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AMINOCHLOROBENZENESULPHONIC ACIDS: SYNTHESIS OF THE MISSING ISOMERS AND CORRECTIONS TO THE LITERATURE

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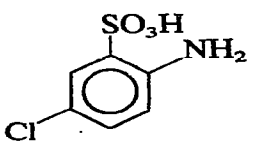
SUMMARY

Unambiguous routes to five aminochlorobenzenesulphonic acids are described. Two of these isomers have not been described before and this work shows that the literature on the other three is confused. The ^{13}C-n.m.r. spectra of all ten isomers have been measured. The isomers have been used to identify the products from the sulphonation of 2-, 3- and 4-chloroaniline in which HPLC analysis has been invaluable.

1. INTRODUCTION

Aminochlorobenzenesulphonic acids and their derivatives are important intermediates in the colour chemical industry.[1] As part of our continuing studies of the effect of the constitution of dyestuffs on their properties we required all ten isomers. Four of these isomers, **1–4** are well known and are available commercially. Of the remaining isomers only one, **5**, has been synthesised by an unambiguous route,[2] two are unknown and on the other three the literature is somewhat contradictory.



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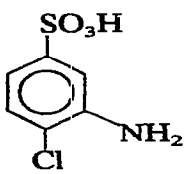

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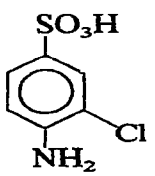

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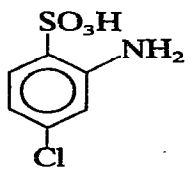

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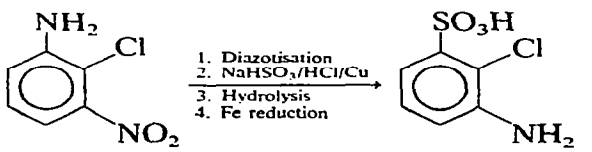
We consequently set out to synthesise the latter five isomers unambiguously and the results of this work form the basis of this paper.

2. RESULTS AND DISCUSSION

2-Amino-3-chlorobenzenesulphonic acid (**8**) is one of the two unknown isomers. We have now synthesised it by well known methods of functional group interchange from 2-amino-6-chloronitrobenzene (**6**). The first step involves diazotisation of the amino group followed by sulphitation of the diazonium salt in concentrated hydrochloric acid in the presence of a copper catalyst[3] to give the sulphonylchloride **7**. This sulphonyl chloride is then hydrolysed and reduced to the desired product **8**.

6 **7** **8**

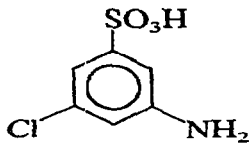
The other unknown isomer is 3-amino-2-chlorobenzenesulphonic acid (**10**). This was synthesised by processes exactly analogous to those described above starting from 3-amino-2-chloronitrobenzene (**9**).



9 **10**

The early literature claims that two of the desired isomers can be made by the sulphonation of 3-chloronitrobenzene with oleum followed by reduction.[4,5] These isomers are said to be 3-amino-5-chlorobenzenesulphonic acid (**11**) and 2-amino-6-chlorobenzenesulphonic acid (**12**).

We have repeated this work and using modern analytical techniques have shown that the earlier results are somewhat inaccurate. The isomeric mixture that is obtained from the sulphonation of 3-chloronitrobenzene contained 31·0 and 33·3% of the two major components **13** and **14** respectively and 13·8% of a third (**15**). Isomer **13** would indeed give rise to **11** on reduction but there was no evidence for **16** which would be required to give **12**. The chemical evidence



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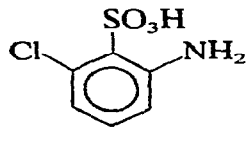

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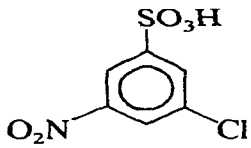
provided by Claus and Bopp[5] for **16** could also be accounted for if their product was a mixture of **14** and **15** which our work shows to be the case.



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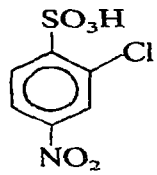

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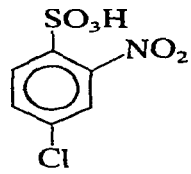

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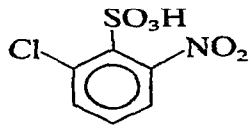

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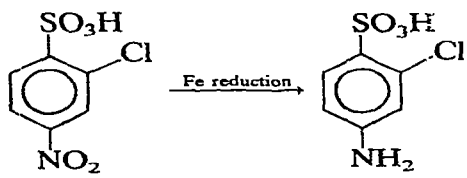
The nitro isomers **13–16** required for our work were all synthesised by independent means as shown in Scheme 1. Their structures were also confirmed by ^{13}C-n.m.r. details of which are given in Table 1.

The aminosulphonic acids **11** and **12** were prepared by iron reduction of **13** and **16**. Therefore the only isomer left to consider is 4-amino-2-chlorobenzenesulphonic acid (**17**). We have synthesised this latter compound by the iron reduction of **14**, prepared as in Scheme 1. The literature on the synthesis of **17** by sulphonation of 3-chloroaniline is discussed below.



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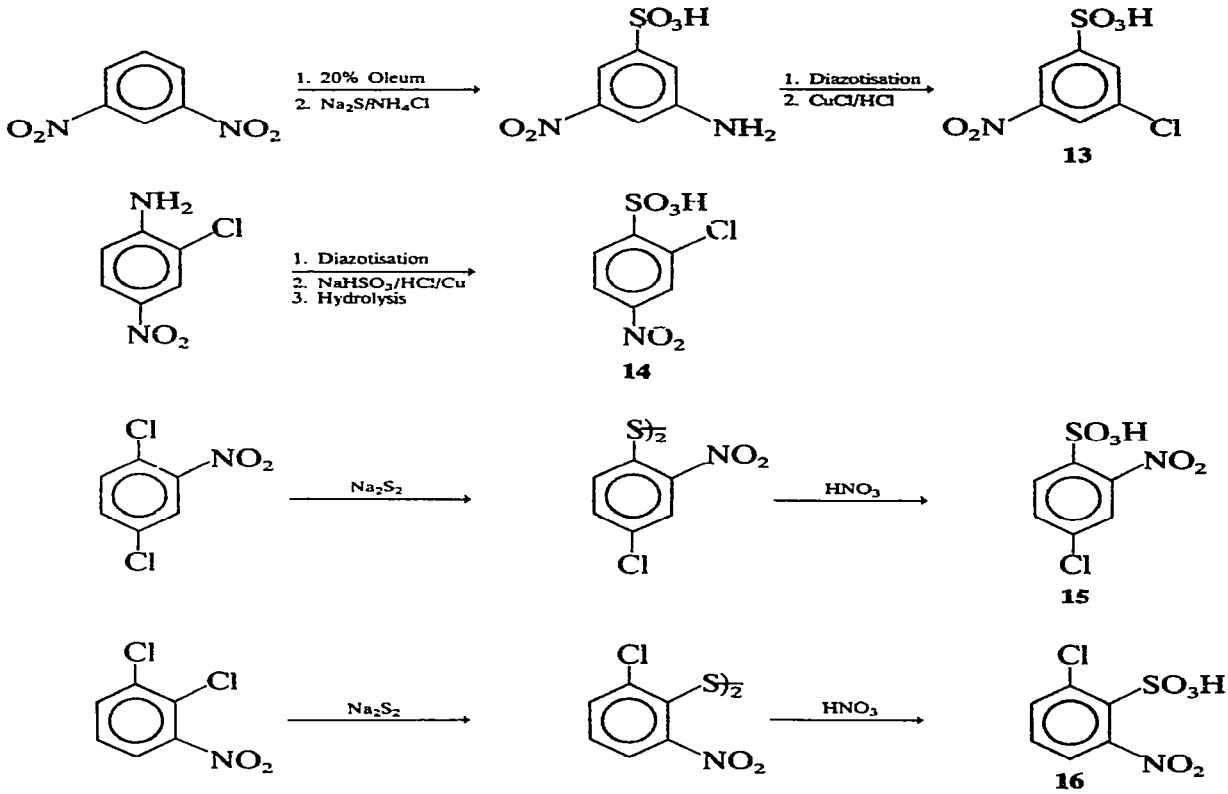
As a final proof of structure, pure samples of all ten isomeric aminochlorobenzenesulphonic acids were prepared and their ^{13}C-n.m.r. spectra measured. The results obtained were compared with the predicted shifts calculated, using as reference, spectra for the 2-, 3- and 4-aminobenzenesulphonic acids as appropriate, in conjunction with the published shift parameters for chlorine.



Scheme 1

TABLE 1

^{13}C-n.m.r. SPECTRA OF FOUR ISOMERIC CHLORONITROBENZENESULPHONIC ACIDS (K SALTS)

Isomer of Chloro-nitrobenzenesulphonic acid		*Observed (top) and calculated (bottom) shifts*					
		C_1	C_2	C_3	C_4	C_5	C_6
2-nitro-4-chloro[a]	obs.	(s) 133·9	(s) 148·2	122·4	(s) 138·1	130·8	130·8
	calc.	135·5	148·9	126·6	138·4	134·0	130·4
2-nitro-6-chloro		(s) 133·9	(s) 151·3	123·5	134·4	136·1	(s) 135·2
		133·7	150·1	127·0	132·6	137·1	133·8
3-nitro-5-chloro		(s) 147·6	120·9	(s) 150·2	127·6	(s) 137·0	133·4
		146·6	121·2	152·4	128·1	136·3	132·5
4-nitro-2-chloro		(s) 147·6	(s) 133·4	127·5	(s) 150·2	123·4	131·5
		148·5	131·1	126·8	154·1	122·8	131·6

[a] D_6DMSO
(s) singlet peak in off resonance spectrum

TABLE 2

^{13}C-n.m.r. SPECTRA OF THE TEN ISOMERIC AMINOCHLOROBENZENESULPHONICACIDS (K SALTS)

Isomer of amino-chlorobenzenesulphonic acid		*Observed (top) and calculated (bottom) shifts*					
		C_1	C_2	C_3	C_4	C_5	C_6
2-amino-3-chloro	obs.	(s) 129·2	(s) 144·6	(s) 121·0	133·9	123·3	128·4
	calc.	129·5	145·9	126·0	134·8	121·0	127·1
2-amino-4-chloro		(s) 127·0	(s) 146·9	118·1	(s) 138·4	118·4	130·4
		126·3	146·8	120·2	140·6	120·2	130·3
2-amino-5-chloro		(s) 129·2	(s) 144·6	121·0	133·9	(s) 123·3	128·4
		129·5	143·6	121·1	134·8	126·0	129·4
2-amino-6-chloro		(s) 125·2	(s) 148·1	118·5	132·6	121·4	(s) 133·8
		128·6	146·8	117·9	135·7	120·2	135·2
3-amino-2-chloro		(s) 142·1	(s) 117·5	(s) 146·5	121·5	129·0	120·5
		146·0	121·5	146·8	122·9	129·8	120·3
3-amino-4-chloro		(s) 143·8	115·3	(s) 145·1	(s) 124·4	131·5	118·1
		143·7	116·6	146·8	127·8	132·1	120·3
3-amino-5-chloro		(s) 146·6	112·7	(s) 150·4	119·6	(s) 136·3	116·9
		146·9	113·4	147·7	122·0	137·9	119·4
3-amino-6-chloro		(s) 147·3	117·6	(s) 141·7	121·3	133·7	(s) 120·9
		146·0	116·6	144·5	122·9	132·1	125·2
4-amino-2-chloro		(s) 132·9	(s) 131·1	118·3	(s) 152·1	114·3	131·6
		134·5	134·9	117·2	152·7	114·9	130·0
4-amino-3-chloro		(s) 134·7	128·0	(s) 120·4	(s) 147·4	117·8	127·0
		135·4	129·1	123·0	151·8	118·1	126·8

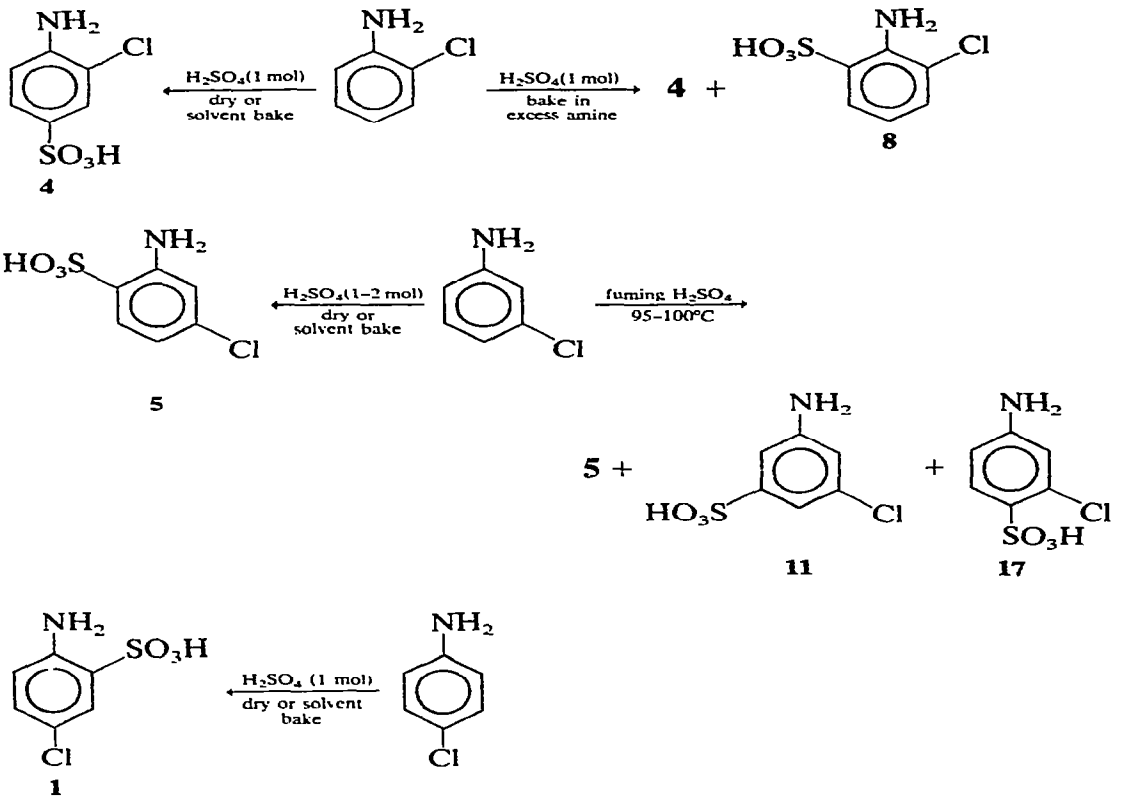
(s) singlet peak in off resonance spectrum

Full data are given in Table 2 and as can be seen there is very good agreement with the observed and predicted values.

Most of the routes described above to the various isomers are very circuitous. This was of course intentional since we required unambiguous synthetic proofs of structures. However, for practical purposes, it would be much more attractive to directly sulphonate the readily available chloroanilines. Having available all of the ten isomers we were then in a position to carry out this study and accurate quantitative HPLC methods of analysis were developed. The synthetically valuable results of this work are given in Scheme 2.

A dry or solvent bake sulphonation of 2-chloroaniline provides a ready synthesis of **4** in high yield.[6] If the solvent used is 2-chloroaniline itself then the product of the reaction is a mixture of **4** and **8** with the former predominating. This method affords a short if low yield (16·5%) route to **8** because it is easily separated from the main component **4** by virtue of the insolubility of its sodium salt in water. The dry or solvent bake suphonations of 4-chloroaniline are well established industrial processes[7] and are obviously the best routes to **1**.

The literature on the sulphonation of 3-chloroaniline is somewhat confused. Solvent bake sulphonation is claimed by Casper *et al.*[8] to give a mixture of **5**



Scheme 2

and **17** whilst Skrowaczewska states that only **5** is obtained.[6] In our hands, dry bake sulphonation of 3-chloroaniline gave only **5** in an isolated yield of 77%. Turning to wet sulphonation the early workers Claus and Bopp[5] claimed that in fuming sulphuric acid the products were **5** and **17** but at a later date some Japanese researchers said that the product was **17**.[9] More recently it was reported that chlorosulphonation followed by hydrolysis gave a mixture of **5** and **17** in very low yield.[10]

We have had a look at the work of Claus and Bopp. Unfortunately the conditions are somewhat imprecise being described as fuming sulphuric acid on a water bath and no yields are given. Carrying out the reaction in 10% oleum at 95–100°C gave the disulphonic acid, 4-amino-6-chlorobenzene-1,3-disulphonic acid as the main component (33·7%). The monosulphonic acids

present were indeed **5** and **17**, 16·2% and 21·5% respectively, but in addition there was a significant quantity (12·2%) of **11** which has not been observed by previous workers.

3. MATERIALS AND METHODS

The i.r. spectra were taken with a Perkin-Elmer 297 Infra Red Spectrophotometer as KBr discs of Nujol mulls. Spectra of all the isomeric aminochlorobenzenesulphonic acids (free acid) were measured and shown to be different.[13]C-n.m.r. spectra at 22·62 MHz were measured using a Bruker WH 90, with D_2O as solvent and dimethyl sulphoxide as internal reference. The shifts were calculated relative to $SiMe_4$ using reference spectra of the isomeric aminobenzenesulphonic acids in conjunction with published shift parameters for the chlorine, nitro and amino group. H-n.m.r. data were recorded in D_2O at 100 MHz on a Varian HA 100 with 3-(trimethylsilyl)-propane sulphonic acid as internal standard. Analysis by High Performance Liquid Chromatography (HPLC) was carried out using a Hewlett Packard 1084B Liquid Chromatograph. Measurements of water content were made on a Karl Fischer-Automat E547. Melting points were recorded on a Buchi SMP-20 apparatus and are uncorrected.

For thin-layer chromatography (t.l.c.) purposes, Eastman Chromagram Silica gel sheet 13181 was used and the mixture ethyl acetate, methanol, 31% ammonium hydroxide (70:30:5) as eluent. All the benzene sulphonic acids prepared were examined by this method and shown to have one component.

Potassium salts were prepared by the following general method unless otherwise stated. The sulphonic acid (5g) was dissolved in water (50 cm^3) at 60°C by the addition of potassium hydroxide (1M). Saturated potassium acetate solution was added at this temperature until the potassium salt began to crystallise. The mixture was cooled to 20°C, the solid collected by filtration, washed with ethanol and dried at 50°C.

The aminochlorobenzenesulphonic acids **1**, **2**, **3** and **4** are commercially available. The chloroanilines were obtained from either B.D.H. Chemicals Ltd or Fisons, 3-chloronitrobenzene from Eastman Kodak Co. and 4-amino-3-chloronitrobenzene from Koch-Light Laboratories Ltd.

The following intermediates were prepared by literature methods: 2,3-dinitrochlorobenzene,[11] 2,6-dintrochlorobenzene,[12] 3,5-dinitrobenzene sulphonic acid,[13] 2,2′-dichloro-6,6′-dinitrodiphenyl disulphide,[14] 4-chloro-2-nitrobenzene sulphonic acid,[2] 2-amino-4-chlorobenzenesulphonic acid,[2] 4-amino-6-chloro-1,3-benzenedisulphonic acid.[15,16] Structures were confirmed where necessary by modern spectral methods.

3.1. 2-*Amino*-3-*chlorobenzenesulphonic acid* (**8**)

2-Amino-6-chloronitrobenzene (4·3 g, 0·02M) was stirred in 36% hydrochloric acid (20 cm^3) at 5–10°C and sodium nitrite solution (1·8 g dissolved in 3 cm^3 water) added dropwise. The mixture was stirred for 0·5 h at 5–10°C and the insoluble material removed by filtration. The solution of diazo compound was added simultaneously with a solution of sodium sulphite, ($Na_2SO_3.7H_2O$, 6·3 g) dissolved in water (10 cm^3), below the surface to a mixture of 36% hydrochloric acid (45 cm^3), copper sulphate ($CuSO_4.5H_2O$, 0·5 g), sodium sulphite ($Na_2SO_3.7H_2O$, 6·3 g) and water (10 cm^3). The addition was made at 3–5°C over 0·25 h and the suspension stirred for a further 0·5 h at the same temperature. The product, 2-nitro-3-chlorobenzenesulphonylchloride was removed by filtration and washed with cold water until acid free. The solid was resuspended in water (100 cm^3) at room temperature and sodium hydroxide solution added. The suspension was stirred for 18 h and insoluble solid separated by filtration. The solution was adjusted to pH 5·0 by the addition of 36% hydrochloric acid and added over 0·25 h to a mixture of iron powder (3 g), ferrous sulphate crystals (0·3 g) and water (10 cm^3) at 90–95°C. The suspension was stirred at this temperature until reduction was complete (1 h, t.l.c.).

The mixture was rendered alkaline by the addition of sodium carbonate (2 g) and the iron residues removed by filtration. The solution was cooled to 0–5°C and 36% hydrochloric acid added to pH 3·5. On stirring, a solid precipitate was formed which was collected by filtration, washed with ice-cold water (2 cm^3) and acetone (20 cm^3) and dried at 60°C. 2-Amino-3-chlorobenzenesulphonic acid sodium salt was obtained (1·7 g, 29·6%).

Found: C, 31·3; H, 2·4; N, 6·0; Cl, 15·2; S, 13·6. $C_6H_5NaClNO_3S$ requires C, 31·4; H, 2·2; N, 6·1; Cl, 15·5; S, 13·9. ν_{max} (Nujol) 3450, 3250 (NH); 1150–1240(SO_3H); 775, 640 cm^{-1}. H-n.m.r. δ (Me_2SO, Na salt) 7·2 (o, m, 1p-H_4), 6·5 (o, o, 1p-H_5), 7·4 (o, m, 1p-H_6).

The free acid may be obtained on acidification with excess hydrochloric acid to pH 1·0.

ν_{max} (KBr) 3090, 2890 (broad); 1485, 1448, 1190–1240 (multiplet, SO_3H); 1100, 1030, 795, 660 cm^{-1}.

3.2. 3-*Amino*-2-*chlorobenzenesulphonic acid* (**10**)

3-Amino-2-chloronitrobenzene (30 g, 0·17 M) was reacted by exactly the same procedure as described above for 2-amino-6-chloronitrobenzene. Acidification of the final solution of aminosulphonic acid with excess hydrochloric acid gave 3-amino-2-chlorobenzenesulphonic acid (25·4 g, 64·7%) as free acid containing one molecule of water of crystallisation.

Found: C, 32·4; H, 3·5; N, 6·0; Cl, 15·9; S, 14·4; H_2O, 8·05. $C_6H_8ClNO_4S$ requires C, 31·9; H, 3·6; N, 6·2; Cl, 15·7; S, 14·2; H_2O,

8·0. ν_{max} (KBr) 3480 (broad, H_2O); 3200, 2740, 2600, (broad); 1550, 1430, 1140–1260 (multiplet, SO_3H); 1025, 785, 755, 705, 635 cm^{-1}. H-n.m.r, δ (K salt) 7·1 (o, m, 1p-H_4), 7·24 (o, o, 1p-H_5), 7·48 (o, m, 1p-H_6).

3.3. 2-*Amino*-6-*chloronitrobenzene*

The compound was prepared as described by Wepster and Verkade[17] by the reduction of 2,3-dinitrochlorobenzene[11] using acetic acid and stannous chloride m.p. 107–108°C (ref. 17: m.p. 108–108·5°C). The structure was confirmed by H-n.m.r., $\delta(CDCl_3, SiMe_4)$ 6·7 (o, m, 1p-H_3), 7·2 (o, o, 1p-H_4), 6·8 (o, m, 1p-H_5).

3.4. 3-*Amino*-2-*chloronitrobenzene*

This compound is well described in the literature[18,19] and was prepared in improved yield from 2,6-dinitrochlorobenzene[12] by the method of Wulfman and Cooper for the mono reduction of dinitroarenes.[20]

2,6-Dinitrochlorobenzene (81 g, 0·4M) was added to glacial acetic acid (1139 cm^3) and the mixture heated to 118°C. Iron powder (Bradley Foster Grade, 67·2 g) was added in portions (5 g) and the reaction mixture heated under reflux for 2·5 h. The hot mixture was added to cold water (6000 cm^3) and the precipitate collected and washed with cold water. The 3-amino-2-chloronitrobenzene was recrystallised from toluene and petroleum ether (1 : 1) (35·9 g, 52%), m.p. 95–6°C (refs. 18 and 19: m.p. 96°C).

3.5. 3-*Amino*-5-*nitrobenzenesulphonic acid*

3,5-dinitrobenzenesulphonic acid, potassium salt,[13] (80·0 g, 0·28M) was dissolved in water (1500 cm^3) at 85–90°C. A solution of sodium sulphide crystals ($Na_2S.9H_2O$, 100·8 g) and ammonium chloride (22·5 g) in water (200 cm^3) was added over 3 h. The pH was adjusted to 6.0 with 36% hydrochloric acid, a small amount of solid removed by filtration and the solution cooled to 20°C. Potassium chloride (400 g) was added and after cooling to 5°C the precipitate was collected, washed with saturated potassium chloride solution (200 cm^3) and dried. The solid was then stirred in water (400 cm^3) at 50°C to dissolve. 36% Hydrochloric acid was added (100 cm^3) and the mixture cooled to 5°C. The precipitate was collected by filtration, washed with cold water (60 cm^3) and acetone (100 cm^3) and dried. (37·3 g, 61·1%). The free acid so obtained was stirred in water (350 cm^3) and potassium hydroxide added (9·5 g) at 60°C. Saturated potassium acetate solution was added (90 cm^3) and after cooling to 20°C the crystalline solid was removed by filtration and washed with ethanol (38·4 g, 53·6%).

Found: C, 28·5; H, 1·1; N, 10·4. $C_6H_5KN_2O_5S$ requires C, 28·1; H, 1·9; N, 10·9. H-n.m.r., δ (K salt) 7·5 (m, 1p), 7·65 (m, 1p), 7·9 (m, 1p). ν_{max} (Nujol) 3490, 3400 (NH); 1240, 1190 (SO_3H); 1050, 765, 745, 660 cm^{-1}.

3.6. 3-*Chloro*-5-*nitrobenzenesulphonic acid*

3-amino-5-nitrobenzenesulphonic acid, potassium salt, (10·2 g, 0·04M) and sodium nitrite (2·8 g) were dissolved in water (140 cm^3). The solution was cooled to 5°C and 36% hydrochloric acid (16 cm^3) added all at once. After stirring the suspension for 0·2 h, excess nitrous acid was removed with 10% sulphamic acid solution. The diazo suspension was added to a solution of cuprous chloride (4·1 g) in 36% hydrochloric acid (120 cm^3) at 10°C over 0·25 h. The mixture was stirred for 18 h at 10°C and the precipitate collected, washed with ice-cold water and then acetone and dried (7 g, 73·6%).

Found: C, 27·6; H, 1·0; N, 5·4. $C_6H_4ClNO_5S.H_2O$ requires C, 28·1; H 1·5; N, 5·5. ν_{max} (Nujol) 3450 (broad, H_2O); 1550 (NO_2), 1170–1240 (multiplet, SO_3H); 1040, 900, 750, 660, 640, 620 cm^{-1}.

3.7. 3-*Amino*-5-*Chlorobenzenesulphonic acid* (**11**)

3-Chloro-5-nitrobenzene sulphonic acid (5·94 g, 0·25M) was reduced using the iron reduction method previously described to yield 3-amino-5-chlorobenzene sulphonic acid in the free acid form (3·2 g, 61·7%).

Found: C, 35·2; H, 3·1; N, 7·0; Cl, 16·5; S, 15·3. $C_6H_6Cl\ NO_3S$ requires C, 34·7; H, 2·9; N, 6·75; Cl, 17·1; S, 15·4. ν_{max} (KBr) 3040 (v. broad); 1430, 1210 (broad, SO_3H); 1040, 860, 815, 665, 625 cm^{-1}. H-n.m.r., δ (K salt) 7·1 (m, 1p), 6·9 (m, 1p), 7·2 (m, 1p).

3.8. 2-*Chloro*-6-*nitrobenzenesulphonic acid* (**16**)

2,2′-Dichloro-6,6′-dinitro diphenyldisulphide[14] (5 g, 0·0133M) was added, with cooling, to nitric acid (12·5 cm^3, SG 1·5) at 25–30°C over 0·25 h. The mixture was stirred for 2·5 h and added to cold water (120 cm^3). After removal of a small amount of insoluble material the solution was evaporated to a small volume several times to leave a final volume of 50 cm^3. The solution may be reduced at this stage or the product isolated in the following way. Potassium hydroxide was added until the solution, at 20°C, was alkaline and the salt precipitated by the addition of saturated potassium acetate solution (30 cm^3) and cooling to 5°C. 2-Chloro-6-nitrobenzenesulphonic acid potassium salt was collected by filtration, washed with ethanol and dried at 50°C (1·25 g, 34·1%).

Found; C, 26·4; H, 0·8; N, 5·1; Cl, 13·3; S, 11·3. $C_6H_3KClNO_5S$ requires C, 26·1; H, 1·1; N, 5·1; Cl, 12·9; S, 11·6. ν_{max} (Nujol) 1540 (NO_2); 1230 (SO_3H); 1120, 1070, 1030, 900, 760, 740, 630 cm^{-1}.

3.9. 2-*Amino*-6-*chlorobenzenesulphonic acid* (**12**)

The solution of 2-chloro-6-nitrobenzenesulphonic acid prepared as described above was reduced using the iron reduction method and 2-amino-6-chlorobenzenesulphonic acid obtained as the free acid (1·6 g, 28·9% based on 2,2′-dichloro-6,6′-dinitro diphenyldisulphide, 84·7% at reduction stage).

Found: C, 34·2; H, 2·8; N, 6·7; Cl, 17·0; S, 14·1. $C_6H_6ClNO_3S$ requires C, 34·7; H, 2·9; N, 6·75; Cl, 17·1; S, 15·4. ν_{max} (KBr) 3040 (v, broad); 1450, 1260, 1200 (broad, SO_3H); 1125, 1065, 780, 755, 660 cm^{-1}. H-n.m.r., δ (K salt) 6·75 (o, m, 1p-H_3 or H_5), 6·85 (o, m, 1p-H_3 or H_5), 7·15 (o, o, 1p-H_4).

3.10. *2-Chloro-4-nitrobenzenesulphonic acid* (**14**)

4-Amino-3-chloronitrobenzene (103·5 g, 0·6M) was diazotised and reacted with sulphur dioxide using the same procedure as described for 2-amino-6-chloronitrobenzene. A solution of 2-chloro-4-nitrobenzenesulphonic acid was isolated by evaporation of the solution to 500 cm^3 followed by the addition of 36% hydrochloric acid (50 cm^3) and cooling at 5°C for 2h. The crystalline solid was collected by filtration, washed with a small volume of ice-cold water and acetone and dried at 55°C (75·7 g, 53·1%). The potassium salt was formed by dissolving the free acid in water at 70°C (640 cm^3), adding potassium hydroxide (17·8 g) and precipitating with saturated potassium acetate solution (640 cm^3). After cooling to 20°C the product was removed by filtration, washed with ethanol and dried at 50°C (69·9 g, 79·6%).

Found: C, 26·7; H, 0·7; N, 4·7; Cl, 12·8; S, 11·7. $C_6H_3KCl\ NO_5S$ requires C, 26·1; H, 1·1; N, 5·1; Cl, 12·9; S, 11·6. ν_{max} (Nujol) 1530 (NO_2); 1240, 1205 (SO_3H); 1070, 1020, 780, 690, 650 cm^{-1}.

3.11. *4-Amino-2-chlorobenzenesulphonic acid* (**17**)

2-Chloro-4-nitrobenzenesulphonic acid (11·87 g, 0·05M) was again reduced by the iron reduction method to give the free acid of 4-amino-2-chlorobenzenesulphonic acid (8·47 g, 81·7%). This was converted to the potassium salt by the general procedure (8·57 g, 85·5%).

Found: C, 29·4; H, 2·0; N, 6·2; Cl, 14·6; S, 12·4. $C_6H_5KCl\ NO_3S$ requires C, 29·3; H, 2·0; N, 5·7; Cl, 14·5; S, 13·0. ν_{max} (KBr) 2900 (v. broad); 1550, 1200 (broad, SO_3H); 1065, 1015, 830 680 cm^{-1}. H-n.m.r., δ(K salt) 6·95 (m, 1p-H_3), 6·7 (o, m, 1p-H_5), 7·73 (o, 1p-H_6).

3.12. *Sulphonation of 3-chloronitrobenzene*

3-Chloronitrobenzene (47·25 g, 0·3M) was added to fuming sulphuric acid (100 cm^3, 20% SO_3) over 0·5 h at 20°C. The mixture was heated to 105–110°C and held at this temperature for 3 h. The reaction was weighed and analysed by HPLC (external standard method) for the four possible chloronitrobenzene sulphonic acids. Column, 20 × 0·46 cm LiChrosorb RP 8 (10 μ); mobile phase, methanol/0·25% acetic acid (5:95); 4·0 ml min^{-1}; detection 254 nm; 10 μl sample; samples dissolved in 50% methanol/water (0·1%).

The retention times (mins) and percentage yields respectively of the four possible products were 2-chloro-4-nitrobenzenesulphonic acid (**14**) 1·29,

33·3%; 3-chloro-5-nitrobenzenesulphonic acid (**13**) 2·52, 31·0%; 4-chloro-2-nitrobenzenesulphonic acid (**15**) 2·01, 13·8%; 6-chloro-2-nitrobenzenesulphonic acid (**16**) 1·02, none detected.

3.13. *Bake sulphonation of 2-chloroaniline*

2-*Amino*-3-*chlorobenzenesulphonic acid* (**8**): To 2-chloroaniline (900 g) was added dropwise 100% sulphuric acid (147 g, 1·5M) over 0·25 h. allowing the temperature to rise to 60°C. The mixture was heated to 170°C and then to 210°C over 3·5 h removing water as it was formed. The reaction was cooled to 80°C, water added (125 cm^3) followed by sodium carbonate until alkaline (150 g). The excess 2-chloroaniline was removed by steam distillation, the solution clarified by filtration at 100°C and cooled to 20°C. The crystalline solid was collected by filtration, washed with cold water and recrystallised again from dilute sodium carbonate solution (975 cm^3 containing 32 g Na_2CO_3) to give pure 2-amino-3-chlorobenzenesulphonic acid sodium salt (46·4 g, 13·5%) having an identical i.r. spectrum to the same compound prepared from 2-amino-6-chloronitrobenzene.

The reaction mixture before isolation was shown by HPLC (external standard method, Fig. 1) to contain only 2-amino-3-chlorobenzenesulphonic acid (16·5%) and 4-amino-3-chlorobenzenesulphonic acid (63·9%).

3.14. *Bake sulphonation of 3-chloroaniline*

2-*Amino*-4-*chlorobenzenesulphonic acid* (**5**): 3-Chloroaniline (95·6 g, 0·75M) was added to 98% sulphuric acid (150 g) over 0·5 h allowing the temperature to rise to 100°C. The mass was heated to 220–225°C for 4 h. The reaction mass after cooling to 80°C was added to water (1000 cm^3) and dissolved by addition of sodium hydroxide. A small amount of insoluble material was removed and the solution acidified to pH 1·0 with 36% hydrochloric acid (70 cm^3). The crystalline solid was collected by filtration at 20°C washed with cold water (400 cm^3) and dried at 70°C (120 g, 77·1%).

The compound had an identical i.r. spectrum to 2-amino-4-chlorobenzenesulphonic acid prepared from 4,4'-dichloro-2,2'-dinitrodiphenyldisulphide.[2]

3.15. *Sulphonation of 3-chloroaniline*

3-Chloroaniline (10 g, 0·078M) was added to fuming sulphuric acid (25 cm^3, 10% SO_3) over 0·25 h at 20°C. The mixture was heated to 95–100°C for 12 h. The resulting solution was weighed and analysed by HPLC (external standard method). Conditions were as described in Fig. 1 but using 15% acetonitrile/0·0251M tetrabutylammoniumphosphate as the mobile phase. The

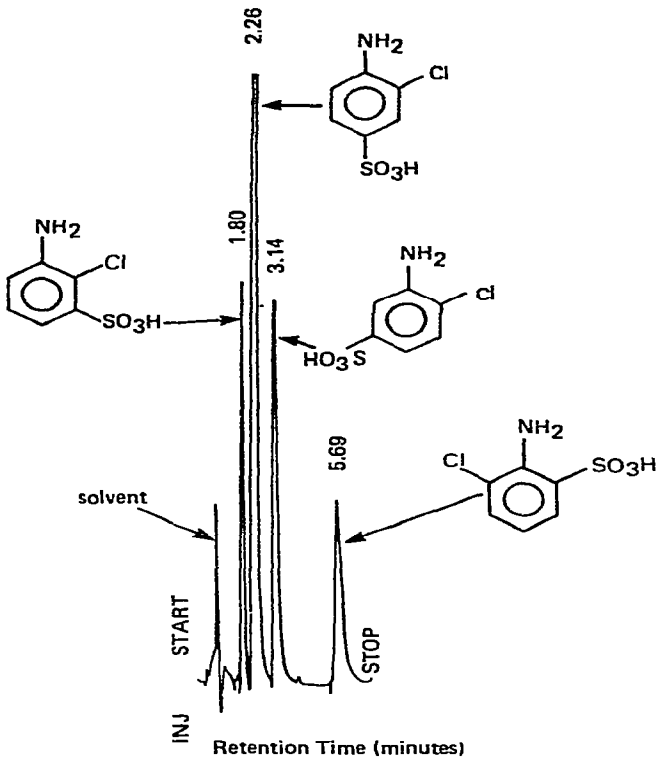


Fig. 1. Separation of the four isomeric aminochlorobenzenesulphonic acids derived from 2-chloroaniline. Column, 25×0·46 cm LiChrosorb RP8 (10 μ); mobile phase, 25% acetonitrile/0·0251 M tetrabutyl ammonium phosphate (pH 7·0); 4·0 cm^3 min^{-1}; detection 250 nm; 10 μl sample; samples dissolved in 50% methanol/water (0·1%).

products, their retention times and percentage yields respectively were as follows: 4-amino-6-chlorobenzene-1,3-disulphonic acid,[15,16] 7·14, 33·7; 4-amino-2-chlorobenzenesulphonic acid (**17**), 1·86, 21·5; 2-amino-4-chlorobenzene sulphonic acid (**5**) 11·99, 16·2; 3-amino-5-chlorobenzene-sulphonic acid (**11**) 6·03, 12·2.

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