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An X-ray crystallographic study of the conformation of arylmethanesulfonamides

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The conformations of eight arylmethanesulfonamides have been studied by X-ray crystallography. The average N–S bond length is significantly shorter than the sum of the covalent radii and the plane C(1)–N–S is rotated with respect to the aromatic ring.

Keywords: arylmethanesulfonamides, X-ray crystallography

There have only been limited studies on the conformation of arylmethanesulfonamides ($ArNHSO_2CH_3$) by X-ray crystallography. This grouping is present in a number of drugs including the tumour inhibitory amsacrine,[1,2] the anti-inflammatory drug nimesulide[3] and some antiarrhythmic drugs related to sotalol[4] whose X-ray crystal structures have been determined. The X-ray crystal structures of a number of toluene-*p*-sulfonamides have been determined but there are only three crystal structures of arylmethane-sulfonamides in the Cambridge Crystallographic Data Base. The conformation of some toluene-*p*-sulfonamides has been discussed[5] and there is a balance between the interactions of the toluene ring and the nitrogen atom with the sulfonyl group. In this paper we describe the X-ray crystal structure of some arylamine *N*-methanesulfonamides and consider some of the factors which may influence the conformation of the methanesulfonamide group relative to the aromatic ring.

The advent of rapid X-ray crystallographic structure determinations has meant that it is possible to study a series of compounds. Nevertheless it is important to note that any interpretation of such information in terms of intramolecular effects must also take into account crystal packing effects and in particular intermolecular hydrogen bonding. In this context compounds **1**, **3**, **4**, **7** and **8** showed intermolecular hydrogen bonds of length $SO_2N(H)$ …O of 2.20, 2.22, 2.20, 2.11 and 2.04 Å respectively. The X-ray crystal structure of *p*-chloroaniline has been determined[6] and it has been shown that the nitrogen is only slightly displaced from the plane of the aromatic ring (c 0.02 Å). The Ar(C)–NH_2 bond is significantly shorter than a normal C–N bond in accord with electron-delocalisation from the nitrogen into the ring.

The plane of the sulfonamide group [C(1)–N–S] in the N-methanesulfonamide of *p*-chloroaniline (see Fig. 1) is rotated by 62° with respect to the aromatic ring (see Table 1). This rotation is increased to 85° in the *N*-methyl-*N*-methanesulfonamide (see Fig. 2) in which hydrogen bonding involving an N–H cannot take place. Hence a significant proportion of the rotation must be steric in origin. A single adjacent methyl group in the methanesulfonamide of 2,5-dimethylaniline does not significantly alter the rotation (see Fig. 3) but a second methyl group as in the methanesulfonamide of 2,6-dimethylaniline produces a greater steric effect (see Fig. 4) (68° in **3**, 85° in **4**). In contrast intramolecular hydrogen bonding to an adjacent nitro or carbomethoxy group (Figs 5 and 6) reduces the rotation to 23° and 32° respectively. The planes of the nitro and carbomethoxy groups are almost parallel with the aromatic ring (13° and 1° rotation respectively). When steric crowding twists the nitro group so that it is no longer co-planar with the aromatic ring as in the *N*-methanesulfonamide of 3,4-dimethyl-2,6-dinitroaniline (see Fig. 7), the sulfonamide rotates to the same extent (89°) as the nitro group. However, the hydrogen bonds are intermolecular in this case.

Table 1 Angle (°) between the plane C(1)–N–S and the aromatic ring

N-Methanesulfonamide *p*-chloroaniline	**1**	62
N-Methyl-*p*-chloroaniline	**2**	86 and 85
2,5-Dimethylaniline	**3**	68
2,6-Dimethylaniline	**4**	85
4-Methoxy-2-nitroaniline	**5**	23
Methyl anthranilate	**6**	32
3,4-Dimethyl-2,6-dinitroaniline	**7**	89
4-Aminoacetanilide	**8**	71

There is an interesting comparison between the methanesulfonamide and acetanilide groups in the structure of the *N*-methanesulfonamide of 4-aminoacetanilide (see Fig. 8). Here the methanesulfonamide is rotated to the extent of 71°

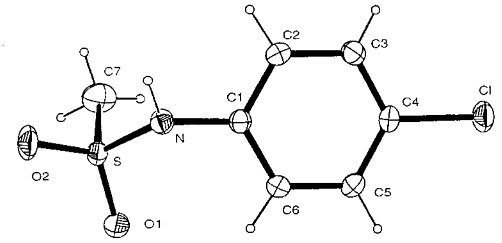

Fig. 1 Crystal structure of *p*-chloroaniline *N*-methanesulfonamide **1**.

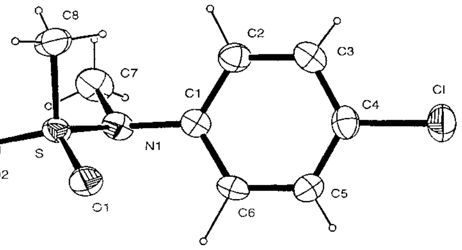

Fig. 2 Crystal structure of *N*-methyl-*p*-chloroaniline *N*-methanesulfonamide **2**.

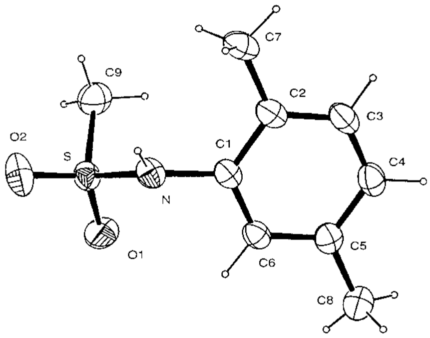

Fig. 3 Crystal structure of 2,5-dimethylaniline *N*-methanesulfonamide **3**.

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* Correspondence.

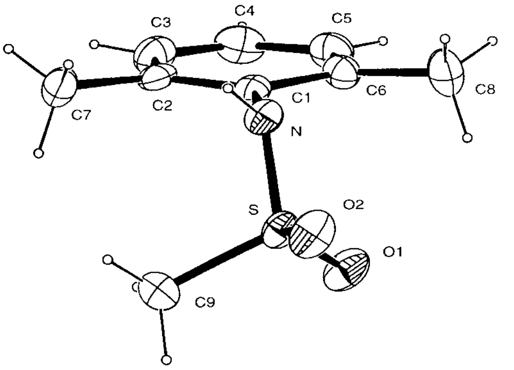

Fig. 4 Crystal structure of 2,6-dimethylaniline *N*-methanesulfonamide **4**.

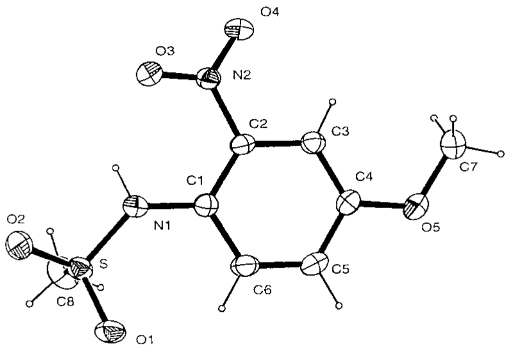

Fig. 5 Crystal structure of 4-methoxy-2-nitroaniline *N*-methanesulfonamide **5**.

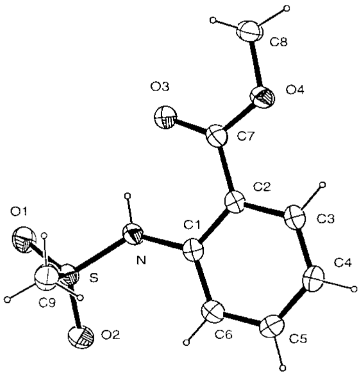

Fig. 6 Crystal structure of 4-methyl anthranilate *N*-methanesulfonamide **6**.

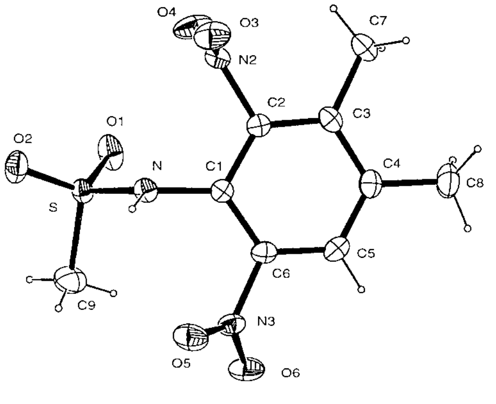

Fig. 7 Crystal structure of 3,4-dimethyl-2,6-dinitroaniline *N*-methanesulfonamide **7**.

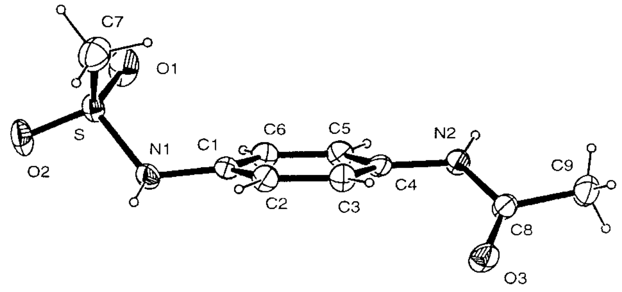

Fig. 8 Crystal structure of 4-aminoacetanilide *N*-methanesulfonamide **8**.

whilst the acetanilide is rotated by 40°. The plane of the amide nitrogen is almost parallel with the aromatic ring and it shows very little pyramidal character. It is only 0.04 Å out of the plane of C(4)–C(8)–H(2). The C(=O)–N bond length is 1.36 Å in keeping with the partial double bond character of the amide.

The methanesulfonamide nitrogens of **1** to **8** form part of a flattened pyramid with the nitrogen lying an average of 0.23 Å out of the plane of the three substituents (see Table 2). A typical pyramidal –$(CH_2)_3N$ nitrogen is in the range 0.46 – 0.54 Å out of the plane of its substituents. The average N–S bond length (see Table 3) in the methanesulfonamides is 1.64 Å which is shorter than the sum of the covalent radii (1.78 Å). The average Ar(C)–N bond length is 1.43 Å which is longer than the corresponding Ar(C)–N bond length in *p*-chloroaniline (1.386 Å).[6] The average C(1)–N–S–O(2) torsion angle (Table 4) is 172.8° indicating an almost *trans* co-planar arrangement. However, there is little difference (av. 0.005 Å) between the two S–O bond lengths in the sulfonamides.

In conclusion these X-ray crystal structures suggest that in these arylamine *N*-methanesulfonamides there may be less electron delocalisation involving the sulfonamide nitrogen and the aromatic ring compared to an acetanilide but that there is an interaction between the nitrogen lone pair and the sulfonyl group. Although the shorter N–S bond lengths and the near 180° C(1)–N–S–O(2) torsion angle could be in accord with a contribution from an 'amide type' resonance, the similarity of the two S–O bond lengths militates against this. Molecular orbital studies of sulfur–nitrogen conjugation have invoked[7] the participation of the 'd' orbitals on sulfur to account for some electron delocalisation in the molecule (S_4N_4).

Table 2 Nitrogen out of plane distance (/Å) from C(1)–N(H)–S

N-Methanesulfonamide *p*-chloroaniline	**1**	0.28
N-Methyl-*p*-chloroaniline	**2**	0.28 and 0.26
2,5-Dimethylaniline	**3**	0.20
2,6-Dimethylaniline	**4**	0.22
4-Methoxy-2-nitroaniline	**5**	0.16
Methyl anthranilate	**6**	0.20
3,4-Dimethyl-2,6-dinitroaniline	**7**	0.17
4-Aminoacetanilide	**8**	0.28

Table 3 C(1)–N and N–S bond lengths (/Å), (esd)

		C(1)–N	N–S
N-Methanesulfonamide *p*-chloroaniline	**1**	1.434(3)	1.640(2)
N-Methyl-*p*-chloroaniline	**2**	1.433(5)	1.646(3)
		1.446(5)	1.644(3)
2,5-Dimethylaniline	**3**	1.4363(17)	1.6251(12)
2,6-Dimethylaniline	**4**	1.440(3)	1.629(2)
4-Methoxy-2-nitroaniline	**5**	1.404(2)	1.6338(14)
Methyl anthranilate	**6**	1.4152(17)	1.6364(12)
3,4-Dimethyl-2,6-dinitroaniline	**7**	1.4218(19)	1.6438(14)
4-Aminoacetanilide	**8**	1.440(2)	1.6262(15)

Table 4 C(1)–N–S–O(2) torsion angles (°)

N-Methanesulfonamide *p*-chloroaniline	**1**	–178.6
N-Methyl-*p*-chloroaniline	**2**	–170.57, –170.39
2,5-Dimethylaniline	**3**	–179.79
2,6-Dimethylaniline	**4**	–167.32
4-Methoxy-2-nitroaniline	**5**	–172.80
Methyl anthranilate	**6**	179.64
3,4-Dimethyl-2,6-dinitroaniline	**7**	162.46
4-Aminoacetanilide	**8**	173.56

Experimental

The *N*-methanesulfonamides were prepared from the corresponding anilines by literature methods[8,9] using methanesulfonyl chloride in pyridine and recrystallised from methanol or aqueous methanol.

Crystal data and structure determinations: (i) *p*-chloroaniline *N*-methanesulfonamide **1** $C_7H_8ClNO_2S$, M_r = 205.65, monoclinic, space group $P2_1/c$(No.14), a = 9.5955(3), b = 5.6963(3), c = 16.0340(6) Å, $\alpha = \gamma = 90°$, β = 97.379(2)°, V = 869.14(6) Å^3, Z = 4, D_{calc} = 1.57 g cm^{-3}, μ = 0.64 mm^{-1}, F(000) = 424, λ = 0.71073 Å, T = 173(2) K. Data were collected using a crystal of size 0.4 × 0.4 × 0.3 mm^3 on an KappaCCD diffractometer. A total of 11740 reflections were collected for $3.80 < \theta < 27.53°$ and $-12 \le h \le 12$, $-7 \le k \le 7$, $-20 \le l \le 20$. There were 1990 independent reflections and 1859 reflections with $I > 2\sigma(\mathrm{I})$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(\mathrm{I})]$, R_1 = 0.048, wR_2 = 0.142 and all data, R_1 = 0.052, wR_2 = 0.145. The largest difference peak and hole was 0.45 and –0.47 e Å^{-3} and the goodness-of-fit on F^2 was 1.213.

(ii) *N*-methyl-*p*-chloroaniline *N*-methanesulfonamide **2** $C_8H_{10}ClNO_2S$, M_r = 219.68, monoclinic, space group Pc (No.7), a = 16.4946(8), b = 5.9918(3), c = 10.1030(4) Å, $\alpha = \gamma$= 90°, β = 90.589(3)°, V = 998.45(8) Å^3, Z = 4, D_{calc} = 1.46 g cm^{-3}, μ= 0.56 mm^{-1}, F(000) = 456, λ = 0.71073 Å, T = 173(2) K. Data were collected using a crystal of size 0.4 × 0.2 × 0.1 mm^3 on an KappaCCD diffractometer. A total of 13776 reflections were collected for $3.95 < \theta < 25.08°$ and $-19 \le h \le 19$, $-7, \le k \le 7$, $-12 \le l \le 11$. There were 3341 independent reflections and 3204 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.039, wR_2 = 0.099 and all data, R_1 = 0.041, wR_2 = 0.101. The largest difference peak and hole was 0.39 and –0.32 e Å^{-3} and the goodness-of-fit on F^2 was 1.094. There were two independent molecules in the unit cell.

(iii) 2,5-dimethylaniline *N*-methanesulfonamide **3** $C_9H_{13}NO_2S$, M_r = 199.26, monoclinic, space group $P2_1/c$ (No.14), a = 8.8657(2), b = 5.8245(2), c = 19.1885(5) Å, $\alpha = \gamma = 90°$, β = 95.658(2)° V = 986.03(5) Å^3, Z = 4, D_{calc} = 1.34 g cm^{-3}, μ = 0.30 mm^{-1}, F(000) = 424, λ = 0.71073 Å, T = 173(2) K. Data were collected using a crystal of size 0.40 × 0.30 × 0.15 mm^3 on an KappaCCD diffractometer. A total of 15358 reflections were collected for $4.10 < \theta < 27.48°$ and $-11 \le h \le 11$, $-7 \le k \le 7$, $-24 \le l \le 24$. There were 2260 independent reflections and 1987 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.033, wR_2 = 0.090 and all data, R_1 = 0.039, wR_2 = 0.094. The largest difference peak and hole was 0.25 and –0.40 e Å^{-3} and the goodness-of-fit on F^2 was 1.065.

(iv) 2,6-dimethylaniline *N*-methanesulfonamide **4** $C_9H_{13}NO_2S$, M_r = 199.26, orthorhombic, space group $P2_12_12_1$ (No.19), a = 4.9267(3), b = 13.2229(12), c = 15.0484(15) Å, $\alpha = \beta = \gamma = 90°$, V = 980.3(2) Å^3, Z = 4, D_{calc} = 1.35 g cm^{-3}, μ = 0.30 mm^{-1}, F(000) = 424, λ = 0.71073 Å, T =173(2) K. Data were collected using a crystal of size 0.3 × 0.1 × 0.1 mm^3 on an KappaCCD diffractometer. A total of 5462 reflections were collected for $4.10 < \theta < 29.97°$ and $-4 \le h \le 6$, $-18 \le k \le 15$, $-14 \le l \le 21$. There were 2769 independent reflections and 2032 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.054, wR_2 = 0.112 and all data, R_1 = 0.084, wR_2 = 0.125. The largest difference peak and hole was 0.26 and –0.38 e Å^{-3} and the goodness-of-fit on F^2 was 1.039.

(v) 4-methoxy-2-nitroaniline *N*-methanesulfonamide **5** $C_8H_{10}N_2O_5S$, M_r = 246.24, monoclinic, space group $P2_1/n$ (No.14), a = 11.2511(4), b = 5.0158(2), c= 18.8266(8) Å, $\alpha = \gamma = 90°$, β = 105.678(2)°, V = 1022.92(7) Å^3, Z = 4, D_{calc} = 1.60 g cm^{-3}, μ = 0.33 mm^{-1}, F(000) = 512, λ = 0.71073 Å, T = 173(2) K. Data were collected using a crystal of size 0.3 × 0.1 × 0.1 mm^3 on a KappaCCD diffractometer. A total of 9119 reflections were collected for $3.76 < \theta < 27.48°$ and $-14 \le h \le 14$, $-6 \le k \le 6$, $-24 \le l \le 24$. There were 2343 independent reflections and 1916 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.036, wR_2 = 0.088 and all data R_1 = 0.048, wR_2 = 0.095. The largest difference peak and hole was 0.27 and –0.37 e Å^{-3} and the goodness-of-fit on F^2 was 1.029.

(vi) methyl anthranilate *N*-methanesulfonamide **6** $C_8H_{11}NO_4S$, M_r = 229.25, monoclinic, space group $P2_1/n$ (No.14), a = 8.4710(2), b = 9.0077(3), c = 13.7050(3) Å, $\alpha = \gamma = 90°$, β = 103.788(2)°, V = 1015.62(5) Å^3, Z = 4, D_{calc} = 1.50 g cm^{-3}, μ = 0.31 mm^{-1}, F(000) = 480, λ = 0.71073 Å, T = 173(2)K. Data were collected using a crystal of size 0.3 × 0.2 × 0.3 mm^3 on an KappaCCD diffractometer. A total of 17606 reflections were collected for $3.81< \theta < 27.52°$ and $-11 \le h \le 10$, $-11 \le k \le 11$, $-17 \le l \le 17$. There were 2314 independent reflections and 2044 reflections with $I > 2\sigma(I)$ were used in refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.032, wR_2 = 0.082 and all data, R_1 = 0.038, wR_2 = 0.085. The largest difference peak and hole was 0.28 and –0.49 e Å^{-3} and the goodness-of-fit on F^2 was 1.075.

(vii) 3,4-dimethyl-2,6-dinitroaniline *N*-methanesulfonamide **7** $C_9H_{11}N_3O_6S$, M_r = 289.27, monoclinic, space group $P2_1/n$ (No.14), a = 4.9187(1), b = 16.5884(6), c = 14.9944(6) Å, $\alpha = \gamma = 90°$, β = 96.009(2)°, V = 1216.72(7) Å^3, Z = 4, D_{calc} = 1.58 g cm^{-3}, μ = 0.30 mm^{-1}, F(000) = 600, λ = 071073 Å, T = 173(2) K. Data were collected using a crystal of size 0.30 × 0.25 × 0.25 mm^3 on an KappaCCD diffractometer. A total of 16660 reflections were collected for $3.93 < \theta < 27.50°$ and $-6 \le h \le 6$, $-21 \le k \le 21$, $-19 \le l \le 19$. There were 2779 independent reflections and 2427 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.036, wR_2 = 0.085 and all data, R_1 = 0.044, wR_2 = 0.090. The largest difference peak and hole was 0.280 and –0.386 e Å^{-3} and the goodness-of-fit on F^2 was 1.047.

(viii) 4-aminoacetanilide *N*-methanesulfonamide **8** $C_9H_{12}N_2O_3S$, M_r = 228.27, orthorhombic, space group $P2_12_12_1$ (No.19), a = 5.0820(1), b = 8.4033(2), c = 24.5945(5) Å, $\alpha = \beta = \gamma = 90°$, V = 1050.32(4) Å^3, Z = 4, D_{calc} = 1.44 g cm^{-3}, μ = 0.30 mm^{-1}, F(000) = 480, λ = 0.71073 Å, T = 173(2) K. Data were collected using a crystal of size 0.2 × 0.1 × 0.1 mm^3 on an KappaCCD diffractometer. A total of 15528 reflections were collected for $4.09 < \theta < 28.37°$ and $-6 \le h \le 6$, $-11 \le k \le 11$, $-32 \le l \le 32$. There were 2599 independent reflections and 2442 reflections with $I > 2\sigma(I)$ were used in the refinement. The structure was solved by direct methods and refined using SHELXL-97. The final R indices were $[I > 2\sigma(I)]$, R_1 = 0.032, wR_2 = 0.078 and all data, R_1 = 0.035, wR_2 = 0.080. The largest difference peak and hole was 0.28 and –0.28 e Å^{-3} and the goodness-of-fit on F^2 was 1.056. The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC 233591 – 233598).

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