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Polymorphism and Isostructurality in Sulfonylhydrazones†

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Abstract

Five methyl and halogen derivatives of the conformationally flexible trimorphic molecule, bis(p-tolyl) ketone p-tosylhydrazone (TMSH, trimethyl sulfonylhydrazone) (Cryst. Growth Des., 2007, 7, 2047) were synthesized to understand polymorphism and isostructurality upon Cl−Me and inter-halogen exchange. The chlorodimethyl derivative CMSH (chlorodimethyl sulfonylhydrazone) is dimorphic whereas TCSH (trichloro sulfonylhydrazone), TBSH (tribromo sulfonylhydrazone), FMSH (fluorodimethyl sulfonylhydrazone), and MISH (methyldiiodo sulfonylhydrazone) have one crystal structure each. Single crystal X-ray diffraction and XPac analysis showed 3D isostructurality between CMSH form I, TCSH and TBSH, as well as for CMSH form II and FMSH. MISH has a different crystal packing compared to the other members due to the large iodo group. The conformational rigidity of the sulfonylhydrazone backbone leads to the observed isostructurality, whereas the presence of sulfonamide dimer and catemer synthons gives different packing motifs and polymorphism.

Introduction

Controlling the solid-state assembly of molecules into periodic solids with tailor-made properties using non-covalent interactions, notably hydrogen bonding, is of considerable importance in crystal engineering, especially for the design and synthesis of functional materials.[1] In this regard, polymorphism, salt preparation, and cocrystallization are a few approaches that are used extensively, more often in the pharmaceutical industry.[2] Polymorphism is the occurrence of a compound in more than one crystalline forms.[3] The differences in crystal packing arrangements result in different physicochemical properties. However a complementary phenomenon, isostructurality, is also possible in which two or more related molecules may have the same or very similar crystalline arrangement. Even through both polymorphism and isostructurality have been independently reported for a long time, the idea of polymorphism and isostructurality in the same system is somewhat less studied.[4] Moreover, isostructural sets of compounds rarely include more than two members.[5] Functional groups which have the ability to adopt the same structural role in crystal structures may lead to the formation of isostructural crystals. Chloro−methyl and halogen groups are often viewed as structurally equivalent functional groups.[6] According to the Kitaigorodskii's principle of close packing[7], chlorine (Cl, 21 Å^3) and methyl (Me, 19 Å^3) groups have a similar size and shape, and so it is possible that Cl and Me interchanged molecules adopt the same crystal structure, known as the chloro−methyl exchange rule.[8] But, it was observed that isostructural Cl−Me interchange occurs relatively infrequently, in about 26% cases only (one fourth), and different crystal structures were observed for the majority 74% (three fourth) in a small sample of 118 structures.[9] The outcome of Cl−Me exchange is not always predictable. Exchange of the halogen group, Cl, Br and I, to give isostructurality is more frequent.[10] Apart from Cl−Me and inter-halogen exchange, isostructurality with respect to a few other groups such as aromatic C−H/N,[11a-c] O−H/N−H,[11d] Br/OH,[11e] C−H/C−F,[11f] etc. are well documented.

Isostructurality is more common in multi-component systems such as cocrystals, notably solvent inclusion compounds, molecular complexes, etc.[12] There are a large number of reports on isostructural

solvent inclusion compounds with guests of different size and shape, for which the overall crystal lattice does not change. However isostructurality in single-component solids is less common, which may be attributed to the sensitivity of crystal packing to molecular structure changes. Single-component isostructural solids may be divided into two categories of conformationally rigid and conformationally flexible molecules. Among the conformationally rigid single-component systems, very few isostructural cases are known.[13] In contrast, the construction of an isostructural organic solid with conformationally flexible molecule is not straight forward because the change in conformation/ shape/ hydrogen bonding groups may lead to a different packing arrangement, or polymorphism, which is the opposite of isostructurality. Among the conformationally flexible isostructural solids,[14] Cl−Me exchange in polymorphic fuchsones by Nangia,.[14a] substituted derivatives of sulfonamide by Caira,[14c] Gelbrich,[14d,e] Chopra,[14f] and Guru-Row[14g] are a few important examples. One major application of isostructurality is the synthesis of desired solids (cocrystal, salt and polymorph) using heteronuclear seeding with isostructural compounds, when routine methods have failed.[13a,15] Some examples of single-component isostructural solids reported in the literature are shown in Scheme 1.

Acetone tosylhydrazone (AMSH) and *p*-tolylketone tosylhydrazone (TMSH) were studied based on their conformational flexibility and polymorphism.[16] Here we report five additional sulfonylhydrazone derivatives with Me, F, Cl, Br and I substituents at the *para*-position of the three phenyl rings. Even as halogen−methyl and inter-halogen exchange can direct the formation of isostructural crystals, achieving isostructural crystals in the sulfonylhydrazone series of compound is a challenge because the likelihood of polymorphism in this family is high due to conformational flexibility (different shape and packing) and possible sulfonamide dimer vs. catemer synthon variance (different H bonding motifs are shown in Scheme 2).[16,17]

Results

Five new derivatives of trimorphic bis(*p*-tolyl)ketone *p*-tosylhydrazone (TMSH, trimethyl sulfonylhydrazone) with varying halogen substituents are shown in Scheme 3.‡ All these compounds were crystallized using common laboratory solvents by dissolving 10-15 mg of the compound in 4-5 mL of methanol, ethanol, nitromethane, or acetonitrile. A single crystal was selected from among the nice block-shaped crystals for X-ray diffraction. All the crystallization batches resulted in a single guest-free structure except for CMSH that crystallized as dimorphs (CMSH-I from nitromethane and CMSH-II from ethanol solvent). The experimental procedures for synthesis and crystallization are detailed in ESI.† The unit cell dimensions and crystal structure analysis showed that CMSH-I, TCSH and TBSH have similar cell parameters, space group *C*2/*c*, and possess the same crystal packing. The unit cell parameters and space group of FMSH are identical (orthorhombic space group *Pbca*) with CMSH-II. MISH has different unit cell parameters and crystal structure compared to other members in the series. Details of crystal cell parameters are listed in Table 1 and hydrogen bond metrics in Table 2.

Crystal Structure Analysis

Polymorphism

CMSH crystallized in two polymorphic forms. Crystallization from nitromethane gave single crystals which solved and refined in the monoclinic space group *C*2/*c*, termed CMSH-I. Form II (CMSH-II) was obtained from ethanol in the orthorhombic space group *Pbca* (*Z*' = 1 in each case). The structural differences between the two polymorphs are shown in Figure 1. Both the polymorphs of CMSH contain the same sulfonamide N−H···O dimer synthon of $R_2^2(8)$ graph set and the dimers are connected by

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C−H···O hydrogen bonds. Both the polymorphs contain similar 2D isostructural units. The crystal structures are different in the third dimension. C−H···Cl interactions (C5−H5···Cl1, 2.80 Å, 127.7°) between two sulfonamide dimers complete the 3D packing in CMSH-II, whereas in CMSH-I they are close packed. In CMSH-I, two close packed dimers are inversion related whereas in CMSH-II they are glide related. The six crystal structures are 2D isostructural due to the same building unit of sulfonamide tapes extending via dimers through C−H···O hydrogen bonds (Figure 2).

Isostructurality

In the crystal structure of TCSH, sulfonamide dimers are connected by C−H···Cl and type I Cl···Cl interactions (where $\theta_1 = \theta_2$) (see Figure S1 in ESI†) to complete the packing. C−H···Me (C3−H3···C20, 3.02 Å, 132.9°) and Me···Me (C20···C20, 3.84 Å, 146.3°) contacts in CMSH-I are exchanged by C−H···Cl (C3−H3···Cl2, 2.83Å, 124.9°) and type I Cl···Cl interactions (3.47 Å, $\theta_1 = \theta_2$ = 143.1°). The crystal structure of TBSH is similar to TCSH. In this crystal structure, C−H···Cl and type I Cl···Cl interactions of TCSH are replaced by C−H···Br (C5−H5···Br3, 2.95 Å, 122.4°) and type I Br···Br interactions (3.59 Å, $\theta_1 = \theta_2$ =142.3°). Therefore, CMSH-I, TCSH and TBSH are isomorphous with identical cell parameters, space group and crystal structures. Isostructurality in these cases is due to the Cl−Me, Br−Me and Cl−Br functional groups exchanges. In the crystal structure of FMSH two sulfonamide dimers related by a glide plane are connected by C−H···F interactions as in CMSH form II where two glide related sulfonamide dimers are connected by C−H···Cl interaction. Therefore isostructurality in this case is due to Cl−F exchange. Now to compare our results with the reported sulfonylhydrazone derivatives, TMSH form I and MCSH (methyldichloro sulfonylhydrazone) are isomorphous to CMSH-I whereas MBSH (methyldibromo sulfonylhydrazone) is isomorphous to CMSH-II, with identical unit cell parameters, space group and structural packing (see Figure S2 and Table S2 in ESI†). MFSH (methyldifluoro sulfonylhydrazone) and MPSH (methyldiphenyl sulfonylhydrazone) have completely different crystal packing. The reported forms II and III of TMSH do not contain the frequent sulfonamide dimer synthon, and so they are not isostructural to any of the sulfonylhydrazone structures.

The packing in MISH is different compared to other crystal structures. Due to the bulky iodo group, the inversion related sulfonylamide dimers cannot come into close proximity similar to the CMSH-I, TCSH or TBSH, rather they point in opposite directions. The C−H···O hydrogen bonds between the sulfonamide dimers result in 2D isostructurality, however, they differ in the third dimension due to the relative offset of adjacent layers (see Figure 3). Isostructurality due to the exchange of Cl−Br and Cl−I are common whereas F generally results in a different crystal packing due to the very high electronegativity of the F atom compared to the other halogens, e.g. see the discussion on isostructural Ag-complexes of halo-pyridyl ureas.[10b] Here we have observed isostructurality in FMSH and CMSH form II due to Cl−F exchange which is unique; and a different crystal packing for MISH compared to the other structures.

XPac analysis

There are several methods for the comparison of two crystal structures, among which XPac is the most promising one in the recent literature to measure isostructurality in a quantitative manner.[18] In the XPac approach, each crystal structure is represented by a cluster of molecules, with a central core of molecule and a shell of contacting molecules. The two clusters are then compared by computing the mean differences between the comprehensive (i.e. all possible combinations) sets of angles (δ_a) and interplanar angles (δ_p), between a chosen group of atoms in the core molecule and the corresponding atoms in one shell molecule (a double subunit) or two shell molecules (a triple subunit). The obtained δ parameters can

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be considered as inverse indicators of structural similarity. The focal point of the XPac method is that the sub-components of two different crystal structures, i.e. the supramolecular construct is similar if the two molecules are of the same type and assembled in the same way. Any recurring periodic or discrete arrangement of molecules with its spatial characteristics may be called a supramolecular construct (SC).

Each crystal structure can be explained as a cluster of molecules which consists of a central molecule (kernel) and all molecules surrounding it to complete the coordination sphere. If two crystal structures contain a common fragment (i.e. a given SC), then their clusters must also contain the common fragment which corresponds to this SC. Hence, the common SCs (if present) of two crystal structures can be identified by comparing their representative clusters. A 'corresponding ordered set of points' (COSP) is a selection of atoms in the molecule that is chosen to best represent the molecular shape. The supramolecular construct of two structures can be discrete (0D, identical isolated units such as a hydrogen bonded dimer), extended 1D (identical chains), 2D (identical sheets) or 3D (complete similar arrangement of molecules).

In the XPac plots of δ_p vs. δ_a for a cluster of 15 molecules with one kernel (central molecule) and n = 14 shell molecules (neighbor molecules), there are n[1+ (n−1)/2)] = 105 data points and the position of each point characterizes the degree of similarity in a particular subunit of the cluster. Closer the (δ_a, δ_p) points to the origin of the coordinate system, the better is the structural match of the two compounds. Thus, the quantitative dissimilarity index (X) is computed as,

$$X = \sum_{i=1}^{M} \left({\delta_{a,i}}^2 + {\delta_{p,i}}^2 \right)^{1/2}$$

Where X is the mean distance (in °) of all M data points from the origin and $\delta_{a,i}$ and $\delta_{p,i}$ are the coordinates of the i-th data point.

For sulfonylhydrazones the number of ordered set of points consists of 22 atomic positions as shown in Scheme 4, indicated by blue circles and it is retained for the whole series of molecules. 3D SCs were identified for the crystal pairs CMSH-I/ TCSH, CMSH-I/ TBSH, TCSH/ TBSH, and CMSH-II/ FMSH, whereas 2D SCs were identified for all other crystal pairs. The dissimilarity index X values are listed below for 2D and 3D SCs in the crystal structures. Colour codes are dark red = 3D and dark green = 2D isostructurality. A lower value of X indicates a better match.

	CMSH-I				
CMSH-II	4.5	CMSH-II			
TCSH	2.7	2.4	TCSH		
TBSH	3.5	2.0	1.1	TBSH	
MISH	5.4	2.9	2.6	2.0	MISH
FMSH	0.8	3.7	2.1	2.8	4.4

XPac plots of δ_p vs. δ_a for a few sulfonylhydrazone pairs are shown in Figure 4. The closer placement of the (δ_a, δ_p) points to the origin of the system defines better match for the sulfonylhydrazone pair. In case

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of CMSH-I/ CMSH-II and CMSH-I/ MISH pairs, XPac points are scattered over a wide area from the origin, indicative of structural dissimilarity (higher value of *X*).

Discussion

Isostructurality was observed in the conformationally flexible sulfonylhydrazones molecules, wherein the crystal structures are governed mainly by strong N−H···O hydrogen bonds. Isostructurality is due to functional group exchangeability of halogen and methyl groups in this series of compounds. The 2D isostructurality is perhaps a result of the robust sulfonamide dimer synthon of $R_2^2(8)$ graph set. The detailed molecular arrangements are directed by the slight changes in the conformation of molecules and weaker interactions. Cl−Me, Br−Me, Cl−Br and Cl−F functional groups proved to be structurally equivalent resulting in isomorphous crystals. Two notable features of the sulfonylhydrazone series are: 1) Cl−F isostructurality (which is generally rare)[19] as the F derivatives generally behave in a different manner due to the small size and high electronegativity of the fluorine atom, and 2) 3D packing of MISH is different compared to the other members indicating the effect of the large iodo group in crystal packing.

Polymorphism was observed only for CMSH where form I is isomorphous with TCSH and TBSH and form II is isomorphous with FMSH. Therefore polymorphs of CMSH show a structural link in sulfonylhydrazones. The isostructural relationship among sulfonylhydrazones is depicted in Scheme 5. Interestingly, despite the molecule being conformationally flexible, as reported independently by Gleason[16a] and Nangia[16b] for different derivatives, polymorphism in the sulfonylhydrazones of the present study is not of the conformational type. They have similar torsion angles in the flexible parts of the molecule in all crystal structures. The molecular overlay (Figure 5) and the torsion angles (Table S1) show the near identity of conformers.

Conclusions

In summary, Cl−Me, Br−Me, Cl−Br and Cl−F exchanged isostructurality is observed in a series of conformationally flexible polymorphic molecules.[16] Three isomorphous crystal structures of sulfonylhydrazones in space group *C*2/*c* and two isomorphous crystals in *Pbca* were discussed. The isostructurality of all the isomorphous crystal structures was calculated using XPac. The 2D isostructurality in sulfonylhydrazones is due to the presence of strong hydrogen bonding sulfonamide dimer N−H···O synthon and the differences in crystal structures are due to slight conformational changes and weak interactions. The polymorphs contain similar packing motifs. A rare and unique set of conformationally flexible molecules which exhibit polymorphism due to strong hydrogen bonding and yet form isostructural crystals by the halogen−methyl and halogen−halogen exchange is discussed. Structural analysis of a few more halo/ methyl-substituted sulfonylhydrazone derivatives, particularly with ortho/ meta substitution to break the symmetry, will provide further insights on the role of steric and electronegativity factors that direct hydrogen bonding, conformation changes, and close packing in this series of derivatives and thereby refine the polymorphism vs. isostructurality categories classification for sulfonylhydrazones.

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Notes and References

† Electronic Supplementary Information (ESI) available: Crystallographic information files (.cif format), experimental details of synthesis and crystallization, melting point, FT-IR, ^{1}H-NMR and torsion angle data. See DOI: 10.1039/b000000x/. CCDC 971250-971255 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

‡ Experimental procedures of synthesis, crystallization and X-ray crystallographic details are listed in the ESI†.

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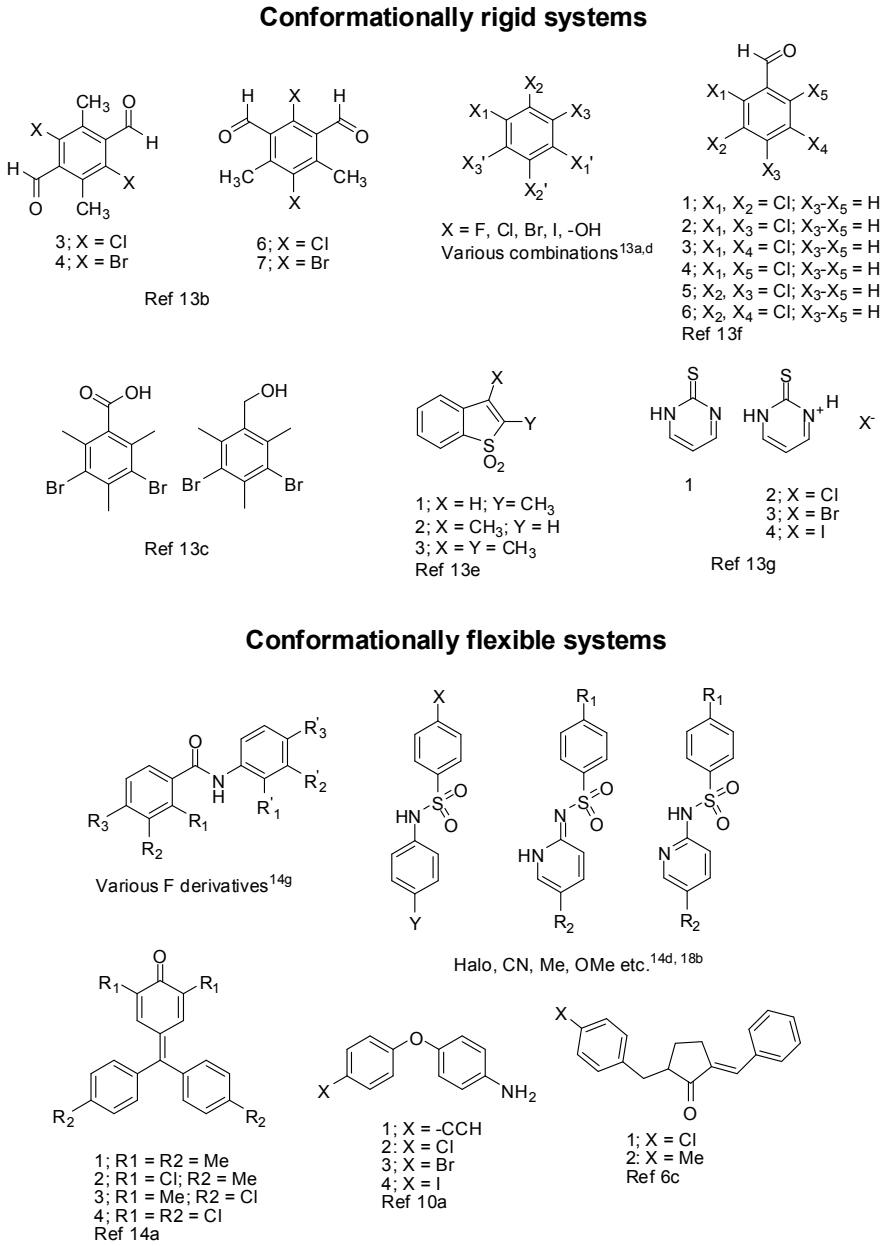
Schemes and Figures



Scheme 1 A few single-component isostructural solids reported in the literature (refs. 6c, 10a, 13, 14, 18b).

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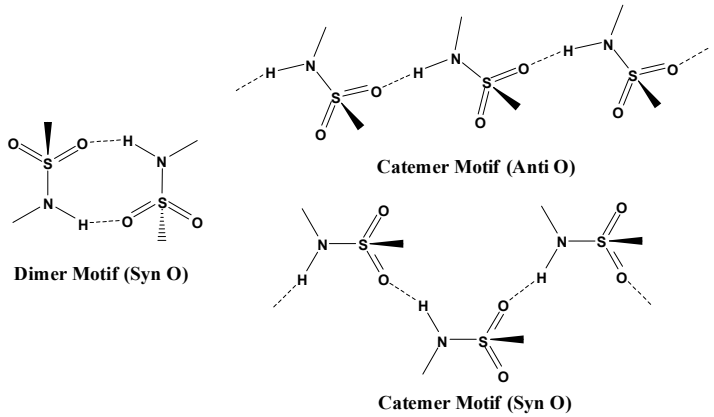
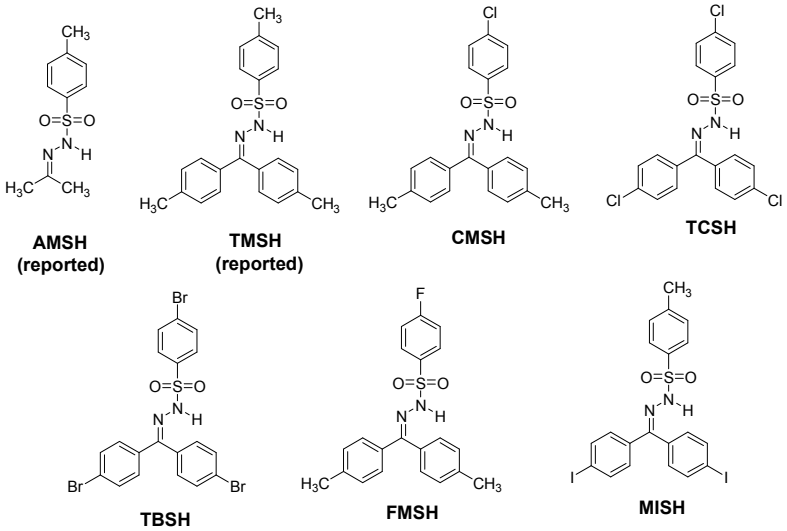


Scheme 2 Dimer and catemer N−H···O synthon of the sulfonamide group. The catemer chain motif can be formed using both syn and anti SO_2NH_2 conformation, but the cyclic dimer arises from the syn conformation only.



Scheme 3 Molecular diagram of AMSH,[16a] TMSH[16b] along with halogenated derivatives of TMSH synthesized, CMSH (chlorodimethyl sulfonylhydrazone), TCSH (trichloro sulfonylhydrazone), TBSH (tribromo sulfonylhydrazone), FMSH (fluorodimethyl sulfonylhydrazone) and MISH (methyldiiodo sulfonylhydrazone).

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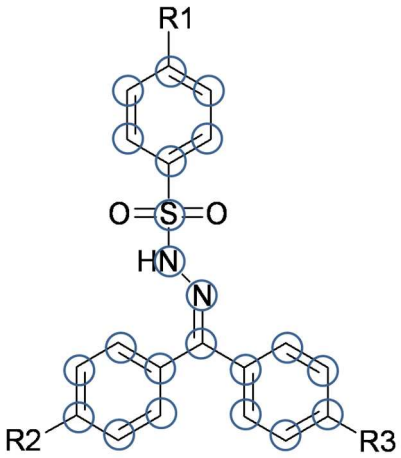
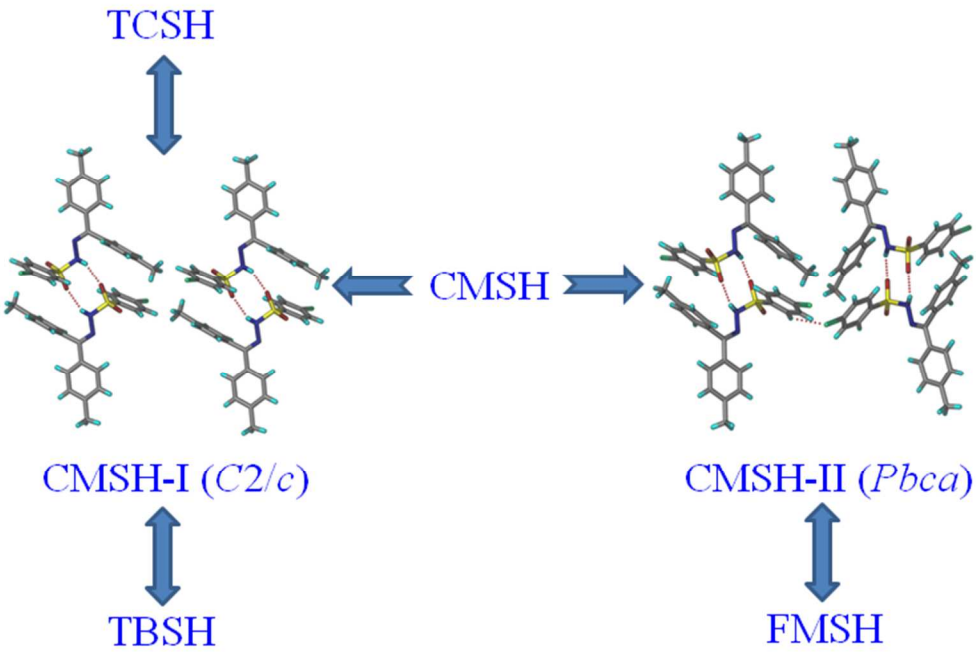


Scheme 4 Common set of points of sulfonylhydrazones (indicated by blue circles) used for XPac analysis.



Scheme 5 Dimorphs of CMSH show a structural link among the crystal structures of sulfonylhydrazones. Double head arrows are used to indicate the isomorphous relationship.

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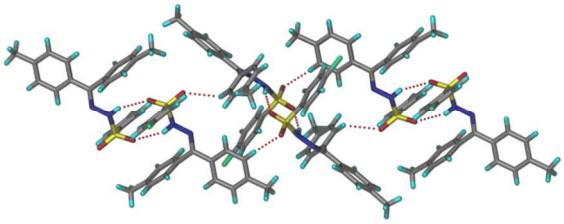
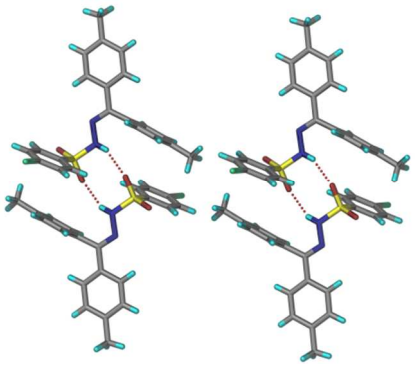
CMSH-I

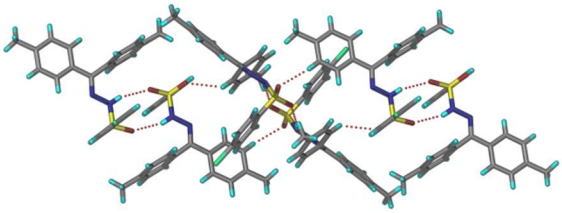


Sulfonamide dimers form 1D tape

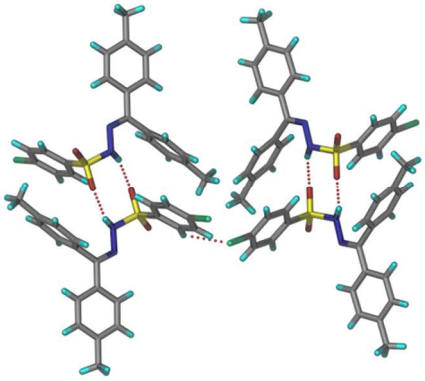


Inversion related sulfonamide dimers

CMSH-II



Sulfonamide dimers form 1D tape



Glide related sulfonamide dimers

Fig. 1 Sulfonamide dimers and molecular packing in the crystal structures of CMSH-I and CMSH-II polymorphs.

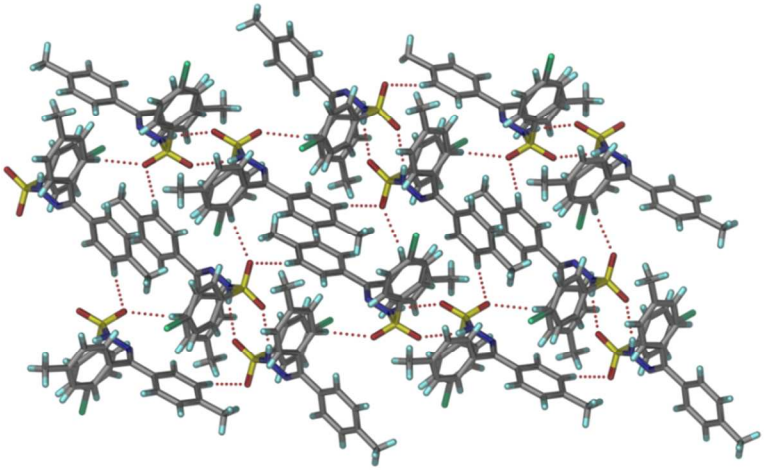


Fig. 2 Isostructural unit of CMSH-I formed by sulfonamide dimer tapes connected by C−H···O hydrogen bonds. This 2D structural unit is present in all the crystal structures.

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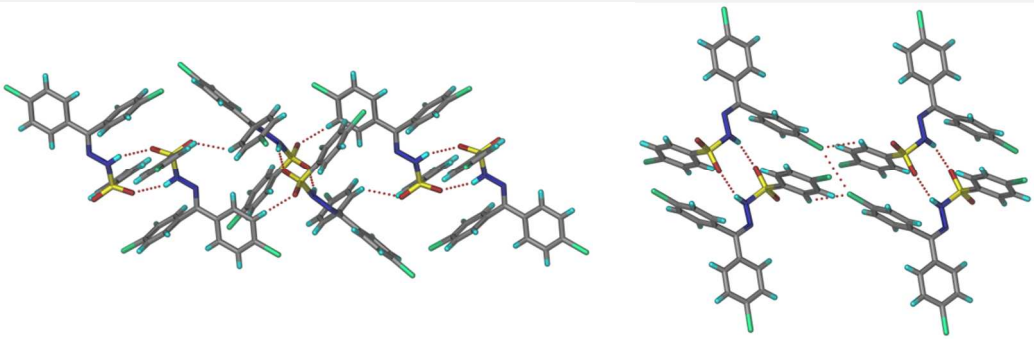
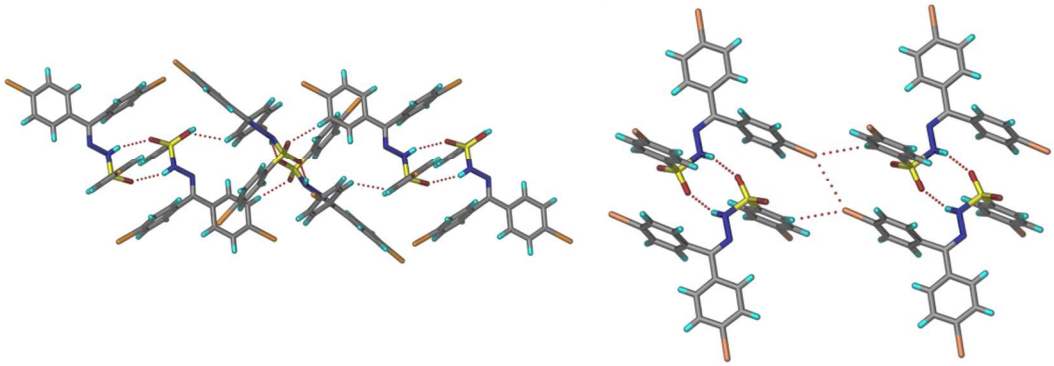
TCSH



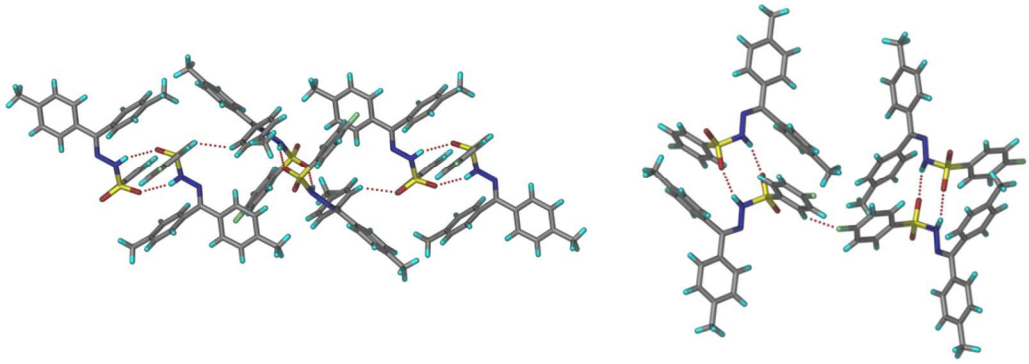
(a) (b)

TBSH



(a) (b)

FMSH



(a) (b)

MISH

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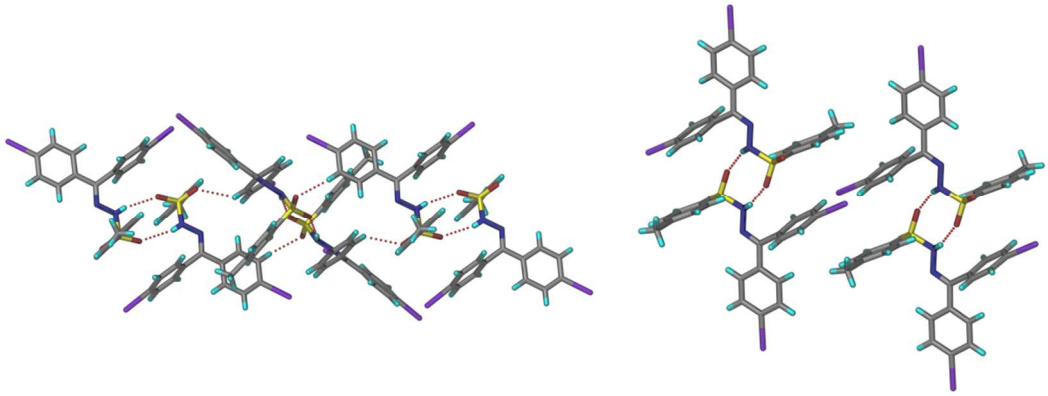

(a) (b)

Fig. 3 Crystal structures of TCSH, TBSH, FMSH and MISH. TCSH and TBSH are isomorphous to CMSH-I in *C*2/*c* space group, and FMSH and CMSH-II are isomorphous crystal pairs in *Pbca* space group. All these crystal structures are 2D isostructural while that of MISH has a different packing. (a) Sulfonamide dimers form 1D tape. (b) Symmetry related sulfonamide dimers.

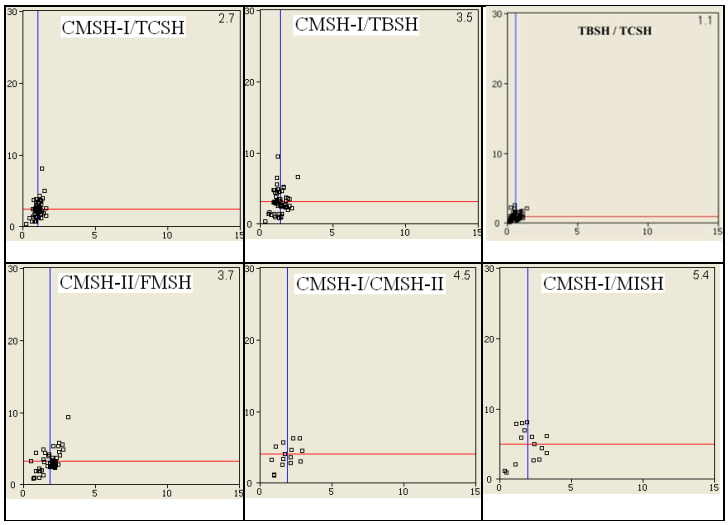

Fig. 4 Selected XPac plots of δ_p against δ_a (in °) show the degree of similarity in different crystal structures pairs of sulfonylhydrazones. The upper right corner of each plot indicates the value of *X*.

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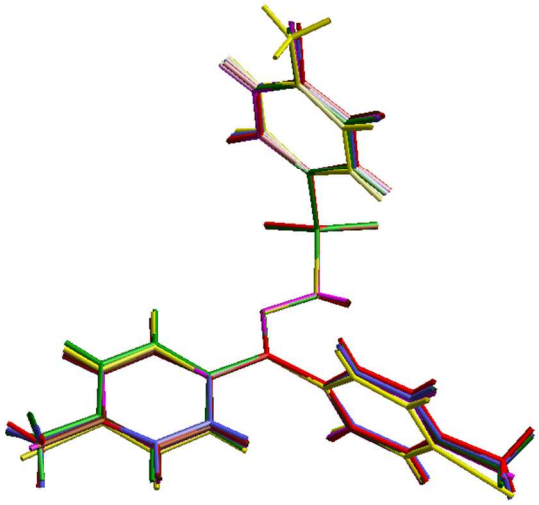

Fig. 5 Six conformers of five different molecules in crystal structures (CMSH is dimorphic). These conformers were overlaid by fixing the sulfonylhydrazone functional group portion (S−N−N−C). Color codes are CMSH-I = red, CMSH-II = green, TCSH = brown, TBSH = magenta, FMSH = blue, and MISH = yellow.

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Table 1 Crystallographic and refinement data.

	CMSH-I	**CMSH-II**	**TCSH**	**TBSH**	**FMSH**	**MISH**
Chemical formula	$C_{21}H_{19}ClN_2O_2S$	$C_{21}H_{19}ClN_2O_2S$	$C_{19}H_{13}Cl_3N_2O_2S$	$C_{19}H_{13}Br_3N_2O_2S$	$C_{21}H_{19}FN_2O_2S$	$C_{20}H_{16}I_2N_2O_2S$
Formula weight	398.89	398.89	439.72	573.10	382.44	602.21
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Monoclinic	Orthorhombic	Monoclinic
Space group	*C*2/*c*	*Pbca*	*C*2/*c*	*C*2/*c*	*Pbca*	$P2_1/c$
T/K	298(2)	298(2)	298(2)	298(2)	298(2)	298(2)
a/Å	22.305(2)	11.726(5)	22.655(4)	23.334(8)	11.939(2)	11.6335(16)
b/ Å	12.0112(12)	15.488(7)	11.6004(18)	11.594(4)	15.261(3)	11.6089(16)
c/ Å	15.3336(15)	22.317(10)	15.428(3)	15.600(5)	21.322(4)	15.843(2)
α/°	90	90	90	90	90	90
β/°	100.953(2)	90	101.926(3)	103.035(5)	90	96.670(2)
γ/°	90	90	90	90	90	90
Z	8	8	8	8	8	4
V/ $Å^3$	4033.1(7)	4053(3)	3967.2(11)	4112(2)	3884.9(12)	2125.1(5)
D_{calc}/g cm^{-3}	1.314	1.307	1.472	1.852	1.308	1.882
μ /mm^{-1}	0.311	0.309	0.584	6.005	0.194	3.075
Reflns. collected	20658	40435	15441	20670	33011	21633
Unique reflns.	3164	3097	2454	2569	3047	3678
R1[I > 2(I)]	0.0514	0.0451	0.0516	0.0399	0.0428	0.0390
wR2 (all)	0.1270	0.1141	0.1124	0.0836	0.1138	0.1003
Goodness-of-fit	1.039	1.050	1.016	1.003	1.048	1.064

CCDC No.	971250	971251	971255	971254	971252	971253
Structure refinement	SHELXL-97	SHELXL-97	SHELXL-97	SHELXL-97	SHELXL-97	SHELXL-97
Data collection	Bruker SMART	Bruker SMART	Bruker SMART	Bruker SMART	Bruker SMART	Bruker SMART

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Table 2 Hydrogen bond metrics for sulfonylhydrazones.

Interaction	H···A/ Å	D···A/ Å	∠D–H···A/º	Symmetry code
		CMSH-I		
N1−H1A···O2	2.05	2.985(2)	153.6	½–x, ½–y, –z
C13−H13···O1	2.52	3.272(2)	125.3	½–x, ½+y, ½–z
C16−H16···O1	2.51	3.589(3)	172.8	x, –y, ½+z
C3−H3 ···O1	2.48	2.888(3)	101.1	---[a]
		CMSH-II		
N1−H1A···O1	2.00	2.965(3)	159.3	1–x, –y,1–z
C3− H3···O1	2.44	3.451(3)	154.5	1–x, –y,1–z
C12−H12···O2	2.49	3.577(3)	173.7	½–x, –½+y, z
C15−H15···O2	2.50	3.364(3)	135.1	½+x, ½–y, 1–z
C5−H5···O2	2.46	2.880(3)	101.8	---[a]
		TCSH		
N1−H1A···O2	2.03	2.984(3)	157.7	½–x, ½–y, –z
C13−H13···O1	2.47	3.266(4)	129.5	½–x, ½+y, ½–z
C16−H16···O1	2.51	3.590(3)	174.0	x, –y, ½+z
C5−H5···O2	2.63	3.617(3)	151.1	½–x, ½–y, –z
C3−H3···O1	2.49	2.896(4)	101.0	---[a]
		TBSH		
N1−H1A···O1	2.03	2.986(4)	158.0	½–x, ½–y,1–z
C5−H5···O2	2.48	2.893(5)	101.1	---[a]
C13−H13···O1	2.47	3.266(4)	129.3	½–x, –½+y, ½–z
C16−H16···O1	2.51	3.590(4)	174.0	x, –y, ½–z
		FMSH		
N1−H1A···O1	1.99	2.955(2)	158.5	1–x,-y,1–z
C9−H9···O2	2.42	3.245(2)	131.5	–½+x, ½–y,1–z
C5−H5···O2	2.47	2.888(3)	101.4	---[a]
C3−H3···O1	2.56	3.568(2)	153.1	1–x, –y, 1–z
		MISH		
N1−H1A···O2	2.00	2.977(4)	162.6	2–x, 1–y, 1–z

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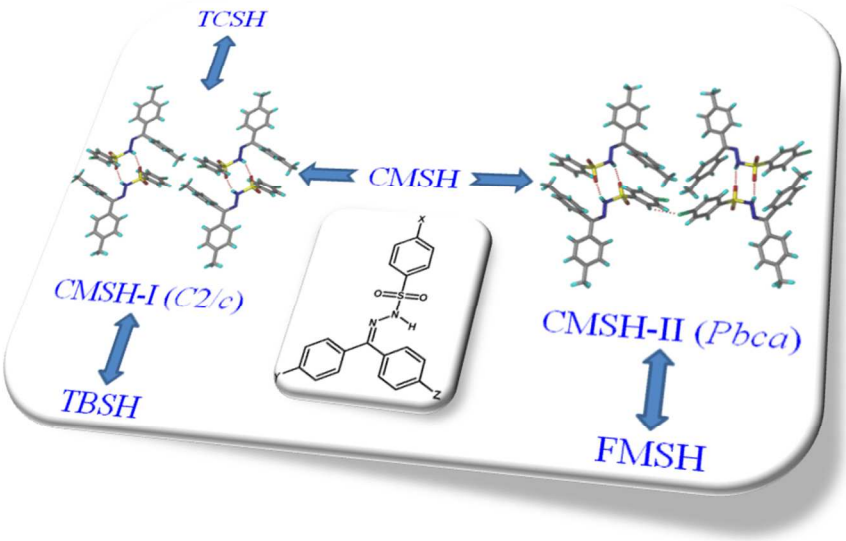
C3−H3···O1	2.50	2.906(6)	101.0	---[a]
C13−H13···O1	2.51	3.322(4)	130.2	2–x, –½+y, ½–z
C5−H5···O2	2.59	3.611(4)	155.7	2–x, 1–y, 1–z

[a] Intramolecular

TOC graphic



Five new methyl and halogen derivatives of triaryl sulfonylhydrazone were synthesized to understand polymorphism and isostructurality upon Cl−Me and inter-halogen exchange. Conformational rigidity and sulfonamide dimer synthon control the isostructurality in this family of crystal structures.