Acta Crystallographica Section B
Structural Science
ISSN 0108-7681

Structural systematics of 4,4′-disubstituted benzenesulfonamidobenzenes. 1. Overview and dimer-based isostructures

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Received 16 January 2007
Accepted 22 March 2007

One hundred 4,4′-disubstituted benzenesulfonamidobenzenes, X–C_6H_5–SO_2–NH–C_6H_5–Y, where X, Y = NO_2, CN, CF_3, I, Br, Cl, F, H, Me, OMe, have been synthesized and their crystal structures determined. The resulting set of 133 structures, which includes polymorphic forms, is used to make a comparative study of the molecular packing and the nature of the intermolecular interactions, including the formation of hydrogen-bonding motifs and the influence of the two substituents X and Y on these features. Nine distinct supramolecular connectivity motifs of hydrogen bonding are encountered. There are 74% of all the structures investigated which exhibit one of two motifs based on N—H···O═S interactions, a dimer or a chain. There are three other, infrequent motifs, also employing N—H···O═S links, which exhibit more complexity. Four different chain motifs result from either N—H···O═N, N—H···C≡N or N—H···OMe interactions, arising from the presence of a nitro (position Y), nitrile (X or Y) or methoxy (Y) substituent. The program *XPac* [Gelbrich & Hursthouse (2005). *CrystEngComm*, **7**, 324–336] was used to systematically analyse the packing relationships between crystal structures. Similar discrete (zero-dimensional) and extended (one-dimensional and two-dimensional) structure components, as well as cases of isostructurality were identified. A hierarchy for the classification of the 56 distinct structure types of this set is presented. The most common type, a series of 22 isostructures containing the simple centrosymmetric N—H···O═S-bonded dimer, is discussed in detail.

1. Introduction

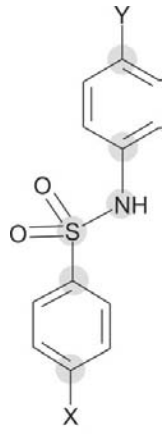
The careful examination of a single-crystal structure of an organic molecule can yield much information about the details of the molecular structure and conformation. It also enables the nature of the crystal packing to be ascertained. However, information on why that molecular conformation or packing exists or on how the chosen crystal growth mechanism might have been favoured is not readily accessible. It is our belief that some pointers towards answering these questions can be gained from a detailed, comparative study of the crystal structures of many compounds, especially when the molecules are similar. In order to develop this knowledge-based approach, we have engaged in a structural systematics study, in which we are following two strands. In one, we are studying polymorphic and associated solid forms (*e.g.* solvates, co-crystals and salts), in which a given molecule occurs in different crystal structures, and in the other we are studying the crystal structures of families of closely related molecules. In all of the sets of structures examined, we are searching for patterns that identify similarities or differences between

members, which might be related to particular features in the individual components of the structures.

A comparison of the structures of polymorphs often shows that the structures encountered seem to represent a very disparate set out of the huge numbers of possible structures that can be generated, for example by calculation (Lancaster *et al.*, 2006). Our work on solvates, co-crystals and salts has also shown irregular behaviour patterns with respect to the nature of the crystalline product formed. A preliminary note on the sulfathiazole system has been published (Bingham *et al.*, 2001) and we will report further on this area in subsequent publications. Here we report on the crystal chemistry of one family from our structural systematics study.

The Cambridge Structural Database (CSD; Allen, 2002) rarely contains substantial sets of closely related crystal structures other than those of aliphatic straight-chain hydrocarbons, acids and some related substituents. We have therefore set out to prepare extensive collections of easily synthesized molecules, which differ slightly in their substituents, and determine their crystal structures. As far as possible a crystal structure of every member of the defined set has been obtained. The main problem with this undertaking lies in obtaining satisfactory crystals from every compound in the set. This can prove time-consuming in respect of what is usually a tiny minority amongst otherwise easily crystallizable compounds.

Many large sets of structures have been examined in these studies, including alkali metal dicarboxylates, chalcones, benzamides, pyridine amides, pyridine sulfonamides, sulfathiazole solvates, tricyclics related to carbamazepine, amine tartrates and alkali metal tartrates. Of these, only part of the work on the alkali metal tartrates (Gelbrich *et al.*, 2004, 2006*a*), and the crystal structure of an aberrant product encountered in the present work (Gelbrich *et al.*, 2006*b*) have so far been published. The present set has been chosen as the first report from this study because of its completeness and relative simplicity of distribution of crystal structure types amongst the compounds in the set. Further papers describing relationships in other compound families are in preparation. The set of compounds of the title, for which the short notation *X*~*Y* is used, comprises every combination of *X* and *Y* in the substituted benzene sulfonamides (I), in which *X* and *Y* are NO_2, CN, CF_3, I, Br, Cl, F, H, Me and OMe. More than 100 structures are available for comparison, because for many of the compounds the crystal structure of more than one form has been obtained.[1] The structural relationships between these have been examined using the computer program *XPac* (Gelbrich & Hursthouse, 2005; Gelbrich, 2006), developed in this laboratory. In this paper, an overview of the structural patterns is presented, together with a detailed examination of a series of 24 isostructures based on an N—H···O=S-bonded dimer. This group is composed of 22 structures of the described set of compounds and additionally the structures of Cl~C≡CH and a mixed crystal $(Cl{\sim}Cl)_{0.8}{\cdot}(Cl{\sim}F)_{0.2}$. This series is unique within the investigated set of benzene sulfonamides, because no other hydrogen-bond motif is associated to the same extent with just one crystal structure type.



(I)

There have been relatively few comparable comparative studies reported in the literature, but the work of Boese on dicarboxylic acids (Thalladi *et al.*, 2000) and that of Kato on bile acid derivatives (Kato *et al.*, 2004) are noteworthy. However, these have a somewhat different focus and relate to the effect on properties of homologues.

2. Experimental

2.1. General synthesis procedure and crystallization

The *para*-substituted benzenesulfonyl chloride (1 mmol) was added to a solution of the *para*-substituted aniline (1 mmol) in pyridine (3 ml). The orange–red colour which formed was discharged on boiling. After boiling for 30 min, the solution was reduced by evaporation to a small volume under nitrogen until white fumes of pyridine hydrochloride began to appear. The cooled residue was treated with water, left to stand and if no solid formed within 12 h, scratched with a rod until it solidified. The product was filtered off the solvent, dissolved in ethanol (5 ml) and allowed to evaporate at room temperature until crystals formed. In some cases, because the product was so soluble in ethanol, only a syrup resulted. Such compounds were crystallized from benzene, toluene or petrol, or from benzene by anti-solvent addition of petrol. In the case of 4-methoxybenzenenesulfonamido-*N*-(4-fluorobenzene), the product was crystallized by two phase crystallization from methanol–hexane.

The formation of polymorphs was attempted *via* solvent change, change of crystallization conditions, cross-seeding, cross-seeding by antisolvent addition of a dilute slurry of seeds, co-crystallization, treatment of the surface of the crystallizing vessel, templating with polymers containing sulfonamide groups and by sublimation. Cross-seeding implies the use of seeds of a related compound with the intention of inducing the crystal packing features of the seed in the product of the crystallizing solution. This has been the most successful

[1] The polymorphic modifications of a compound *X*~*Y* are arbitrarily labelled α, β, γ *etc.*

Table 1
Crystallographic parameters for structures of the **A1.1** type (trigonal space group $R\bar{3}$, $Z = 18$).

Phase	a (Å)	c (Å)	V (Å^3)	M_r	θ_{max} (°)	R_{int}	Completeness	R, wR, S	No. of variables	No. of reflections
α-Br~CF_3†	28.0220 (6)	9.5386 (3)	6486.5 (3)	380.18	25.1	0.050	0.995	0.040, 0.112, 0.99	231	2552
α-Br~I‡	28.134 (4)	9.0240 (18)	6185.8 (18)	438.07	25.1	0.120	0.980	0.060, 0.180, 1.10	176	2401
α-Br~Br‡	27.3197 (11)	9.2582 (6)	5984.2 (5)	391.08	25.0	0.186	0.836	0.086, 0.206, 1.07	166	1962
Cl~Br‡	27.045 (4)	9.1556 (10)	5799.5 (13)	346.62	25.0	0.104	0.910	0.0499, 0.113, 0.94	172	2049
Cl~CF_3†	27.805 (3)	9.4583 (12)	6332.8 (12)	335.72	26.0	0.147	0.993	0.056, 0.139, 0.90	257	2745
Cl~Cl‡	26.5773 (11)	9.3206 (4)	5701.6 (4)	302.16	26.0	0.153	0.983	0.056, 0.121, 1.08	175	2451
Cl~I‡	27.812 (4)	9.0055 (18)	6032.6 (17)	393.61	26.1	0.052	0.980	0.026, 0.058, 1.01	173	2603
CN~CF_3‡	27.6017 (8)	9.4505 (3)	6235.3 (3)	326.29	25.1	0.068	0.992	0.067, 0.170, 1.21	268	2439
CN~I‡	27.4867 (7)	9.3972 (7)	6148.6 (5)	384.18	26.0	0.104	0.880	0.049, 0.129, 0.94	176	2357
CN~Br‡	27.0722 (8)	9.4838 (8)	6019.5 (6)	337.19	26.0	0.111	0.974	0.047, 0.113, 1.02	184	2569
CN~Cl‡	26.8055 (15)	9.5489 (6)	5942.0 (6)	292.73	26.0	0.099	0.952	0.044, 0.121, 1.05	184	2482
α-CN~Me‡	26.9964 (6)	9.5869 (5)	6050.9 (4)	272.32	26.0	0.102	0.994	0.043, 0.108, 1.03	192	2632
F~CF_3†	27.4403 (4)	9.5034 (3)	6197.1 (2)	319.27	26.0	0.057	0.982	0.0477, 0.140, 1.01	249	2654
F~I‡	27.3131 (5)	9.1331 (2)	5900.5 (2)	377.16	26.0	0.036	0.993	0.032, 0.083, 1.10	176	2564
F~Br‡	26.5333 (4)	9.2014 (3)	5610.1 (2)	330.17	26.0	0.054	0.996	0.031, 0.081, 1.03	176	2449
F~Cl‡	25.9241 (8)	9.3533 (5)	5443.8 (4)	285.71	25.1	0.115	0.953	0.056, 0.154, 1.00	175	2048
α-F~F‡	24.9922 (5)	9.5804 (4)	5182.3 (3)	269.26	26.0	0.065	0.953	0.040, 0.099, 1.03	176	2157
Me~CF_3†	27.7243 (7)	9.8101 (5)	6530.2 (4)	315.31	25.1	0.063	0.988	0.055, 0.153, 1.14	222	2548
Me~I‡	27.7443 (14)	9.3639 (9)	6242.2 (7)	373.20	25.1	0.095	0.949	0.045, 0.119, 1.04	166	2338
Me~Br‡	27.1912 (10)	9.4503 (7)	6051.1 (5)	326.21	25.0	0.113	0.983	0.044, 0.099, 0.97	177	2334
Me~Cl‡	26.7454 (4)	9.5265 (3)	5901.5 (2)	281.75	26.0	0.050	0.998	0.037, 0.103, 1.09	179	2577
α-OMe~I‡	27.3759 (8)	9.9002 (4)	6425.6 (4)	389.20	26.0	0.140	0.990	0.054, 0.129, 1.06	176	2769
(Cl~Cl)$_{0.8}$·(Cl~F)$_{0.2}$‡	26.4119 (8)	9.3936 (5)	5674.9 (4)	298.87	26.0	0.088	0.988	0.048, 0.126, 1.05	186	2455
Cl~CCH‡	27.3848 (15)	9.2241 (7)	5990.6 (6)	291.74	25.1	0.091	0.853	0.072, 0.176, 0.93	180	2006

† $T = 293$ K ‡ $T = 120$ K.

method of generating polymorphs in our other structural systematic studies (cited in §2.1).

IR spectra were run by the diamond ATR technique on a Nicolet Omnic spectrometer over the range 3700–370 cm^{-1}. From our set of 100 compounds only four crystal structures had been previously reported, those of NO_2~I, I~NO_2 (Kelly *et al.*, 2002), OMe~OMe (Pokrywiecki *et al.*, 1973) and H~Br (Rérat, 1969). The structures obtained for the first three of these compounds were the same as those in the literature, while our crystals of H~Br proved to be a new polymorphic form.

2.2. Single-crystal structure determination

Intensity data were collected using Mo $K\alpha$ radiation (λ = 0.71073 Å) monochromated by 10 cm confocal mirrors, on a Bruker–Nonius KappaCCD diffractometer with a Bruker–Nonius FR591 rotating anode. The data were corrected for absorption using *SADABS* (Sheldrick, 2003). The structures were solved by direct methods and refined on F^2 by least-squares procedures (Sheldrick, 1997). The H atoms were located in difference maps and those attached to C were treated as riding. The positions of H atoms attached to N were refined using the *DFIX* instruction in *SHELXL*. Crystallographic parameters and refinement details for the 24 isostructures discussed in §3.4 are listed in Table 1. Parameters of the hydrogen-bond geometry in these structures are available as supplementary information.[2]

[2] Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM5045). Services for accessing these data are described at the back of the journal.

2.3. Identification of packing similarity

The set of $n = 133$ structures and $(n^2 - n)/2 = 8778$ structure pairs was investigated for packing similarity, using the *XPac* program in the previously described manner (Gelbrich & Hursthouse, 2005, 2006) with standard cut-off parameters. In order to rationalize procedures, once the complete three-dimensional arrangements of molecules in two structures were identified as being the same (isostructures), only one of them was retained for subsequent operations. The underlying assumption was that the comparison of either of the two structures with a third structure would always lead to the same result. All comparisons were carried out with parameter lists derived from corresponding ordered sets of points. These were obtained from the six atoms highlighted in (I). The geometry of this set of points is not affected by a possible rotation of the two benzene rings about the C—C and the C—N bond.

3. Results and discussion

3.1. Classification of crystal structures

All the compounds examined here are *para–para* substituted. Our experiences of the comparison of different substitution patterns showed a tendency of *ortho*- and *meta*-substituted compounds to form distinct structures and for *ortho* compounds to favour hydrates and solvates. This would complicate any discussion of similarities. All the substituents, except for NO_2 and OMe, are rotationally symmetrical or pseudo-symmetrical, which reduces the options for different packing owing to group rotation. Even with these restrictions

a very large number of unique structures result, despite the fact that the overwhelming portion of the molecule remains constant in every case.

Structural units of molecules in a crystal that are linked by known or conceivable intermolecular interactions may be called *supramolecular synthons*, a term introduced by Desiraju (1995). It is convenient to describe the linkage between molecules by conventional interactions with a few geometric parameters, for instance a distance $D\cdots$H and an angle (DHA) in the case of a D—H$\cdots A$ bond. Graph-set methods can be employed to characterize the topology of an interaction (Bernstein *et al.*, 1995). Recently, we have described a new approach, whereby the actual spatial arrangements of molecules in two crystal structures are compared (Gelbrich & Hursthouse, 2006). This enables the identification of structural components that are geometrically similar and occur in more than one structure. We have termed such common components *supramolecular constructs* (SCs) and these can either be discrete (zero-dimensional) or extended (one-, two- or three-dimensional). Molecules may pack in a similar fashion, but this is not necessarily due to a conventional, easily recognisable intermolecular interaction. For example, a previous study on a set of 25 structures based on the carbamazepine molecule has shown very robust packing motifs that cannot be explained in terms of classical hydrogen bonds, even though the packing in the underlying crystal structures is clearly dominated by such interactions (Gelbrich & Hursthouse, 2006). Thus, for a comprehensive understanding of the complex relationships among the structures in a given set we must investigate *both* the spatial arrangement of molecules (the SCs) *and* the linkage of molecules by recognisable intermolecular interactions (or supramolecular connectivity motifs).

We have identified all SCs of the X~Y system using *XPac* (see§2.3 for details). The N—H$\cdots A$ interactions in each structure were investigated separately. We have then analysed the information obtained from these two independent steps. For this set, it became apparent that each SC was connected to one specific supramolecular connectivity motif (we emphasize that this outcome is not trivial, as the carbamazepine system has shown). It follows that for the present set of X~Y structures, the two complementary types of information, namely about connectivity and about packing, can be combined. This leads to a rational system of structural classification which is presented below. It serves as a framework for more detailed structure discussions that will follow in subsequent papers. This categorization of the 133 observed structures is carried out in four steps according to:

(i) the type of acceptor A employed in D—H$\cdots A$ interactions;

(ii) the supramolecular connectivity motif of this hydrogen bond;

(iii) the spatial arrangement of molecules arising from this motif;

(iv) the structure type, *i.e.* the distinct three-dimensional packing mode of molecules in the crystal.

The distinction in steps (i) and (ii) is due to connectivity, in steps (iii) and (iv) it is due to the spatial arrangement of molecules. Fig. 1 summarizes the resulting classification. Note that the term 'structure type' is used here not in its conventional meaning of an inorganic structure type (Lima-de-Faria *et al.*, 1990). Instead, it represents the unique characteristics of one particular three-dimensional packing arrangement of X~Y molecules, so that a whole set of isostructures can be rationalized as a single structure type.

3.1.1. Types of acceptor. A common characteristic of all 100 X~Y compounds is the presence of N—H as the only donor group for hydrogen bonds and that of two sulfonyl O atoms as potential acceptors. In 49 compounds there is no other potential acceptor. No distinction is drawn between the two sulfonyl O atoms at this stage. There are 51 of the X~Y compounds which contain at least one ring substituent that can accept a hydrogen bond, that is X and/or Y = NO_2, CN or OMe. Of the 133 resulting structures, 108 (81%) are N—H$\cdots$O=S bonded, six are N—H$\cdots$O (NO_2), 18 N—H$\cdots$N (CN) and one is N—H$\cdots$O (OMe) linked. We have found no example where different acceptor types are employed in the same structure. However, there are several cases where different acceptor types are used in different polymorphs of a single compound. These compounds are NO_2~NO_2, Br~NO_2, Cl~NO_2 [all N—H$\cdots$O=S *versus* N—H$\cdots$O (NO_2)], CN~F

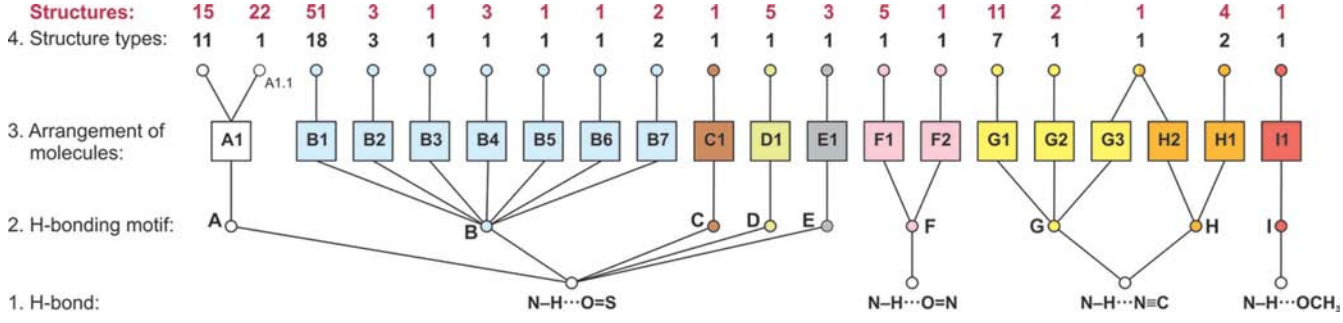


Figure 1
Classification of 133 structures X~Y according to the acceptor A employed in intermolecular N—H$\cdots A$ interactions (step 1, bottom), hydrogen-bonding motif (step 2), the spatial arrangement of molecules linked in a particular motif (step 3) and 56 unique three-dimensional crystal packing arrangements (step 4). Second line from top (black numbers): number of structure types arising from each arrangement. Top line: total number of structures in each type. A colour version of this figure is available in the online version of the journal.

Table 2
56 structure types; *Ms.n* was observed for 100 benzenesulfonamidobenzenes *X*~*Y* *M* = hydrogen-bonding motif [see Scheme (II)], *s* = number denoting the *s*th distinct spatial arrangement arising from a given motif *M* (Fig. 3), *n* = running number denoting the *N*th structure type containing a given arrangement *ms*.

M	*s*	*n*	Phases	Space group	*Z*′
N—H···O═S					
A	**1**	**1**	CN~CF_3, CN~I, CN~Br, CN~Cl, α-CN~Me, α-Br~CF_3, α-Br~I, α-Br~Br, Cl~CF_3, Cl~I, Cl~Br, Cl~Cl, F~CF_3, α-F~I, F~Br, F~Cl, α-F~F, Me~CF_3, Me~I, Me~Br, Me~Cl, α-OMe~I†	$R\bar{3}$	1
A	**1**	**2**	α-Br~Me, α-Cl~Me, Me~Me	$P\bar{1}$	1
A	**1**	**3**	F~NO_2, α-H~Cl	$P2_1/c$	1
A	**1**	**4**	H~F	$C2/c$	1
A	**1**	**5**	β-F~F	$P\bar{1}$	1
A	**1**	**6**	NO_2~F	$P2_1/n$	1
A	**1**	**7**	α-Cl~H	$P2_1/c$	2
A	**1**	**8**	β-H~Cl	$P2_1/c$	1
A	**1**	**9**	α-Me~H	$P2_1/n$	1
A	**1**	**10**	α-OMe~Br, α-OMe~Cl	*Pbca*	1
A	**1**	**11**	α-CF_3~NO_2	$P2_1/c$	1
A	**1**	**12**	β-Me~H	$C2/c$	1
B	**1**	**1**	Br~H, Cl~F, β-Cl~H	*Pc*	2
B	**1**	**2**	CF_3~H	$P2_1/c$	1
B	**1**	**3**	I~Br, I~Cl, I~Me	$P2_1/c$	1
B	**1**	**4**	CF_3~Br, CF_3~Cl, CF_3~F, CF_3~Me, Br~Cl, β-Br~Me	$P\bar{1}$	1
B	**1**	**5**	CF_3~CF_3, I~NO_2, α-Br~NO_2, β-Br~Br	$P2_1/n$	1
B	**1**	**6**	I~I	*Cc*	5
B	**1**	**7**	I~H	$P\bar{1}$	2
B	**1**	**8**	NO_2~I, NO_2~Br, NO_2~Cl, NO_2~H, α-NO_2~OMe	*Cc*	1
B	**1**	**9**	I~F, Br~F, OMe~F	$Pna2_1$	1
B	**1**	**10**	CN~H, CN~OMe, CF_3~OMe, I~OMe, Br~OMe, Cl~OMe, F~OMe, β-OMe~Cl	$Pna2_1$	1
B	**1**	**11**	I~CF_3, β-Br~CF_3	$Pna2_1$	1
B	**1**	**12**	Me~F, β-OMe~Br	$P2_1$	1
B	**1**	**13**	Me~OMe	$P2_1$	1
B	**1**	**14**	OMe~Me, α-OMe~OMe	$P2_1$	1
B	**1**	**15**	OMe~H	$P2_12_12_1$	1
B	**1**	**16**	CN~F, β-CN~Me, Br~Me, β-Cl~Me	$P2_1$	1
B	**1**	**17**	β-OMe~I	$P2_1$	1
B	**1**	**18**	CF_3~I, β-Br~I	$P2_1/n$	1
B	**2**	**1**	α-NO_2~NO_2	$Pna2_1$	2
B	**2**	**2**	β-CF_3~NO_2	$P2_1/c$	2
B	**2**	**3**	F~H	$P2_12_12_1$	1
B	**3**	**1**	H~H	$P4_32_12$	1
B	**4**	**1**	NO_2~CF_3, NO_2~Me, β-NO_2~OMe	$R\bar{3}$	1
B	**5**	**1**	H~CN	$P4_1$	1
B	**6**	**1**	α-H~Br‡	*Pbca*	1
B	**7**	**1**	H~CF_3	$P2/c$	2
B	**7**	**2**	H~OMe	*Aba*2	1
C	**1**	**1**	γ-OMe~I	$P\bar{1}$	2
D	**1**	**1**	β-F~I, F~Me, H~I, β-H~Br, H~Me	$P2_1/c$	2
E	**1**	**1**	Me~CF_3, Me~I, γ-Me~Br	$P2_1/c$	3
N—H···O = N					
F	**1**	**1**	β-Br~NO_2, β-Cl~NO_2, H~NO_2, Me~NO_2, OMe~NO_2	$P2_1/c$	1
F	**2**	**1**	β-NO_2~NO_2	$P2_1/c$	1
N—H···C					
G	**1**	**1**	α-I~CN, α-Br~CN, Cl~CN, F~CN	$P2_1/c$	1
G	**1**	**2**	β-Br~CN	$P2_1/c$	1
G	**1**	**3**	γ-Br~CN	$P2_1/n$	3
G	**1**	**4**	α-CF_3~CN, β-I~CN	$C2/c$	1
G	**1**	**5**	α-Me~CN	$P2_1/n$	1
G	**1**	**6**	OMe~CN	$P2_1/c$	1
G	**1**	**7**	β-Me~CN	$P2_1$	5
G	**2**	**1**	NO_2~CN, β-CF_3~CN	$P2_1/c$	1
H	**1**	**1**	α-CN~NO_2, α-CN~CN, β-CN~F	$C2/c$	1
H	**1**	**2**	β-CN~NO_2	$P2/c$	1
G / **H**	**3** / **2**	**1**	β-CN~CN	$P2_1$	2
N—H···OMe					
I	**1**	**1**	β-OMe~OMe	$P2_1/n$	1

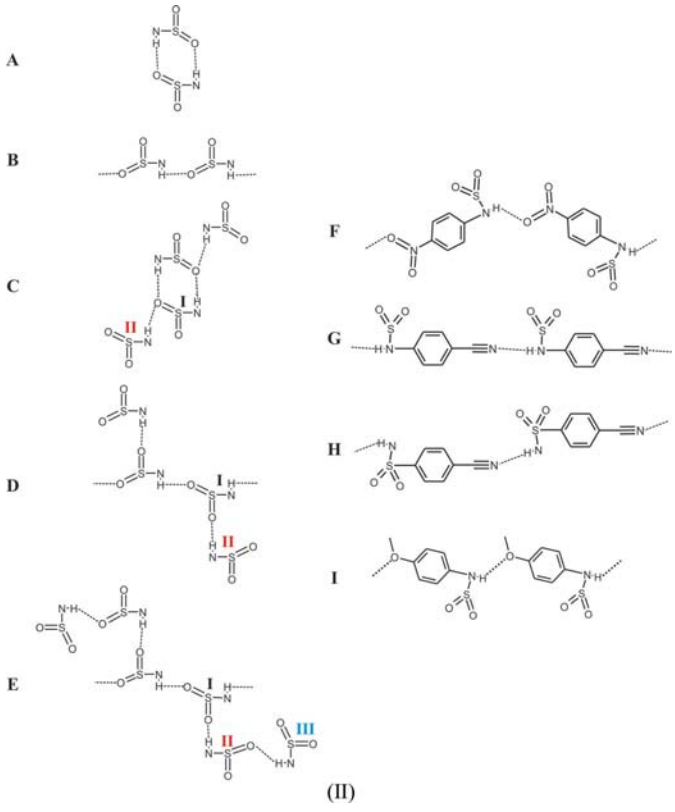
† Isostructural with $(Cl{\sim}Cl)_{0.8}{\cdot}(Cl{\sim}F)_{0.2}$ and Cl~C≡CH. ‡ A report on another **B6.1** structure, γ-H~Cl (Perlovich *et al.*, 2006), came to our attention during the final stages of the preparation of this publication.

[N—H···O═S *versus* N—H···N (CN)] and OMe~OMe [N—H···O═S *versus* N—H···O (OMe)]. Thus, Etter's rule that 'the best proton donors and acceptors ... form intermolecular hydrogen bonds to one another' (Etter, 19910) cannot strictly apply for at least one form in each of these pairs.

3.1.2. Hydrogen-bonding motifs. Scheme (II) shows nine different modes of connection, **A**–**I**. The first five motifs, **A**–**E**, are the result of N—H···O═S interactions. Motif **A** leads to a dimer with a $R_2^2(8)$ ring. **B** is a one-dimensional $C(4)$ chain where just one sulfonyl O atom per molecule is engaged in hydrogen bonding. Both these motifs can exist in structures with $Z' = 1$. By contrast, **C** and **D** always lead to a structure with $Z' = 2$ and **E** to a structure with $Z' = 3$. **C** is a finite tetrameric unit. One sulfonyl O atom of each of the central two molecules acts as a bifurcated N—H···O═S bond acceptor, while neither O atom of the other two molecules is engaged in hydrogen bonding. Alternatively, **C** may also be interpreted as an extension of the dimer **A**. By contrast, the one-dimensional chain motif **D** can be derived from **B**. Both O atoms of one independent molecule, marked as I in Scheme (II), are employed as hydrogen-bond acceptors. This molecule is bonded to one molecule of its own type (I) and to one molecule of type II. The SO_2 group of molecule II is not involved in hydrogen bonding. The motif **E** has three independent molecules (I, II and III). It is formally obtained from **D** by the insertion of a molecule into each of the dangling side chains that are attached to the central strand. The connection between molecules I and II is the same as in motif **D**. Additionally, one O of molecule II acts as an acceptor for the N—H group of molecule III, and the SO_2 unit of the latter molecule is not involved in any N—H···O═S interactions. **A** is found in 37, **B** in 62, **D** in five, **E** in three structures and **C** occurs only once.

The formation of each of the four other motifs **F**–**I** relies on the presence of a specific substituent, that is $Y = NO_2$ (**F**), Y = CN (**G**), X = CN (**H**) or Y = OMe (**I**). The one-dimensional $C(8)$ chain **F** is formed by N—H···O (NO_2) interactions involving one O atom of the nitro group in six NO_2~Y structures. There are 14 structures obtained from eight compounds with the composition CN~Y which contain N—H···N (CN) bonded one-dimensional $C(9)$ chains of type **G**. The $C(8)$ motif H is an N—H···N (CN) chain formed in five X~CN structures.

Note that β-CN~CN contains **G** chains as well as H chains. Finally, the β form of OMe~OMe is the only example where N—H···O (OMe) interactions are present. The OMe substituent in the *Y* position is employed in this interaction which results in one-dimensional *C*(7) chains.



(II)

The pattern of distribution of the motifs **A**–**H** among the 100 *X*~*Y* compounds is explored in Fig. 2. The arrangement of substituents in the 10 × 10 matrix (vertical: *X*, horizontal: *Y*) is in decreasing electron-withdrawing power as recorded by the Hammett sigma value (Hansch *et al.*, 1991), and the substituent size also decreases from CF_3 to H. Each combination of *X* and *Y*, *e.g.* each compound *X*~*Y*, is represented by a box.[3] If more than one crystalline form was observed for a compound, then the corresponding box is divided into more sections accordingly. For example, the Me~I box has four sections which correspond to four polymorphs with four different N—H···O=S motifs **A**, **B**, **C** and **E**.

An inspection of Fig. 2 immediately shows that the system is dominated by the simple motifs **A** and **B**, which together account for 108 of the 133 structures. **A** is favoured by medium *X* substituents and large *Y* substituents and it is a particular feature if *Y* = halogen. Motif **B** is favoured by large *X* substituents and enhanced by smaller *Y* substituents. Motif **D** is favoured by small *X*, *i.e.* fluorine and hydrogen. However, there are exceptions to these generalizations which cannot be simply related to a particular feature of group *X* or group *Y*, or indeed to any obvious combination of the characteristics of *X* and *Y*. The groups **G** and **H** are restricted of course to the nitrile substituents, but not all nitriles belong to these groups. The dominant role of **G** in the *X*~CN column is remarkable. Group **F** is restricted to those compounds containing a nitro group *Y*, but again it does not include all the possible compounds.

3.1.3. Spatial arrangement of molecules and structure types. We have assigned each distinct structure type with a code *Ms.n*, where *M* is a capital letter from **A** to **I** denoting the hydrogen-bonding motif present [see Scheme (II)], *s* is a number denoting the *s*th spatial arrangement of the molecules involved in a given motif *M* (see Figs. 3–5) and *n* is a number for the *n*th structure type containing a given arrangement of molecules *Ms*. The resulting structure code(s) for each compound are listed in Fig. 2 and Table 2. The centrosymmetric structure **A1** is the only observed geometry for the dimeric motif **A**. This observation is in contrast with the results obtained for the closely related benzenesulfonamidopyridines X–C_6H_4–SO_2–NH–C_5H_3N–Y, where dimers with twofold symmetry are also encountered (Gelbrich *et al.*, 2007). **A1** is found in 37 structures which represent 12 different structure types, termed **A1.1**–**A1.12**. However, most of these structures (22) belong to just one type: **A1.1** (discussed in §3.4). The inversion symmetry of the **A1** unit is crystallographic in all obtained structures including the only $Z' = 2$ example (αCl~H, type 1.7).

Motif **B** leads to seven fundamentally different one-dimensional spatial arrangements **B1**–**B7**, shown in Fig. 4. Adjacent molecules in these **B** chains are related by translation (**B1**), 2_1 (**B2** and **B3**), 3_1 (**B4**), 4_1 (**B5**) and glide (**B6** and **B7**) symmetry. The two sulfonyl oxygen positions can be distinguished as *anti* and *gauche* according to the two torsion angles (C, N, S, O) formed (their observed values are actually *ca* 175 and 50°). The O in the *anti* position is employed as a hydrogen-bond acceptor in **B2**, **B3**, **B5** and **B7** chains, while the *gauche*-O position is used in **B1**, **B4** and **B6**. The most remarkable feature of all the **B** structures is the versatility of the simple **B1** chain. No less than 18 unique structure types with this arrangement have been obtained. These are the types **B1.1**–**B1.18**. In other words, at least 18 fundamentally different ways exist in which a valid three-dimensional structure can be generated by arranging multiple copies of **B1**. At least 50 structures crystallize in one of these 18 types.

Tetramer **C** is found exclusively in the γ form of OMe~I (centrosymmetric, structure type **C1.1**). Just one spatial arrangement and just one structural type were observed for the hydrogen-bonded chain motifs **D** and **E**. The chains **D1** and **E1** both have 2_1 symmetry. The resulting **D1.1** and **E1.1** structure types represent sets of five and three isostructures, respectively. A one-dimensional chain based on motif **F** and exhibiting glide symmetry is present in five *X*~NO_2 isostructures of the **F1.1** type. In contrast, **F2** has glide symmetry and is present in the α form of NO_2~NO_2 (type **F2.1**). The chain motif **G** appears in three geometries. The first of these is **G1** (translation symmetry) and gives rise to seven distinct structure types, **G1.1**–**G1.7**. The **G2** geometry (glide symmetry)

[3] These boxes are coloured according to the motif present (**A** = white, **B** = blue, **C** = brown, **D** = green, **E** = grey, **F** = pink, **G** = yellow, **H** = orange, **I** = red, corresponding to Fig. 1) in the online version of this paper.

X \ Y	NO_2	CN	CF_3	I	Br	Cl	F	H	Me	OMe
NO_2	B2.1 F2.1	G2.1	B4.1	B1.8	B1.8	B1.8	A1.6	B1.8	B4.1	B1.8 B4.1
CN	H1.1 H1.2	H1.1 G3H2.1	A1.1	A1.1	A1.1	A1.1	H1.1 B1.16	B1.10	A1.1 B1.16	B1.10
CF_3	A1.11 B2.2	G1.4 G2.1	B1.5	B1.18	B1.4	B1.4	B1.4	B1.2	B1.4	B1.10
I	B1.5	G1.1 G1.4	B1.11	B1.6	B1.3	B1.3	B1.9	B1.7	B1.3	B1.10
Br	B1.5 F1.1	G1.1 G1.2 G1.3	B1.11 A1.1	B1.18 A1.1	B1.5 A1.1	B1.4	B1.9	B1.1	A1.2 B1.4 B1.16	B1.10
Cl	B1.5 F1.1	G1.1	A1.1	A1.1	A1.1	A1.1	B1.1	A1.7 B1.1	A1.2 B1.16	B1.10
F	A1.3	G1.1	A1.1	D1.1 A1.1	A1.1	A1.1	A1.1 A1.5	B2.3	D1.1	B1.10
H	F1.1	B5.1	B7.1	D1.1	D1.1 B6.1	A1.3 A1.8	A1.4	B3.1	D1.1	B7.2
Me	F1.1	G1.5 G1.7	A1.1	A1.1	A1.1	A1.1	B1.12	A1.9 A1.12	A1.2	B1.13
OMe	F1.1	G1.6	E1.1	A1.1 B1.17 C1.1 E1.1	A1.10 B1.12 E1.1	A1.10 B1.10	B1.9	B1.15	B1.14	I1.1 B1.14

Figure 2
Distribution of 56 unique three-dimensional packing arrangements (see Fig. 1) among compounds represented by square boxes in a matrix *X versus Y*. See caption of Table 2 for an explanation of the notation *Ms.n* for structure types.

appears exclusively in crystals of NO_2~CN (type **G2.1**). Motif **H** leads to chain **H1** with 2_1 symmetry. It is formed in four CN~*Y* structures that belong to two different types, **H1.1**, **H1.2**. Furthermore, the chain geometries **H2** and **G3**, both with translation symmetry, are present only in a modification of CN~CN (type **G3H2.1**). Finally, the β form of OMe~OMe is the only structure with an **I** chain (2_1 symmetry), structure type **I1.1**.

We have found in this study that similar packing is largely restricted to structures with the same hydrogen-bonding motif. The structures in this set will be discussed according to the classification given above and in Fig. 1. Type **A1.1**, which represents the most populated series of isostructures, will be dealt with in §3.4. Its relationships to the remaining 11 **A1** types will be explored in subsequent papers.

3.2. Polymorphism

This study is not primarily an exercise in polymorphism: rather it is an exercise in trying to understand some of the factors tending to favour particular crystal structures. Nevertheless, some attempt has been made to generate polymorphs. One reason was to establish whether any of the structures represent metastable polymorphs which have formed fastest. In this case there may be more stable forms, the structures of which would be in greater conformity with the overall distribution of structures within the matrix of Table 1. A second reason was to test the robustness of the forms. This was particularly so for the blue group, to be discussed in detail in a later paper. In this group a large number of distinct but closely related structures were present. It was initially thought, as a result of observing the somewhat random distribution of those forms amongst the blue entries, that it might be possible to produce any of these compounds in any of the forms. This does not seem to be the case. The specific polymorphic form for a given compound appears under a variety of crystallizing conditions and so it must be assumed that there are good reasons why a particular packing offers stability for particular substituents, even if this is not apparent to superficial examination. A third reason for seeking polymorphs was to try to establish better recognition of the universe of structures that is available to this collection of compounds.

There are many more polymorphs than are shown in Table 1. It is often not possible to obtain the structure of polymorphs, particularly of metastable forms, because under the growth conditions appropriate to the formation of large crystals suitable for single-crystal structure determination, transformation to a more stable form occurs. The inherent strain which must be an intrinsic part of a metastable form often favours minute crystals or defect structures. For example, three different solid forms of Me~CN were identified from IR spectra, but the most commonly encountered habits in this sample, clear, well formed crystalline plates or rods, invariably give an uninterpretable diffraction pattern. By contrast, the minor blocks, although appearing less crystalline to the eye, produce an acceptable crystal structure, but of a different polymorph. Polymorphism is much less prevalent in the benzenesulfonamidobenzenes examined here than in the close analogues, the benzenesulfonamidopyridines (Gelbrich *et al.*, 2007).

3.3. IR spectra

The polymorphism of samples was detected only from crystal habit and IR spectra. Although it has become unfashionable to regard IR spectra as a suitable tool for the detection of polymorphs, in our experience, except for large molecules and those without hydrogen bonding, IR spectra rarely fail to show differences between polymorphs, although those differences might be quite small. In a study such as this, in which many hundreds of crystallizations are carried out it is essential to have a rapid screening method. The total time to present a sample and obtain the spectrum on a modern ATR-FTIR system is less than 3 min.

The spectra display all the expected bands owing to the phenyl rings, the sulfonamido group and the substituents, but the only feature of relevance here is the NH stretching frequency. In all but three cases a single isolated NH stretching band was observed. The exceptions were the **E1.1** structures (forms of OMe~*Y* with *Y* = CF_3, I, Br). Here, a triplet corresponding to the three distinct, differently bonded molecules forming the helix in this unusual $Z' = 3$ [see **E** in Scheme (II) and **E1** in Fig. 3] structure was observed. In some cases the NH band was unsymmetrical owing to the presence of a shoulder. This suggests in those cases where the band failed to persist under recrystallization the presence of low concentrations of a polymorph. It was rarely possible to obtain the crystal structure of the other component, presumably owing to its low concentration or to its small crystal size.

3.4. Isostructures of the type A1.1

In this section, a large block of structures represented in white in Figs. 1 and 2 is discussed; an attempt is made to understand why there are so many isostructural compounds and what the limitations for the formation of this structure are. The *XPac* procedure confirmed that these 22 structures (Table 2) containing motif **A** are isostructures. Additionally, Cl~CCH and a mixed crystal of the composition $(Cl{\sim}Cl)_{0.80}{\cdot}(Cl{\sim}F)_{0.20}$ crystallize in the same trigonal $R\bar{3}$ structure with one molecule per asymmetric unit. It is worth mentioning that the **B4.1** type results in structures with the same space group, Z' and similar *c*/*a* ratios, but this is merely coincidental, and **A1.1** and **B4.1** are not connected by any form of packing similarity. Fig. 3 shows the geometry of the characteristic centrosymmetric dimer **A1**, where the *anti*-O (see §3.1.3) is employed as a hydrogen-bond acceptor. The space-filling diagram in Fig. 6 shows that the dimer is of an irregular shape, with the phenyl groups set like the sails of a windmill. The vast majority of the compounds in the **A** group are **A1.1** isostructures, presumably because there are a limited number of good packing possibilities for such a shape. The IR absorption spectra show that the

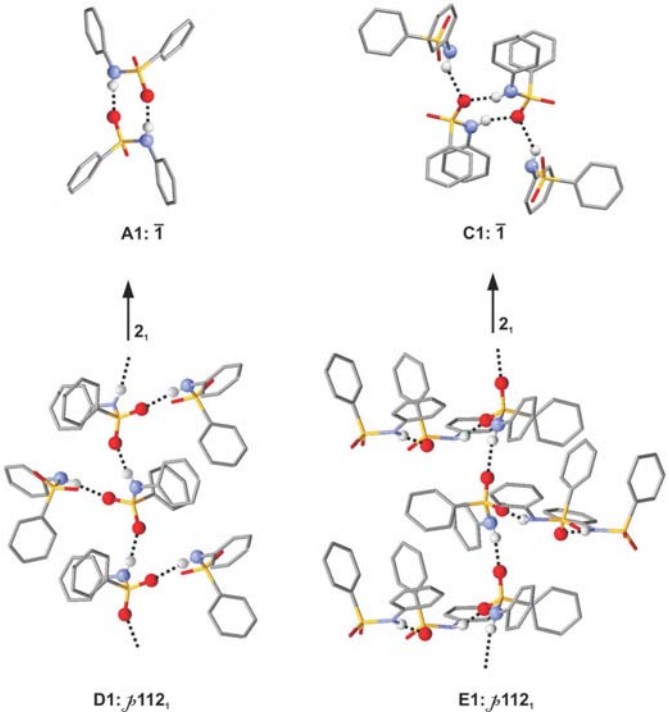


Figure 3
The observed spatial arrangements for molecules connected by N—H···O′S bonded motifs **A**, **C**, **D** and **E**. Point groups of the discrete arrangements **A1** and **C1** and rod groups of the one-dimensional arrangements **D1** and **E1** are given. N, H and O atoms participating in hydrogen bonding are drawn as balls. *X* and *Y* substituents have been omitted for clarity.

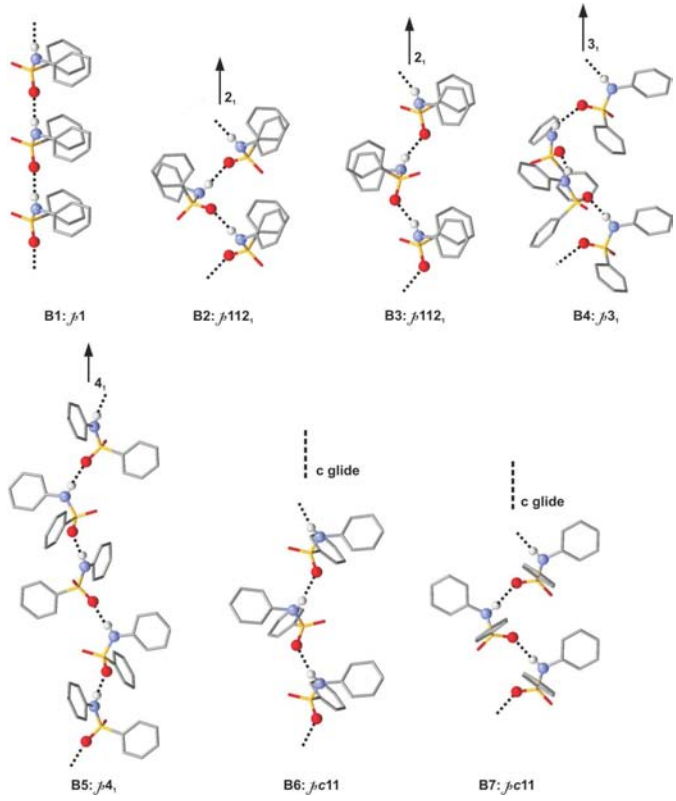


Figure 4
The seven distinct spatial arrangements for molecules connected by N—H···O═S bonded chain motif **B** and their rod groups. N, H and O atoms participating in hydrogen bonding are drawn as balls. *X* and *Y* substituents have been omitted for clarity.

N—H···O=S bonds upon which these dimers depend are relatively strong in comparison with the alternative motifs of **B**, **C**, **D** and **E**. The NH vibrational frequencies vary between 3239 and 3219 cm^{-1} and thus represent a compact group relatively unaffected by substituent effects and presumably also to packing changes.

The largest unit-cell volume among the **A1.1** isostructures is found in Me~CF_3. It is 121% of the smallest volume, observed for F~F, although the difference may be somewhat exaggerated by a difference in temperature at which the data were collected. The *c*/*a* ratios range between 0.32 (Br~I) and 0.38 (F~F). The most striking feature of the packing diagram of this structure type (Fig. 7*a*) is the arrangement of *Y* substituents around the $\bar{3}$ axis. Six adjacent *Y* units originating from six different dimers form a trigonal antiprism. This antiprism contains two independent $Y\cdots Y$ contacts, d_1 and d_2, where d_1 is the $Y\cdots Y$ distance between two molecules related by threefold symmetry, see Fig. 7(*b*). The following pattern of distribution of **A1.1** isostructures among the *X*~*Y* compounds emerges from the matrix in Fig. 2:

(i) preferred in compounds with *Y* = CF_3, I, Br, Cl;

(ii) preferred in compounds with *X* = CN, Br, Cl, F, Me;

(iii) no examples of *Y* = H and only one with *Y* = F;

(iv) no examples of *Y* = NO_2, CN or OMe;

(v) no examples with *X* = NO_2, only one example with *X* = OMe;

(vi) no examples with *X* = H, CF_3 or I.

Obvious factors that may lead to a relative preference of **A1.1** against other possible types are the shape and effective volume of the *X* and *Y* substituents. These are either small: H < F, medium: Cl < CN < CCH < NO_2 < Br < Me or large: I < OMe < CF_3. In general, **A.1.1** is favoured most if a combination *X* = small/medium and *Y* = medium/large is present. It is easy to understand that a packing in Y_6 units is preferred if the *Y* substituent is spherical (halogens) or exhibits at least rotational symmetry (CCH). The lack of any examples with *Y* = NO_2 or OMe is highly significant in this respect, while the absence of any examples with *Y* = CN may also be attributed to the general predominance of the motif **G** in *Y*~CN compounds (see Fig. 2). The molecular shape associated with small H or F substituents in *X*~H, H~*Y* and *X*~F compounds seems to make other three-dimensional packing alternatives of the **A1** dimer relatively more viable, so that the types **A1.2** to **A1.9** and **A1.12** are obtained. However, the F~*Y* row is still dominated by **A1.1** structures. We note that the population of **A1.1** in the *X*~*Y* system of Fig. 2 is 22, whereas the other **A1** types are sparsely populated, **A1.2** with three, **A1.3** and **A1.10** with two and all remaining types with just one example. Hence, it is likely that at least some of these other **A1** types are very specific for a particular combination of *X* and *Y*. Different polymorphs that contain motif **A** are known for F~F, H~Cl and Me~H (see Fig. 2). The formation of an **A1.1** structure by CN~Me and Cl~CCH is confirmation that the antiprismatic Y_6 arrangement does not rely on *Y* being a halogen. We conclude that the arrangement in these units must to a large extend be driven by space-filling effects and that the formation of the **A1.1** type cannot rely on intermolecular halogen···halogen interactions within Y_6 units. Is it now possible to further rationalize the pattern of occurrence of the **A1.1** type from the observed geometric variations in the antiprismatic Y_6 unit?

A casual inspection shows that the geometry of this unit strongly depends on the nature (size) of **Y**. The values of d_1 and d_2 are almost equal for large *Y* substituents, *i.e.* CF_3, I and

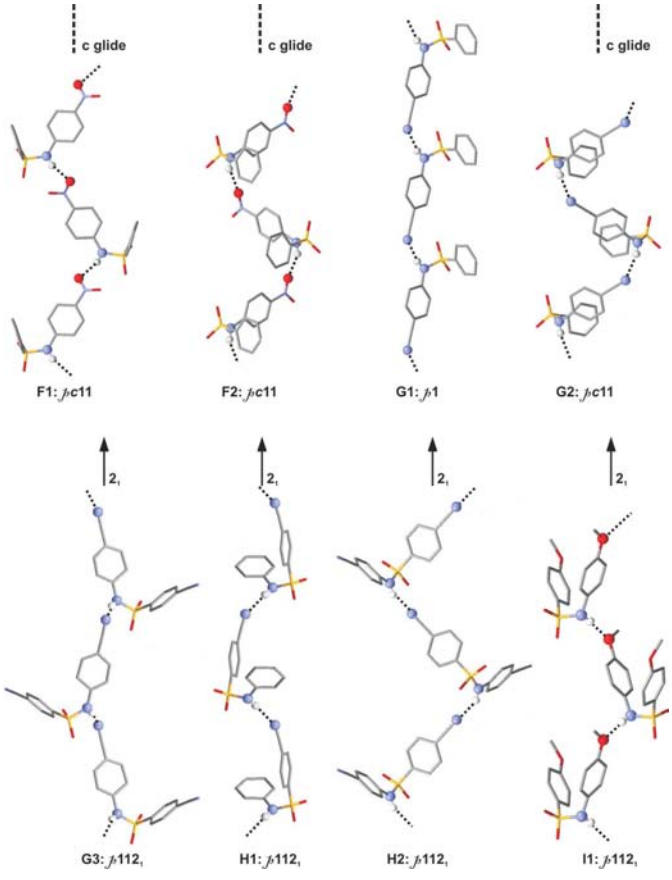


Figure 5
The observed spatial arrangements arising from N—H···O (NO_2) motif **F**, N—H···O (CN) motifs **G** and **H**, and N—H···O (OMe) motif **I**. The rod group of each arrangement is given. N, H and O atoms participating in hydrogen bonding are drawn as balls.

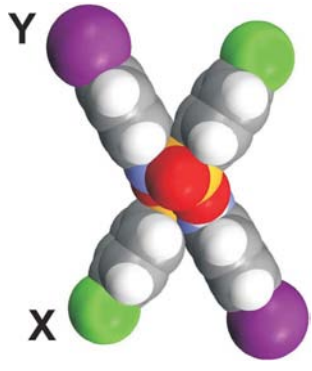


Figure 6
Space-filling diagram of the centrosymmetric **A1** dimer.

Br [α-Br~Br: d_1 = 4.102 (2), d_2 = 3.994 (2) Å], so that the trigonal antiprism is almost uniform (regular octahedron). By contrast, the much smaller *Y* substituent of α-F~F is correlated with a marked negative $\Delta d = d_1 - d_2$ value [d_1 = 3.195 (2), d_2 = 4.133 (2) Å]. The geometries of the intermolecular $Y\cdots Y$ contacts (*Y* = halogen) in the **A1.1** structure type are consistent with van der Waals interactions.

The diagram in Fig. 8 shows the intermolecular $Y\cdots Y$ distances d_1 (data points connected by dotted lines) and d_2 (data points connected by solid lines) for the five *X*~*Y* series with *X* = CN, Br, Cl, F and Me. As expected, the d_1 values generally decrease with the volume of *Y* (the dotted lines go down from left to right). For example, d_1 is 4.169 Å in F~I and 3.195 Å in F~F. A rather different correlation is observed between d_2 and the size of *Y*. For *Y*~I (left column of data points), d_2 is in general shorter than d_1. For *Y* = Br, the d_2 values remain in the same range, but they also increase relative to d_1. A second relative d_2 against d_1 shift in the same direction occurs in the *Y* = Cl column. However, this change is rather sharp in the case of CN~Cl. The *X* = F column has just one example, F~F, where a sharp increase in d_2 is observed in addition to a sharp drop in d_1.

The difference $\Delta d = d_1 - d_2$ is positive for all *Y* = I structures and has a small positive or negative value for *Y* = Br. For *Y* = Cl all Δd values are negative and the smallest absolute value of Δd is found in F~Cl (Δd = −0.102 Å). For a given substituent *Y*, Δd is usually inversely correlated with the size of *X*. Nevertheless, Δd decreases to −0.938 Å in F~F, the only known **A1.1** structure with *Y* = F, even though the substituent *X* is also F.

The overall change in Δd from I~F (Δd = 0.293 Å) to F~F accounts for approximately 30% of the original $Y\cdots Y$ separation in I~F. It is surprising that the principle arrangement of molecules is maintained while such a considerable deformation of the geometry in the region around the $\bar{3}$ axis takes place. The extrapolation of the trends in Fig. 8 leads the prediction that the Δd values for other, hypothetical *X*~F isostructures of the **A1.1** type would be even higher than in F~F and the geometry of their Y_6 units even more severely distorted. In this respect, it is interesting to note that within the five **A1.1** isostructural *X*~*Y* series of Fig. 8 there are five occurrences for *Y* = I and *Y* = Br, four for *Y* = Cl, but just one for *Y* = F. **A1.1** structures are completely absent for *X*~F compounds with medium and large *X*. This seems to confirm that the **A1.1** structure is most stable if Δd is low, when the Y_6 geometry is nearly octahedral.

Furthermore, although Cl~Cl crystallizes in the **A1.1** type, several attempts to produce an **A1.1** modification of pure Cl~F were unsuccessful. Instead, a **B1.1** form was obtained each time. This observation is in accordance with our interpretation of the trends in Fig. 8. It is also interesting that F~F is the only **A1.1** compound of which a second **A1** polymorph is known (type **A1.5**). We have carried out additional crystallization experiments using a 1:1 molar solution of Cl~F and Cl~Cl. Unit-cell parameters were determined for five different crystals obtained in these experiments and a structure analysis was carried out for two of them. The results showed that mixed crystals of the composition $(\mathrm{Cl{\sim}Cl})_x\cdot(\mathrm{Cl{\sim}F})_{1-x}$ had formed, with x = 0.80 in the first and x = 0.68 in the second experiment. The **A1.1** structure was adopted in each case. Thus, it is not possible to produce a pure **A1.1** form of Cl~F, but one can admix up to one third of Cl~F into the **A1.1** matrix of Cl~Cl. The *Y* position of the resulting structure is statistically disordered. The geometrical destabilization caused by the occupation of two *Y* positions in each Y_6 unit by small F atoms is tolerated.

Some compounds form a polymorph with an **A1** dimer and another modification with a **B1** chain (white–blue boxes in Fig. 2). The **A** forms were made by crystallization from hydrocarbon solvents and the **B** forms by crystallization from alcoholic solvents. This was achieved deliberately, based on the belief that a dimeric structure in solution would be favoured by low polarity solvents because their external

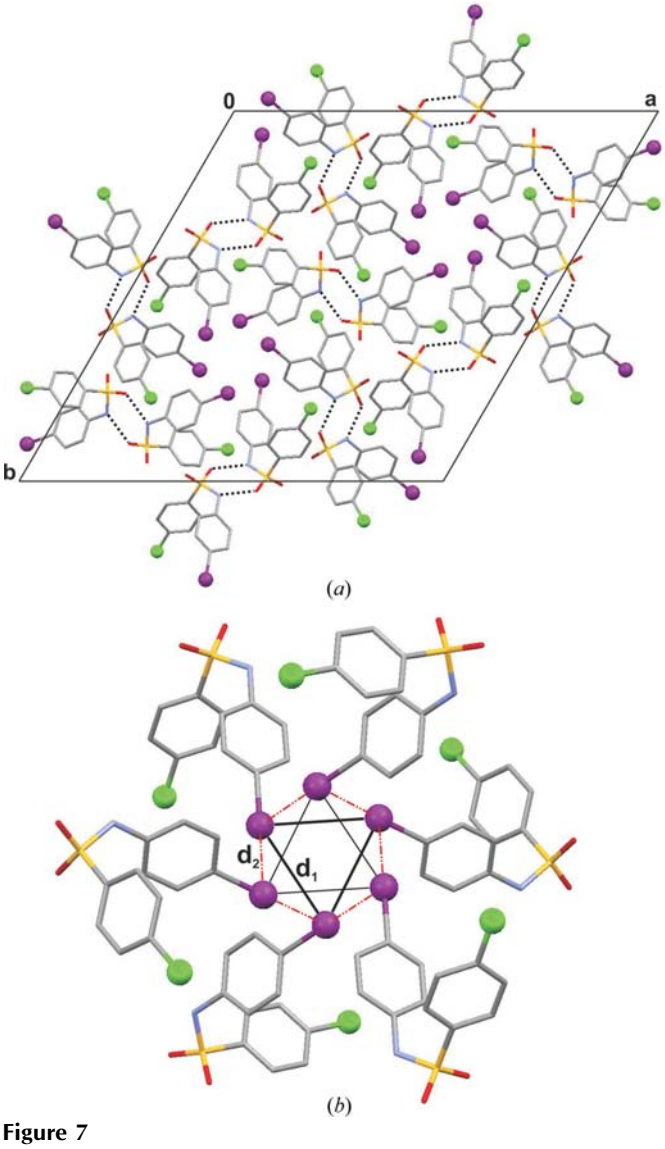


Figure 7
(*a*) Packing diagram for structure type **A1.1**, viewed along the *c* axis. *X* and *Y* substituents are depicted as balls. (*b*) Detailed view of six molecules arranged around the $\bar{3}$ axis. There are two independent sets of $Y\cdots Y$ edges, drawn black and red, which define a trigonal antiprism. Their lengths are d_1 and d_2.

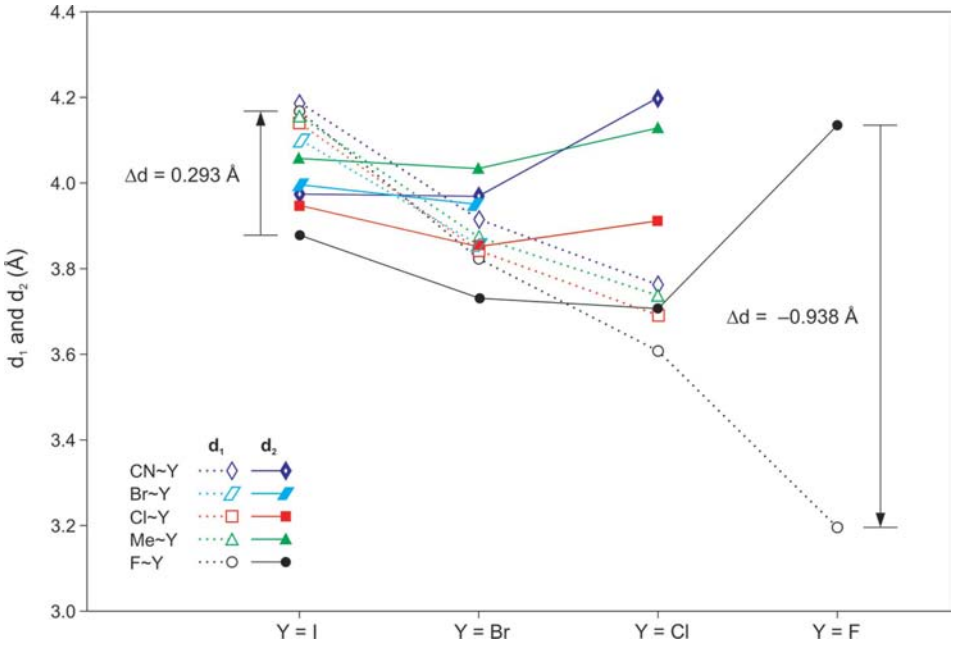


Figure 8
Illustration of the effect of different substituent combinations of X and Y on the geometry trigonal antiprismatic Y_6 units in the structure type **A1.1**, indicating possible limitations for its formation. Progression of the intermolecular $Y\cdots Y$ distances d_1 (solid lines) and d_2 (dashed lines) in five series of **A1.1** structures: CN~Y, Br~Y, Cl~Y, Me~Y and F~Y. See Fig. 7(b) for the definition of d_1 and d_2. Structure type **A1.1** seems to be preferred if the trigonal antiprismatic Y_6 unit is nearly uniform ($\Delta d \simeq 0$). The extrapolation of observed trends to hypothetical Y~F structures (Y = CN, Br, Cl, Me) leads to the conclusion that the Y_6 geometries in these structures would probably be severely distorted.

surfaces would be of a hydrocarbon nature, whilst the chain (**B**) structures would be favoured by a polar solvent with hydrogen-bond acceptor and donor groups. It is one of the few examples we have encountered in which consideration of solvent–solute interactions has resulted in the formation of the expected polymorphic structure.

4. Conclusions

This study shows that related compounds frequently tend to form related crystal structures. It complements and extends a previous paper (Gelbrich & Hursthouse, 2006), in which it was shown that the manifold forms (polymorphs, solvates, co-crystals) of a specific compound, carbamazepine, present a set of interrelated structures. This interrelationship also extends to analogues of carbamazepine. The present results enhance our conviction, drawn from some published observations (Vrcelj *et al.*, 2003; Gelbrich *et al.*, 2004; Gerber *et al.*, 2004; Gelbrich & Hursthouse, 2005; Aragoni *et al.*, 2007) and many unpublished ones, of the widespread occurrence, perhaps extending even to universality, of this phenomenon. The 133 crystal structures of benzenesulfonamidobenzenes forming the present set are elaborated from only nine basic supramolecular connectivity motifs. It is perhaps obvious that there will be sulfonamide (N—H$\cdots$O=S) hydrogen-bonded chains which relate many structures, but the structural equivalences are carried to much deeper levels than the mere presence of similar hydrogen-bonding patterns. Packing similarities can transcend hydrogen-bonding patterns, as was shown in the carbamazepine series. In a large set such as the benzenesulfonamides, the number of structures bearing no similarities to others is very limited, and tends to diminish with the identification of further polymorphs. An intensive, but not exhaustive, attempt to generate polymorphs has demonstrated the robustness of most of the structures originally produced. We cannot be sure that a particular structure represents the most stable polymorph, but we think the amount of effort put into these investigations makes it very likely. However, there was difficulty in generating new forms even from those compounds presenting structures lying at the edge of islands of structural types within the matrix, Fig. 2. This suggests that it is improbable that substantial variation of the overall pattern of structures will arise from further polymorph screening.

The possibility of making the necessary vast numbers of structural comparisons between large numbers of related structures is entirely dependent on the use of the *XPac* program. The 8778 pairwise comparisons would scarcely be possible manually. Although similar cell parameters are often indicative of isostructurality, there are several examples in the present study for which closely similar cell parameters represent different structures. There is one example of virtually identical parameters arising from entirely different structures. In other cases rather different cell parameters hide isostructurality. The 24 isostructural dimers investigated in detail here show a variation of up to 20% in cell length.

It is shown that the occurrence of these dimers amongst the benzenesulfonamidobenzenes is largely dependent on the size of substituents. The failure to produce any further structures of this type beyond those originally encountered, despite many crystallization attempts on apparently likely compounds, reinforces this theoretical analysis in terms of substituent size.

The authors gratefully acknowledge support of the crystallographic facilities at Southampton by the EPSRC.

References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Aragoni, M. C., Arca, M., Demartin, F., Devillanova, F. A., Gelbrich, T., Garau, A., Hursthouse, M. B., Isaia, F. & Lippolis, V. (2007). *Cryst. Growth Des.* Accepted for publication.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bingham, A. L., Hughes, D. S., Hursthouse, M. B., Lancaster, R. W., Tavener, S. & Threlfall, T. L. (2001). *Chem. Commun.* pp. 603–604.
Desiraju, G. R. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 2311–2327.
Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
Gelbrich, T. (2006). *Comput. Commun. Newsl.* **7**, 139–144.
Gelbrich, T. & Hursthouse, M. B. (2005). *CrystEngComm*, **7**, 324–336.
Gelbrich, T. & Hursthouse, M. B. (2006). *CrystEngComm*, **8**, 448–460.
Gelbrich, T., Threlfall, T. L., Huth, S. & Seeger, E. (2006*a*). *Polyhedron*, **25**, 937–944.
Gelbrich, T., Threlfall, T. L. & Hursthouse, M. B. (2006*b*). *Acta Cryst.* C**62**, o470–0472.
Gelbrich, T., Threlfall, T. L., Huth, S., Seeger, E. & Hursthouse, M. B. (2004). *Z. Anorg. Allg. Chem.* **630**, 1451–1458.
Gelbrich, T., Threlfall, T. L. & Hursthouse, M. B. (2007). Unpublished results.
Gerber, S., Krautscheid, H., Gelbrich, T. & Vollmer, H. (2004). *Z. Anorg. Allg. Chem.* **630**, 1427–1432.
Hansch, C., Leo, A. & Taft, R. W. (1991). *Chem. Rev.* **91**, 165–195.
Kato, K., Sugahara, M., Tohnai, N., Sada, K. & Miyata, M. (2004). *Cryst. Growth Des.* **4**, 263–272.
Kelly, C. J., Skakle, J. M. S., Wardell, J. L., Wardell, S. M. S. V., Low, J. N. & Glidewell, C. (2002). *Acta Cryst.* B**58**, 94–108.
Lancaster, R. W., Karamertzanis, P. G., Hulme, A. T., Tocher, D. A., Covey, D. F. & Price, S. L. (2006). *Chem. Commun.* pp. 4921–4923.
Lima-de-Faria, J., Hellner, E., Liebau, F., Makovicky, E. & Parthé, E. (1990). *Acta Cryst.* A**46**, 1–11.
Perlovich, G. L., Tkachev, V. V., Schaper, K.-J. & Raevsky, O. A. (2006). *Acta Cryst.* E**62**, o376–o378.
Pokrywiecki, S., Weeks, C. M. & Duax, W. L. (1973). *Cryst. Struct. Commun.* **2**, 63–66.
Rérat, B. (1969). *Acta Cryst.* B**25**, 1392–1403.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Sheldrick, G. M. (2003). *SADABS*, Version 2.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Thalladi, V. R., Nuesse, M. & Boese, R. (2000). *J. Am. Chem. Soc.* **122**, 9227–9236.
Vrcelj, R. M., Sherwood, J. N., Kennedy, A. R., Gallagher, H. G. & Gelbrich, T. (2003). *Cryst. Growth Des.* **3**, 1027–1032.