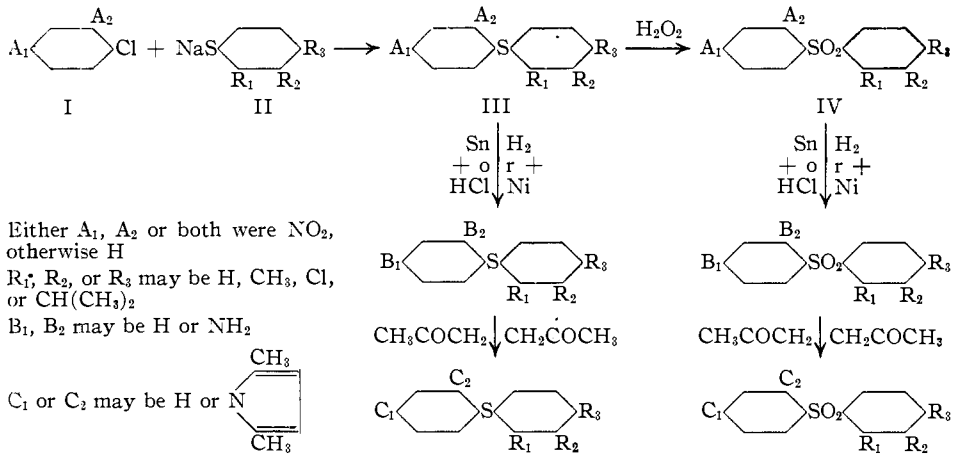
BY HENRY GILMAN AND H. SMITH BROADBENT

Studies on the treatment of tuberculosis by chemotherapeutic agents have disclosed that among the compounds of most promise are Diasone,[1] Promin,[2] and Promizole.[3,4] The first two of these are derivatives of 4,4′-diaminodiphenyl sulfone whereas in the last, one of the *p*-aminophenyl groups is replaced by the 2-aminothiazolyl-5 group. Moreover, early trials on the treatment of experimental avian and simian malaria with 4,4′-diaminodiphenyl sulfone[5] derivatives had been promising. It seemed likely, therefore, that other basically substituted derivatives of diphenyl sulfide and diphenyl sulfone might display activity against tuberculosis and malaria.

Accordingly, a number of 4-amino-, 2-amino- and 2,4-diaminodiphenyl sulfides and sulfones and some of their 2,5-dimethyl-1-pyrryl derivatives were prepared and submitted to chemotherapeutic tests. The other, unsubstituted, benzene ring was varied by the introduction of methyl, chloro and isopropyl groups.

By the time the compounds were ready for testing, there appeared little likelihood that a sulfanilamide type of compound would show promise as an antimalarial; therefore, these compounds were given only *in vitro* tests for potential antituberculous activity.[6]

The general scheme by which these compounds were prepared is outlined below.



The nitrochlorobenzenes, thiophenols and the thiocresols were obtained from the Eastman Kodak Company. The preparation of *o*-, *m*- and *p*-chlorothiophenol was patterned after a modification of Leuckhardt's method[7] for converting arylamines to thiophenols through the S-aryl ethyl xanthates. They were obtained in 67, 65 and 49% yields, respectively. *p*-Isopropylthiophenol was prepared from the corresponding sulfonyl chloride,[8] which has never been isolated in the pure form, by reduction with zinc and sulfuric acid in 63.5% over-all yield from cumene.

The general procedure of Bourgeois and Huber[9] was followed in condensing I and II to form III. 2-Nitrochlorobenzene generally requires one-half to one hour for complete reaction, 4-nitrochlorobenzene requires two to three hours, and 2,4-dinitrochlorobenzene requires about fifteen minutes. In the last case, more prolonged refluxing often

(1) Raiziss, *Science*, **98**, 350 (1943).

(2) Feldman, Hinshaw and Moses, *Proc. Staff Meeting, Mayo Clinic*, **15**, 695 (1940); **16**, 187 (1941).

(3) Bambas, THIS JOURNAL, **67**, 671 (1945).

(4) Feldman and Hinshaw, *ibid.*, **19**, 25 (1944).

(5) Coggeshall, Maier and Best, *J. Am. Med. Assoc.*, **117**, 1077 (1941).

(6) These tests for tuberculocidal activity were performed by Dr. Guy P. Youmans of the Northwestern University Medical School, Chicago, Illinois, and will be reported elsewhere.

(7) Schwarzenbach and Egli, *Helv. Chim. Acta*, **17**, 1176 (1934).

(8) Huntress and Autenrieth, THIS JOURNAL, **63**, 3446 (1941).

(9) Bourgeois and Huber, *Rec. trav. chim.*, **31**, 38 (1912).

results in the formation of a very much poorer product. For instance, *m*-thiocresol reacting at reflux temperatures for thirty minutes with 2,4-dinitrochlorobenzene yielded only tar, whereas when the reactants were just heated to reflux in ethanolic solution and cooled, a 64.5% yield of 3'-methyl-2,4-dinitrochlorobenzene was obtained. Tarry reduction products of the nitrohalobenzenes caused by the reducing action of the alkaline solution of thiophenol always tend to form; however, the amount is usually small, varying from one compound to another in a rather unpredictable manner. *m*-Thiocresol was the most troublesome in this respect and the chlorothiophenols the least so. All of the nitrodiphenyl sulfides were conveniently crystallized from methanol or ethanol.

The nitrosulfones (IV) were all prepared in very good yields by oxidizing the corresponding sulfides with an excess of 30% hydrogen peroxide in glacial acetic acid solution at steam-bath temperatures.

In the past catalytic reduction of sulfur-containing compounds has been regarded as impracticable because of the poisoning of the catalyst that frequently takes place. Deem and Kaveckis[10] describe the poisoning of Raney nickel during the hydrogenation of various substances in the presence of sulfur compounds of various degrees of oxidation. Mozingo, *et al.*,[11] state that Raney nickel is not generally useful for the hydrogenation of sulfur-containing compounds because of the hydrogenolysis to hydrogen sulfide and aryl hydrocarbons that occurs when diaryl sulfides are warmed with rather large amounts of Raney nickel.[12] They did find, however, that supported palladium catalyst was active in hydrogenating sulfur-containing compounds under some conditions, but that the hydrogenolysis of nuclear halogens usually accompanying the use of palladium readily takes place. On the other hand, Morgan and Hamilton[13] report a lone instance wherein they reduce *p*-nitrophenyl β-hydroxyethyl sulfide to the amine in 99% crude yield using Raney nickel catalyst. However, our experience has been that nitrodiaryl sulfides and sulfones can be readily reduced to the corresponding amines in excellent yields with small amounts of Raney nickel catalyst at room temperature using hydrogen under one to four atmospheres pressure. In the seventeen cases now reported, the average yield by catalytic reduction of as little as 0.01 mole to as much as 0.25 mole was 78% after recrystallizing the extremely soluble products to a constant melting point. The crude yields appeared to be practically quantitative. In only one case was difficulty encountered in reduction. Even then, other samples of the same compound were reduced with complete success.

(10) Deem and Kaveckis, *Ind. Eng. Chem.*, **33**, 1373 (1941).

(11) Mozingo, Harris, Wolf, Hoffhine, Easton and Folkers, THIS JOURNAL, **67**, 2092 (1945).

(12) Mozingo, Wolf, Harris and Folkers, *ibid.*, **65**, 1013 (1943).

(13) Morgan and Hamilton, *ibid.*, **66**, 874 (1944).

Since the completion of most of this work reports have become available wherein nitrodiaryl sulfones have been reduced to amines using Raney nickel.[14]

Some of the nitro compounds were reduced in ethanolic solution with tin and hydrochloric acid as noted in the tables. This method suffered from the difficulty frequently encountered of separating the amine from the tin-containing residues obtained by the addition of alkali to the complex of amine with chlorostannous or chlorostannic acid. There was a great tendency for colloidal suspensions containing tin compounds to form. However, as soon as the success of the catalytic reduction procedure became apparent, all of the nitro compounds were reduced thereafter in this way. In addition to giving a cleaner, more easily purified product, the latter method is more economical and gives better yields.

The 2,5-dimethyl-1-pyrryl derivatives were prepared essentially in accordance with procedure B of Hazelwood, Hughes and Lions[15] by condensing the amines with 2,5-hexanedione.

Three derivatives of 3'-methyl-4-aminodiphenyl sulfide, one of the most promising of the compounds in the early tests, were prepared. They are the ureido, formylamino and acetylamino compounds. The last two of these were prepared after the completion of the rest of the work following a report by Heymann and Fieser[16] that formylation of 4,4'-diaminodiphenyl sulfone increased its activity against avian malaria and decreased its toxicity.

The preparation of 2,4-dinitrophenyl sulfides and sulfones is a convenient method for derivatizing thiophenols and mercaptans.[17] Those prepared in this investigation further extend the number of known derivatives available for reference in characterizing thiols by this method.

Experimental

4-Isopropylthiophenol.—The method of Huntress and Autenrieth[5] was followed in making *p*-isopropylbenzenesulfonyl chloride except that the quantities they specify were multiplied one hundred-fold. An estimate on the yield of the crude sulfonyl chloride, secured by converting a small portion to the sulfonamide,[5] indicated that the chlorosulfonation of cumene was substantially complete.

Concentrated sulfuric acid, 293.5 g. (2.84 mole), was added to 900 g. of ice in a 2-liter, three-necked flask, and the mixture kept at −5 to 0° with an ice–salt-bath while 91 g. (0.414 mole) of the crude sulfonyl chloride was run in with vigorous stirring. Then 147 g. (2.10 atoms) of zinc dust (90%) was added as rapidly as maintaining the temperature at 0° would allow (approximately thirty minutes). After one and one-half hours stirring at 0°, the mixture was allowed to warm to room temperature and finally refluxed for five hours, at which time it became clear. The mixture was steam distilled as long as an oil separated from the distillate. The chilled distillate was extracted with ether, and the extract dried over anhydrous

(14) Burton and Hoggarth, *J. Chem. Soc.*, 14, 468 (1945); 542 (1946).

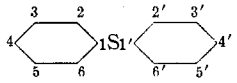
(15) Hazelwood, Hughes and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 92 (1937) [*C. A.*, **32**, 1695 (1938)].

(16) Heymann and Fieser, THIS JOURNAL, **67**, 1979 (1945).

(17) Bost, Turner and Norton, *ibid.*, **54**, 1985 (1932).

TABLE I

SULFIDES



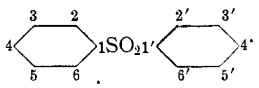
No.	Name	M. p.,[a] °C.	Yield, %	Formula	Analyses,[b] % Nitrogen Calcd.	Nitrogen Found	Sulfur Calcd.	Sulfur Found
1	2-Nitro[c]	80.5	95	$C_{12}H_9O_2NS$				
2	2′-Methyl, 2-nitro[d]	87–88	84	$C_{13}H_{11}O_2NS$				
3	3′-Methyl, 2-nitro[e]	86–86.5	91	$C_{13}H_{11}O_2NS$			13.1	13.3
4	4′-Methyl, 2-nitro[e]	89–90	93	$C_{13}H_{11}O_2NS$			13.1	13.0
5	4-Nitro[c]	55	86	$C_{12}H_9O_2NS$				
6	2′-Methyl, 4-nitro	64–65	60	$C_{13}H_{11}O_2NS$			13.1	13.1
7	3′-Methyl, 4-nitro	47	87	$C_{13}H_{11}O_2NS$	5.72	5.75		
8	4′-Methyl, 4-nitro[f]	80–81	87	$C_{13}H_{11}O_2NS$				
9	2′-Chloro, 4-nitro	113–114	80	$C_{12}H_8O_2NClS$			12.1	12.2
10	3′-Chloro, 4-nitro	71–71.5	73	$C_{12}H_8O_2NClS$			12.1	12.3
11	4′-Chloro, 4-nitro[g]	83–84	68	$C_{12}H_8O_2NClS$			12.1	12.1
12	4′-Isopropyl, 4-nitro	47.5–48.5	65	$C_{15}H_{15}O_2NS$			11.7	11.9
13	2-Amino[h,o]	43	50	$C_{12}H_{11}NS$				
14	2′-Methyl, 2-amino[o]	89–90.5	75	$C_{13}H_{13}NS$			14.9	14.9
15	3′-Methyl, 2-amino[i,o]	b. p., 174–177 (1 mm.)	88	$C_{13}H_{13}NS$			14.9	14.8
16	4′-Methyl, 2-amino[j]	48.5–49	80	$C_{13}H_{13}NS$			14.9	15.0
17	4-Amino[k]	95	89	$C_{12}H_{11}NS$				
18	2′-Methyl, 4-amino[l,o]	51.5–52	40	$C_{13}H_{13}NS$				
19	3′-Methyl, 4-amino	72.5–73	80	$C_{13}H_{13}NS$			14.9	14.8
20	4′-Methyl, 4-amino[m]	72–73	78	$C_{13}H_{13}NS$				
21	2′-Chloro, 4-amino	77–78	78	$C_{12}H_{10}NClS$			13.6	13.6
22	3′-Chloro, 4-amino	72–72.5	82	$C_{12}H_{10}NClS$			13.6	13.7
23	4′-Chloro, 4-amino[n]	60–61	79	$C_{12}H_{10}NClS$			13.6	13.8
24	4′-*i*-Propyl, 4-acetylamino[p]	93.5–94.5 108–109	45[p]	$C_{17}H_{19}ONS$			11.2	11.4
25	3′-Methyl, 2,4-dinitro	99.5–100.5	65	$C_{13}H_{10}O_4N_2S$			11.0	11.1
26	3′-Chloro, 2,4-dinitro	108–109	65	$C_{12}H_7O_4N_2ClS$			10.3	10.4
27	4′-Chloro, 2,4-dinitro	121–122	68	$C_{12}H_7O_4N_2ClS$			10.3	10.4
28	4′-*i*-Propyl, 2,4-dinitro	95.5–96.5	55	$C_{15}H_{14}O_4N_2S$			10.1	10.1
29	3′-Methyl, 2,4-diamino	112–112.5	87	$C_{13}H_{14}N_2S$			13.9	13.9
30	3′-Chloro, 2,4-diamino	94–95	78	$C_{12}H_{11}N_2ClS$			12.8	12.6
31	4′-Chloro, 2,4-diamino	141–142	87	$C_{12}H_{11}N_2ClS$			12.8	12.7
32	4′-*i*-Propyl, 2,4-diamino	93.5–94	82	$C_{15}H_{18}N_2S$			12.4	12.5
33	3′-Methyl, 4-acetylamino	121–122	..	$C_{15}H_{15}ONS$			12.5	12.4
34	3′-Methyl, 4-formylamino	72.5–73.5	67	$C_{14}H_{13}ONS$			13.2	13.5
35	3′-Methyl, 4-ureido	150–151	42	$C_{14}H_{14}ON_2S$	10.8	10.9		
36	2-(2,5-Dimethyl-1-pyrryl)	114–115	60	$C_{18}H_{17}NS$	5.03	5.05		
37	2′-Methyl, 2-(2,5-dimethyl-1-pyrryl)	107–108	80	$C_{19}H_{19}NS$			10.9	11.1
38	4′-Methyl, 2-(2,5-dimethyl-1-pyrryl)	78–82	38	$C_{19}H_{19}NS$			10.9	11.0
39	4-(2,5-Dimethyl-1-pyrryl)	86.5–87	84	$C_{18}H_{17}NS$	5.03	5.22		
40	2′-Methyl, 4-(2,5-dimethyl-1-pyrryl)	111.5–112.5	86	$C_{19}H_{19}NS$			10.9	11.1
41	3′-Methyl, 4-(2,5-dimethyl-1-pyrryl)	66	75	$C_{19}H_{19}NS$	4.78	4.70		

[a] The melting points are uncorrected. [b] All analyses for nitrogen were made using the micro Dumas method. Those for sulfur were performed with a macro Parr bomb. [c] Prepared by Bourgeois and Huber, *Rec. trav. chim.*, **31,** 38 (1912), using the same method. [d] Prepared by Mauthner, *Ber.*, **39,** 3598 (1906); also by Varma, *et al., J. Indian Chem. Soc.*, **19,** 354 (1942), who gives its melting point as 86°. [e] A report of the preparation of this compound was published by Varma, *et al., J. Indian Chem. Soc.*, **19,** 354 (1942), after we had also prepared it. [f] Prepared by Law and Johnson, THIS JOURNAL, **52,** 3623 (1930). Melting point reported as 81.5°. [g] Burton and Hogarth, *J. Chem. Soc.*, 468 (1945), published the preparation of this compound after we had prepared ours. They give 88° as the melting point. Repeated recrystallization failed to raise the melting point of our sample above 84°. [h] Bourgeois and Huber, *Rec. trav. chim.*, **31,** 30 (1912) employed reduction with stannous chloride and hydrochloric acid. Cullinane and Davies, *Rec. trav. chim.*, **55,** 885 (1936), recommend iron and water instead, which is the method we used. Our product was recrystallized from ligroin. They give 35.5° as the melting point. On the basis of our experience catalytic reduction of the nitro sulfide with Raney nickel should be much superior to either of the foregoing methods. [i] A colorless oil when freshly distilled. It quickly turns a deep blue on exposure to the air, sp. gr. $^{20}_{20}$ 1.159; $n^{20}D$ 1.6518; M_D calcd. 67.31, found 67.8. [j] This is an example of the superiority of the catalytic reduction method over the tin and hydrochloric acid reduction method in preparing these amines. Two 0.08-mole runs by the former procedure gave only 50% yields and great difficulty was encountered in se-

curing pure crystals free of tin. By the latter technique a 0.02-mole run gave 80% of a product purer without any recrystallization than the first method afforded after two or three recrystallizations. [k] Kehrmann and Bauer, *Ber.*, **29,** 2364 (1896). We obtained a 74% yield of pure compound by tin and hydrochloric acid reduction and 89% on reducing 50 g. of the nitro compound catalytically. This was the only case in the many tried wherein we encountered any difficulty in catalytic reduction of nitrodiaryl sulfides. On one run only a small fraction of the required hydrogen was absorbed. A few grams of flat, greenish-gold platelets of bis-(*p*-phenylthio)-azobenzene, melting point 117–118°, was isolated from the mixture. This azo compound was first prepared by J. Iriarte (unpublished studies). A mixed melting point taken with our compound showed no depression. Another attempt to reduce the slightly purer nitro compound to the amine catalytically met with complete success. [l] Heiduschka and Langkammerer, *J. prakt. Chem.*, [2] **88,** 439 (1913), have prepared this compound by heating aniline and *o*-toluenesulfinic acid, melting point, 50°. Freeing our crude product from tin proved to be very laborious. [m] Prepared by Law and Johnson, THIS JOURNAL, **52,** 3623 (1930), by reduction of the nitro compound with stannous chloride and hydrochloric acid, melting point 73.5°. [n] This compound is listed in the literature, German Patent 632,572, *Chem. Zentr.*, **107,** II, 3148 (1936), but no data on its properties are given. [o] These amines were prepared from the corresponding nitro compounds by reduction in ethanolic solution with tin and hydrochloric acid. All those unmarked were prepared by catalytic reduction. [p] Yield based on the crude nitro starting material. Catalytic reduction of the crude nitro compound gave a viscous oil which was distilled *in vacuo* and acetylated. After repeated recrystallizations from dilute ethanol, the resulting white needles gave the double melting point recorded, without change. The change from the lower to the higher melting form is evidently irreversible, because if a sample is once heated to 110° and allowed to solidify, it exhibits only the higher of the two melting points thereafter.

TABLE II

SULFONES



No.	Name	M. p.,[a] °C.	Yield, %	Formula	Analyses,[b] % Nitrogen Calcd.	Nitrogen Found	Sulfur Calcd.	Sulfur Found
1	4-Nitro[c]	143	98	$C_{12}H_9O_4NS$				
2	2'-Methyl-2-nitro	144–145	80	$C_{13}H_{11}O_4NS$			11.6	11.7
3	2'-Methyl-4-nitro	106–108	73	$C_{13}H_{11}O_4NS$			11.6	11.3
4	3'-Methyl-4-nitro[d]	121–122	91	$C_{13}H_{11}O_4NS$			11.6	11.6
5	4'-Methyl-4-nitro[e]	171–172	91	$C_{13}H_{11}O_4NS$				
6	2'-Chloro-4-nitro	160–161	95	$C_{12}H_8O_4NClS$			10.8	10.9
7	3'-Chloro-4-nitro	142–144	97	$C_{12}H_8O_4NClS$			10.8	10.7
8	4'-Chloro-4-nitro[f]	182–183	90	$C_{12}H_8O_4NClS$	4.71	4.74		
9	4'-*i*-Propyl-4-nitro	109–111	87	$C_{15}H_{15}O_4NS$			10.5	10.7
10	4-Amino[g,k]	174–175	68	$C_{12}H_{11}O_2NS$				
11	2'-Methyl-4-amino[d,k]	151–152	69	$C_{13}H_{13}O_2NS$			13.0	13.1
12	3'-Methyl-4-amino[k]	184.5–185.5	58	$C_{13}H_{13}O_2NS$			13.0	13.0
13	4-Methyl-4-amino[h,k]	181–182	68	$C_{13}H_{13}O_2NS$				
14	2'-Chloro-4-amino	142–144	80	$C_{12}H_{10}O_2NClS$			12.0	11.8
15	3'-Chloro-4-amino	189–190	76	$C_{12}H_{10}O_2NClS$			12.0	12.0
16	4'-Chloro-4-amino[i]	184–185	31	$C_{12}H_{10}O_2NClS$	5.24	5.38		
17	4'-*i*-Propyl-4-amino	154.5–155.5	86	$C_{15}H_{17}O_2NS$			11.7	11.7
18	3'-Methyl-2,4-dinitro	128–129	90	$C_{13}H_{10}O_6N_2S$			9.94	10.1
19	3'-Chloro-2,4-dinitro	155–156	97	$C_{12}H_7O_6N_2ClS$			9.37	9.28
20	4'-Chloro-2,4-dinitro[j]	168–169	94	$C_{12}H_7O_6N_2ClS$				
21	4'-*i*-Propyl-2,4-dinitro	118–119	53	$C_{15}H_{14}O_6N_2S$			9.16	9.18
22	3'-Methyl-2,4-diamino	153–154	68	$C_{13}H_{14}O_2N_2S$			12.2	12.4
23	4'-Chloro-2,4-diamino	200.5–201.5	81	$C_{12}H_{11}O_2N_2ClS$			11.3	11.5
24	4-(2,5-Dimethyl-1-pyrryl)	153–154	39	$C_{18}H_{17}O_2NS$	4.50	4.58	10.3	10.5
25	3'-Methyl, 4-(2,5-dimethyl-1-pyrryl)	121–122	65	$C_{19}H_{19}O_2NS$	4.13	4.18	9.87	10.2
26	4'-Methyl, 4-(2,5-dimethyl-1-pyrryl)	148–149	84	$C_{19}H_{19}O_2NS$			9.87	9.80

[a] The melting points are uncorrected. [b] See note *b* of Table I. [c] Prepared by Ullmann and Pasdermadjian, *Ber.*, **34,** 1154 (1901), from benzene-sulfinic acid and *p*-nitrobromobenzene and by Bourgeois and Huber, *Rec. trav. chim.*, **31,** 38 (1912). [d] Two crystallizations from dilute ethanol yielded fine, yellow needles. [e] First prepared by Loudon, *J. Chem. Soc.*, 220 (1936), from sodium *p*-toluenesulfinate and *p*-nitrobromobenzene. He gives its melting point as 170°. [f] Burton and Hogarth, reference [g], Table I, published the preparation of this compound after we had prepared ours; however, they list its melting point as 154°. Ganapathi and Venkatamaran, *Proc. Indian Acad. Sci.*, **21A,** 34 (1945) [*C. A.*, **39,** 3524 (1945)] reported m. p. 174–175°. [g] Prepared by Ullmann and Pasdermadjian, reference [c], by reduction of the nitro compound. They give its melting point as 176°. [h] Bamberger and Rising, *Ber.*, **34,** 244 (1901), first prepared this compound from *p*-toluenesulfinic acid and phenylhydroxylamine and from *p*-toluenesulfonic acid, aniline hydrochloride and phosphorus pentoxide at 150°. They give the melting point as 181.5°. Loudon, reference [e], also reports its synthesis. [i] Yield shown was taken after at least ten recrystallizations from various solvents. Burton and Hogarth, reference [g], Table I, published the preparation of this compound after we had prepared ours. They give its melting point as 182–183°. A mixed melting point with our nitro sulfone (m. p., 182–183°; Burton and Hogarth report 154° for theirs) and our amino sulfone (m. p., 184–185°) was depressed 35°. [j] First prepared by Loudon, reference [e], from the sodium sulfinate. He reports the melting point as 168°. [k] See reference [o] of Table I.

sodium sulfate. After evaporation of the ether, the residue was distilled from a twelve-inch Vigreux column. With no forerun, 40 g. (63.5%) of colorless, mobile oil distilling at 100–104.5° (14 mm.) was obtained: $n^{20}D$ 1.5542; d^{26}_4 1.0009; M_D calcd. 47.9, found 48.7.[18]

Anal. Calcd. for $C_9H_{12}S$: S, 21.1. Found: S, 21.2.

3′-Methyl-4-nitrodiphenyl Sulfide.—The procedures which follow were typical of all the members in their class. In preparing the nitro sulfides the times of reaction mentioned in the body of the paper were followed approximately.

To a solution of 62 g. (0.5 mole) of *m*-thiocresol in 400 ml. of absolute ethanol was added 11.5 g. (0.5 atom) of sodium. When the sodium had dissolved, a solution of 101 g. (0.5 mole) of *p*-nitrobromobenzene in 700 ml. of ethanol was added. (The chloro compound was equally satisfactory.) The mixture was refluxed with stirring (to prevent bumping) for three hours. The deposited sodium bromide was filtered off, and the solution cooled. Two more crops of crystals were obtained from the mother liquors. Recrystallization from ethanol gave a total of 106.2 g. (87%) of compact, yellow crystals.

3′-Methyl-4-aminodiphenyl Sulfide. A. Tin and Hydrochloric Acid Reduction Method.—Twenty grams (0.816 mole) of 3′-methyl-4-nitrodiphenyl sulfide dissolved in 150 ml. of hot ethanol was placed in a flask with 30 g. of mossy tin. Then 125 ml. of concentrated hydrochloric acid was added slowly with stirring. After refluxing one hour, the solution was poured into cracked ice, and 200 ml. of 50% sodium hydroxide solution was stirred in. The precipitate was filtered off, dried and extracted with boiling ethanol. On cooling fine, white platelets separated out. The product was recrystallized from dilute ethanol to a constant melting point of 72.5–73°. The yield was 14 g. (80%).

All the amino compounds were very soluble in ethanol and methanol, some so extremely soluble that they could not be readily crystallized from the pure solvent; however, by the use of mixtures of ethanol and water carefully adjusted to incipient crystallization without causing oiling out as determined by trial in each case, it was possible to crystallize all of them (excepting the one liquid compound) quite satisfactorily.

B. **Catalytic Reduction Method.**—A suspension of 61.25 g. (0.25 mole) of 3′-methyl-4-nitrodiphenyl sulfide in 300 ml. of absolute ethanol together with 4–5 g. of Raney nickel catalyst was shaken at room temperature under 1–3 atm. pressure in a standard Parr low-pressure hydrogenation apparatus until the required amount of hydrogen had been absorbed (one to two hours). The solution, filtered free of catalyst, was concentrated to 150 ml., diluted with 20 ml. of water and cooled. On seeding a mass of crystals formed. On filtering and drying, 47 g. (87.5%) of white plates melting at 72–73° were obtained.

Approximately the same procedures were followed in preparing the amino sulfones.

(18) The experience of Suter and Hansen, THIS JOURNAL, **54**, 4101 (1932), indicates that an exaltation in the atomic refraction of sulfur is common. The calculated value was computed from Eisenlohr's values.

2′-Chloro-4-nitrodiphenyl Sulfone.—Fifteen grams of 2′-chloro-4-nitrodiphenyl sulfide dissolved in 100 ml. warm glacial acetic acid was treated with 25 ml. of 30% hydrogen peroxide and heated on the steam plate for one hour. On dilution with water to incipient crystallization and cooling, pale, yellow well-formed crystals deposited. The crystals were filtered off, dried and recrystallized from ethanol–benzene (1:1). The product, which melted at 160–161°, weighed 16 g. (95%).

***p*-(2,5-Dimethyl-1-pyrryl)-phenyl *m*-Tolyl Sulfide.**—In the presence of one ml. of glacial acetic acid as a catalyst, 6.45 g. (0.03 mole) of 3′-methyl-4-aminodiphenyl sulfide and 3.4 g. (0.03 mole) of 2,5-hexanedione were condensed together in 15 ml. of absolute ethanol by refluxing for one and one-half hours. The solution was poured into 200 ml. of water; the solid product was filtered off, dried and recrystallized from dilute ethanol. The yield was 6.5 g. (75%) of white crystals melting at 66°.

The pyrryl sulfones were prepared in a similar manner.

3′-Methyl-4-formylaminodiphenyl Sulfide.—Five grams of the amine was refluxed for five hours with 50 ml. of 87% formic acid. The mixture was poured into an excess of cracked ice. The light pink blades which separated out on standing were filtered off, dried, and twice recrystallized from dilute ethanol giving 3.7 g. (67%) of product melting at 72.5–73.5°. The starting material itself melts at 72–73°, but a mixed melting point is depressed to 50–55°.

3′-Methyl-4-ureidodiphenyl Sulfide.—Five grams (0.023 mole) of 3′-methyl-4-aminodiphenyl sulfide was dissolved in 50 ml. of 50% ethanol containing 2.2 ml. (0.025 mole) of concentrated hydrochloric acid and refluxed for thirty minutes with 2.1 g. (0.026 mole) of potassium cyanate. During the course of the reaction 25 ml. of ethanol was added. The solution was filtered hot to remove a small amount of suspended solid and cooled. The product showed a pronounced tendency to oil out. It was redissolved in ethanol, filtered, cooled and filtered. After two recrystallizations from a mixture of 3 ml. of ethanol and 100 ml. of benzene, a pure, white powder was obtained melting at 150–151°, and unchanged by further recrystallization. The yield was 2.5 g. (42%).

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Summary

A series of basically substituted diaryl sulfides and sulfones and their precursors have been synthesized for testing for antituberculous activity.

Catalytic reduction of the nitro sulfides and sulfones with Raney nickel has been found to proceed smoothly in good yield without poisoning the catalyst.

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