

# When two symmetrically independent molecules must be different: “Crystallization-induced diastereomerization” of chiral pinanyl sulfone<sup>†‡</sup>

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According to X-ray data, homochiral pinanyl sulfone crystallizes as an asymmetric dimer formed by pairwise H-bonds involving stereochemically different oxygen atoms of sulfonyl groups of molecules A and B. Thus, a pro-*R* atom is invoked for the construction of a relevant H-bond in molecule A, but in the case of molecule B only a pro-*S* atom is involved. Newly formed chiral sulfur atoms take opposite chirality in molecules A and B, while the configuration of the pinane skeleton remains unchanged. Such a stereochemical transformation is called “crystallization-induced diastereomerization”. The stability of the asymmetric dimer found in the crystal was evaluated within the framework of DFT (B3LYP, 6-31G (d,p)) and studied *via* IR spectroscopy in solution.

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## Introduction

The phenomenon of  $Z' > 1$  crystal structure formation has been extensively studied for the last few years.<sup>1–8</sup> The origins of this phenomenon are still largely unclear, though various reasons have been put forward to explain them. Thus, Desiraju<sup>2</sup> has recently suggested that some high  $Z'$  structures may be metastable relics of fast growing crystal nuclei. There have been a range of particularly significant studies in the past year alone.

Anderson<sup>3</sup> has shown that the tendency towards high  $Z'$  structures can be increased by introducing a competition between strongly directional hydrogen-bonded motifs and other packing forces (*e.g.*,  $\pi$ -stacking), which can frustrate molecules causing arrangements with large values of  $Z'$ .

The incidence of  $Z' > 1$  is known to be higher for chiral space groups than for the centrosymmetric space group. Structures with more than one independent molecule often show some pseudosymmetry where pairs of independent molecules are related by approximate  $-1$ ,  $2$ , or  $2_1$  operations. Chiral molecules cannot be related to each other by some of the more common symmetry operations, consequently they often exhibit pseudosymmetry.

Anderson<sup>6</sup> supposed that the likelihood of a chiral molecule forming a pseudo-centrosymmetric arrangement is greatly enhanced if the molecule is already predisposed to pack in a centrosymmetric manner, for example, if it contains a strongly directional supramolecular synthon with a preference for centrosymmetry. This idea has previously been represented generally as the “shape mimicry” concept by Whitesell and Davis.<sup>9</sup> It would therefore be expected that these species would still show a strong preference to form a centrosymmetric dimer, but that the packing of the molecules would necessarily have to adapt to allow formation of this dimer because of the absence of a crystallographic inversion center. Hence there should be a strong tendency for the compound to crystallize with more than one molecule in the asymmetric unit.

Until now, there have been a total of 5 strongly directional supramolecular synthons with a preference for centrosymmetry described, among which there are carboxylic acid dimers, amide dimers, and some others (Fig. 1).<sup>6</sup> For all the five synthons, a rather large number of chiral structures are distinguished, which crystallize with more than one independent molecule. At the same time, for all the five synthons, there are chiral structures that crystallize with one independent

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<sup>†</sup> Dedicated to the memory of Professor Evgenii Naumovich Klimovitskii, with whom we developed the original ideas which are expanded here.

<sup>‡</sup> Electronic supplementary information (ESI) available: Selected geometrical parameters of the compounds studied by X-ray structural analysis (Table S1), DFT calculations (Table S2), experimental and calculated frequencies of the  $\nu(\text{OH})$  IR bands (Table S3) and IR spectrum (Fig. S1). CCDC 970674. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ce42642d

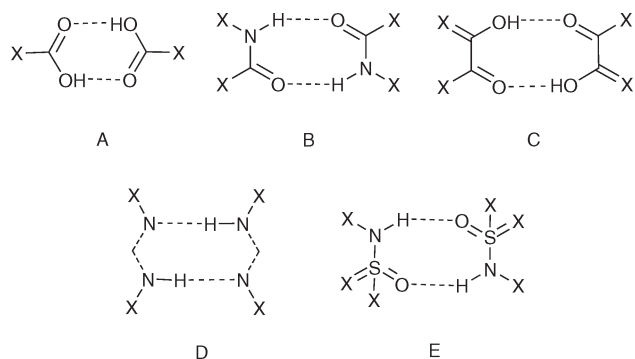


Fig. 1 The centrosymmetric hydrogen bond motifs,<sup>6</sup> X = any non-hydrogen atom. Dashed lines indicate hydrogen bonds.

molecule – this is possible in the case where the dimer is situated on a 2-fold rotation axis.

Regarding the differences between independent molecules in a crystal, in most cases the molecules A and B are in pseudosymmetric relations and, consequently, their difference is geometrically insignificant. So, in the common volume of publications on the issue of  $Z' > 1$ , the statement of J. Steed is widely known: “the second independent molecule is not significantly different from the first”.<sup>1</sup> The significantly fewer amount of  $Z' = 2$  structures, which are presented in the literature, are characterized by distinctions in kind between molecules A and B, which can consist of either conformation or (which is more uncommon) configuration of one or more stereogenic centers of a molecule, which are cases of co-crystallization of diastereomers.<sup>10–17</sup>

Previously, we have discovered and studied the stable co-crystallization of diastereomeric (by a sulfur atom) pinanyl sulfoxides.<sup>17</sup> These compounds are crystallized as H-bonded dimers, constructed by forming a new centrosymmetrical stereogenic sulfur-containing synthon F (Fig. 2).

In this paper we present an unexpected  $Z' = 2$  crystallization type of homochiral pinanyl sulfone, associated with the formation of a similar supramolecular synthon.

We analyze the reasons of inclusion of an “additional” molecule into a cell and answer the question: how does the second independent molecule significantly differ to the first one?

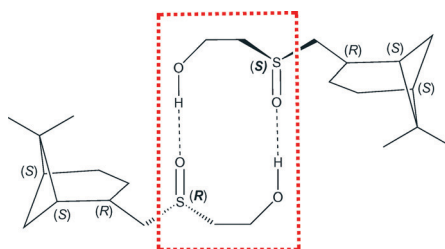
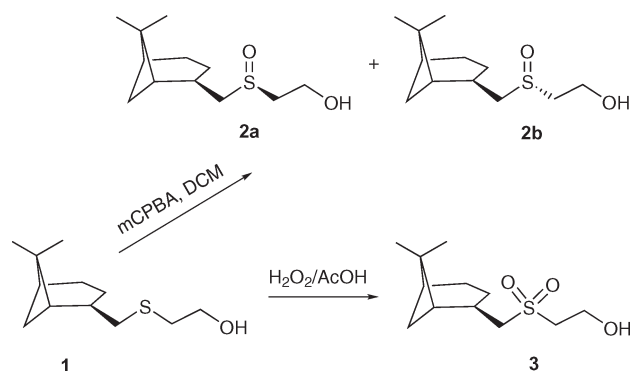


Fig. 2 The H-bonded dimer, formed by diastereomeric pinanyl sulfoxides.<sup>17</sup> Dashed lines indicate hydrogen bonds and the red dashed box shows the supramolecular synthon F.

## Results and discussion

In a previous publication we have described the phenomenon of stable co-crystallization of diastereomeric pinanyl sulfoxides **2a** and **2b**, obtained by the oxidation of sulfide **1** by the use of *m*-chloroperbenzoic acid (Scheme 1).<sup>17</sup> As a minor product in this reaction, the corresponding sulfone **3** is formed, which can be also easily prepared from sulfide **1** according to a known method using hydrogen peroxide in combination with acetic acid.



Scheme 1 Preparation of compounds **2** and **3**.

### Crystal structures

For the co-crystal of diastereomeric pinanyl sulfoxides **2a** and **2b**, we have found two modifications – triclinic and monoclinic – wherein in both cases the compound is presented by the hydrogen-bonded dimer (Fig. 3).

For the diastereomeric molecules **2a** and **2b**, different conformations along the bond C<sup>2</sup>–C<sup>10</sup> were observed: a *trans* conformation around C<sup>10</sup>–S<sup>1</sup> and C<sup>2</sup>–C<sup>3</sup> bonds takes place for

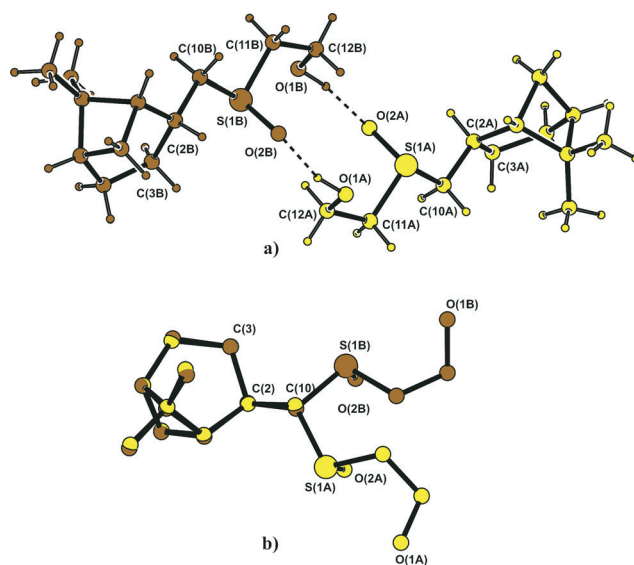


Fig. 3 (a) The hydrogen-bonded dimer of **2a** + **2b**; (b) the overlap of molecules A and B in the crystal structure of **2**.

the isomeric molecule **2a** bearing an  $R_S$  configuration of the stereogenic sulfur atom, at the same time a  $C^2-C^1$  bond of a bicyclic skeleton adopts a *trans* orientation relative to the  $C^{10}-S^1$  bond in **2b** with a  $S_S$  configuration of the heteroatom. Oxygen atoms of both sulfinyl groups are placed far away from the carbocyclic fragment to avoid unfavorable steric contacts (see Table S1†).

Thus, in the co-crystals of diastereomeric sulfoxides, the two independent molecules A and B have significantly different conformations, which is generally typical for isomeric molecules.

Surprisingly, we have found a similar H-bonded dimer, formed by independent molecules A and B, differing in conformation along the key bond  $C^2-C^{10}$  in the crystal structure of pinanyl sulfone **3**, where all sulfone molecules are identical in stereochemical aspect. What is the reason of inclusion of an “extra” molecule into the unit cell in this case?

In order to answer this question, we will examine the structure of dimer **3** (Fig. 4). This situation resembles that of the parent sulfoxide **2**, featuring the presence of  $S=O\cdots H-O$  interactions in a 12-membered cycle. The conformation around the  $C^2-C^{10}$  bond for molecules A and B is different again, as it was for sulfoxide **2**. It is obvious that the tendency of the oxygen atoms invoked in H-bonding (more encumbered) is to occupy a *transoid* position relative to the *gem*-dimethyl fragment of the pinane skeleton. A *gauche*-form of the  $-S^1C^{11}C^{12}O^1-$  fragment in **3**, similar to **2**, was also established, while a *gauche*-conformation around the  $S^1-C^{11}$  bond is typical for the sulfone molecule only. In dimer **3**, H-bonds between the sulfone molecules are not identical: the  $O^{1A}-H^{1A}\cdots O^{3B}$  bond is significantly shorter than that of  $O^{1B}-H^{1B}\cdots O^{2A}$  (Table 1). Most probably, the  $S^{1B}=O^{3B}$  bond appeared to be enlarged in comparison with  $S^{1B}=O^{2B}$  and  $S^{1A}=O^{2A}$  as a result. An analogous situation was established for  $O^{1A}-C^{12A}$  and  $O^{1B}-C^{12B}$  bonds (Table S1†).

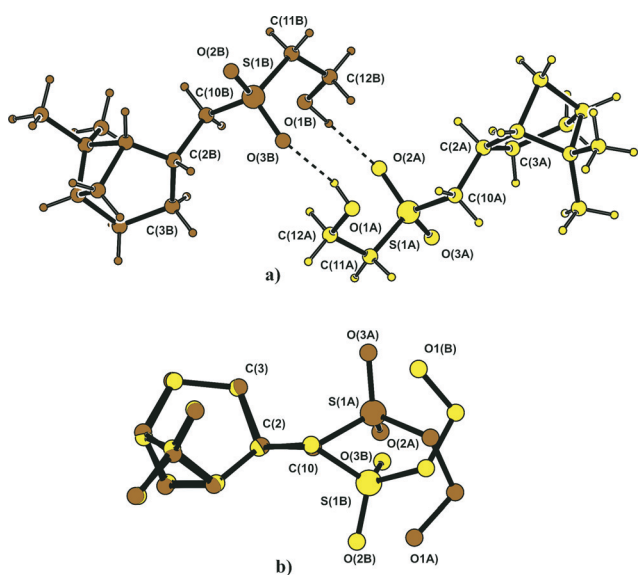


Fig. 4 (a) The hydrogen-bonded dimer of **3**; (b) the overlap of molecules A and B in the crystal structure of **3**.

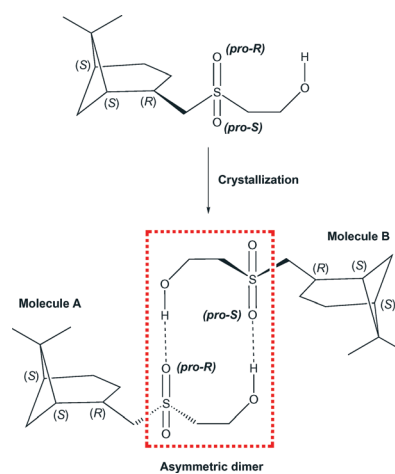
Table 1 Hydrogen bonds in the crystal structure of **3**

Bond	D-H, Å	H $\cdots$ A, Å	D $\cdots$ A, Å	$\angle$ D-H $\cdots$ A, °
$O^{1A}-H^{1A}\cdots O^{3B}$	0.90(6)	1.91(5)	2.781(5)	165(5)
$O^{1B}-H^{1B}\cdots O^{2A}$	0.99(3)	1.85(3)	2.826(5)	169(2)

Stereochemical representation seems to be somewhat delicate and deserves a special comment. The sulfur atom in sulfone **3** is not stereogenic as in isomeric sulfoxide **2**. Molecules of isolated sulfone **3** are stereochemically homogeneous (homochiral), bearing three stereogenic carbons  $C^1$ ,  $C^2$  and  $C^5$  incorporated into a pinane moiety and an acyclic achiral fragment  $HOCH_2CH_2SO_2-$  as a substituent. Crystal phase analysis of the molecule under consideration prompted us to propose that the geminal oxygen atoms of both sulfone groups incorporated in the cyclic dimer molecule may be referred to as heterotopic (as C in XABC<sub>2</sub>). Consequently, the descriptors *pro-R* and *pro-S* can be used. Thus, the  $O^2$  *pro-R* atom is invoked for construction of a relevant H-bond in molecule A, but in the case of molecule B, only the *pro-S*  $O^3$  atom is involved. There is reason to believe that the 12-membered cycles of both **2** and **3** are formed by  $-SO(O)_{n=0,1}CH_2CH_2OH$  moieties having an opposite configuration. If this is the case as we have encountered with heterochiral dimer **3**, the sulfur atom should be referred to as stereogenic.

The fundamental difference between **2** and **3** is based on the stereochemistry of a  $\beta$ -hydroxy sulfoxide (sulfone) involved in the dimerization process. Optically active diastereomeric sulfoxides **2a** and **2b** serve as a starting material. Dimer **3** is formed from two identical molecules of sulfone and diastereomerization takes place at the stage of the 12-membered H-bonded cycle building (Scheme 2).

It should be noted that the dimer of sulfone **3**, due to its stereochemical features, is not simply homochiral but also fully asymmetric. Since placement on the 2-fold rotation axis, which is the only possibility of placement in the crystal without including an additional molecule into the unit cell



Scheme 2 Crystallization-induced diastereomerization of pinanyl sulfone **3**. The red dashed box shows the supramolecular synthon F.

available to the typical homochiral dimers, is not available for it, it invariably forms a  $Z' \geq 2$  crystal. Despite the features of crystallization of homochiral dimers having attracted attention previously (see Introduction), associates of this type have not been described in the literature before.

At the same time, a search *via* CSD<sup>18</sup> allowed us to find similar asymmetric dimers of five chiral sulfonamides (refcodes ATOVIO, AXAGOV, CAZFEP, NAKNAO, and NISBIB). Crystals of these compounds contain centrosymmetrical synthon F (see Introduction). The scheme of formation of such dimers is similar to 3: two crystallographically independent molecules involved stereochemically nonequivalent oxygen atoms of a sulfone group in hydrogen binding. It is notable that in the 5 above mentioned cases, the crystallographically independent molecules are found in crystals in different conformations, which is typical for different diastereomeric forms.

We suggest to use the new term “crystallization-induced diastereomerization” for the description of the stereochemical process leading to the formation of sulfone dimer 3 and the five above mentioned sulfones (in contrast to the conventional term of the modern literature CIDT – “crystallization-induced diastereomeric transformation” – for the designation of the inverse process – the compound crystallization of equilibrating diastereomers in only a diastereomeric form).<sup>19</sup>

In addition to asymmetric homochiral dimer research, we have attempted to obtain associates on the basis of camphanyl sulfone prepared from (+)-camphene – in other words, we have attempted to replace the chiral fragment while keeping the centrosymmetric synthon. However, due to synthetic difficulties,<sup>20</sup> we obtained a racemic camphanyl sulfone, which in the crystal structure forms a common centrosymmetric dimer (containing synthon F as well, see Fig. 5).

We also took an interest in how stable the fully asymmetric dimer is, which we have found in the pinanyl sulfone crystal.

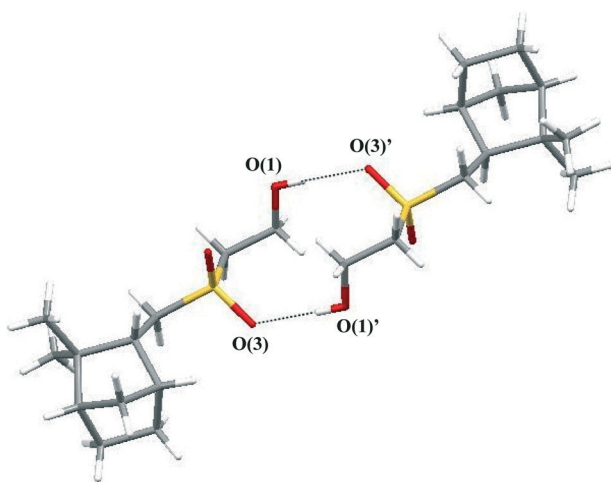


Fig. 5 Centrosymmetric dimer of camphanyl sulfone, from our previous work,<sup>20</sup> space group  $P\bar{1}$ ,  $Z' = 1$ .

## DFT calculations

We have calculated a dimer and various types of monomers with DFT (B3LYP, 6-31G (d,p)).

The geometry of the dimer is reproduced quite well within quantum chemistry (Fig. 6). It can be noted that nonequivalence of H-bonds remains in the gas phase as well (because of the asymmetric structure of the dimer): distance  $O^{1A} \cdots O^{3B}$  is 2.79 Å, and distance  $O^{1B} \cdots O^{2A}$  is 2.81 Å.

Regarding monomers, for the sulfone molecule we have optimized four various forms (Fig. 6). According to the calculations, the conformations of molecules A and B, observed in crystal structures, are stable in the isolated state as well – these are the forms **mon1** and **mon2**. These two forms are stabilized by two C–H $\cdots$ O interactions (1 and 2 for **mon1**, and 3 and 4 for **mon2** in Fig. 6). The same interactions are typical for the optimized conformation of dimer 3 (parameters of C–H $\cdots$ O interactions are given in Table S2<sup>†</sup>). Furthermore, it is possible to transform structures **mon1** and **mon2** into two diastereomeric forms of the monomer, which are stabilized by an intramolecular classical hydrogen bond by means of either a  $O^2$  atom (**mon1\_Hbond**) or a  $O^3$  atom (**mon2\_Hbond**). Intramolecular H-bonds in monomeric structures are characterized by weaker parameters as compared to those in the cyclic dimer, so distance  $O^1 \cdots O^2$  is 2.87 Å in **mon1\_Hbond** and distance  $O^1 \cdots O^3$  is 2.91 Å in **mon2\_Hbond**. The energy characteristics of dimer and monomer forms are compared in Table 2. It is notable that the forms **mon1** and **mon2** are not at a big disadvantage in energy compared to monomers **mon1\_Hbond** and

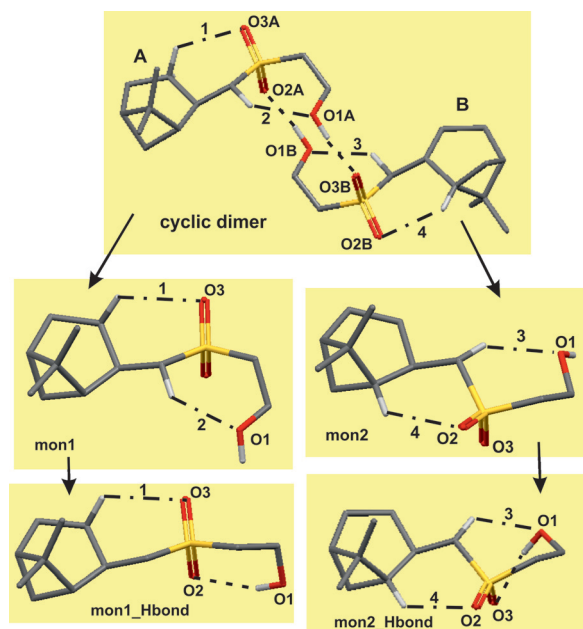


Fig. 6 The optimized geometry of dimer 3 (top) and stable conformations of the monomers (bottom), O–H $\cdots$ O interactions are marked with dotted lines, C–H $\cdots$ O interactions are marked with chain lines, numbers 1–4 mean that the C–H $\cdots$ O interactions were observed both in the cyclic dimer and in the monomers. Only the hydrogen atoms involved in O–H $\cdots$ O and C–H $\cdots$ O interactions are shown.



**Table 2** The relative Gibbs free energies of pinanyl sulfone monomers *versus* the most stable conformation and dimerization energy, kcal mol<sup>-1</sup>

	Cyclic dimer <sup>a</sup>	mon1	mon2	mon1_Hbond	mon2_Hbond
$\Delta G_{298}$ , kcal mol <sup>-1</sup>	-2.66	0.92	1.40	0	0.49

$$^a \Delta G_{298}\text{dim} = G_{\text{dim}} - G_{\text{mon1}} - G_{\text{mon2}}$$

**mon2\_Hbond.** This suggests that the former coexists in solution with the latter. It does facilitate the dimerization significantly, because in forms **mon1** and **mon2** the molecules of sulfone are conformationally pre-organized for the formation of the cyclic asymmetric dimer.

### IR study

To find out whether the dimers found in crystal structures can also exist in a solution of sulfone, IR spectra of sulfone **3** in the crystal structure and in CCl<sub>4</sub> solutions were studied.

The vibrational frequencies and IR intensities computed by the B3LYP/6-31G (d,p) method for OH stretching bands  $\nu(\text{OH})$  of different forms of associates are in good agreement with the observed values.

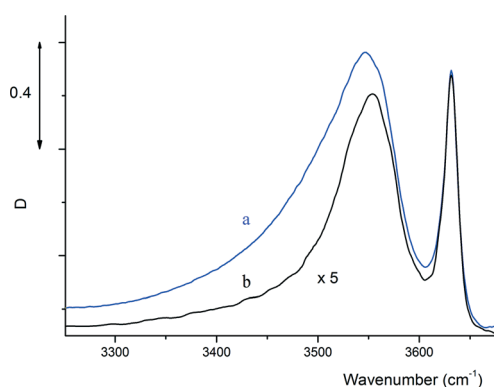
In the IR spectrum of the sulfone **3** crystalline phase, a symmetrical contour centered at 3472 cm<sup>-1</sup> ( $\nu(\text{OH})_{\text{ass}}$ ) is observed (Fig. S1<sup>†</sup>).

For an estimation, using IR spectroscopy, of the stability of dimer **3**, the behavior of the pinanyl sulfone was studied in CCl<sub>4</sub> solutions at concentrations of 10<sup>-2</sup> mol L<sup>-1</sup> and 10<sup>-3</sup> mol L<sup>-1</sup> (see Fig. 7).

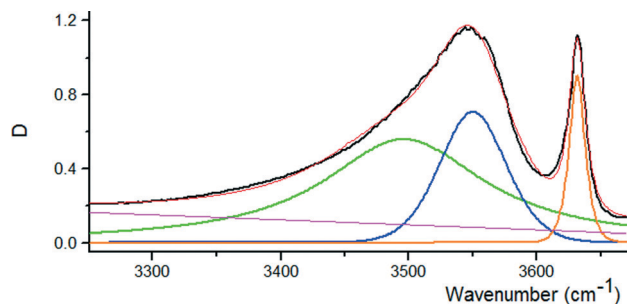
A curve fitting procedure can be applied to calculate quantitatively the area of each individual component representing the Gaussian-Lorentz function. Fig. 8 shows the result of the fitting procedure for a spectrum of sulfone in a CCl<sub>4</sub> solution at a concentration of 10<sup>-2</sup> mol L<sup>-1</sup>, which was obtained using the OPUS software.

Dilution from 10<sup>-2</sup> to 10<sup>-3</sup> mol L<sup>-1</sup> causes a decrease of its half-width and a shift of its maximum to a high frequency region as a result of the complex associates being partially destroyed.

IR spectra of the CCl<sub>4</sub> solution at a concentration of 10<sup>-2</sup> mol L<sup>-1</sup> also exhibit a band of free OH vibration ( $\nu(\text{OH})_{\text{free}}$ )



**Fig. 7** The  $\nu(\text{OH})_{\text{ass}}$  contour in the IR spectra of sulfone **3** in CCl<sub>4</sub> solutions at concentrations (a) 10<sup>-2</sup> mol L<sup>-1</sup> and (b) 10<sup>-3</sup> mol L<sup>-1</sup>.



**Fig. 8** Hydroxyl absorption curve fitting procedure for a 10<sup>-2</sup> mol L<sup>-1</sup> CCl<sub>4</sub> solution of sulfone **3**.

at 3631 cm<sup>-1</sup>, and the broad band in the 3200–3600 cm<sup>-1</sup> range originated from associated OH groups,  $\nu(\text{OH})_{\text{ass}}$ .

The comparison of the solid state spectrum of dimer **3** with those of solutions demonstrates, as expected, a more complicated picture due to the appearance of associates with different hydrogen bond energies. Along with the cyclic dimer possessing two intermolecular hydrogen bonds and the monomer bearing no hydrogen bond and having a free OH group, two associates can be expected in addition: a linear dimer (or more high-associated structures) formed by one intermolecular hydrogen bond and a monomer with an intramolecular hydrogen bond. An experimental contour centered at 3631 cm<sup>-1</sup> may be attributed to  $\nu(\text{OH})_{\text{free}}$  of the monomer forms **mon1** and **mon2**.<sup>18</sup>

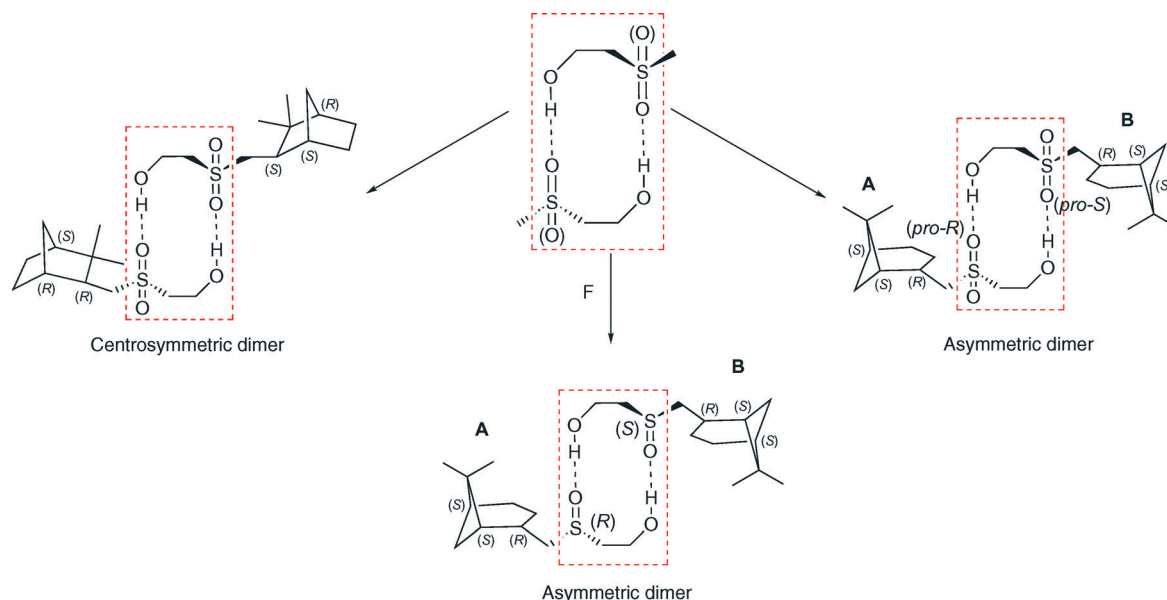
Hydroxyl absorption curves (10<sup>-2</sup> and 10<sup>-3</sup> mol L<sup>-1</sup>) were also subjected to deconvolution. It appears that the cyclic dimer still persists in the 10<sup>-2</sup> mol L<sup>-1</sup> CCl<sub>4</sub> solution [ $\nu_{\text{OH}}$  (dimer) 3496 cm<sup>-1</sup>] along with a new band at 3550 cm<sup>-1</sup>, whereas the band that has been adopted by the linear dimer with an intermolecular hydrogen bond disappeared. The 10<sup>-3</sup> mol L<sup>-1</sup> spectrum of **3** displays both components again, though a drop in intensity of the low frequency band takes place as a result of the cyclic dimer diminishing.

The hydroxyl absorption at 3550 cm<sup>-1</sup> seems to originate either from the linear dimer or the monomer with an intramolecular H-bond. This band is most likely attributed to the linear dimer based on the good agreement with the calculation data (see Table S3<sup>†</sup>).

Thus, we have established, that the non-typical asymmetric dimer, detected by X-ray crystallography in the crystal phase, exists in solutions of various concentrations as well as the other associates.

## Conclusions

For the first time, the stereochemical transformation accompanying the crystallization of homochiral pinanyl sulfone,



**Scheme 3** New centrosymmetric stereogenic sulfur-containing synthon F in chiral and racemic crystals.

and also some chiral sulfonamides, is found and studied. We suggest to use a new term – “crystallization-induced diastereomerization” – to designate this phenomenon. From the viewpoint of crystal engineering, this phenomenon is interesting as it invariably results in a  $Z' = 2$  structure, in which molecules A and B are essentially different in their conformations as they represent two diastereomeric forms.

From a supramolecular chemistry point of view, we can speak of the finding of a new robust and reproducible synthon F (Scheme 3). The tendency to form such a synthon is caused by the fragment structure, most critical for its hydrogen bonding. Namely, the chirality of a sulfoxide sulfur atom (or the prochirality of the sulfone sulfur atom), combined with the fixed *gauche*-conformation of the  $-\text{SO}(\text{O})-\text{CH}_2-\text{CH}_2-\text{OH}$  fragment, determines the specific spatial organization of the group in general, for which the formation of a cyclic dimer with a group of the contrary configuration is preferable. The “finished”  $-\text{SO}(\text{O})-\text{CH}_2-\text{CH}_2-\text{OH}$  groups complying with this condition contain the isomeric molecules of the sulfoxides. For sulfone, the problem of choosing geometrically corresponding fragments is solved by involvement of stereochemically different (diastereotopic) oxygen atoms from two different molecules in the interactions.

From a stereochemical point of view, an “*enantiophilic*” fragment was discovered – a  $\beta$ -hydroxy sulfoxide (sulfone) group, capable of recognizing its mirror image both in an explicit (a racemic camphanyl sulfone) and concealed state (a diastereomeric pair of sulfoxides and a homochiral pinanyl sulfone).

## Experimental

### General

For isolation and purification of the reaction products the method of adsorption chromatography on silica gel L (100/160  $\mu$ )

was applied. As eluents, methylene chloride–acetone mixtures were used. The reaction progress and the quality of the separation of the reaction mixtures were monitored by TLC on Silufol plates and developers  $\text{I}_2$  and ethanol–sulfuric acid–anisaldehyde mixture (90:5:5) were used. To remove water and purify the solvents we used known techniques described in the literature.<sup>21</sup>

NMR spectra were obtained on a Bruker Avance instrument (Germany) with the operating frequencies 400.13 and 100.61 MHz for  $^1\text{H}$  and  $^{13}\text{C}$  nuclei, respectively, and internal reference TMS was used.

Melting points of substances were determined on a Koeffler apparatus and were uncorrected.

The infrared spectra were recorded on a FTIR Bruker Vector 22 spectrometer ( $400\text{--}4000\text{ cm}^{-1}$ ). The interferograms were collected with a resolution of  $2\text{ cm}^{-1}$ , 128 scans, and Fourier transformed using a Blackman–Harris apodization function. We have analyzed the spectra of solid (crystal) samples and solutions in  $\text{CCl}_4$ . For registration of the spectra of the solutions,  $\text{CaF}_2$  cells were used with different spacers (0.1–50.0 mm) to achieve the best signal/noise ratio. The concentrations of compounds varied from 0.01 to 0.2 M.

### Gaussian curve-fitting

Spectral data were processed with the OPUS-7.0 software (Bruker Optik GmbH) using spectra averaging, baseline correction and peak picking techniques. The curve-fitting was performed to acquire single Gaussian–Lorentz function components of overlapping bands.

### X-Ray diffraction‡

The X-ray diffraction data for the crystals of 3 were collected on a Smart Apex II automatic diffractometer (Bruker, Germany) using graphite monochromated radiation  $\text{MoK}\alpha$  ( $\lambda$  0.71073),

$T = 293$  K. Details of the crystal data, data collection, and refinement are given in Table 3. The structures were solved by direct method using the SHELXS<sup>22</sup> program and refined by full-matrix least-squares using the SHELXL97<sup>23</sup> program. All the non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H(C) atoms were constrained as riding atoms, with C–H set to 0.95 Å. The hydroxyl H atoms were located from a difference Fourier map and refined isotropically in the final stages of refinement. All figures were made using the program PLATON.<sup>24</sup> Crystallographic data (excluding structure factors) for structure 3 reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as the supplementary publication number CCDC 970674.

### DFT calculations

Geometry optimizations and vibrational frequencies were carried out at a basic DFT level using the B3LYP<sup>25,26</sup> 6-31G(d,p) basis set available in the Gaussian-03 package.<sup>27</sup> These values were corrected using scale factor 0.9613 [DFT]<sup>28</sup> and the corrected frequencies and proposed assignments are summarized in Table S3† along with the observed values. These values indicate that there is a close agreement between the calculated values and observed values.

### Experimental procedure and spectral characterization of the synthesized compound

The oxidation of sulfide 1 with peracetic acid:<sup>29</sup> to a solution of sulfide 1 (20 mmol) in 15 mL of glacial acetic acid, 27% hydrogen peroxide (48 mmol) was added dropwise. The reaction mixture was kept at room temperature for 24 h, then diluted with water and extracted with ether. The ether extract was washed with saturated aqueous K<sub>2</sub>CO<sub>3</sub> and water until neutral, and dried with MgSO<sub>4</sub>. The crystalline mass was filtered off, the residue was concentrated in a vacuum and

the compound was purified by column chromatography. Sulfone 3 is a transparent thin plate, recrystallized from a mixture of petroleum ether and ethyl acetate (1 : 1).

2-(((1*S*,2*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-yl)methyl)sulfonyl)ethanol (3). Yield 81%; mp 68.5–69 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  1.05 (s, 3H, H-9), 1.24 (s, 3H, H-8), 1.07 (m, 1H, H-7), 1.72 (m, 1H, H-3), 1.72 (m, 1H, H-3), 1.88–2.08 (m, 4H, H-1, H-2, 2H-4), 2.42 (m, 1H, H-5), 2.61 (br s, 1H, OH), 3.18–3.31 (m, 2H, H-10), 3.21 (m, 2H, SO<sub>2</sub>CH<sub>2</sub>), 4.16 (m, 2H, CH<sub>2</sub>OH); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  22.85 (C-3), 23.81 (C-9), 26.57 (C-4), 28.29 (C-8), 33.25 (C-7), 35.04 (C-5), 39.11 (C-6), 41.34 (C-1), 47.45 (C-2), 56.40 (C-10), 57.11 (CH<sub>2</sub>OH), 62.78 (SO<sub>2</sub>CH<sub>2</sub>).

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**Table 3** Crystallographic data and parameters of the X-ray diffraction experiment

Compound reference	3
Chemical formula	C <sub>12</sub> H <sub>22</sub> O <sub>3</sub> S
Formula mass	246.36
Crystal system	Monoclinic
$a/\text{Å}$	13.982(3)
$b/\text{Å}$	6.474(2)
$c/\text{Å}$	15.002(4)
$\beta/^\circ$	100.430(3)
Unit cell volume/Å <sup>3</sup>	1335.4(5)
Temperature/K	296(2)
Space group	$P2_1$
No. of formula units per unit cell, $Z$	4
Absorption coefficient, $\mu/\text{mm}^{-1}$	0.234
No. of reflections measured	11 312
No. of independent reflections	5957
$R_{\text{int}}$	0.0524
Final $R_1$ values ( $I > 2\sigma(I)$ )	0.0601
Final $wR(F^2)$ values ( $I > 2\sigma(I)$ )	0.1446
Final $R_1$ values (all data)	0.1310
Final $wR(F^2)$ values (all data)	0.1743
Flack parameter	0.0(1)

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