

Polymorphic Inclusion Structure Types of Solvated 2,4-Dichloro-5-Carboxy-Benzsulfonimide. A Study of Solvation Patterns and their Influence on Molecular Conformation

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Abstract. The inclusion behavior of 2,4-dichloro-5-carboxy-benzsulfonimide in protic (water, acetic acid and methanol) and aprotic (*N,N*-dimethylacetamide) environments has been examined by crystal structure determinations of the solvated compound, providing an illustration of the relationship between solvation effects and structural polymorphism. Three different crystal structure types of the corresponding complexes in which the benzsulfonimide moiety, $C_{14}H_7Cl_2NO_8S_2$, exhibits different conformations have been observed [I (with 4 mol of water) – $P\bar{1}$, $a = 8.227$, $b = 8.964$, $c = 16.945$ Å, $\alpha = 89.64$, $\beta = 97.51$, $\gamma = 114.28^\circ$; II (with acetic acid + 2 H_2O) – $P\bar{1}$, $a = 7.857$, $b = 11.379$, $c = 13.831$ Å, $\alpha = 92.50$, $\beta = 101.21$, $\gamma = 101.12^\circ$ and III (with methanol + 2 H_2O) – $P\bar{1}$ or $P1$, $a = 7.840$, $b = 11.235$, $c = 13.697$ Å, $\alpha = 95.56$, $\beta = 102.05$, $\gamma = 102.21^\circ$; IV (with 2 *N,N*-dimethylacetamide + 2 H_2O) – $P2_12_12_1$, $a = 14.838$, $b = 14.818$, $c = 14.500$ Å]. Crystallization from water and from acetic acid leads to layered structures consisting of alternating zones of the host (with a folded conformation) and the solvent. Crystals obtained from *N,N*-dimethylacetamide are composed of a three-dimensional lattice of loosely packed host species (with an extended conformation) which are interspaced by solvent molecules. This polymorphism can be correlated to hydrogen bonding in that the extended conformation of the title compound is favored in a solvent which is a poor hydrogen donor, while the folded conformation is induced in solvation environments that are good donors of hydrogen bonds.

Key words: solvation patterns, structural polymorphism, solvent inclusion.

Supplementary Data relating to this article are deposited with the British Library as Supplementary Publication No. SUP 82005 (8 pages). To obtain copies, see p. ii of this issue.

1. Introduction

We have recently characterized a series of inclusion systems formed in the solid by highly polar compounds of pharmaceutical interest [1]. They represent channel-type clathrates in which the host lattice is stabilized by dipolar forces and can accommodate various guest molecules in continuous channels running through the crystal. In the present work we extend our structural investigation to a different type of inclusion behavior in polar media which can be directly correlated to hydrogen bonding.

As a suitable example we have chosen to study the structural properties of 2,4-dichloro-5-carboxy-benzsulfonimide. This compound contains a large number of polar functions and potential donors and acceptors of hydrogen bonds and appears to have only a few conformational degrees of freedom associated with soft modes of torsional isomerism. It co-crystallizes with a variety of solvents, a phenomenon which is associated with the occurrence of

different structural forms and conformational polymorphism [2,3]. The following crystalline complexes of 2,4-dichloro-5-carboxy-benzulfonimide are reported in this account: with 4 mol of water (**I**), with acetic acid and 2 H₂O (**II**), with methanol and 2 H₂O (**III**; this structure has not been fully analyzed and its composition is therefore uncertain) and with 2 mol of *N,N*-dimethylacetamide and 2 H₂O (**IV**). The larger benzulfonimide component is referred to as host and the included solvent as guest species throughout this report. A possible explanation of polymorphism in this series of compounds is proposed by relating the conformational flexibility of the host to the type and hydrogen bonding potential of the solvating species.

2. Experimental and Structure Determination

The title compound was kindly supplied by TEVA Pharmaceutical Industries Ltd. Single crystals of the inclusion compounds **I**, **II**, **III** and **IV** suitable for crystallographic study were obtained upon recrystallization of 2,4-dichloro-5-carboxy-benzulfonimide (C₁₄H₇Cl₂NO₈S₂) from water, acetic acid, methanol and *N,N*-dimethylacetamide respectively using evaporation techniques.

Diffraction data were measured at ca. 18 °C on an CAD4 diffractometer equipped with a graphite monochromator, using MoK α ($\lambda = 0.71069 \text{ \AA}$) radiation and the $\omega - 2\theta$ scan technique. The cell constants (from 25 accurately positioned reflections of high θ value) and pertinent details of the experimental conditions are summarized in Table I. The methanol compound **III** is relatively unstable. It appears to be isomorphous to **II**, but a detailed study of its structure was not completed. The other crystals were checked for deterioration, monitoring the intensities of three standard reflections from different zones, which was found to be negligible during the measurements. The data sets were corrected for Lorentz and polarization

Table I. Summary of crystal data and experimental parameters

	I	II	III	IV
M_r	595.2	619.2	591.2	733.4
Space group	$P\bar{1}$	$P\bar{1}$	$P1$ or $P\bar{1}$	$P2_12_12_1$
Z	2	2	2	4
a , \AA	8.227(1)	7.857(3)	7.840(4)	14.838(3)
b , \AA	8.964(2)	11.379(2)	11.235(2)	14.818(4)
c , \AA	16.945(2)	13.831(3)	13.697(3)	14.500(3)
α , deg	89.64(2)	92.50(1)	95.56(2)	90.0
β , deg	97.51(1)	101.21(2)	102.05(2)	90.0
γ , deg	114.28(2)	101.12(2)	102.21(2)	90.0
V , \AA^3	1127.9	1186.0	1140.5	3188.1
d_x , g cm^{-3}	1.752	1.734	1.721	1.528
2θ limits, deg	0–54	0–54	^a	0–54
Scan range, deg	$1.4 + 0.3 \tan \theta$	$0.9 + 0.3 \tan \theta$	^a	$0.9 + 0.3 \tan \theta$
No. of unique data	4397	4721	^a	3465
Data with $I \geq 3\sigma_I$	3583	3970	^a	2552
Refined parameters	299 ^b	316 ^b	^a	388 ^b
R	0.046	0.035	^a	0.044
R_w	0.061	0.050	^a	0.044
Error of fit, e	1.96	1.65	^a	1.60

^a Not analysed.

^b Parameters of H-atoms are not included.

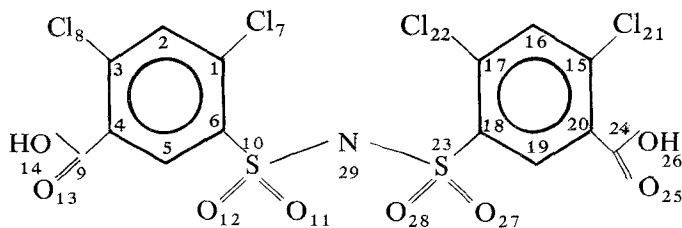
effects, background counts and variable measuring time (the scan rate varied between 1 and 5° min^{-1}). Absorption corrections were not applied.

The crystal structures were solved by a combination of direct methods (MULTAN 78 and MULTAN 80) and Fourier techniques. Extensive use of the latter was required in the final elucidation of structure **IV**, as well as in the location of solvent components of the other compounds. The hydrogen atoms were also found directly from electron density difference maps at an intermediate stage of the refinement, and were assigned isotropic temperature factors. In **I** and **II** the location of all H-atoms, with an exception of H(33b) in **I**, was unambiguous; the corresponding peak heights ranged from 0.35 to $0.65 \text{ e } \text{Å}^{-3}$. However, no peaks which could correspond to hydrogen atoms have been found in the immediate vicinity of the imide nitrogen. Instead, additional peaks were located near the water oxygen sites. The difference Fourier analyses thus suggested a possible proton transfer between the acidic imide nitrogen and one of the water molecules, leading to the formation of oxonium ions in these crystals (see below). In structure **IV**, where the results have lower precision, the imide and two carboxylic hydrogens of the host molecule as well as 4 out of 18 H-atoms of the *N,N*-dimethylacetamide moieties could not be located; the latter have subsequently been introduced in calculated positions.

The refinement of the three structural models was carried out by the full matrix least-squares method, including the positional and anisotropic thermal parameters of all the nonhydrogen atoms. The atomic parameters of the H-atoms were not refined, except for a partial adjustment of the coordinates with low-order data below $\sin \theta/\lambda = 0.50 \text{ Å}^{-1}$. Least-squares calculations were based on the experimental weights [$w = 1/\sigma^2(F_0)$] in **I** and **II** and on unit weights in **IV**, the quantity minimized being $w(\Delta F)^2$. At convergence no parameter shift was greater than 0.3 esd. Atomic scattering factors were taken from [4].

The final difference Fourier maps showed no indication of incorrectly placed or missing atoms; some residual electron density (ranging from -0.5 to $0.5 \text{ e } \text{Å}^{-3}$ in **I**, from -0.4 to $0.3 \text{ e } \text{Å}^{-3}$ in **II**, and from -0.2 to $0.4 \text{ e } \text{Å}^{-3}$ in **IV**) appeared in the vicinity of the second row S and Cl atoms. The final atomic parameters are given in Tables II, III and IV.

The crystallographic atom labeling scheme used for the title compound is shown below



Molecular dimensions obtained for the various molecules are in good agreement with the values found for such bonds and angles in other molecules. The observed bond lengths for $\text{C}(sp^2)\text{—Cl}$, $\text{C}(sp^2)\text{—S(VI)}$, N—S and S=O vary within 1.721–1.737, 1.780–1.793, 1.585–1.590 and 1.421–1.449 Å, respectively. The two C—O bonds in the carboxylic acid groups have different lengths ($\text{C=O} = 1.20 \pm 0.01 \text{ Å}$, $\text{C—OH} = 1.30 \pm 0.01 \text{ Å}$), indicating that hydrogen bonds associated with these groups are not disordered. (Relevant data have been deposited.)

The molecules of *N,N*-dimethylacetamide which occupy large intermolecular voids in structure **IV**, have relatively large thermal motion. The loose packing of molecules in **IV** is also

Table II. Positional and isotropic thermal parameters of compound I^a

Atom	x	y	z	U_{eq}/U (Å ²)
C(1)	-0.2503(4)	-0.3531(4)	0.3411(2)	0.0291
C(2)	-0.1195(5)	-0.2281(4)	0.3914(2)	0.0343
C(3)	0.0064(4)	-0.0934(4)	0.3596(2)	0.0307
C(4)	0.0012(4)	-0.0806(4)	0.2780(2)	0.0299
C(5)	-0.1289(4)	-0.2095(4)	0.2280(2)	0.0271
C(6)	-0.2523(4)	-0.3465(3)	0.2591(2)	0.0254
Cl(7)	-0.4036(1)	-0.5156(1)	0.3847(2)	0.0423
Cl(8)	0.1728(1)	0.0457(1)	0.4281(2)	0.0509
C(9)	0.1272(4)	0.0581(4)	0.2353(2)	0.0339
S(10)	-0.3957(1)	-0.5117(1)	0.1904(1)	0.0242
O(11)	-0.5794(3)	-0.5535(3)	0.2039(1)	0.0352
O(12)	-0.3578(3)	-0.4554(3)	0.1127(1)	0.0342
O(13)	0.1484(4)	0.0415(3)	0.1677(2)	0.0544
O(14)	0.2053(3)	0.1969(3)	0.2779(2)	0.0472
C(15)	0.2868(4)	-0.3295(4)	0.3743(2)	0.0309
C(16)	0.1589(4)	-0.4651(4)	0.4030(2)	0.0332
C(17)	0.0170(4)	-0.5777(4)	0.3518(2)	0.0279
C(18)	0.0034(4)	-0.5537(3)	0.2701(2)	0.0243
C(19)	0.1351(4)	-0.4192(4)	0.2422(2)	0.0287
C(20)	0.2797(4)	-0.3044(4)	0.2929(2)	0.0289
Cl(21)	0.4558(1)	-0.1975(1)	0.4449(2)	0.0507
Cl(22)	-0.1369(1)	-0.7436(1)	0.3926(1)	0.0433
S(23)	-0.1772(1)	-0.6831(1)	0.1976(1)	0.0249
C(24)	0.4142(4)	-0.1708(4)	0.2518(2)	0.0381
O(25)	0.4296(4)	-0.1847(4)	0.1834(2)	0.0629
O(26)	0.5121(5)	-0.0402(4)	0.2961(2)	0.1091
O(27)	-0.1221(3)	-0.6291(3)	0.1214(2)	0.0350
O(28)	-0.2088(3)	-0.8502(3)	0.2137(2)	0.0375
N(29)	-0.3522(3)	-0.6634(3)	0.2155(2)	0.0272
O(30)	0.3137(5)	0.5963(4)	0.0336(2)	0.0747
O(31)	0.1349(5)	0.8032(5)	0.0468(2)	0.0790
O(32)	0.1993(5)	0.2436(4)	0.0331(2)	0.0659
O(33)	0.6485(5)	0.9255(5)	0.0503(2)	0.0863
H(2)	-0.116	-0.234	0.453	0.060
H(5)	-0.129	-0.202	0.168	0.060
H(14)	0.293	0.289	0.250	0.060
H(16)	0.157	-0.489	0.460	0.060
H(19)	0.128	-0.401	0.182	0.060
H(26)	0.603	0.049	0.269	0.060
H(30a)	0.257	0.499	0.060	0.060
H(30b)	0.317	0.600	-0.024	0.060
H(30c)	0.238	0.653	0.045	0.060
H(31a)	0.146	0.867	0.095	0.060
H(31b)	0.024	0.800	0.012	0.060
H(32a)	0.195	0.178	0.083	0.060
H(32b)	0.268	0.200	0.000	0.060
H(33a)	0.610	0.911	0.101	0.060

^a Numbers (30) through (33) denote atoms of the four water molecules.

Table III. Positional and isotropic thermal parameters of compound II^a

Atom	x	y	z	$U_{eq}/U (\text{\AA}^2)$
C(1)	0.5381(3)	0.1426(2)	0.2301(2)	0.0319
C(2)	0.4834(3)	0.0517(2)	0.1544(2)	0.0380
C(3)	0.3884(3)	-0.0590(2)	0.1707(2)	0.0351
C(4)	0.3473(3)	-0.0803(2)	0.2625(2)	0.0312
C(5)	0.3982(3)	0.0139(2)	0.3365(2)	0.0294
C(6)	0.4944(3)	0.1257(2)	0.3222(2)	0.0283
Cl(7)	0.6635(1)	0.2759(1)	0.2057(1)	0.0474
Cl(8)	0.3173(1)	-0.1675(1)	0.0722(1)	0.0563
C(9)	0.2561(3)	-0.2000(2)	0.2862(2)	0.0344
S(10)	0.5458(1)	0.2404(1)	0.4209(1)	0.0298
O(11)	0.7289(2)	0.2959(2)	0.4337(1)	0.0476
O(12)	0.4892(2)	0.1830(2)	0.5034(1)	0.0392
O(13)	0.2927(3)	-0.2937(2)	0.2623(2)	0.0488
O(14)	0.1347(2)	-0.1911(2)	0.3378(1)	0.0445
C(15)	-0.0843(3)	0.0012(2)	0.1837(2)	0.0325
C(16)	0.0112(3)	0.0949(2)	0.1440(2)	0.0356
C(17)	0.1036(3)	0.1962(2)	0.2032(2)	0.0314
C(18)	0.1047(3)	0.2044(2)	0.3044(2)	0.0268
C(19)	0.0048(3)	0.1107(2)	0.3425(2)	0.0280
C(20)	-0.0917(3)	0.0079(2)	0.2839(2)	0.0285
Cl(21)	-0.1922(1)	-0.1217(1)	0.1018(1)	0.0546
Cl(22)	0.2134(1)	0.3112(1)	0.1469(1)	0.0478
S(23)	0.2327(1)	0.3283(1)	0.3869(1)	0.0304
C(24)	-0.1982(3)	-0.0892(2)	0.3297(2)	0.0346
O(25)	-0.2726(3)	-0.1857(2)	0.2893(2)	0.0550
O(26)	-0.2045(3)	-0.0562(2)	0.4221(1)	0.0515
O(27)	0.1966(2)	0.3017(2)	0.4830(1)	0.0420
O(28)	0.1872(3)	0.4364(2)	0.3490(2)	0.0481
N(29)	0.4346(3)	0.3374(2)	0.3810(1)	0.0304
C(30)	0.7382(4)	0.5275(2)	0.0765(2)	0.0470
C(31)	0.9231(5)	0.5583(4)	0.1315(3)	0.0755
O(32)	0.7150(3)	0.4739(2)	-0.0114(2)	0.0613
O(33)	0.6155(3)	0.5514(2)	0.1108(1)	0.0601
O(34)	0.9820(3)	0.6004(2)	0.3869(1)	0.0448
O(35)	0.5710(3)	0.5774(2)	0.3195(2)	0.0615
H(2)	0.512	0.067	0.086	0.050
H(5)	0.365	0.000	0.404	0.050
H(14)	0.078	-0.264	0.357	0.060
H(16)	0.010	0.089	0.069	0.050
H(19)	0.003	0.118	0.416	0.050
H(26)	-0.280	-0.122	0.443	0.060
H(31a)	1.008	0.597	0.099	0.080
H(31b)	0.972	0.490	0.143	0.080
H(31c)	0.945	0.613	0.186	0.080
H(32)	0.592	0.472	0.043	0.070
H(34a)	1.051	0.545	0.385	0.060
H(34b)	1.000	0.614	0.456	0.060
H(35a)	0.616	0.579	0.255	0.070
H(35b)	0.537	0.491	0.343	0.070
H(35c)	0.694	0.615	0.371	0.070

^a Numbers (30)–(33), (34) and (35) denote atoms of the acetic acid and the two water molecules respectively.

Table IV. Positional and isotropic thermal parameters of compound IV^a

Atom	x	y	z	$U_{eq}/U (\text{\AA}^2)$
C(1)	0.2860(5)	0.4908(4)	0.4545(4)	0.0435
C(2)	0.3149(5)	0.5731(4)	0.4833(4)	0.0494
C(3)	0.3154(5)	0.6451(4)	0.4235(4)	0.0418
C(4)	0.2878(4)	0.6363(4)	0.3332(4)	0.0424
C(5)	0.2597(5)	0.5506(4)	0.3038(4)	0.0432
C(6)	0.2584(5)	0.4786(4)	0.3619(4)	0.0407
Cl(7)	0.2868(2)	0.4036(1)	0.5331(1)	0.0703
Cl(8)	0.3571(2)	0.7461(1)	0.4649(1)	0.0654
C(9)	0.2856(5)	0.7111(4)	0.2634(5)	0.0482
S(10)	0.2241(1)	0.3715(1)	0.3174(1)	0.0451
O(11)	0.2978(4)	0.3100(3)	0.3343(3)	0.0598
O(12)	0.2013(4)	0.3875(3)	0.2232(3)	0.0604
O(13)	0.3179(4)	0.7016(3)	0.1876(3)	0.0723
O(14)	0.2478(4)	0.7844(4)	0.2920(4)	0.0815
C(15)	-0.0650(5)	0.2787(5)	0.0928(5)	0.0492
C(16)	-0.0495(5)	0.2168(4)	0.1613(5)	0.0497
C(17)	-0.0179(5)	0.2470(5)	0.2451(5)	0.0510
C(18)	-0.0008(5)	0.3375(4)	0.2607(4)	0.0437
C(19)	-0.0159(5)	0.3976(4)	0.1908(4)	0.0441
C(20)	-0.0470(5)	0.3697(4)	0.1040(4)	0.0436
Cl(21)	-0.1103(2)	0.2364(2)	-0.0088(1)	0.0698
Cl(22)	0.0007(2)	0.1646(1)	0.3280(1)	0.0753
S(23)	0.0447(1)	0.3794(1)	0.3670(1)	0.0502
C(24)	-0.0569(5)	0.4422(5)	0.0320(5)	0.0528
O(25)	-0.0737(5)	0.5181(3)	0.0522(4)	0.0765
O(26)	-0.0453(5)	0.4151(4)	-0.0516(3)	0.0910
O(27)	0.0452(4)	0.4763(3)	0.3578(3)	0.0627
O(28)	-0.0073(4)	0.3421(4)	0.4400(3)	0.0748
N(29)	0.1424(4)	0.3366(4)	0.3780(4)	0.0488
O(30)	0.3263(4)	0.1708(4)	0.4610(4)	0.0818
O(31)	0.1470(5)	0.1907(3)	0.5297(4)	0.0955
N(32)	0.2169(5)	0.0531(4)	0.1622(5)	0.0722
C(33)	0.2204(7)	0.1469(5)	0.1953(7)	0.0889
C(34)	0.1910(8)	0.0393(6)	0.0645(6)	0.0930
C(35)	0.2345(6)	-0.0148(6)	0.2125(5)	0.0625
C(36)	0.2578(7)	-0.0026(6)	0.3121(5)	0.0775
O(37)	0.2310(4)	-0.0934(3)	0.1774(4)	0.0705
N(38)	0.4925(7)	0.4981(7)	0.2051(7)	0.1092
C(39)	0.5141(7)	0.5978(6)	0.2307(7)	0.0904
C(40)	0.4461(10)	0.4874(8)	0.1149(7)	0.1353
C(41)	0.5119(9)	0.4394(9)	0.2598(10)	0.1143
C(42)	0.4896(7)	0.3446(6)	0.2306(6)	0.0817
O(43)	0.5471(5)	0.4571(5)	0.3371(4)	0.0953
H(2)	0.335	0.578	0.551	0.070
H(5)	0.240	0.545	0.234	0.070
H(16)	-0.062	0.149	0.151	0.070
H(19)	-0.006	0.467	0.202	0.070
H(30a)	0.264	0.176	0.474	0.070
H(30b)	0.339	0.190	0.399	0.070
H(31a)	0.135	0.135	0.500	0.070
H(31b)	0.138	0.240	0.486	0.070

Table IV (continued)

Atom	x	y	z	$U_{eq}/U (\text{\AA}^2)$
H(33a)	0.284	0.149	0.222	0.070
H(33b)	0.170	0.149	0.241	0.070
H(33c)	0.212	0.197	0.150	0.070
H(34a)	0.216	0.095	0.028	0.070
H(34b)	0.220	-0.020	0.035	0.070
H(34c)	0.124	0.031	0.050	0.070
H(36a)	0.324	0.027	0.306	0.070
H(36b)	0.257	-0.059	0.350	0.070
H(36c)	0.217	0.042	0.352	0.070
H(39a)	0.566	0.593	0.268	0.070
H(39b)	0.461	0.628	0.268	0.070
H(39c)	0.520	0.639	0.175	0.070
H(40a)	0.478	0.439	0.078	0.070
H(40b)	0.442	0.545	0.079	0.070
H(40c)	0.379	0.467	0.124	0.070
H(42a)	0.426	0.337	0.206	0.070
H(42b)	0.499	0.296	0.282	0.070
H(42c)	0.534	0.322	0.180	0.070

^a Numbers (30), (31), (32)–(37) and (38)–(43) denote atoms of the two water and the two *N,N*-dimethylacetamide molecules, respectively.

reflected in the low density (1.528 g cm^{-3}) of this material. Correspondingly, the atomic positions of *N,N*-dimethylacetamide were determined with lower accuracy and the refined model of the molecular structure is thus slightly distorted. In addition, the data-to-parameters ratio in the least-squares refinement of compound **IV** is considerably smaller than those in the refinements of **I** and **II**. As a result, the estimated standard deviations of atomic parameters in **IV** are twice to three times larger than in **I** and **II**.

3. Discussion of Results

Structures **I**, **II** and **IV** represent three different patterns of co-crystallization of the host compound with various guest molecules, all being stabilized by extensive hydrogen bonding networks. Two of the crystal structure types (**I** and **II**) have alternating layers of the host and the solvent, and resemble intercalation compounds. The third polymorph (**IV**) has a three-dimensional lattice of loosely-packed host species interspaced by channel-type zones which accommodate the solvent guest components. The overall conformation of the benzenesulfonamide molecule is different in the two inclusion types as illustrated in Figure 1. The stoichiometric ratios between host and guest in these multimolecular inclusion structures are well defined, and the positions of guest molecules in the crystal lattice have been determined with a satisfactory precision. There was no evidence of structural disorder in any of the constituent species.

Crystallization experiments of 2,4-dichloro-5-carboxy-benzenesulfonamide from protic media led to the formation of layered structures. In **I** continuous layers of water alternate with *bilayers* of host molecules, defining two distinct regions in the solid (Figure 2a). Within the bilayer region the large molecules form parallel sets of hydrogen-bonded chains along the $a + b$ direction, each molecule being linked to its neighbors in a chain through four $\text{COOH} \cdots \text{O}_2\text{S}$

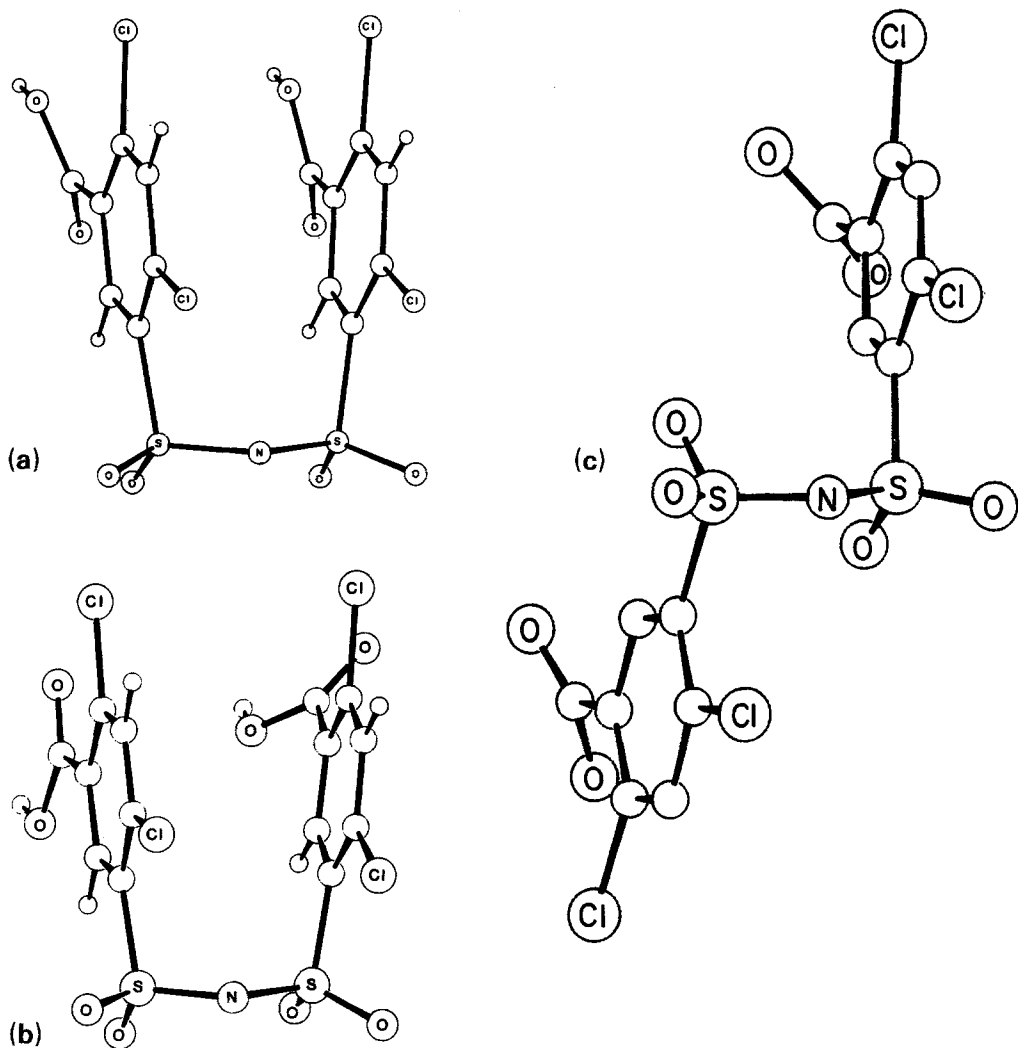


Fig. 1. Molecular structure of 2,4-dichloro-5-carboxy-benzulfonamide in compounds (a) I, (b) II, and (c) IV.

hydrogen bonds. The C—Cl groups turn inward and take part in dipolar interactions between adjacent chains displayed along c , which stabilize the bilayer. This is illustrated for example by non-bonding chlorine-chlorine distances of 3.275 Å, a value considerably smaller than the sum of the appropriate van der Waals radii. All the oxygen-containing functions of the host point outward on both sides of the bilayer, and are linked efficiently to the adjacent hydration layers. The hydrogen-bonding network in the latter is shown in Figure 2b. The water molecules form polymeric chains which include *homodromic* and *antidromic* six-membered hydrogen-bonded circles similar to those recently reported by Chacko and Saenger [5]. These two types of circular bonds are arranged in an alternating manner along the chains and have one side in common, H₂O(31)...H₂O(32). The homodromic rings have a chair-type conformation, while the antidromic circles are roughly planar. Each one of the water species is either threefold or fourfold coordinated, donating at least one hydrogen bond to the surface of a

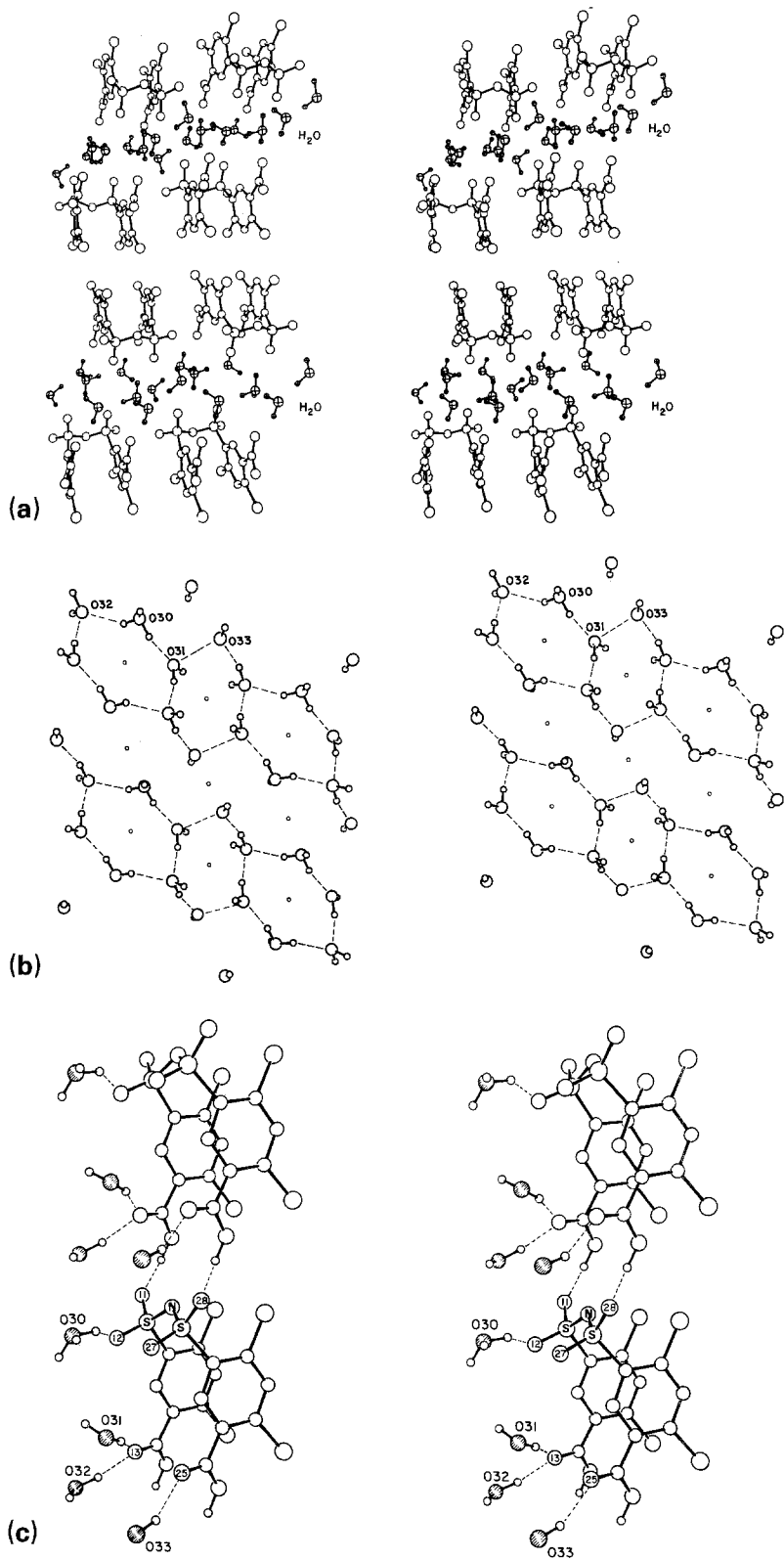


Fig. 2. Stereoviews of (a) the crystal structure of compound I approximately down the *b* axis, (b) a single solvation layer showing chains of circular hydrogen bonds between water molecules, and (c) host-host and host-solvent hydrogen bonding interactions.

Table V. Geometry of the hydrogen bonds

Donor (RH)	Acceptor (R')	Site	R—H (Å)	R...R' (Å)	H...R' (Å)	R—H...R' (deg)
<i>Compound I</i>						
OH(14)	O(11)	1 + x, 1 + y, z	1.01	2.646 ^a	1.64	174
OH(26)	O(28)	1 + x, 1 + y, z	1.00	2.777	1.82	159
HOH(30a)	O(32)	x, y, z	0.94	2.905	2.17	134
HOH(30b)	O(12)	-x, -y, -z	0.98	2.920	2.14	136 ^b
	O(27)	-x, -y, -z		2.960	2.24	130 ^b
HOH(30c)	O(31)	x, y, z	0.99	2.825	1.87	164
HOH(31a)	O(13)	x, 1 + y, z	0.97	2.929	1.99	161
HOH(31b)	O(32)	-x, 1 - y, -z	1.01	2.767	1.78	166
HOH(32a)	O(13)	x, y, z	1.03	2.869	1.85	171
HOH(32b)	O(33)	1 - x, 1 - y, -z	1.03	2.812	1.81	166
HOH(33a)	O(25)	x, 1 + y, z	0.95	2.979	2.09	156
HOH(33b)	O(31)	1 - x, 2 - y, -z	-	2.990	-	- ^c
<i>Compound II</i>						
OH(14)	O(34)	x - 1, y - 1, z	0.94	2.624	1.69	176
OH(26)	O(12)	-x, -y, 1 - z	0.96	2.817	1.95	149
OH(32)	O(33)	1 - x, 1 - y, -z	0.98	2.647	1.68	170
HOH(34a)	O(28)	x + 1, y, z	0.91	2.785	1.89	167
HOH(34b)	O(27)	1 - x, 1 - y, 1 - z	0.94	2.804	2.25	117 ^b
	O(11)	2 - x, 1 - y, 1 - z		3.038	2.38	127 ^b
HOH(35a)	O(33)	x, y, z	1.02	2.983	2.01	160
HOH(35b)	N(29)	x, y, z	1.05	2.960	1.92	170
HOH(35c)	O(27)	1 - x, 1 - y, 1 - z	1.08	3.074	2.13	144 ^b
	O(34)	x, y, z		3.139	2.27	136 ^b
<i>Compound IV</i>						
OH(14)	O(37)	x, y + 1, z	-	2.471	-	- ^d
OH(26)	O(43)	$\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$	-	2.489	-	- ^d
HOH(30a)	O(31)	x, y, z	0.95	2.858	1.93	166
HOH(30b)	O(11)	x, y, z	0.96	2.794	2.10	128
HOH(31a)	O(25)	-x, y - $\frac{1}{2}, \frac{1}{2} - z$	0.95	3.023	2.10	165
HOH(31b)	N(29)	x, y, z	0.98	3.085	2.12	169

^a The average standard deviations for R...R' distances are 0.005, 0.004 and 0.008 Å in **I**, **II** and **IV**, respectively.

^b Bifurcated bonds. ^c Atom H(33b) in **I** has not been located. ^d Atoms H(14) and H(26) in **IV** have not been located.

neighboring bilayer. Geometric parameters related to the intermolecular associations and solvent coordination (Figure 2c), which are summarized in Table V, conform to normal values of bond lengths and angles for O—H...O bonds. [As shown in Table V, it is assumed in the above description that H₂O(33) donates one of its hydrogens to O(31); this H-atom could not be found, however, in the corresponding difference map.]

A different intermolecular arrangement occurs in compound **II**. The solvent layers which contain 2 mol of water as well as 1 mol of acetic acid are included now between *monolayers* of the host, as illustrated in Figure 3a. Consequently, the relative orientation of individual host molecules with respect to the solvation layer is different than in structure **I** to allow a simultaneous interaction of the host with two neighboring bands of the guest species. In fact, each benzenesulfonimide molecule has its SO₂ groups turned toward one layer while the carboxylic functions point in the opposite direction.

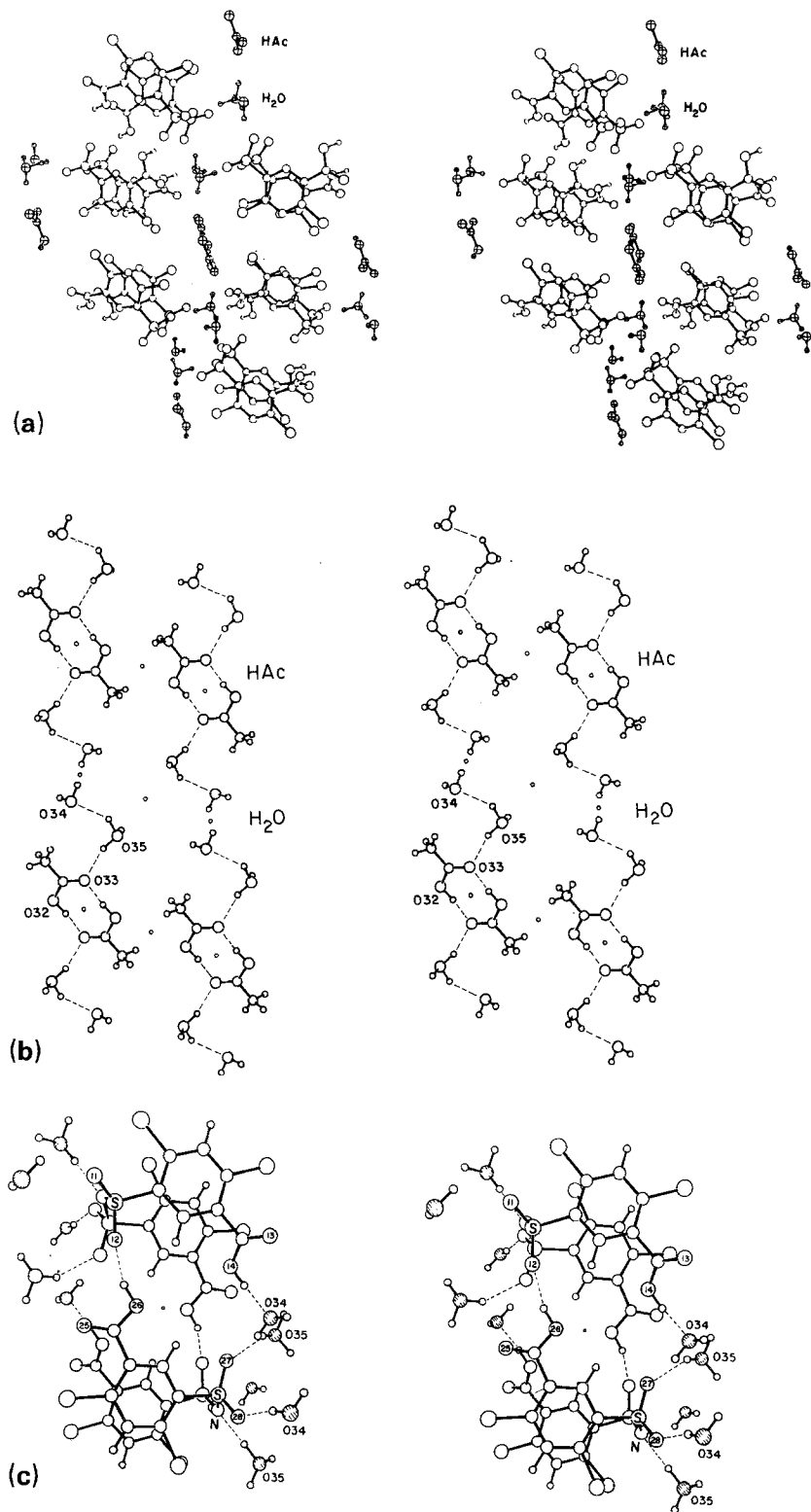


Fig. 3. Stereoviews of (a) the crystal structure of compound **II** approximately down the *a* axis, (b) a single layer of guest molecules showing the cyclic carboxy dimers of acetic acid and their solvation by water species, and (c) host-host and host-solvent hydrogen bonding interactions.

The solvent zone itself consists of alternating rows of the acetic acid and of water and oxonium cations (Figure 3b). Acid molecules related by crystallographic inversion form, as in many other crystal structures containing monocarboxylic acids [6], a cyclic hydrogen-bonded pattern with a characteristic $O_D \dots O_A$ distance of 2.647 Å. Nevertheless, the appearance of such dimers within the layered solvent structure is an interesting observation because crystals of pure acetic acid were found to consist of hydrogen-bonded chains of molecules rather than of carboxy dimers [7]. The existence of the latter modification has, in fact, been suggested only from far infrared spectra [8]. The cyclic dimers are solvated by the water species, with the oxonium ions linking directly to the carbonyl end of the acid. Each of these carbonyl oxygens thus serves as an acceptor of two hydrogens. The host species are involved in $O-H \dots O=S$ hydrogen bonds between themselves as well as with the surrounding molecules of water (Figure 3c and Table V). In this structure there are more nucleophilic sites than acidic protons. As a result, while adjacent benzulfonimide species bind to each other by two $COOH \dots O_2S$ bonds in **I**, there is only one such bond in **II**, allowing the remaining functions to interact with the solvation layer. Moreover, the O(13) and O(25) potential acceptor sites are not involved in hydrogen bonding. Instead they approach the H_3O^+ (35) aqua cations at 2.87 and 2.82 Å, respectively, contributing pole-dipole attractions to the overall interaction scheme.

The molecular conformation of the host found in structures **I** and **II** is characterized by an unfavorable alignment of dipoles, the two substituted phenyl rings as well as the two SO_2 groups being arranged *cis* to each other in relation to the intramolecular $S \dots S$ axis. For example, the tetrahydrate compound contains pairs of almost exactly parallel $C-Cl$ bonds and $COOH$ groups at an average distance of 3.7 Å. However, this is undoubtedly more than compensated for by the strong hydrogen-bonding ($\geq 5 \text{ kcal mol}^{-1}$) attractions between layers of the dielectric solvent and hydrophilic functions of the host. In **I** the planes of the carboxylic group deviate from coplanarity with the respective adjacent phenyl ring by about 22° .

In spite of the fact that the layered arrangement of molecules in **II** is different from that in **I**, the overall geometry of the host species remained similar. The optimization of intermolecular forces (there are no short contacts between the two overlapping halves of the molecule indicative of significant intramolecular *steric* interactions) was found to be associated with minor conformational variations only. It is reflected in the change of relative orientations of the carboxyl groups. Thus, in **II** one of the $COOH$ groups is nearly coplanar with the adjacent ring (the twist angle about the $C(\text{phenyl})-C(\text{carboxyl})$ bond being only 8°), while the plane of the second carboxylic function is rotated by about 43° with respect to the corresponding phenyl. The effect of the intermolecular interactions on this conformational feature is more emphasized when the present observations are compared to relevant data reported in the literature. For example, in benzoic acids the angle of rotation of carboxyl group about the exocyclic $C-C$ bond out of the plane of the benzene ring is consistently between 10 and 20° for mono-*o*-substituted derivatives, below 10° for compounds without an ortho substituent [9] and between 48 and 59° for 2,6-disubstituted benzoic acid molecules [10]. The overlap between the two substituted-phenyl residues is almost complete in **I**, the $C(\text{phenyl})-S \dots S-C(\text{phenyl})$ torsion angle being 2° . It is slightly distorted in **II** where the respective angular value of torsion about the $S \dots S$ axis is about 15° .

At this stage it was decided to extend the crystallization experiments to aprotic polar solvents in order to try to induce a different conformation of the host. Indeed, upon recrystallization of the title compound from *N,N*-dimethylacetamide a distinctly different structure type occurs (**IV**). In the initially aprotic environment the host adapted a stretched conformation

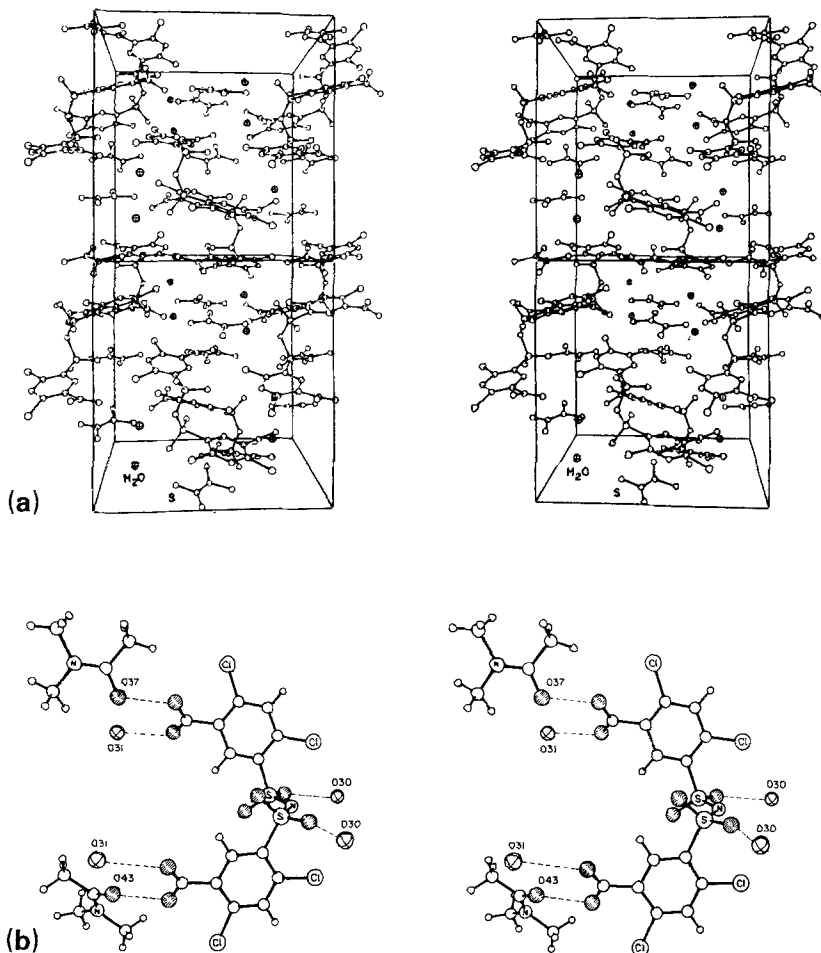


Fig. 4. Stereoviews of (a) the crystal structure of compound **IV** approximately down the c axis (S denotes a molecule of N,N -dimethylacetamide), and (b) the solvating environment of a single host molecule.

with a nonparallel arrangement of the phenyl rings and the $S=O$ dipoles (the $C(\text{phenyl})-S\cdots S-C(\text{phenyl})$ torsion angle is now 136°), releasing some of the intramolecular electrostatic repulsions that exist in **I** and **II** (see above). On the other hand a relatively strong $O-H(\text{acid})\cdots O(\text{amide})$ hydrogen-bonding association can be formed without steric interference, leading to a host-guest stoichiometric ratio of 1 : 2. The crystal structure that forms is not a layered one (Figure 4a). Rather, the packing of the elongated host molecules extends in three dimensions inducing channels in the lattice. Molecules of the N,N -dimethylacetamide solvate are contained in the wide intermolecular voids, exhibiting a considerable thermal motion. It should be noted that a satisfactory crystallization of **IV** was achieved only when a *very concentrated* solution of the benzsulfonimide host in N,N -dimethylacetamide was left in the open air for about 48 h and allowed to absorb some moisture. The included molecules of water complete the solvation layer around the sulfone oxygen nucleophiles. They are arranged in hydrogen bonded pairs within continuous channels along the a direction of the

crystal. The OH \cdots O distance between such pairs is relatively large, 5.18 Å, as each pair is partially surrounded by the polar functions of neighboring host molecules.

Interactions of the benzulfonimide species with surrounding molecules are shown in Figure 4b and details of their geometry are included in Table V. Clearly, six out of the eight oxygen sites are involved in significant dipolar and hydrogen bonding. In order to optimize their bonding pattern (particularly the strong interaction with the amide O-atoms of the solvent) in a similar manner, the two carboxy groups had to be rotated by different amounts about the respective C(carboxyl)—C(phenyl) bonds. The observed angles of twist out of the plane of the benzene ring are 29.5 and 48.5°; such values are considerably larger than expected for an ortho-substituted derivative of benzoic acid (see above). The O(amide) function is a rather strong proton acceptor; but in the present structure the observed O \cdots O distances between the interacting sites (2.47 and 2.49 Å) are shorter than those usually found for similar H-bonds [11]. The corresponding C—O(acid) \cdots O(amide) angles are 112 and 116°, in agreement with the expected geometries.

The coordination features of water molecules can be summarized as follows. The H₂O(31) molecule donates hydrogen bonds to the N(29) and O(25) sites of two different hosts, lying within a van der Waals distance from a carboxyl group of a third host at O(31) \cdots O(13) = 2.84 Å. It acts also as a hydrogen bond acceptor from the second water molecule. The H₂O(30), in turn, lies within an interacting distance from the sulfone groups of two different hosts [O(30) \cdots O(11) = 2.79 Å and O(30) \cdots O(28) = 2.86 Å], and donates its other hydrogen to one of them. Direct interactions between the benzulfonimide molecules in this structure are mainly through dipolar and dispersion forces. Short intermolecular distances include Cl(22) \cdots O(25) (at $-x, y - \frac{1}{2}, \frac{1}{2} - z$) = 2.98 Å and Cl(7) \cdots O(13) (at $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$) = 3.14 Å.

The acidity of the H-atom bound to nitrogen in the benzulfonimide is relatively high, the N—H group being activated by the two electron-withdrawing sulfones. In fact, the present examples provide consistent structural evidence that in aqueous media this hydrogen is readily transferred to water. Thus, oxonium ions have been characterized in structures **I** and **II**, and the imide nitrogen was found to serve as an acceptor of nearly linear hydrogen bonds (with N \cdots H distances between 1.9 and 2.1 Å) from the water species in **II** and **IV** (Table V). The aqua cations have an approximate pyramidal geometry, in agreement with previous indications from other crystal structures [12]; the observed HOH bond angles are 99, 106 and 123° in **I** and 99, 102 and 114° in **II**. The solvent clusters in these structures do not contain particularly short contacts between the H₂O and H₃O⁺ moieties as in some crystal structures of acid polyhydrates. It should be kept in mind, however, that in view of the very weak X-ray diffraction power of the hydrogen atoms, particularly at room temperature, the above data are of only moderate accuracy and provide only qualitative indications.

Conformational flexibility of the benzulfonimide framework is confined to rotations about the sulfur-carbon and sulfur-nitrogen bonds, torsional adjustment about the latter having the largest effect on the overall conformation of the molecule. The observed torsion angles about the S(10)—N bond are -75.9(2), 84.3(2) and 74.8(4)° in **I**, **II** and **IV**, respectively, those corresponding to the S(23)—N bond being 78.3(2), -68.6(2) and 74.0(4)°. Thus, the two torsions about S—N bonds have similar magnitudes but different relative signs in the three compounds. Interestingly, the benzene rings remain nearly parallel to each other in both types of the molecular structure. This can be attributed to the presence of steric as well as electrostatic repulsions between chlorine atoms (those substituted in 2-positions of the rings) and adjacent sulfone groups, which hinder free rotation about the S—C single bonds. Short intramolecular Cl \cdots O distances, varying between 3.086 and 3.204 Å, reflect these inter-

actions. As described above, torsional variations about the C(phenyl)–C(carboxyl) bonds in the individual structures are associated mainly with the optimization of hydrogen bonding patterns.

It is clear that the solid structures presented in this study are dominated by hydrogen bonding. Although the three crystalline forms are quite different one from another they all contain the maximum number of hydrogen bonds, in agreement with previous observations on solid acids and amides [13]. The present analysis also suggests that O(sulfone) as well as O(amide) are stronger proton acceptors than O(carboxyl). The energies of similar hydrogen bonds have recently been estimated to be greater than 5 kcal mol^{-1} [11]. Since each host molecule is involved in several O—H \cdots O bonds, the contribution of these interactions to the total energy of each structure is thus far more important than that associated with intramolecular repulsions between local dipoles or with torsional deformations about the relatively weak N—S bonds. Correspondingly, the observed modes of crystallization and molecular conformation of the title compound were found to be primarily dependent on the nature of the solvent environment. The differences in functionality of the solvating media in the three structures are clearly reflected in the number of carboxy protons that are exposed by the host to solvent hydrogen bonding; this number increased (from zero to two) as the proton-donating capability of the solvent decreased. Because of the strong binding forces between molecular species involved in these structures, it is possible that the above described features for static crystalline phases may also characterize structural domains that exist (in dynamic equilibria with other forms) in a concentrated solution phase.

This study thus provides an interesting illustration of the ability to induce and isolate different polymorphic structures of highly polar and conformationally flexible molecules by varying their environment in solution. Further structural investigations of such phenomena, taking into account the available information on characteristic interaction patterns, hydrogen bonding capabilities and binding energies associated with various functional groups, may lead to a better understanding of solvation forces and solvation-structure-activity relationships in polymorphic systems.

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