DERIVATIVES OF CHLOROBENZENE-2,4-DISULPHONIC ACID[1]

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ABSTRACT

Chlorobenzene-2,4-disulphonates (II), -disulphones (IV), and -disulphonamides (V) have been prepared from chlorobenzene-2,4-disulphonyl chloride (I). The properties and reactions of I–V have been compared with those of related derivatives of *p*-chlorobenzenesulphonic acid and phenoxybenzene-4,4′-disulphonic acid.

Recent investigations have shown that *p*-chlorophenyl (5) and β-chloroethyl *p*-chlorobenzenesulphonates (3) are toxic to insects. In a further search for insecticides, it was decided to prepare for testing derivatives of chlorobenzene-2,4-disulphonic acid. This report of the investigation describes the preparation of II–V from chlorobenzene-2,4-disulphonyl chloride (I) (10); and compares the properties and reactions of I–V with those of related derivatives of *p*-chlorobenzenesulphonic acid (6) and phenoxybenzene-4,4′-disulphonic acid (12). Information regarding the insecticidal activity of these compounds is provided by another communication (8).

Chlorobenzene-2,4-disulphonyl chloride (I) is not affected by chlorine at 160°. This is contrary to the behavior of *p*-chlorobenzenesulphonyl chloride which is converted to *p*-dichlorobenzene under similar conditions (6). The disulphonyl chloride (I) reacts normally with alcohols and phenols to form II when in the presence of sodium hydroxide but only in poor yields or not at all when organic base is used. Thus the reaction products of I, ethylene chlorohydrin, and pyridine were ethylene dichloride and chlorobenzene-2,4-disulphonic acid. Esters of chlorobenzene-2,4-disulphonic acid and allyl alcohol, 1,1,1-trichloro-3-nitro-2-propanol, and 1,1,1-trichloro-2-methyl-2-propanol could not be obtained under any conditions.

Unlike *p*-chlorobenzenesulphinic acid and phenoxybenzene-4,4′-disulphinic acid, chlorobenzene-2,4-disulphinic acid (III) is very soluble in water and liberates sulphur dioxide rapidly when warmed in dilute mineral acid solution. However the sodium salt of III is sufficiently stable to form chlorobenzene-2,4-disulphones (IV) with reactive halogen compounds. *p*-Chlorobenzenesulphinic acid and phenoxybenzene-4,4′-disulphinic acid react readily with aqueous formaldehyde as does *p*-toluenesulphinic acid (2) to form the corresponding hydroxymethyl aryl sulphones but no IV ($R = CH_2OH$) could be isolated from an aqueous solution of III and formaldehyde. Although *p*-chloro- and *p*-nitrobenzenesulphonyl chlorides undergo the Friedel-Crafts reaction with methoxybenzenes to form diaryl sulphones (1) along with other products, diaryl chlorobenzene-2,4-disulphones (IV, R = aryl) could not be prepared from I and anisole, veratrole, and *m*-dimethoxybenzene using zinc chloride as the condensing agent.

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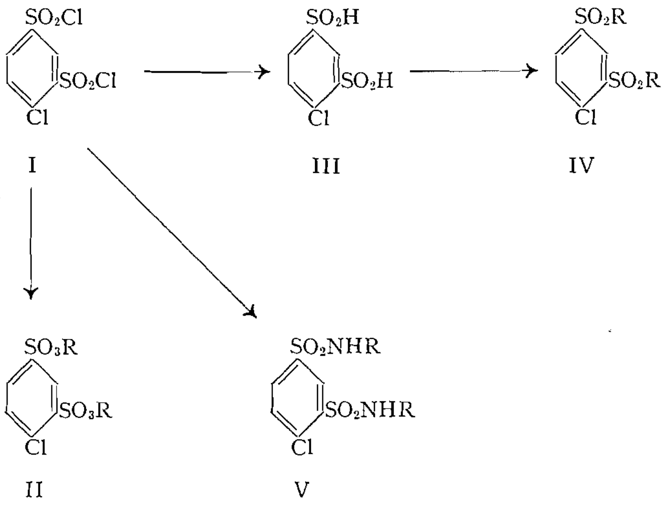

No difficulty was experienced in the preparation of chlorobenzene-2,4-disulphonamides (V) from I and excess amine. It must be cautioned that 1,N,N,N′,N′-pentachlorobenzene-2,4-disulphonamide, which was obtained from chlorobenzene-2,4-disulphonamide (V, R = H) (9) and chlorine, is extremely reactive. A solution of the N,N,N′,N′-tetrachloro-V (R = H) in xylene when warmed on the steam bath resulted in a violent explosion.

Aqueous hydrazine can react with chlorobenzene-2,4-disulphonyl chloride (I) to form either chlorobenzene-2,4-disulphonhydrazide (V, R = NH_2) or the disulphinic acid (III) depending on conditions. When I is treated with excess aqueous hydrazine, V (R = NH_2) precipitates and if this is not filtered it gradually dissolves to form the water soluble III. This shows that the hydrazide must be an intermediate when hydrazine is used in the reduction of an arylsulphonyl halide to the corresponding arylsulphinic acid.

EXPERIMENTAL

1. *Chlorobenzene-2,4-disulphonyl Chloride (I)*

A solution of *p*-chlorobenzenesulphonyl chloride (6) (120 gm.) and chlorosulphonic acid (300 ml.) was heated at 130° for 20 hr. The cooled reaction mixture was cautiously poured onto cracked ice and the precipitated solid extracted with benzene. The benzene extract was quickly washed with cold water, dried, and the solvent distilled off. Crystallization of the residue from carbon tetrachloride yielded 120 gm. (69%) of white solid melting 89–90°; Lit. (10) m.p. 90–91°.

In other experiments the use of a lower reaction temperature resulted in incomplete reaction and the use of less chlorosulphonic acid decreased the yield.

2. *Diethyl Chlorobenzene-2,4-disulphonate (II, R = C_2H_5)*

To a solution of chlorobenzene-2,4-disulphonyl chloride (I) (31 gm.) in benzene (300 ml.) was added absolute ethanol (125 ml.) and pellet sodium hydroxide (8 gm.) and the reaction mixture stirred at 15–20° for five hours. The resulting mixture was washed with water, the benzene solution dried, and the solvent removed. Crystallization of the residue from ethanol and from benzene – petroleum ether yielded 12 gm. (30%) of white needles melting at 72–73°. Anal. calc. for $C_{10}H_{13}O_6ClS_2$: C, 36.54; H, 3.96. Found: C, 36.52, 36.25; H, 3.85, 4.01.

3. *Dimethyl Chlorobenzene-*2,4*-disulphonate* (*II*, $R = CH_3$)

This was prepared in 55% yield, using methanol instead of ethanol (see section 2), m.p. 118–119°. Anal. calc. for $C_8H_9O_6ClS_2$: C, 31.96; H, 3.00. Found: C, 32.49, 32.35; H, 3.13, 2.95.

4. *bis-*(2*-Chloroethyl*) *Chlorobenzene-*2,4*-disulphonate* (*II*, $R = CH_2CH_2Cl$)

A reaction mixture of chlorobenzene-2,4-disulphonyl chloride (I) (30 gm.), ethylene chlorohydrin (80 ml.), and pellet solid hydroxide (8 gm.) was stirred for two hours, the temperature being maintained at 20–30°. Cooling on an ice water bath was essential at the beginning. After it had been allowed to stand overnight, the reaction mixture was extracted with ether, the ether extract washed with water, and the solvent removed. Crystallization of the residue from methanol yielded 30 gm. (75%) of white prisms melting at 72–73°. Anal. calc. for $C_{10}H_{11}O_6Cl_3S_2$: C, 30.20; H, 2.77. Found: C, 30.38, 30.06; H, 2.98, 2.97.

5. *bis*(2*-Chloroethyl*) *Phenoxybenzene-*4,4′*-disulphonate*

This was prepared in 75% yield from phenoxybenzene-4,4′-disulphonyl chloride (12) and ethylene chlorohydrin (see section 4). It crystallized from benzene–methanol as colorless prisms melting at 82–83°. Anal. calc. for $C_{16}H_{16}O_7Cl_2S_2$: C, 42.20; H, 3.52. Found: C, 42.84, 42.77; H, 3.45, 3.30.

6. *bis*(*p-Chlorophenyl*) *Chlorobenzene-*2,4*-disulphonate* (*II* $R = p\text{-}ClC_6H_4$)

To a solution of *p*-chlorophenol (35 gm.), sodium hydroxide (9 gm.), and water (35 ml.) was added a solution of chlorobenzene-2,4-disulphonyl chloride (I) (30 gm.) in benzene (300 ml.) and the reaction mixture was stirred for five hours. The temperature was maintained at 25–35° by occasional cooling. The benzene solution was separated, washed with aqueous sodium hydroxide and water, and then concentrated to about 50 ml. On cooling there crystallized 43 gm. (92%) of white prisms which on recrystallization from benzene–methanol melted at 141–142°. Anal. calc. for $C_{18}H_{11}O_6Cl_3S$: C, 43.78; H, 2.23. Found: C, 43.77; H, 2.23.

7. *bis*(*p-Nitrophenyl*) *Chlorobenzene-*2,4*-disulphonate* (*II*, $R = p\text{-}NO_2C_6H_4$)

This compound was prepared in 75% yield from *p*-nitrophenol and I (see section 6). (Reaction time 18 hr.) The white prisms melted at 147–148° after crystallization from benzene. Anal. calc. for $C_{18}H_{11}N_2O_{10}ClS_2$: C, 42.00; H, 2.14. Found: C, 42.24, 42.08; H, 2.28, 2.45.

8. *bis*(8*-Quinolyl*) *Chlorobenzene-*2,4*-disulphonate* (*II*, $R = C_9H_6N$)

This was prepared in 82% yield from 8-hydroxyquinoline and I (see section 6). The light-tan prisms melted at 174–175° after crystallization from acetone.

Anal. calc. for $C_{24}H_{15}N_2O_6ClS_2$: C, 54.70; H, 2.85. Found: C, 54.26, 54.80; H, 2.84, 2.84.

9. *bis(p-Chlorophenyl) Phenoxybenzene-*4,4′*-disulphonate*

This was prepared in 80% yield from phenoxybenzene-4,4′-disulphonyl chloride (12) and *p*-chlorophenol (see section 6). It crystallized from methanol as colorless prisms and melted at 104–105°. Anal. calc. for $C_{24}H_{16}O_7Cl_2S_2$: C, 52.26; H, 2.90. Found: C, 52.34, 52.63; H, 2.74, 2.55.

10. 8-*Quinolyl p-Chlorobenzenesulphonate*

This was prepared in 70% yield, from *p*-chlorobenzenesulphonyl chloride and 8-hydroxyquinoline (see section 6). The light-tan needles melted at 120–121° after crystallization from methanol. Anal. calc. for $C_{15}H_{10}NO_3ClS$: C, 56.34; H, 3.13. Found: C, 56.23; 56.18; H, 3.03, 3.14.

11. *Chlorobenzene-*2,4*-disulphinic Acid* (*III*)

To a stirred solution of sodium sulphite (175 gm.) in water (500 ml.) was added chlorobenzene-2,4-disulphonyl chloride (I) (50 gm.) and benzene (50 ml.) and the reaction mixture was stirred at 50–60° for five hours. The reaction mixture was allowed to stand overnight, and then was treated with concentrated hydrochloric acid with cooling at 15–20° and the sulphur dioxide was removed *in vacuo* at room temperature. The resulting solution was extracted with five 500-ml. portions of ether and the solvent removed from the extract. The residual oil which was unstable in the presence of warm hydrochloric acid would not crystallize. It was used directly for the preparation of the sulphones (see below).

12. *Dimethyl Chlorobenzene-*2,4*-disulphone* (IV, $R = CH_3$)

A solution of crude chlorobenzene-2,4-disulphinic acid (III) (15 gm.), water (100 ml.), and chloroacetic acid (15 gm.) was treated with sodium carbonate until just alkaline. The resulting solution was heated on the steam bath for two days. The precipitated sulphone (11 gm. or 70%) was filtered, washed, and crystallized from ethanol. The white needles melted at 174–175°. Anal. calc. for $C_8H_9O_4ClS_2$: C, 35.76; H, 3.35. Found: C, 35.79, 35.93; H, 3.47, 3.40.

13. *bis(Chloromethyl) Chlorobenzene-*2,4*-disulphone* (IV, $R = CH_2Cl$)

This was prepared in 25% yield from dichloroacetic acid and III (see section 12). The white solid melted at 137–138° after crystallization from methanol. Anal. calc. for $C_8H_7O_4Cl_3S_2$: C, 28.45; H, 2.07; Cl, 31.56. Found: C, 28.30; H, 1.99; Cl, 31.20.

14. *bis(Chloromethyl) Phenoxybenzene-*4,4′*-disulphone*

This was prepared in 50% yield from phenoxybenzene-4,4′-disulphinic acid and dichloroacetic acid (see section 12). It crystallized from methanol as white needles melting at 139–140°. Anal. calc. for $C_{14}H_{12}O_5Cl_2S_2$: C, 42.53; H, 3.04. Found: C, 42.83; H, 2.80.

15. *Dimethyl Phenoxybenzene-4,4'-disulphone*

This was prepared in 75% yield from phenoxybenzene-4,4'-disulphinic acid and chloroacetic acid (see section 12). It crystallized from methanol as white prisms melting at 182–183°. Anal. calc. for $C_{14}H_{14}O_5S_2$: C, 51.53; H, 4.29. Found: C, 52.06, 51.82; H, 3.96, 4.16.

16. *Hydroxymethyl p-Chlorophenylsulphone*

Following the method of von Meyer (7) for the preparation of hydroxymethyl *p*-tolylsulphone, *p*-chlorobenzenesulphinic acid (50 gm.) and 40% formaldehyde (100 ml.) were stirred for one hour. The white solid (52 gm. or 90%) was filtered, washed, dried, and crystallized from benzene, m.p. 111–112°. Anal. calc. for $C_7H_7O_3ClS$: C, 40.67; H, 3.39. Found: C, 40.93, 40.66; H, 3.27, 3.36. Heating this compound with phenyl isocyanate did not yield the urethane.

17. *bis(Hydroxymethyl) Phenoxybenzene-4,4'-disulphone*

This was prepared in 90% yield from phenoxybenzene-4,4'-disulphinic acid (prepared in a manner similar to that of III in section 11) and formaldehyde (see section 16). It crystallized from dilute formaldehyde as a white solid melting at 151–153° (with decomposition). Anal. calc. for $C_{14}H_{14}O_7S_2$: C, 46.92; H, 3.91. Found: C, 47.05, 47.02; H, 3.95, 4.14.

18. *p-Chlorophenyl 3,4-Dimethoxyphenylsulphone*

The method of Burton and Hoggarth (1) was employed. A reaction mixture of *p*-chlorobenzenesulphonyl chloride (40 gm.), veratrole (40 gm.), and zinc chloride (30 gm.) was stirred in an open beaker and heated at 120–130° for 15 min. Hydrogen chloride was evolved with considerable frothing. The cooled reaction mixture was treated with dilute hydrochloric acid and then extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, with aqueous alkali, and with water and the solvent was removed. The residue was fractionally distilled yielding essentially two fractions, one boiling at 170–180° (0.2 mm.) and the other at 180–200° (0.2 mm.). The first fraction was crystallized from ethanol to yield white needles (16 gm. or 28%) melting at 99–100° alone or in admixture with *o-methoxyphenyl p-chlorobenzenesulphonate* (see section 19). This is apparently formed through demethylation of veratrole and reaction of the resulting guaiacol with *p*-chlorobenzenesulphonyl chloride.

The second fraction which consisted mainly of *p-chlorophenyl 3,4-dimethoxyphenylsulphone* was boiled for three hours with aqueous–alcoholic alkali to free it from *o*-methoxyphenyl *p*-chlorobenzenesulphonate. The alcohol was removed and the precipitate crystallized from ethanol. The white needles (4 gm. or 7%) melted at 140–141°. Anal. calc. for $C_{14}H_{13}O_4ClS$: C, 53.75; H, 4.16. Found: C, 54.17, 54.21; H, 4.33, 4.12.

19. *o-Methoxylphenyl p-Chlorobenzenesulphonate*

This was prepared in 70% yield from *p*-chlorobenzenesulphonyl chloride and guaiacol (see section 6). The white needles melted at 99–100° after crystallization from ethanol. Anal. calc. for $C_{13}H_{11}O_4ClS$: C, 52.26; H, 3.68; OCH_3, 10.39. Found: C, 52.66, 52.46; H, 3.67, 3.77; OCH_3, 10.37, 10.53.

20. *p-Chlorophenyl p-Methoxyphenylsulphone*

This was prepared in 15% yield from *p*-chlorobenzenesulphonyl chloride and anisole (see section 18). The white prisms melted at 70–71° after crystallization from methanol. Anal. calc. for $C_{13}H_{11}O_3ClS$: C, 55.22; H, 3.89. Found: C, 55.41, 55.20; H, 3.58, 4.16.

21. *p,p'-Dichlorobenzhydryl p-Chlorophenylsulphone*

The method of Hinsberg (4) was employed. A solution of *p,p'*-dichlorobenzhydrol (11) (5 gm.), *p*-chlorobenzenesulphinic acid (5 gm.), acetic acid (25 ml.), and two drops of concentrated hydrochloric acid were heated under reflux for four hours. The cooled reaction mixture was poured into water, extracted with ether, the ether extract washed with dilute aqueous sodium hydroxide and with water, and the solvent removed. The residue crystallized from benzene–methanol as white needles (6.1 gm.) which melted at 105–106°. Anal. calc. for $C_{19}H_{13}O_2Cl_3S$: C, 55.41; H, 3.16. Found: C, 55.56; H, 3.24.

22. 1,*N*,*N*,*N'*,*N'-Pentachlorobenzene*-2,4-*disulphonamide*

To a stirred solution of chlorobenzene-2,4-disulphonamide (9) (15 gm.) in sodium hydroxide (6 gm.) and water (250 ml.) was added chloroform (300 ml.) and then excess chlorine was passed in for one hour. The temperature was maintained at 25–30° by occasional cooling. The chloroform layer was separated, washed with water, concentrated to about 30 ml., and allowed to cool. White crystals (16 gm. or 64%) separated which melted at 148–149°. Anal. calc. for $C_6H_3N_2O_4Cl_5S_2$: C, 17.62; H, 0.73. Found: C, 18.01, 18.22; H, 0.94, 1.06.

This compound is a dangerous chlorinating agent. When equimolecular quantities of it and *p*-xylene were mixed and heated on the steam bath a violent explosion resulted.

23. *N*,*N*,*N'*,*N'-Tetramethyl*-1-*chlorobenzene*-2,4-*disulphonamide*

Chlorobenzene-2,4-disulphonyl chloride (20 gm.) and 40% aqueous dimethylamine (100 ml.) were heated on the steam bath and stirred for two hours. The white precipitate was filtered, washed, and crystallized twice from methanol, m.p. 132–133°; yield, 19 gm. or 60%. Anal. calc. for $C_{10}H_{15}N_2O_4ClS_2$: C, 36.75; H, 4.60. Found: C, 37.16; H, 4.69.

24. *N*,*N'-Di*-2-*pyridyl*-1-*chlorobenzene*-2,4-*disulphonamide* (*V*, *R* = 2-*pyridyl*)

To a solution of 2-aminopyridine (35 gm.) in benzene (75 ml.) was added a solution of chlorobenzene-2,4-disulphonyl chloride (25 gm.) in benzene (100 ml.). The resulting reaction mixture was heated under reflux for one-half hour and then poured into cold water. The yellow precipitate was filtered and washed with dilute hydrochloric acid, water, benzene, and acetone. It was then redissolved in dilute aqueous potassium hydroxide, the solution filtered, and the filtrate was acidified with acetic acid. The precipitate (27 gm.

or 80%) was filtered, washed, and dried, m.p. 280° (with decomposition). Anal. calc. for $C_{16}H_{13}N_4O_4ClS_2$: C, 45.21; H, 3.06. Found: C, 44.92, 45.02; H, 3.59, 3.36.

25. *N-2-Pyridyl-p-chlorobenzenesulphonamide*

This was prepared in 80% yield from 2-aminopyridine and *p*-chlorobenzenesulphonyl chloride (see section 24). It crystallized from methanol in the form of white needles which melted at 193–194°. Anal. calc. for $C_{11}H_9N_2O_2ClS$: C, 49.17; H, 3.35. Found: C, 49.21, 49.56; H, 3.29, 3.37.

26. *N,N′-bis(2-Hydroxyethyl)-1-chlorobenzene-2,4-disulphonamide* (*V*, $R = CH_2CH_2OH$)

This was prepared in 35% yield from chlorobenzene-2,4-disulphonyl chloride and ethanolamine using chloroform as solvent instead of benzene (see section 24). It crystallized from benzene–methanol as white needles melting at 127–128°. Anal. calc. for $C_{10}H_{15}N_2O_6ClS$: C, 33.48; H, 4.18. Found: C, 33.70, 33.86; H, 4.12, 4.11.

27. *Chlorobenzene-2,4-disulphonyl-N,N′-bis(1,2,3,4-tetrahydroquinoline)*

This was prepared in 54% yield from 1,2,3,4,-tetrahydroquinoline and chlorobenzene-2,4-disulphonyl chloride (see section 24). It crystallized from benzene as pink prisms melting at 116–117°. Anal. calc. for $C_{24}H_{23}N_2O_4ClS_2$: C, 57.32; H, 4.58. Found: C, 57.34, 57.48; H, 4.48, 4.41.

28. *N-(p-Chlorophenylsulphonyl)-1,2,3,4-tetrahydroquinoline*

This was prepared in 60% yield from 1,2,3,4-tetrahydroquinoline and *p*-chlorobenzenesulphonyl chloride (see section 24). It crystallized from methanol as white needles melting at 94–95°. Anal. calc. for $C_{15}H_{14}NO_2ClS$: C, 58.55; H, 4.55; N, 4.55. Found: C, 58.13, 58.43; H, 4.30, 4.46; N, 4.91, 4.70.

29. *Chlorobenzene-2,4-disulphonyl bis-Hydrazide* (*V*, $R = NH_2$)

To a stirred cold solution of chlorobenzene-2,4-disulphonyl chloride (20 gm.) in benzene (70 ml.) was added a chilled solution of 85% hydrazine hydrate (20 ml.) in water (20 ml.). The reaction mixture was stirred and cooled at 10° for not more than two hours. (Further reaction occurs to form chlorobenzene-2,4-disulphinic acid if more time is allowed.) The white precipitate (16 gm. or 80%) was filtered, washed, dried, and crystallized quickly from pyridine–ether, m.p. 133° (with decomposition). Anal. calc. for $C_6H_9N_4O_4ClS_2$: C, 23.96; H, 3.00. Found: C, 23.90; H, 2.79.

This compound is insoluble in benzene, methanol, ether, and cold water. It is soluble in hot water but decomposition occurs on prolonged heating.

In another experiment twice the amount of hydrazine hydrate was used and the reaction mixture was allowed to stand overnight. The chlorobenzene-2,4-disulphonyl bis-hydrazide, which first precipitated, gradually dissolved. The aqueous solution was separated, acidified with 50% sulphuric acid, the precipitated hydrazine sulphate was filtered, and the filtrate extracted exhaustively with ether. Removal of the ether left the oily chlorobenzene-2,4-disulphinic acid (8 gm.). This, when treated with chloroacetic acid (see section 12), yielded a sulphone which did not depress the melting point of dimethyl chlorobenzene-2,4-disulphone (IV, R = CH_3).

30. *p-Chlorophenylsulphonhydrazide*

This was prepared in 92% yield from *p*-chlorobenzenesulphonyl chloride and hydrazine (see section 29). It crystallized from benzene as white woolly needles melting at 117–118° (with decomposition). Anal. calc. for $C_6H_7N_2O_2ClS$: C, 34.85; H, 3.39; N, 13.56. Found: C, 35.30, 34.72; H, 3.36, 3.74; N, 13.63.

In another experiment where the reaction was carried out at steam bath temperature, a 70% yield of *p*-chlorobenzenesulphinic acid was obtained.

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