

Enantiomeric Self-Resolution through Dimethylsulfoxide Complexation

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Abstract. The alicyclic diol **2** is known to adopt five different types of crystal lattice: the pure solid, cocrystalline compounds with water or certain phenols, and two different types of lattice inclusion system (helical tubulates and ellipsoidal clathrates). Self-resolution only occurs on forming the helical tubulate inclusion compounds. Its close analogue 2,7-bis(trifluoromethyl)tricyclo[4.3.1.1^{3,8}]undecane-*syn*-2,*syn*-7-diol **4** was synthesised to examine the influence of replacing CH₃- by CF₃-groups. It no longer forms lattice inclusion compounds but does form a cocrystalline solid with dimethyl sulfoxide (DMSO). Crystal structures of **4** [C₁₃H₁₆O₂F₆, *P*2₁/*c*, *a* 7.8636(6), *b* 13.1020(7), *c* 25.319(2) Å, β 101.526(4)°, *Z* 8, *R* 0.044] and (**4**)₂·DMSO [(C₁₃H₁₆O₂F₆)₂·C₂H₆SO, *P*2₁2₁2₁, *a* 7.249(1), *b* 16.064(3), *c* 25.347(4) Å, *Z* 4, *R* 0.033] were determined. In solid diol **4** the molecules are linked through (—O—H)₄ rings to produce layers of chirally pure enantiomers but the net crystal structure, which comprises layers of alternating handedness, is achiral. In contrast, complexation of **4** with DMSO by means of two —O—H ··· O=S hydrogen bonds induces complete enantiomeric self-resolution.

Key words: hydrogen bonding, conglomerates, self-resolution, co-crystals, fluorine interactions, helical tubulands.

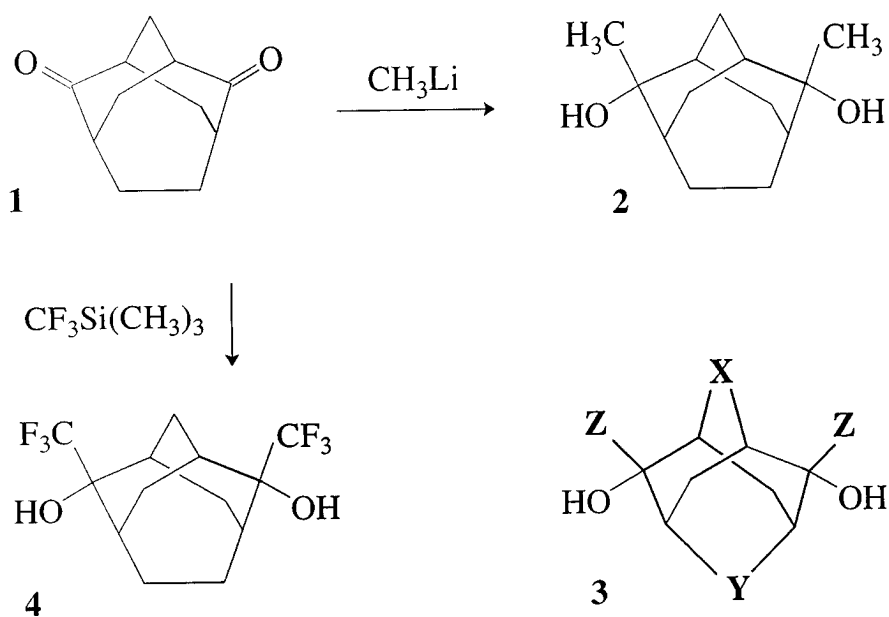
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1. Introduction

Reaction of the alicyclic diketone **1** with methyl lithium yields the apparently simple molecule 2,7-dimethyltricyclo[4.3.1.1^{3,8}]undecane-*syn*-2,*syn*-7-diol **2** which, however, exhibits especially versatile solid state behaviour [1]. Currently, five distinct types of hydrogen bonded crystalline lattices involving **2** are known:

- (i) Pure **2**, a layer structure in space group *P*2₁/*c* [2].
- (ii) The hemihydrate (**2**)₂·(H₂O), a layer structure in space group *Pbca* [3].
- (iii) The ellipsoidal clathrate inclusion lattice, a doubly interpenetrating network in space group *I*4₁/*acd*, formed when **2** is crystallised from smaller organic guests [4,5].

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- (iv) The helical tubuland inclusion lattice, a network lattice in space group $P3_121$ (or $P3_221$), formed when **2** is crystallised from larger organic guests [4,5].
- (v) Co-crystalline diol-phenol solids, layer structures in space group $P2_1/c$, formed when **2** is crystallised from some small phenols [6].

All of these structural types, except (iv), contain both diol enantiomers. In contrast, formation of the helical tubuland lattice (iv) results in formation of a conglomerate whereby spontaneous self-resolution has taken place during crystallisation [7,8]. These five structural types have been compared and contrasted in a recent review article [1].

In previous papers we have explored the effect of systematic change on the general diol structure **3** where we have varied the sizes of the interconnecting molecular bridges **X** and **Y**. Many of the resulting diols also show lattice inclusion behaviour and we have been able to propose a number of structural rules allowing us to predict new examples with a high degree of success [9]. In contrast, our attempts to retain inclusion properties by changing the substituents **Z** from methyl to C_2H_5 - or H-groups have all failed [1]. This present paper describes the preparation of diol **4**, the bis(trifluoromethyl) analogue of **2**, and its unusual solid state behaviour.

2. Experimental

2.1. SYNTHETIC DESIGN

To test the effect of varying the substituents **Z**, diketone **1** was chosen as the key intermediate since it was known that alkylations took place with high selectivity on the more exposed methano bridge side of the carbonyl groups. In addition, as outlined above, diol **2** has a rich inclusion chemistry which might well be shared by a new analogue.

Trifluoromethyl substituents were chosen since they were the smallest possible one-carbon groups with identical symmetry to the methyl groups present in **2**. Fluorine atoms are larger than hydrogens (van der Waals radii 1.47 and 1.20 Å respectively) but this effect is not large. Furthermore, although fluorine is highly electronegative, C—F groups rarely interact with O—H groups if cooperative H—O···H—O···H—O hydrogen bonding arrangements are possible [10,11]. Indeed, the electron withdrawing CF₃-groups should make the hydroxyl protons stronger donors in **4** than in **2** [12]. Therefore we did not expect that the trifluoromethyl groups would disrupt any hydroxy hydrogen bonding arrangements. It is known that (trifluoromethyl)trimethylsilane [13] behaves as a trifluoromethide equivalent in reactions with ketones [14,15] and hence this was the ideal reagent for conversion of **1** into the target molecule **4**.

2.2. PREPARATIVE WORK

¹H (300 MHz) and ¹³C (75 MHz) NMR spectra were recorded using a Bruker ACF300 instrument and are reported as chemical shifts (δ) relative to SiMe₄. The substitution of carbon atoms was determined by the DEPT procedure. Melting points were determined with a Kofler instrument and are uncorrected. IR data were recorded on a Perkin Elmer 298 spectrophotometer, and MS (electron impact) data on a VG Quattro triple quadrupole instrument by Dr. J.J. Brophy. The combustion analysis was carried out at UNSW by Dr. H.P. Pham.

2,7-Bis(trifluoromethyl)tricyclo[4.3.1.1^{3,8}]undecane-syn-2,syn-7-diol 4

Tricyclo[4.3.1.1^{3,8}]undecane-2,7-dione **1** [16] (0.30 g, 1.68 mmol) was added with stirring to a solution of (trifluoromethyl)trimethylsilane [13] (0.98 g, 6.9 mmol) in dry tetrahydrofuran (30 mL) under Ar using anhydrous conditions. The solution was cooled in ice and tetrabutylammonium fluoride hydrate catalyst (60 mg) added. After 20 min. the solution had turned light brown, and after a further 4 h a slight excess of aq. HCl (3 M) was added and then stirring continued overnight. The mixture was transferred to a separating funnel using water and diethyl ether. Organic material was extracted (ether) and the combined extracts dried (MgSO₄). Evaporation of solvent from the filtrate gave a yellow solid which was recrystallised from benzene to give diol **4** (0.35 g, 66%), m.p. 173–176 °C, as colourless

crystals. [Found: C, 49.29; H, 5.17. $C_{13}H_{16}F_6O_2$ requires C, 49.06; H, 5.07%]. ν_{\max} . (paraffin mull) 3545m, 3480s, 3460s, 1285m, 1220m, 1205m, 1170m, 1160s, 1095m, 1080m, 1065m, 970s, 955m, 730m cm^{-1} . m/z (>20%) 300 (M-18, 20%), 282 (26), 249 (72), 231 (21), 213 (36), 159 (38), 148 (39), 147 (83), 141 (23), 136 (23), 127 (41), 91 (36), 79 (48), 77 (39), 69 (58), 68 (20), 67 (61), 66 (22), 65 (22), 55 (100). 1H NMR δ [(CD_3) $_2$ SO] 5.70, s, 2H, —OH; 2.25, m, 2H; 2.15–1.70, m, 10H; 1.52–1.39, m, 2H. ^{13}C NMR δ [(CD_3) $_2$ SO] 128.1 (q, $J = 289.7$ Hz, CF_3), 75.4 (q, $J = 24.6$ Hz, $C-CF_3$), 35.1 (CH), 31.3 (CH_2), 30.6 (CH), 28.3 (CH_2), 27.9 (CH_2).

Compound **4** gave no indication of inclusion properties when crystallised from a range of organic solvents which formed ellipsoidal clathrates (e.g. benzene) or helical tubulates (e.g. ethyl acetate) with the original diol **2**. However, the compound (**4**) $_2$ ·DMSO, m.p. 151–155 °C, was obtained by allowing a solution of **4** in dimethyl sulfoxide (DMSO) to stand for a week at room temperature and then removing the crystals by filtration.

2.3. X-RAY DATA COLLECTION, PROCESSING, AND REFINEMENT FOR THE STRUCTURES

2.3.1. Structure of **4**

Data were recorded for a crystal of **4** grown from a benzene solution by using an Enraf-Nonius CAD4 X-ray diffractometer in $\theta/2\theta$ scan mode. The procedures for data collection and processing have been described [17]. Corrections were made for absorption [18]. The structure was solved using direct phasing (MULTAN) followed by Fourier syntheses. Anisotropic refinement was carried out using full matrix least squares (BLOCKLS, a local version of ORFLS) [19]. Hydrogen atoms were included in calculated positions with their temperature factors being set equal to the isotropic equivalent of those of the atoms to which they were bound. Reflection weights used for refinement were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual was defined as $R_w = (\sum w \Delta F^2 / \sum w F_o^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray Crystallography [20]. The final residual was 0.044. The largest peak in the final difference map was $0.27 e \text{ \AA}^{-3}$.

2.3.2. Structure of (**4**) $_2$ ·DMSO

A similar procedure was used to that described above, except that the DMSO molecule was disordered so refinement was completed using program RAELS [22]. The DMSO was included in the refinement as two identical groups whose occupancies, 0.825(2) and 0.175, were refined. A single fifteen parameter TLX group (where T is the translation tensor, L is the libration tensor and X is the origin of libration) was used to define the thermal motion of the disordered DMSO. The

Table I. Numerical details of the solution and refinement of the structures.

| | | |
|---|---|---|
| Structure | 4 | (4)₂·(DMSO) |
| Formula | C ₁₃ H ₁₆ O ₂ F ₆ | (C ₁₃ H ₁₆ O ₂ F ₆) ₂ ·C ₂ H ₆ SO |
| Formula mass | 318.26 | 714.65 |
| Crystal description | {010}{001}{10-2}{012} {100}{05-7}{043} | |
| Space group | <i>P</i> 2 ₁ / <i>c</i> | <i>P</i> 2 ₁ 2 ₁ 2 ₁ |
| <i>a</i> /Å | 7.8636(6) | 7.249(1) |
| <i>b</i> /Å | 13.1020(7) | 16.064(3) |
| <i>c</i> /Å | 25.319(2) | 25.347(4) |
| β /° | 101.526(4) | (90) |
| <i>V</i> /Å ³ | 2555.9(3) | 2951.6(8) |
| Temp/°C | 21(1) | 21(1) |
| <i>Z</i> | 8 | 4 |
| <i>D</i> _{calc.} /g cm ⁻³ | 1.65 | 1.61 |
| Radiation, λ /Å | CuK α , 1.5418 | CuK α , 1.5418 |
| μ /cm ⁻¹ | 14.74 | 20.07 |
| Crystal dimensions/mm | 0.22 × 0.36 × 0.20 | 0.36 × 0.09 × 0.12 |
| Scan mode | $\theta/2\theta$ | $\theta/2\theta$ |
| $2\theta_{\text{max.}}$ /° | 140 | 140 |
| ω scan angle | 0.60 + 0.15 tan θ | 0.60 + 0.15 tan θ |
| No. of intensity measurements | 5188 | 3225 |
| Criterion for observed reflection | $I/\sigma(I) > 3$ | $I/\sigma(I) > 3$ |
| No. of independent obsd. reflections | 3986 | 2129 |
| No. of reflections (<i>m</i>) and variables (<i>n</i>) in final refinement | 3986 379 | 2129 434 |
| $R = \Sigma^m \Delta F / \Sigma^m F_o $ | 0.044 | 0.033 |
| $R_w = [\Sigma_w^m \Delta F ^2 / \Sigma_w^m F_o ^2]^{1/2}$ | 0.064 | 0.039 |
| $s = [\Sigma_w^m \Delta F ^2 / (m - n)]^{1/2}$ | 2.37 | 1.26 |
| Crystal decay | none | 1 to 0.77 |
| Max., min. transmission coefficients | 0.80, 0.63 | 0.85, 0.70 |
| Largest peak in final diff. map/e Å ⁻³ | 0.27 | 0.36 |
| <i>R</i> for 192 multiple measurements | 0.022 | – |

final residual was 0.033, the *R* factor for the alternative enantiomer being 0.038, and the largest peak in the final difference map 0.36 e Å⁻³.

Table I lists numerical details of the solution and refinement of the two structures. The fractional coordinates for the refined atoms of structures **4** and **(4)₂·DMSO** appear in Tables II and III respectively. Bond lengths and bond angles are listed in Tables IV and V respectively. Hydrogen bonding dimensions associated with the structure **(4)₂·DMSO** are given in Table VI. A DEC Alpha AXP workstation was used for calculations and the structural diagrams were drawn using ORTEP [21] running on a Macintosh IICx. The material deposited for both structures comprises

Table II. Fractional coordinates for the non-hydrogen atoms of structure **4**.

| | <i>x</i> | <i>y</i> | <i>z</i> |
|--------|------------|------------|-----------|
| F(1)A | -0.2964(2) | -0.0193(1) | 0.8291(1) |
| F(2)A | -0.2405(2) | -0.1663(1) | 0.8647(1) |
| F(3)A | -0.1243(2) | -0.0335(1) | 0.9061(1) |
| F(1)'A | 0.3346(2) | -0.4533(1) | 0.8015(1) |
| F(2)'A | 0.5212(2) | -0.3525(1) | 0.7792(1) |
| F(3)'A | 0.4621(2) | -0.3418(1) | 0.8576(1) |
| OA | 0.0352(2) | 0.0217(1) | 0.8238(1) |
| O'A | 0.1966(2) | -0.3105(1) | 0.7275(1) |
| C(1)A | 0.1105(3) | -0.2541(2) | 0.8664(1) |
| C(2)A | 0.1416(2) | -0.1388(1) | 0.8643(1) |
| C(3)A | -0.0136(2) | -0.0823(1) | 0.8288(1) |
| C(4)A | -0.0727(2) | -0.1321(1) | 0.7728(1) |
| C(5)A | -0.0783(2) | -0.2496(1) | 0.7760(1) |
| C(6)A | -0.1680(3) | -0.0764(2) | 0.8574(1) |
| C(7)A | 0.0279(3) | -0.0952(2) | 0.7306(1) |
| C(2)'A | 0.0859(2) | -0.2976(1) | 0.8093(1) |
| C(3)'A | 0.2454(2) | -0.2810(1) | 0.7831(1) |
| C(4)'A | 0.3151(2) | -0.1701(1) | 0.7890(1) |
| C(5)'A | 0.3119(2) | -0.1242(1) | 0.8450(1) |
| C(6)'A | 0.3909(3) | -0.3566(2) | 0.8057(1) |
| C(7)'A | 0.2269(3) | -0.0985(1) | 0.7440(1) |
| F(1)B | 0.3787(2) | 0.3800(1) | 0.5274(1) |
| F(2)B | 0.1308(2) | 0.3070(1) | 0.5066(1) |
| F(3)B | 0.1796(2) | 0.4472(1) | 0.4687(1) |
| F(1)'B | 0.7176(2) | 0.0031(1) | 0.4596(1) |
| F(2)'B | 0.9522(2) | 0.0864(1) | 0.4608(1) |
| F(3)'B | 0.8203(2) | 0.0157(1) | 0.3881(1) |
| OB | 0.1518(2) | 0.2910(1) | 0.3997(1) |
| O'B | 0.7951(2) | 0.2205(1) | 0.3836(1) |
| C(1)B | 0.5447(3) | 0.1879(2) | 0.4966(1) |
| C(2)B | 0.3651(3) | 0.1888(2) | 0.4593(1) |
| C(3)B | 0.3073(2) | 0.2973(2) | 0.4402(1) |
| C(4)B | 0.4480(3) | 0.3574(1) | 0.4183(1) |
| C(5)B | 0.6306(3) | 0.3418(2) | 0.4524(1) |
| C(6)B | 0.2504(3) | 0.3578(2) | 0.4860(1) |
| C(7)B | 0.4435(3) | 0.3367(2) | 0.3581(1) |
| C(2)'B | 0.6792(2) | 0.2298(2) | 0.4664(1) |
| C(3)'B | 0.6930(2) | 0.1670(2) | 0.4157(1) |
| C(4)'B | 0.5138(2) | 0.1426(1) | 0.3800(1) |
| C(5)'B | 0.3751(3) | 0.1150(1) | 0.4127(1) |
| C(6)'B | 0.7951(3) | 0.0676(2) | 0.4313(1) |
| C(7)'B | 0.4464(2) | 0.2260(2) | 0.3389(1) |

Table III. Fractional coordinates for the non-CH atoms of structure (4)₂-DMSO.

| | <i>x</i> | <i>y</i> | <i>z</i> |
|---------------------|------------|------------|-----------|
| F(1)A | −0.6790(3) | 0.5082(2) | 0.6552(1) |
| F(2)A | −0.7815(4) | 0.5088(2) | 0.7343(1) |
| F(3)A | −0.9514(4) | 0.4643(1) | 0.6721(1) |
| F(1) [′] A | −1.5301(3) | 0.6998(2) | 0.5564(1) |
| F(2) [′] A | −1.4151(4) | 0.8215(2) | 0.5621(1) |
| F(3) [′] A | −1.2600(4) | 0.7241(2) | 0.5266(1) |
| OA | −0.7495(3) | 0.6631(2) | 0.6955(1) |
| O [′] A | −1.4332(3) | 0.7482(2) | 0.6569(1) |
| C(1)A | −1.0999(5) | 0.5929(2) | 0.5961(1) |
| C(2)A | −0.9280(5) | 0.6340(2) | 0.6184(1) |
| C(3)A | −0.8990(5) | 0.6131(2) | 0.6774(1) |
| C(4)A | −1.0761(5) | 0.6261(2) | 0.7108(1) |
| C(5)A | −1.2512(5) | 0.5947(2) | 0.6830(1) |
| C(6)A | −0.8293(5) | 0.5241(2) | 0.6843(1) |
| C(7)A | −1.1001(5) | 0.7164(2) | 0.7305(1) |
| C(2) [′] A | −1.2710(5) | 0.6236(2) | 0.6257(1) |
| C(3) [′] A | −1.2979(5) | 0.7191(2) | 0.6211(1) |
| C(4) [′] A | −1.1176(5) | 0.7684(2) | 0.6320(1) |
| C(5) [′] A | −0.9448(5) | 0.7280(2) | 0.6081(1) |
| C(6) [′] A | −1.3748(6) | 0.7415(3) | 0.5664(2) |
| C(7) [′] A | −1.0906(5) | 0.7880(2) | 0.6912(1) |
| F(1)B | 0.8125(4) | 0.1055(2) | 0.4479(1) |
| F(2)B | 0.9810(3) | −0.0013(1) | 0.4567(1) |
| F(3)B | 0.7123(3) | 0.0013(2) | 0.4914(1) |
| F(1) [′] B | 1.2870(4) | −0.0634(2) | 0.6724(1) |
| F(2) [′] B | 1.4618(4) | 0.0315(2) | 0.7034(1) |
| F(3) [′] B | 1.5606(4) | −0.0473(1) | 0.6425(1) |
| OB | 0.8045(4) | 0.1438(1) | 0.5497(1) |
| O [′] B | 1.4940(3) | 0.1130(1) | 0.6116(1) |
| C(1)B | 1.1358(5) | −0.0384(2) | 0.5638(2) |
| C(2)B | 0.9662(5) | 0.0162(2) | 0.5760(1) |
| C(3)B | 0.9386(5) | 0.0849(2) | 0.5339(1) |
| C(4)B | 1.1181(5) | 0.1341(2) | 0.5220(1) |
| C(5)B | 1.2912(5) | 0.0788(2) | 0.5189(1) |
| C(6)B | 0.8610(5) | 0.0473(2) | 0.4827(2) |
| C(7)B | 1.1483(6) | 0.2080(2) | 0.5592(2) |
| C(2) [′] B | 1.3101(5) | 0.0157(2) | 0.5642(1) |
| C(3) [′] B | 1.3423(5) | 0.0574(2) | 0.6179(1) |
| C(4) [′] B | 1.1689(5) | 0.1026(2) | 0.6391(1) |
| C(5) [′] B | 0.9913(5) | 0.0521(2) | 0.6316(1) |
| C(6) [′] B | 1.4126(5) | −0.0060(2) | 0.6584(2) |
| C(7) [′] B | 1.1495(5) | 0.1920(2) | 0.6188(1) |

Table III. Continued.

| | <i>x</i> | <i>y</i> | <i>z</i> |
|------|-------------|------------|------------|
| HOA | −0.7395(58) | 0.6591(25) | 0.7323(15) |
| HO'A | −1.5213(59) | 0.7125(24) | 0.6590(15) |
| HOB | 0.7172(61) | 0.1201(25) | 0.5612(15) |
| HO'B | 1.5265(59) | 0.1379(22) | 0.6403(16) |
| S | 0.1967(1) | 0.2075(1) | 0.3062(0) |
| O | 0.1401(4) | 0.2986(2) | 0.3033(1) |
| CA | 0.1670(7) | 0.1778(3) | 0.3735(2) |
| CB | 0.0080(8) | 0.1513(3) | 0.2783(2) |
| S' | 0.0486(12) | 0.2132(4) | 0.3185(2) |
| O' | 0.1527(27) | 0.2963(10) | 0.3015(6) |
| CA' | 0.1042(43) | 0.1511(15) | 0.2652(9) |
| CB' | 0.1910(40) | 0.1736(16) | 0.3676(10) |

atomic coordinates for the hydrogen atoms, thermal parameters, and structure factors.

3. Results and Discussion

3.1. DESCRIPTION OF THE STRUCTURE OF **4**

The crystal structure of the solvent-free analogue diol **2** is complex [2]. There are three molecules (A—C) in the asymmetric unit. All of these participate in hydrogen bonding to give a layer structure and both of the hydroxy groups of B form one donor and one acceptor bond. However, the A and C molecules exhibit less complete hydrogen bonding with one group of each participating in two hydrogen bonds and the other only in one. Furthermore, molecule C is disordered, with the minor component (17.6%) hydrogen bonded differently. These packing difficulties in pure **2** are no doubt a fundamental cause for it seeking the alternative arrangements outlined in the Introduction. The calculated densities for forms (i), (ii), (iii) benzene compound, (iv) ethyl acetate compound, and (v) *p*-methoxyphenol compound, are 1.19, 1.20, 1.19, 1.20 and 1.20 g cm^{−3} respectively – which indicates that increased packing density is not a significant driving force. However, in all of these other forms every diol hydroxy group participates in one donor and one acceptor hydrogen bond [3,6].

The crystal structure of the solvent-free bis(trifluoromethyl) analogue **4** contains two independent molecules (A and B) in the asymmetric unit, and the monoclinic unit cell contains eight molecules in space group *P2*₁/*c*. Figure 1 shows the molecular structure of diol **4** together with the crystallographic numbering system used for both crystal structures.

This structure has some similarity with that of pure **2** in that hydrogen bonded layers are formed, both diol enantiomers are present, and the space group is the

Table IV. Bond lengths and standard deviations (Å) for structures **4** and (**4**)₂·DMSO.

| Bond | 4 | | (4) ₂ ·DMSO | |
|-------------|----------|----------|---------------------------------|----------|
| | A | B | A | B |
| F(1)—C(6) | 1.342(3) | 1.334(3) | 1.340(4) | 1.333(4) |
| F(2)—C(6) | 1.338(3) | 1.340(3) | 1.337(4) | 1.342(4) |
| F(3)—C(6) | 1.337(3) | 1.333(3) | 1.343(5) | 1.325(5) |
| F(1)'—C(6)' | 1.339(2) | 1.332(3) | 1.334(5) | 1.344(5) |
| F(2)'—C(6)' | 1.335(2) | 1.332(3) | 1.322(5) | 1.338(4) |
| F(3)'—C(6)' | 1.335(3) | 1.337(3) | 1.337(4) | 1.325(5) |
| O—C(3) | 1.429(2) | 1.432(2) | 1.424(4) | 1.414(4) |
| O'—C(3)' | 1.435(2) | 1.434(2) | 1.417(4) | 1.425(4) |
| C(1)—C(2) | 1.533(3) | 1.535(3) | 1.519(5) | 1.541(5) |
| C(1)—C(2)' | 1.528(3) | 1.527(3) | 1.532(5) | 1.533(5) |
| C(2)—C(3) | 1.551(3) | 1.541(3) | 1.547(5) | 1.547(5) |
| C(2)—C(5)' | 1.527(3) | 1.538(3) | 1.538(5) | 1.535(5) |
| C(3)—C(4) | 1.545(3) | 1.548(3) | 1.552(5) | 1.552(5) |
| C(3)—C(6) | 1.534(3) | 1.541(3) | 1.526(5) | 1.538(5) |
| C(4)—C(5) | 1.543(3) | 1.534(3) | 1.537(5) | 1.540(5) |
| C(4)—C(7) | 1.529(3) | 1.541(3) | 1.543(5) | 1.533(5) |
| C(5)—C(2)' | 1.529(3) | 1.540(3) | 1.531(5) | 1.536(5) |
| C(7)—C(7)' | 1.534(3) | 1.531(3) | 1.523(5) | 1.531(5) |
| C(2)'—C(3)' | 1.548(3) | 1.546(3) | 1.551(5) | 1.536(5) |
| C(3)'—C(4)' | 1.549(2) | 1.548(3) | 1.554(5) | 1.547(5) |
| C(3)'—C(6)' | 1.535(3) | 1.539(3) | 1.537(5) | 1.533(5) |
| C(4)'—C(5)' | 1.545(3) | 1.538(3) | 1.536(5) | 1.533(5) |
| C(4)'—C(7)' | 1.531(3) | 1.530(3) | 1.545(5) | 1.533(5) |
| O—HO | 0.95 | 0.92 | 0.94(4) | 0.79(4) |
| O'—HO' | 0.90 | 0.93 | 0.86(4) | 0.86(4) |
| S—O | | | | 1.521(3) |
| S—CA | | | | 1.783(4) |
| S—CB | | | | 1.786(5) |

same. A major difference is that all hydroxy groups of **4** are now fully hydrogen bonded (one donor and one acceptor each), which removes the urgency for **4** to seek more complete hydrogen bonding through formation of lattice inclusion compounds. In crystalline **4** hydroxy groups from four different diol molecules associate to form (—OH)₄ rings, a type of supramolecular motif encountered frequently in alicyclic diol structures [23].

Four further (—OH)₄ rings are subtended from the other diol hydroxy groups producing corrugated layers which stack through dispersion forces. A high degree of enantiomeric ordering has taken place during crystallisation since each individual layer is composed of enantiomerically pure diol **4** molecules, but layers of

Table V. Bond angles and standard deviations ($^{\circ}$) for structures **4** and **(4)₂·DMSO**.

| Angle | 4 | | (4)₂·DMSO | |
|---|----------|----------|-----------------------------|----------|
| | A | B | A | B |
| C(2)—C(1)—C(2)' | 109.0(1) | 109.4(2) | 110.0(3) | 109.5(3) |
| C(1)—C(2)—C(3) | 112.2(2) | 112.2(2) | 112.2(3) | 111.8(3) |
| C(1)—C(2)—C(5)' | 106.9(2) | 106.6(2) | 107.4(3) | 107.6(3) |
| C(3)—C(2)—C(5)' | 113.2(2) | 113.4(2) | 112.8(3) | 112.4(3) |
| O—C(3)—C(2) | 108.2(1) | 109.1(2) | 107.0(3) | 111.8(3) |
| O—C(3)—C(4) | 111.0(2) | 110.0(2) | 112.2(3) | 106.9(3) |
| O—C(3)—C(6) | 104.1(2) | 103.5(2) | 103.9(3) | 104.5(3) |
| C(2)—C(3)—C(4) | 112.9(1) | 113.2(2) | 112.7(3) | 112.9(3) |
| C(2)—C(3)—C(6) | 110.9(2) | 110.6(2) | 111.0(3) | 110.4(3) |
| C(4)—C(3)—C(6) | 109.5(2) | 110.1(2) | 109.8(3) | 110.0(3) |
| C(3)—C(4)—C(5) | 112.2(2) | 112.7(2) | 112.9(3) | 113.5(3) |
| C(3)—C(4)—C(7) | 113.9(2) | 112.9(2) | 113.3(3) | 113.2(3) |
| C(5)—C(4)—C(7) | 112.1(2) | 111.5(2) | 111.3(3) | 111.2(3) |
| C(4)—C(5)—C(2)' | 114.2(1) | 114.6(2) | 114.4(3) | 114.5(3) |
| F(1)—C(6)—F(2) | 105.6(2) | 106.3(2) | 106.0(3) | 104.6(3) |
| F(1)—C(6)—F(3) | 106.6(2) | 105.5(2) | 105.8(3) | 106.6(3) |
| F(1)—C(6)—C(3) | 111.0(2) | 114.5(2) | 112.7(3) | 112.3(3) |
| F(2)—C(6)—F(3) | 106.2(2) | 106.6(2) | 104.9(3) | 106.6(3) |
| F(2)—C(6)—C(3) | 114.8(2) | 111.7(2) | 111.5(3) | 114.0(3) |
| F(3)—C(6)—C(3) | 112.0(2) | 111.7(2) | 115.2(3) | 112.1(3) |
| C(4)—C(7)—C(7)' | 119.0(2) | 118.9(2) | 119.6(3) | 118.5(3) |
| C(1)—C(2)' ¹ —C(5) | 107.6(2) | 107.0(2) | 106.9(3) | 107.2(3) |
| C(1)—C(2)' ² —C(3)' | 113.1(2) | 113.3(2) | 112.5(3) | 112.2(3) |
| C(5)—C(2)' ³ —C(3)' | 111.8(2) | 111.9(2) | 112.6(3) | 112.8(3) |
| O' ¹ —C(3)' ¹ —C(2)' ¹ | 107.6(1) | 110.5(2) | 111.4(3) | 106.9(3) |
| O' ² —C(3)' ² —C(4)' | 111.5(1) | 108.5(2) | 107.4(3) | 111.9(3) |
| O' ³ —C(3)' ³ —C(6)' | 103.1(1) | 103.7(2) | 104.5(3) | 103.6(3) |
| C(2)' ¹ —C(3)' ¹ —C(4)' | 113.1(1) | 112.8(2) | 112.7(3) | 112.9(3) |
| C(2)' ² —C(3)' ² —C(6)' | 110.9(2) | 110.9(2) | 110.3(3) | 110.8(3) |
| C(4)' ¹ —C(3)' ¹ —C(6)' | 110.2(1) | 110.0(2) | 110.3(3) | 110.4(3) |
| C(3)' ¹ —C(4)' ¹ —C(5)' | 112.6(2) | 113.3(2) | 113.6(3) | 113.0(3) |
| C(3)' ² —C(4)' ² —C(7)' | 113.9(2) | 113.7(2) | 112.6(3) | 113.4(3) |
| C(5)' ¹ —C(4)' ¹ —C(7)' | 110.8(2) | 110.4(2) | 111.4(3) | 112.1(3) |
| C(2)—C(5)' ² —C(4)' | 114.9(1) | 114.5(2) | 114.4(3) | 114.4(3) |
| F(1)' ¹ —C(6)' ¹ —F(2)' | 105.7(2) | 106.8(2) | 106.6(3) | 105.4(3) |
| F(1)' ² —C(6)' ² —F(3)' | 106.5(2) | 106.1(2) | 106.1(3) | 106.6(3) |
| F(1)' ³ —C(6)' ³ —C(3)' | 111.7(2) | 113.8(2) | 111.1(3) | 114.0(3) |
| F(2)' ¹ —C(6)' ¹ —F(3)' | 106.1(2) | 106.3(2) | 106.1(3) | 105.6(3) |
| F(2)' ² —C(6)' ² —C(3)' | 112.1(2) | 111.4(2) | 112.5(3) | 111.1(3) |
| F(3)' ¹ —C(6)' ¹ —C(3)' | 114.1(2) | 112.0(2) | 113.9(3) | 113.4(3) |
| C(7)—C(7)' ¹ —C(4)' | 118.2(2) | 118.9(2) | 118.3(3) | 119.3(3) |
| O—S—CA | | | | 105.8(2) |
| O—S—CB | | | | 105.1(2) |
| CA—S—CB | | | | 98.7(2) |

Table VI. Dimensions associated with hydrogen bonding in structure $(\mathbf{4})_2 \cdot \text{DMSO}$.

| | | | |
|--|----------|------------------------|----------|
| C(3)A—OA···O'A ^a | 140.8(2) | OA···O'A ^a | 2.844(3) |
| OA···O'A ^a —C(3)'A ^a | 128.3(2) | OA···O ^b | 2.911(3) |
| OA···HO'A ^a —O'A ^a | 152(4) | OA···O ^b | 2.85(2) |
| C(3)A—OA···O ^b | 128.9(2) | OB···O'B ^c | 2.787(3) |
| OA···O ^b —S ^b | 100.2(1) | O'B···O ^d | 2.792(3) |
| OA—HOA···O ^b | 151(4) | O'B···O ^d | 2.88(2) |
| C(3)A—OA···O ^b | 128.2(4) | OA···HO'A ^a | 2.06(4) |
| OA···O ^b —S ^b | 124.3(7) | HOA···O ^b | 2.05(4) |
| OA—HOA···O ^b | 151(4) | HOA···O ^b | 2.00(4) |
| C(3)B—OB···O'B ^c | 126.6(2) | HOB···O'B ^c | 2.07(4) |
| OB···O'B ^c —C(3)'B ^c | 142.9(2) | HO'B···O ^d | 1.94(4) |
| OB—HOB···O'B ^c | 151(4) | HO'B···O ^d | 2.03(4) |
| C(3)'B—O'B···O ^d | 121.6(2) | | |
| O'B···O ^d —S ^d | 123.6(1) | | |
| O'B—HO'B···O ^d | 169(4) | | |
| C(3)'B—O'B···O ^d | 122.6(4) | | |
| O'B···O ^d —S ^d | 91.6(6) | | |
| O'B—HO'B···O ^d | 167(4) | | |

Equivalent position indicators:

^a $1 + x, y, z.$ ^b $-1/2 - x, 1 - y, 1/2 + z.$ ^c $-1 + x, y, z.$ ^d $1/2 + x, 1/2 - y, 1 - z.$

alternating chirality result in a net achiral lattice. We have not encountered this chirality phenomenon previously for pure diol layer structures, but it is rather similar to that encountered in the cocrystalline adducts of diol **2** and phenols [6]. The surfaces of the layers comprise C—H and C—F groups, and where adjacent layers abut multiple C—F···H—C and C—F···F—C contacts occur. The values of the latter interactions (under 3.20 Å) are 2.83, 3.01, 3.05, 3.07, 3.18 and 3.19 Å. These various modes of assembly are illustrated in Figure 2.

3.2. DESCRIPTION OF THE STRUCTURE OF $(\mathbf{4})_2 \cdot \text{DMSO}$

The crystal structure of $(\mathbf{4})_2 \cdot \text{DMSO}$ contains two independent molecules (A and B) in the asymmetric unit, and the orthorhombic unit cell contains eight diol and four DMSO molecules in the chiral space group $P2_12_12_1$. Spontaneous self-resolution has taken place during the formation of $(\mathbf{4})_2 \cdot \text{DMSO}$ thereby producing a conglomerate, a mixture of chirally pure (+)- and (–)-crystals [7,8].

Strands of diol **4** molecules are hydrogen bonded together H—O···H—O···H—O in the *a* direction. Two such strands surround DMSO molecules to form a ribbon where each DMSO molecule accepts two O—H···O=S hydrogen bonds (one from

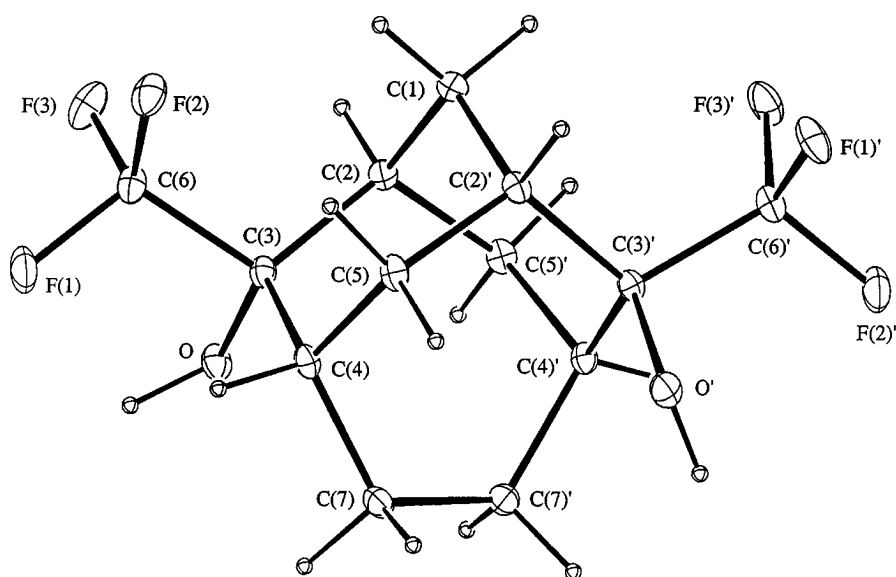


Figure 1. Molecular structure of 2,7-bis(trifluoromethyl)tricyclo[4.3.1.1^{3,8}]undecane-*syn*-2,7-diol (independent molecule A in pure **4**) showing the crystallographic numbering system used for both crystal structures.

each of the neighbouring strands). Hence in the structure (**4**)₂·DMSO each diol molecule is actually less completely hydrogen bonded than in pure solid **4**. The first hydroxy group participates in one donor and one acceptor hydrogen bond, but the second only participates as a donor, as shown in Figure 3. Although the DMSO molecules are disordered, with the occupancy of the major component being 0.825(2), the position of the oxygen atom remains relatively unchanged and there is no disruption of the hydrogen bonding.

Both C–H and C–F groups comprise the outer surfaces of the ribbons and there are multiple C–F···H–C and C–F···F–C contacts present between both adjacent strands and adjacent ribbons. The values of F···C for the latter interactions (under 3.20 Å) are 2.83 Å between strands, and 2.94, 2.95, 3.01, 3.07 and 3.19 Å between ribbons. In addition to the C–F···H–C aliphatic contacts, several —C–F···H–CH₂—SO— interactions involving the weakly acidic DMSO hydrogens provide further inter-ribbon stabilisation as illustrated in Figure 4. The F···C distances (under 3.50 Å) are 3.34, 3.35 and 3.38 Å to one neighbouring ribbon and 3.39 Å to a second.

3.3. COMPARISON OF (**4**)₂·DMSO WITH OTHER DMSO COMPLEXES

There are many compounds reported which contain trapped DMSO, and crystal structures of 244 examples are listed in the October 1996 version of the Cambridge

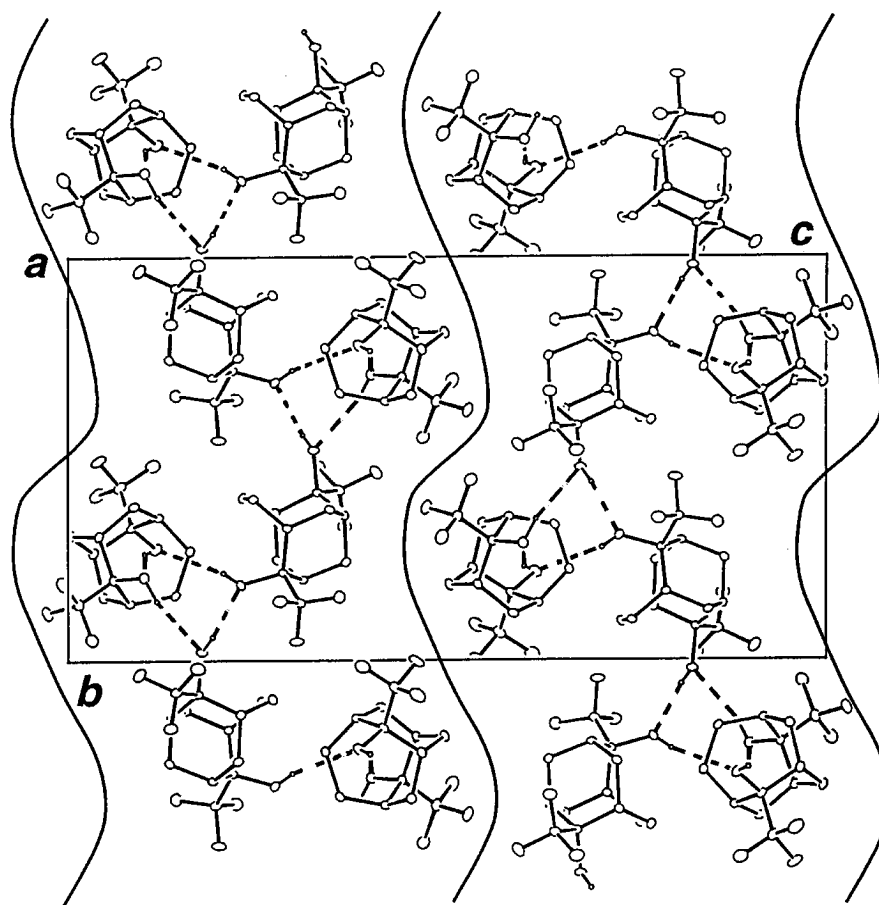


Figure 2. Lattice arrangement of crystalline **4** showing an edge-on view of two corrugated layers of diols with the edges of these being delineated by undulating solid lines. Each layer is built from enantiomerically pure diol molecules, but adjacent layers have opposite chirality. There are multiple C—F ··· H—C and C—F ··· F—C contacts between these adjacent layers. Hydrogen bonded (O—H)₄ rings (dashed lines) link the diol molecules within each layer. Hydrocarbon hydrogen atoms are omitted for clarity.

Structural Database [24]. Of these, nine cases exhibit a DMSO hydrogen bonding pattern similar to that observed here:

| | |
|-----------|---|
| ACDMSM: | α -Cyclodextrin-DMSO-methanol dihydrate [25] |
| BURDMS: | 5-Bromouridine-2,2'-dicarboxylic acid-DMSO [26] |
| CIWJEX10: | 1,1'-Binaphthyl-2,2'-dicarboxylic acid-DMSO [27] |
| DIZMII: | 1,1,1,3,3,3-Hexachloro-2,2-dihydroxypropane-DMSO [28] |
| KUMHEF: | 2,5-Bis(9-hydroxyfluorenyl)thiophene-DMSO [29] |
| PREGSF: | Pregn-4-ene-17 α , 21-diol-3,20-dione-DMSO [30] |
| TMADMS: | Trimesic acid-DMSO [31] |
| ZITNUL: | 2,2'-Binaphthyl-3,3'-dicarboxylic acid-DMSO [32] |
| ZITPAT: | 1,1':3',1''-Terphenyl-2',4,4''-tricarboxylic acid-DMSO [32] |

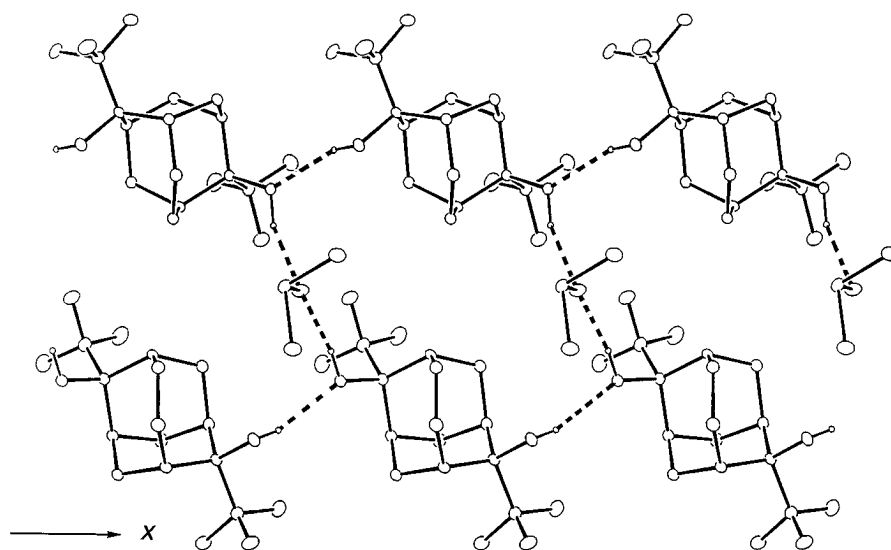


Figure 3. Lattice arrangement of crystalline $(4)_2 \cdot \text{DMSO}$ showing two strands of hydrogen bonded diol molecules and the interconnecting DMSO molecules cross-linking these to complete a hydrogen bonded ribbon. The hydrogen bonds are indicated by dashed lines, and hydrocarbon hydrogen atoms are omitted.

In all these examples either two —O—H or two CO—O—H groups act as hydrogen bond donors to the DMSO molecule. The regular occurrence of this motif across such a wide range of different donor structures indicates that this is a particularly favourable supramolecular interaction for the sulfoxide functionality.

4. Conclusions

The above results support our earlier work indicating that methyl groups are critical for generation of the helical tubular lattice [1]. Even the minor modification made here to **Z** of the general structure **3** resulted in loss of these properties, although quite different inclusion behaviour was still observed for the new type of lattice produced.

Self-resolution is a fascinating chemical phenomenon which represents the simplest means of obtaining pure enantiomers from a racemic solution. It is not just restricted to laboratory separations since the technique has been employed in industrial-scale preparations of materials such as *L*-glutamic acid, chloroamphenicol, and *L*- α -methyldopa [7,8]. The methodology employed in such cases has been reviewed [33]. Since conglomerate formation is an unpredictable and comparatively uncommon property the observations here are most interesting. In this particular instance, inclusion complexation can sufficiently influence enantiomeric assembly from solution to change the resulting crystal structure from a racemate to a conglomerate. Inclusion complexation therefore has some potential as a means

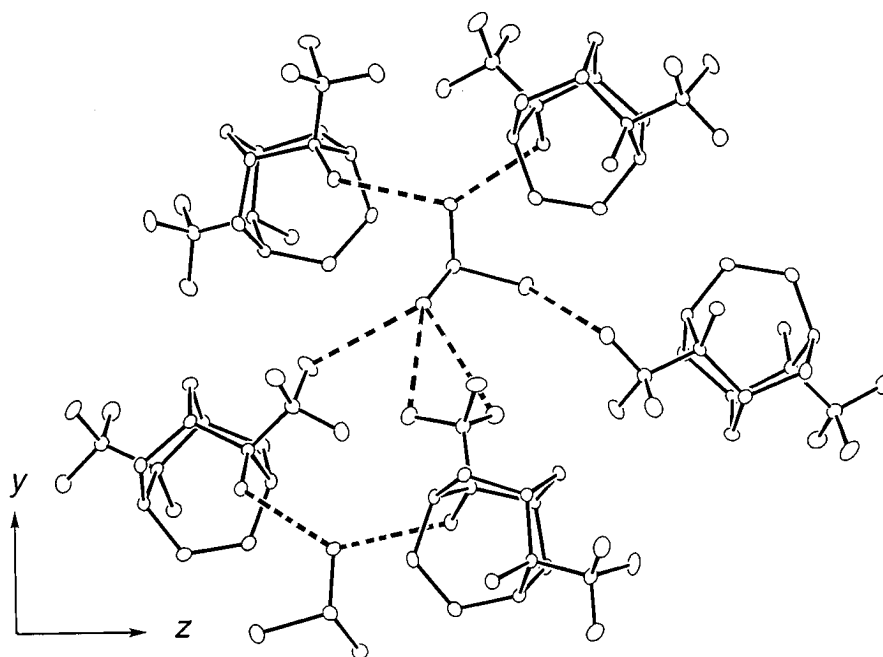


Figure 4. The primary and secondary interactions of DMSO in solid $(\mathbf{4})_2 \cdot \text{DMSO}$ are shown here using dashed lines. Pairs of $\text{O—H} \cdots \text{O=S}$ hydrogen bonds link adjacent strands of diol $\mathbf{4}$ molecules to form ribbons (running along x). One such ribbon is linked with two other neighbours through four $\text{—C—F} \cdots \text{H—CH}_2\text{—SO—}$ interactions ($\text{F} \cdots \text{C}$ distances under 3.50 \AA). All hydrogen atoms are omitted from this figure for clarity.

of inducing enantiomeric self-resolution and we intend studying this property in greater detail.

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