CLXIV.—4-*Sulpho-3-hydroxybenzoic Acid.*

By MADHAVLAL SUKHLAL SHAH.

THE sulpho-*m*-hydroxybenzoic acid which is obtained by the sulphonation of *m*-hydroxybenzoic acid has now been prepared by a more convenient method than those described by Barth (*Annalen*, 1868, **148**, 38), Senhofer (*ibid.*, 1869, **152**, 102), and Remsen (*Z. Chem.*, 1871, 295) : it consists in heating a mixture of *m*-hydroxybenzoic acid and sulphuric acid at 90° for 2 hours; the sulpho-*m*-hydroxybenzoic acid crystallises in large yield on cooling and there is no sign of any other product. The acid, when recrystallised from water, separates as $C_7H_6O_6S,2\frac{1}{2}H_2O$, m. p. 206°. Barth and Senhofer describe the acid, m. p. 208°, crystallising with 1½ molecules of water.

The author has confirmed Barth's observation (*loc. cit.*; *Annalen*, 1871, **159**, 230; contrast Remsen, *loc. cit.*) that no organic acid other than protocatechuic acid, m. p. 199°, is produced by fusion of the sulpho-*m*-hydroxybenzoic acid with alkali. Hence the sulphonic acid appears to be 4-sulpho-3-hydroxybenzoic acid.

In order to obtain further evidence the author studied the methyl ether of this acid, comparing it with the oxidation products of isomeric 3-methoxytoluenesulphonic acids described by Haworth and Lapworth (J., 1923, **123**, 2982; 1924, **125**, 1299). The sulphonic acid methyl ether (I) crystallised as $C_8H_8O_6S,2H_2O$ and gave characteristic *barium* and *potassium hydrogen* salts. The latter on trituration with phosphorus pentachloride produced a chlorosulphonyl-3-methoxybenzoyl chloride, m. p. 87°, which gave on treatment (*a*) with water, a chlorosulphonyl-3-methoxybenzoic acid, m. p. 214°, and (*b*) with ammonia, a sulphonamido-3-methoxybenzamide, m. p. 255°. The former when digested with ammonia and the latter when hydrolysed with hydrochloric acid yielded the same sulphonamido-3-methoxybenzoic acid (II), m.p. 290° (decomp.).

Haworth and Lapworth (*loc. cit.*) state that their potassium hydrogen 4-sulpho-3-methoxybenzoate obtained from 3-methoxytoluene-4-sulphonic acid yielded 4-sulphonamido-3-methoxybenzoic acid, m. p. 255°, by the action of ammonia on the sulphonyl chloride, which was not isolated. From the author's results the substance, m. p. 255°, which Haworth and Lapworth describe under the name of sulphonamido-3-methoxybenzoic acid appears to be 4-sulphonamido-3-methoxybenzamide, m. p. 255°. In order to clear up this matter the experimental work of Haworth and Lapworth was repeated.

3-Methoxytoluene-4-sulphinic acid (III), prepared from 4-nitro-*m*-cresol *via* 4-nitro- and 4-amino-3-methoxytoluenes, was oxidised and 3-methoxytoluene-4-sulphonic acid and 4-*sulpho*-3-*methoxybenzoic acid* (I) were obtained. The latter gave, on treatment similar to that described above, 4-*chlorosulphonyl*-3-*methoxybenzoyl chloride*, m. p. 87°, 4-*chlorosulphonyl*-3-*methoxybenzoic acid*, m. p. 214°, 4-*sulphonamido*-3-*methoxybenzamide*, m. p. 255°, and 4-*sulphonamido*-3-*methoxybenzoic acid* (II), m. p. 290° (decomp.), identical with those obtained from the author's sulpho-*m*-hydroxybenzoic acid methyl ether, the conclusions being confirmed in each case by the mixed melting point test.

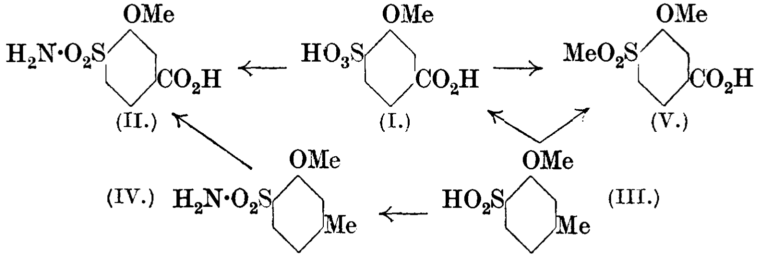
Haworth and Lapworth also state that their sulphonamido-3-methoxybenzoic acid, m. p. 255°, was produced when 3-methoxytoluene-4-sulphonamide (IV) was oxidised with alkaline permanganate. The author, however, obtained only 4-sulphonamido-3-methoxybenzoic acid, m. p. 290° (decomp.).

For full information the author converted (A) 4-sulpho-3-methoxybenzoic acid (I) and (B) 3-methoxytoluene-4-sulphinic acid (III), which yields 4-sulpho-3-methoxybenzoic acid as shown above, into 3-methoxybenzoic acid 4-methylsulphone (V).

(A) 4-Chlorosulphonyl-3-methoxybenzoic acid, m. p. 214°, prepared from sulpho-*m*-hydroxybenzoic acid methyl ether (I), was reduced by Gattermann's method (*Ber.*, 1899, **32**, 1136) and the 4-*thiol*-3-*methoxybenzoic acid* (monothiovanillic acid), m. p. 180°, which was obtained was converted on methylation into 4-*methylthiol*-3-*methoxybenzoic acid* (monothioveratric acid), m. p. 193°. The latter on oxidation gave 3-*methoxybenzoic acid* 4-*methylsulphone* (V), m. p. 227°.

(B) When 3-methoxytoluene-4-sulphinic acid (III) was similarly reduced, 4-*thiol*-3-*methoxytoluene*, b. p. 254°, was produced. This passed on methylation into 4-*methylthiol*-3-*methoxytoluene*, b. p. 269—270°. When the latter was oxidised with alkaline permanganate, the same 3-methoxybenzoic acid 4-methylsulphone (V), m. p. 227°, as described in (A) was produced : a mixture of the two showed no depression in melting point. This proves that sulpho-*m*-methoxybenzoic acid (I) corresponds to 3-methoxytoluene-4-sulphinic acid (III) and that the sulpho-*m*-hydroxybenzoic acid is 4-sulpho-3-hydroxybenzoic acid.

The sulpho-*m*-hydroxybenzoic acid methyl ether (I) was also fused with sodium hydroxide and with potassium hydroxide with a view to get vanillic acid, but the product was protocatechuic acid. Partial fusion at a low temperature gave sulpho-*m*-hydroxybenzoic acid together with protocatechuic acid, which indicates that in alkali fusion 4-sulpho-3-methoxybenzoic acid (I) is first demethylated and then converted into 3 : 4-dihydroxybenzoic acid, *i.e.*, protocatechuic acid. Vanillic, *iso*vanillic, and veratric acids have been found to be similarly demethylated and to yield protocatechuic acid.



EXPERIMENTAL.

*Sulpho-*m*-hydroxybenzoic Acid.*—*m*-Hydroxybenzoic acid (40 g.) was mixed with sulphuric acid containing 3% of sulphur trioxide (60 c.c.) and heated at 90° for 2 hours. The brown solution obtained solidified on cooling to a hard crystalline mass; this was crushed, washed with dilute sulphuric acid, and pressed and dried on porous tile. The crude substance crystallised from water (charcoal) in greenish-yellow needles or truncated prisms containing $2\frac{1}{2}H_2O$, m. p. 206° (yield, 61 g.). The substance effloresced on exposure to air and developed an intense violet fluorescence in dilute alkaline solutions (Found : equiv., 264, 263. Calc. for $C_7H_6O_6S,2\frac{1}{2}H_2O$: equiv., 263). Desiccation removed $1\frac{1}{2}$ molecules of water and left an opaque white mass, m. p. 213° (Found : equiv., 235·6. Calc. for $C_7H_6O_6S,H_2O$: equiv., 236).

The acid sodium, potassium and ammonium salts were prepared (1) by neutralising one half of an aqueous solution of sulpho-*m*-hydroxybenzoic acid with alkali and then mixing it with the other half, (2) by acidifying the neutral solution with hydrochloric acid.

The *sodium hydrogen* salt separated in shining plates and was recrystallised for analysis (Found: Na, 8·6; H_2O, 10·1; equiv., 267·1. $C_7H_5O_6SNa,1\frac{1}{2}H_2O$ requires Na, 8·6; H_2O, 10·1%; equiv., 267). The *potassium hydrogen* salt crystallised in prismatic plates and is more soluble than the acid sodium salt (Found: K, 14·1; H_2O, 6·51; equiv., 274·3. $C_7H_5O_6SK,H_2O$ requires K, 14·2; H_2O, 6·6%; equiv., 274·1). The *ammonium hydrogen* salt separated in needles (Found: N, 6·1; equiv., 234·9. $C_7H_9O_6SN$ requires N, 5·96%; equiv., 235·0).

4-*Sulpho*-3-*methoxybenzoic Acid* (I).—The sulpho-*m*-hydroxybenzoic acid (22 g. in 50 c.c. of water) was neutralised and treated alternately with 25% potassium hydroxide solution (500 c.c.) and methyl sulphate (80 c.c.) until the violet fluorescence disappeared; the mixture was then heated with potassium hydroxide in excess to hydrolyse the ester formed, neutralised with sulphuric acid, concentrated, and cooled. The filtered solution, when acidified with hydrochloric acid, gave *potassium hydrogen sulpho*-m-*methoxybenzoate* in rhombic plates, which were washed and recrystallised from water for analysis (yield, 23 g.) (Found for the hydrated salt: K, 13·5; H_2O, 6·5; equiv., 286·8, 288·2. $C_8H_7O_6SK,H_2O$ requires K, 13·6; H_2O, 6·3%; equiv., 288·1. Found for the anhydrous salt: K, 14·4. $C_8H_7O_6SK$ requires K, 14·4%).

The *sodium hydrogen* salt, prepared by using sodium hydroxide, presented much difficulty in its separation, as it carried sodium chloride along with it and was not easily isolated by filtration. For analysis it was recrystallised several times from water, separating as a glossy microcrystalline mass (Found for the anhydrous salt: Na, 8·9. $C_8H_7O_6SNa$ requires Na, 9·05%).

The *barium* salt: The above acid potassium salt was neutralised with ammonia, and the neutral solution treated with barium acetate solution. The precipitated barium salt, crystallised from water, formed transparent beady crystals containing $4H_2O$, of which $3H_2O$ were easily removed at 120° (Found: Ba, 31·1; loss at 120°, 13·4. $C_8H_6O_6SBa,4H_2O$ requires Ba, 31·3; $3H_2O$, 12·3%).

The barium salt, dissolved in water, was treated with the equivalent amount of sulphuric acid, and the filtered solution concentrated to a small bulk; 4-*sulpho*-3-*methoxybenzoic acid* crystallised in long shining plates containing $2H_2O$, m. p. 228° (Found: S, 11·85; equiv., 133·5. $C_8H_8O_6S,2H_2O$ requires S, 11·9%; equiv., 134).

Fusion of 4-*Sulpho*-3-*hydroxybenzoic Acid with Alkali.*—Finely powdered acid potassium or sodium sulpho-*m*-hydroxybenzoate (7 g.) was added to fused potassium hydroxide or sodium hydroxide (22 g.) in a nickel crucible at 220° and the mass was well stirred. When the temperature was raised gradually, considerable frothing was observed; at 300° the mass became a clear liquid, which was further heated at 310° for ½ hour. The fused mass was dissolved in water and neutralised with sulphuric acid, and the filtered solution acidified and extracted with ether. The extract on evaporation left a residue which crystallised from water in needles (3 g.), m. p. 199° (Found : equiv., 153·8. Calc. for $C_7H_6O_4$: equiv., 154). The acid gave all the characteristic reactions of protocatechuic acid, showed no depression in melting point in admixture with this acid, and gave veratric acid, m. p. 181°, on methylation. It formed a diacetyl derivative, m. p. 152° (compare Herzig, *Monatsh.*, 1885, **6**, 872).

Fusion of 4-*Sulpho*-3-*methoxybenzoic Acid with Alkali.*—Acid potassium 4-sulpho-3-methoxybenzoate (15 g.) was similarly fused at 310°, and the fused mass examined as described above. The ethereal extract gave a product, m. p. 199°, identical with protocatechuic acid (yield, 6 g.).

In other fusions the temperature was maintained at 270° and 280°, and the mass examined. The neutral solution after concentration was acidified with hydrochloric acid; acid potassium sulpho-*m*-hydroxybenzoate then crystallised in prismatic plates, showing in alkaline solutions the violet fluorescence of sulpho-*m*-hydroxybenzoic acid (Found : K, 14·2; H_2O, 6·5%; equiv., 274·0). The acid mother-liquor on extraction with ether gave some protocatechuic acid, which showed that in the fusion of sulpho-*m*-methoxybenzoic acid with alkali demethylation preceded the replacement of the sulpho-group by hydroxyl.

4-*Chlorosulphonyl*-3-*methoxybenzoyl Chloride.*—The anhydrous acid potassium salt of 4-sulpho-3-methoxybenzoic acid (I) (15 g.) was triturated with phosphorus pentachloride (35 g.) and heated on a water-bath for 5 hours. The mixture became syrupy and hydrogen chloride was copiously evolved. The mixture was poured into ice-water and the insoluble portion was washed and dried (yield, 14 g.). The substance gradually changed in cold water, and in boiling water was readily hydrolysed to 4-sulpho-3-methoxybenzoic acid. It dissolved freely in benzene and toluene and moderately readily in carbon tetrachloride. 4-*Chlorosulphonyl*-3-*methoxybenzoyl chloride* separated in rectangular plates, m. p. 87° (Found : S, 11·8; Cl, 26·15. $C_8H_6O_4Cl_2S$ requires S, 11·9; Cl, 26·4%).

4-*Chlorosulphonyl*-3-*methoxybenzoic Acid.*—Finely powdered 4-chlorosulphonyl-3-methoxybenzoyl chloride (8 g.) was shaken with cold water (800 c.c.), the course of the hydrolysis being followed by the rise observed in the melting point of the product. After 8 days, the residue, which consisted solely of 4-*chlorosulphonyl*-3-*methoxybenzoic acid*, m. p. 214°, was collected, washed, and dried (yield, 5 g.). The substance, which was sparingly soluble in all organic solvents, crystallised from toluene in small plates [Found : S, 12·7; Cl, 14·1; equiv. (excess of NaOH solution and back-titration), 83·0. $C_8H_7O_5ClS$ requires S, 12·8; Cl, 14·2%; equiv. (if SO_2Cl becomes $-SO_3H$ and HCl), 83·5].

4-*Sulphonamido*-3-*methoxybenzamide* was obtained in quantitative yield by heating finely powdered 4-chlorosulphonyl-3-methoxybenzoyl chloride (5 g.) with ammonia (*d* 0·88; 50 c.c.) until the excess of ammonia was expelled. It crystallised from water in fine needles or plates, m. p. 255° (Found : S, 13·8; N, 12·2. $C_8H_{10}O_4N_2S$ requires S, 13·9; N, 12·2%).

4-*Sulphonamido*-3-*methoxybenzoic Acid* (II).—(1) 4-Chlorosulphonyl-3-methoxybenzoic acid (3 g.) was dissolved in concentrated aqueous ammonia (30 c.c.), and the excess of ammonia expelled by boiling. The solution on acidification gave 2·9 g. of 4-*sulphonamido*-3-*methoxybenzoic acid* (II), m. p. 290° (decomp.).

(2) 4-Sulphonamido-3-methoxybenzamide (2 g.) was boiled under reflux with concentrated hydrochloric acid (20 c.c.) for 24 hours and the solid product after cooling was collected, washed, and dried (yield, 2 g.). It had m. p. 290° (decomp.) and was identical with that obtained in (1).

(3) Another method of preparation is described on p. 1300.

The sulphonamido-3-methoxybenzoic acid was readily soluble in methyl alcohol, ethyl alcohol and acetone, moderately readily soluble in hot water, and almost insoluble in benzene and toluene. It crystallised from 50% alcohol in small rhombic plates [Found : S, 13·8; N, 6·1; equiv. (excess of NaOH solution and back-titration), 115·2. $C_8H_9O_5NS$ requires S, 13·85; N, 6·1%; equiv. (if $SO_2{\cdot}NH_2$ becomes SO_3H and NH_3), 115·5].

4-*Thiol*-3-*methoxybenzoic Acid* (monothiovanillic acid).—4-Chlorosulphonyl-3-methoxybenzoic acid (5 g.) was treated with tin (15 g.) and hydrochloric acid (40 c.c.) in the cold. After 2 hours the mixture was heated on a water-bath until the tin had dissolved. Excess of hydrochloric acid was then added and, after cooling, the solid, which floated on the surface, was collected, washed with dilute hydrochloric acid, dried (yield, 4 g.), and purified by repeated dissolution in sodium hydroxide and precipitation with hydrochloric acid. The *acid* dissolved readily in almost all organic solvents but with difficulty in water. It separated from dilute alcohol in microcrystalline form, m. p. 180° (Found : S, 17·3. $C_8H_8O_3S$ requires S, 17·4%).

3-*Methoxybenzoic Acid* 4-*Disulphide*.—4-Chlorosulphonyl-3-methoxybenzoic acid (1 g.) was dissolved in alcohol and reduced with zinc dust (1·5 g.) and hydrochloric acid (10 c.c.) in the cold. After removal of the excess of zinc dust the clear liquid was treated with solid ferric chloride in presence of hydrochloric acid and kept for 1 hour. The *disulphide*, which separated on dilution with water, was washed, dissolved in aqueous sodium carbonate, and reprecipitated with hydrochloric acid; it then crystallised from dilute alcohol as a fine white powder (0·9 g.), m. p. 270°, to a dark red liquid after softening at 250° [Found : equiv., 181·8. $(C_8H_7O_3)_2S_2$ requires equiv., 183].

4-*Methylthiol*-3-*methoxybenzoic acid* (monothioveratric acid) was prepared from the thiol acid (3 g.), 25% sodium hydroxide solution (40 c.c.), and methyl sulphate (6 c.c.) in the usual way. A sodium salt which separated in short silky needles redissolved on addition of water. The solution on acidification gave a flocculent mass, which crystallised readily from all organic solvents, except chloroform and carbon tetrachloride, in lustrous needles (3 g.), m. p. 193° (Found : S, 16·1 ; equiv., 197·8. $C_9H_{10}O_3S$ requires S, 16·2% ; equiv., 198·0).

3-*Methoxybenzoic Acid* 4-*Methylsulphone* (V).—4-Methylthiol-3-methoxybenzoic acid (2 g.) was dissolved in aqueous sodium hydroxide and treated with 5% potassium permanganate solution on a boiling water-bath until the purple colour persisted. After addition of a little alcohol and filtration, the solution was concentrated to a small bulk and acidified; 3-*methoxybenzoic acid* 4-*methylsulphone* then separated in well-defined plates (1·9 g.), m. p. 227°, which were recrystallised from dilute alcohol (Found : S, 13·9; equiv., 230·1. $C_9H_{10}O_5S$ requires S, 13·9% ; equiv., 230·0). The sulphone is readily soluble in alcohol and acetone, moderately easily soluble in hot water, and almost insoluble in benzene, toluene, chloroform, and carbon tetrachloride.

[With Mr. C. T. BHATT.] 3-*Methoxytoluene*-4-*sulphinic Acid* (III) *and* 3-*Methoxytoluene*-4-*sulphonic Acid*.—These were prepared by following the experimental work of Haworth and Lapworth (*loc. cit.*). *m*-Cresol was nitrated by Staedel's method (*Annalen*, 1883, **217**, 49; 1890, **259**, 208) and 4-nitro-*m*-cresol, m. p. 56°, was separated from its 6-isomeride by distillation with steam. 4-Nitro-*m*-cresol thus obtained was dissolved in xylene, treated with potassium carbonate and methyl sulphate and converted into 4-nitro-3-methoxytoluene (m. p. 61°) by heating under reflux for 20 hours. The methyl ether on reduction with stannous chloride and hydrochloric acid produced 4-amino-3-methoxytoluene, which was distilled with steam, diazotised, and treated with sulphur dioxide in presence of finely divided copper, all the necessary precautions suggested by Haworth and Lapworth in the conversion of diazo-salt into sulphinic acid being taken.

3-Methoxytoluene-4-sulphinic acid (III), which crystallised in long needles, m. p. 111°, was digested with barium carbonate, and its barium salt oxidised with 1% barium permanganate solution. The barium 3-methoxytoluene-4-sulphonate which was thus held in solution was recovered and treated with the equivalent of potassium carbonate to give the corresponding potassium salt. The anhydrous potassium salt when digested with phosphorus pentachloride gave 3-methoxytoluene-4-sulphonyl chloride, m. p. 79°, which on treatment with ammonia produced 3-methoxytoluene-4-sulphonamide (IV), m. p. 169°. Haworth and Lapworth give 79° and 168° respectively.

4-*Sulpho*-3-*methoxybenzoic Acid* (I) *from* 3-*Methoxytoluene*-4-*sulphinic Acid* (III).—The above potassium 3-methoxytoluene-4-sulphonate, prepared from 3-methoxytoluene-4-sulphinic acid (III) (5 g.), was oxidised with 5% permanganate solution. After the manganese dioxide had been removed, the filtrate was concentrated and acidified with hydrochloric acid; the characteristic acid potassium 4-sulpho-3-methoxybenzoate, then obtained in well-shaped rhombic plates (3 g.), was recrystallised from water (Found : K, 13·5; H_2O, 6·35%; equiv., 287·5). This salt was successively converted into 4-chlorosulphonyl-3-methoxybenzoyl chloride, m. p. 87°, 4-chlorosulphonyl-3-methoxybenzoic acid, m. p. 214°, 4-sulphonamido-3-methoxybenzamide, m. p. 255°, and 4-sulphonamido-3-methoxybenzoic acid, m. p. 290° (decomp.), which were identical with those prepared from sulpho-*m*-hydroxybenzoic acid methyl ether (I).

4-*Sulphonamido*-3-*methoxybenzoic Acid* (II) *from* 3-*Methoxytoluene*-4-*sulphonamide* (IV).—3-Methoxytoluene-4-sulphonamide (IV) (2 g.) was oxidised with 5% potassium permanganate solution and the filtered liquid was concentrated and acidified with hydrochloric acid. 4-Sulphonamido-3-methoxybenzoic acid crystallised in small rhombic plates (1·8 g.) which, alone or mixed with specimens obtained by the two methods already described, melted and decomposed at 290° (Found : equiv., 115·4).

4-*Thiol*-3-*methoxytoluene*.—3-Methoxytoluene-4-sulphinic acid (III) (5 g.) was reduced with tin (15 g.) and hydrochloric acid (40 c.c.) by the method described on p. 1298. 4-*Thiol*-3-*methoxytoluene*, isolated by steam-distillation and extraction with ether, was obtained as a colourless oil (4 g.), b. p. 254°, readily soluble in organic solvents (Found : S, 20·7. $C_8H_{10}OS$ requires S, 20·8%). In alcoholic solution it gave with mercuric chloride a white mercaptide and with lead acetate a canary-yellow *mercaptide* [Found : Pb, 40·1. $(C_8H_9OS)_2Pb$ requires Pb, 40·4%]. The benzoyl derivative, prepared by shaking an alkaline solution of 4-thiol-3-methoxytoluene with benzoyl chloride, crystallised from dilute methyl alcohol in thin plates, m. p. 76°. The disulphide separated readily when a solution of iodine in potassium iodide was added to a solution of the mercaptan in sodium hydroxide; it crystallised from methyl alcohol in prismatic plates, m. p. 83°.

4-*Methylthiol*-3-*methoxytoluene*.—The above mercaptan (3 g.), dissolved in 25% sodium hydroxide solution (30 c.c.), was heated with methyl sulphate (6 c.c.) on a water-bath for 2 hours. The *methylthiol*, which separated as an oil and was extracted with ether, had an aromatic odour and boiled at 269—270° (yield, 3 g.) (Found : S, 19·0. $C_9H_{12}OS$ requires S, 19·0%). When oxidised with hot alkaline 5% potassium permanganate solution, it was converted into 3-methoxybenzoic acid 4-methylsulphone, which, alone or mixed with the specimen described above, melted at 227° (Found : S, 13·8%; equiv., 229·6).

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