Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Dipolar S═O···C═O and C—H···O interactions in the molecular organization of 4,6-di-*O*-acetyl-2-*O*-tosyl-*myo*-inositol 1,3,5-orthoesters

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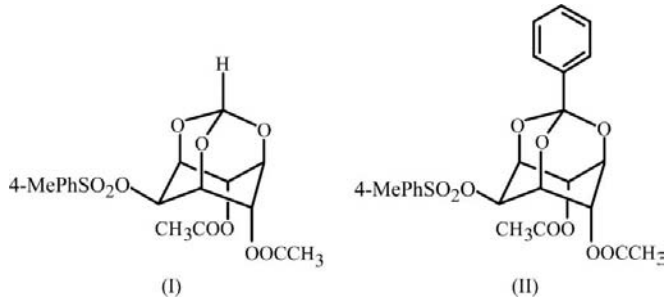
Received 14 April 2009
Accepted 7 May 2009
Online 13 June 2009

In the absence of conventional hydrogen bonding, the molecules of 4,6-di-*O*-acetyl-2-*O*-tosyl-*myo*-inositol 1,3,5-orthoformate, $C_{18}H_{20}O_{10}S$, (I), and 4,6-di-*O*-acetyl-2-*O*-tosyl-*myo*-inositol 1,3,5-orthobenzoate, $C_{24}H_{24}O_{10}S$, (II), are associated *via* C—H···O interactions. Molecules of (II) are additionally linked *via* dipolar S═O···C═O contacts. It is interesting to note that the sulfonyl O atom involved in the dipolar S═O···C═O contacts does not take part in any other interaction, indicating the competitive nature of this contact relative to the weak hydrogen-bonding interactions.

Comment

Noncovalent intermolecular interactions play a vital role in the specificity associated with molecular recognition in chemical and complex biological processes (Glusker, 1998). This necessitates an understanding of the various types and strengths of noncovalent interactions that bind molecules in crystal structures. These studies are significant because of their application in crystal engineering, supramolecular chemistry, and the design of functional materials and drugs (Desiraju & Steiner, 1999). For instance, the importance of dipolar interactions such as C═O···C═O and C—F···C═O has been recognized in the conformational stabilization of proteins (Maccallum *et al.*, 1995) and in structure-based drug design (Hof & Diedrich, 2004). We have previously reported (Manoj *et al.*, 2006) the significance of dipolar S═O···C═O contacts between the diastereomers of camphorsulfonate derivatives of *myo*-inositol for the formation of solvent-inclusion crystals. The title compounds, (I) and (II), were synthesized to explore the activity of S═O···C═O interactions in sulfonylated *myo*-inositol derivatives containing sulfonyl and acyl groups. Sulfonylated *myo*-inositol orthoesters are key intermediates (Sureshan *et al.*, 2003) for the synthesis of biologically important phosphorylated inositols, which play a significant role in cellular signal transduction (Potter & Lampe, 1995).



Crystallization of (I) and (II) from common organic solvents resulted in triclinic and monoclinic crystals, respec-

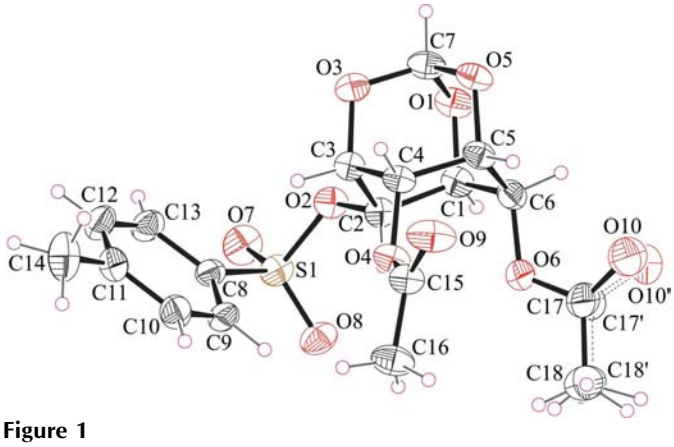


Figure 1
A view of (I), showing the atom-numbering scheme and the disordered atoms labelled with primes. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

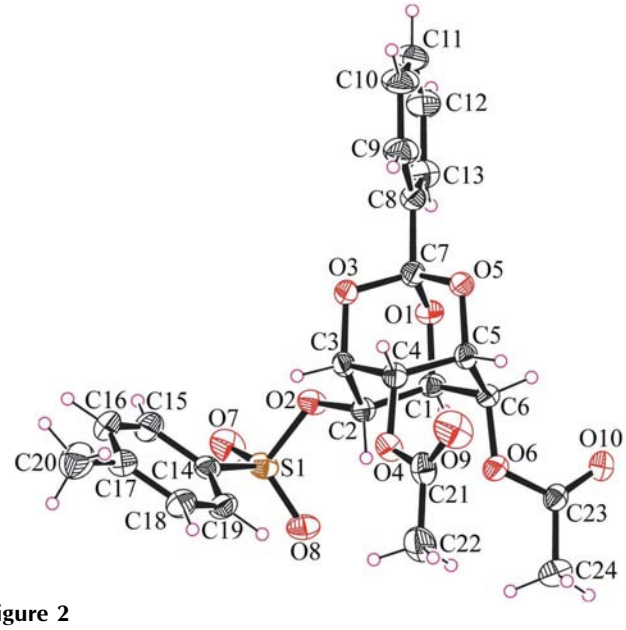


Figure 2
A view of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

 doi:10.1107/S0108270109017211

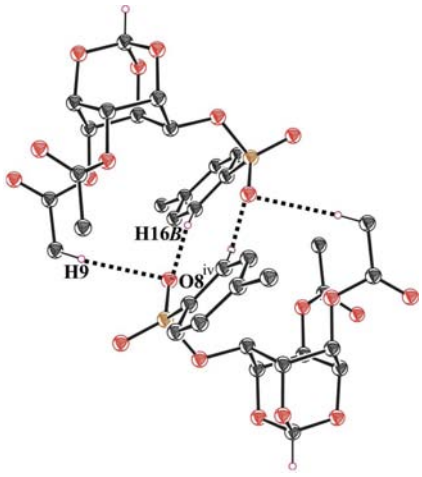


Figure 3
The dimer in the crystal structure of (I) [symmetry code: (iv) $-x + 2$, $-y + 1$, $-z + 1$].

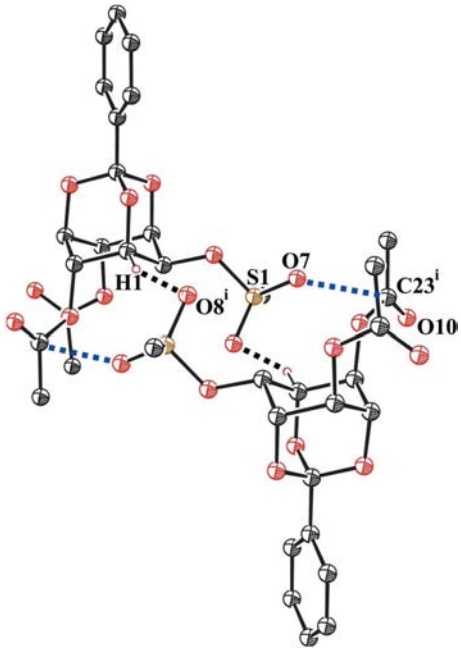


Figure 4
The dimer in the crystal structure of (II) [symmetry code: (i) $-x + 2$, $-y + 2$, $-z + 1$].

tively. The molecules adopt similar conformations (Figs. 1 and 2) in both compounds, although the orthoester H atom in (I) is substituted by a phenyl group in (II). The regioisomers (racemic 2,4-di-*O*-acetyl-6-*O*-tosyl-*myo*-inositol orthoformate and its orthoacetate analogue) produce conformational polymorphs with different orientations of the tosyl group about the O—S bond (Manoj *et al.*, 2009).

Molecules of (I) and (II) associate centrosymmetrically in their crystal structures to form dimers *via* different non-covalent interactions involving sulfonyl O atoms. In compound (I), sulfonyl atom O8 is engaged in the formation of bifurcated C—H···O interactions with atoms H9^{iv} and H16*B*^{iv} (Fig. 3 and Table 1), whereas in (II), sulfonyl atom O7

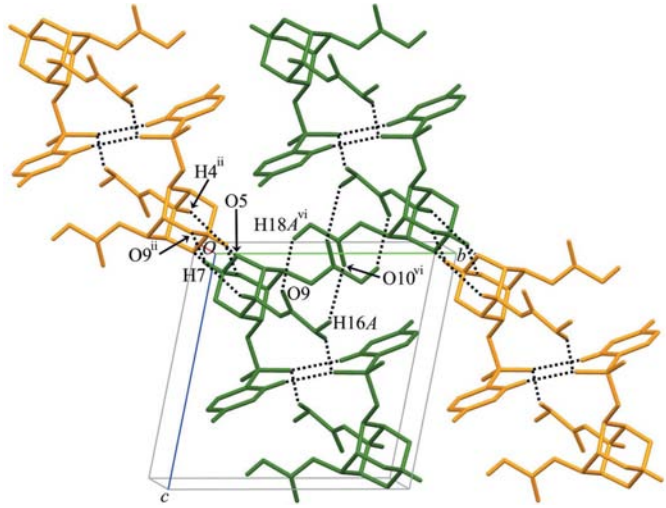


Figure 5
The organization of the dimers (shown in Fig. 3) in the structure of (I) [symmetry codes: (ii) $-x + 1$, $-y$, $-z$; (vi) $-x + 1$, $-y + 1$, $-z$].

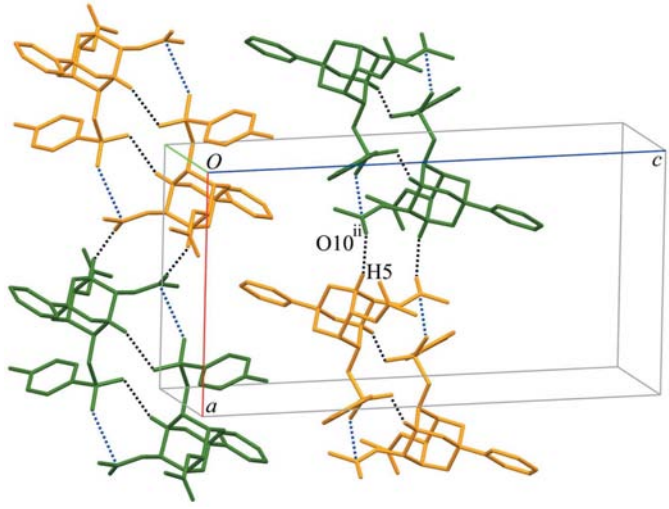


Figure 6
The organization of the dimers (shown in Fig. 4) in the structure of (II) [symmetry code: (ii) $-x + 1$, $-y + 2$, $-z + 1$].

is involved in a dipolar S═O···C═O contact with carbonyl atom C23^{i} and atom O8 makes a short C—H···O contact with inositol ring atom H1^{i} across the inversion centre (Fig. 4 and Table 2). In these S═O···C═O contacts, the S═O group is perpendicular to the C═O group (Manoj *et al.*, 2007) and the geometric parameters [O7···C23^{i} = 3.194 (3) Å, O7···C23^{i}═O10^{i} = 84.4 (2)° and S1═O7···C23^{i} = 147.9 (2)°; symmetry code: (i) $-x + 2$, $-y + 2$, $-z + 1$] indicate that the interaction motif is of Type I (Allen *et al.*, 1998). It is worthy of note that sulfonyl atom O7 which is involved in the S═O···C═O contacts (Manoj *et al.*, 2007) does not take part in any other weak interaction. We have previously observed that S═O···C═O contacts are complementary to C—H···O interactions in camphorsulfonyl derivatives of *myo*-inositol orthoformate (Manoj *et al.*, 2006).

The organization of the dimers (Figs. 3 and 4) in (I) and (II) is observed to be similar [in the *bc* plane in (I) and the *ac* plane in (II)]. The dimers translate to form chains *via* weak van der Waals contacts along the direction of the *b* axis in (I) (Fig. 5) and along the *c* axis in (II) (Fig. 6). These chains form a layered arrangement in the *bc* plane in (I) with four weak hydrogen-bonding interactions, namely C4—H4···O5^{ii}, C7—H7···O9^{ii}, C16—H16*A*···O10^{vi} and C18—H18*A*···O9^{vi}, whereas in (II) the chains are linked by a C5—H5···O10^{ii} interaction (see Tables 1 and 2 for symmetry codes).

These molecular layers are packed in the third dimension by translation of the dimers *via* C—H···O interactions (see supplementary material for figures), *viz.* C1—H1···O9^{i} and C16—H16*B*···O8^{iv} in (I) (Table 1), and C22—H22*C*···O10^{iii} and C24—H24*B*···O9^{iv} in (II) (Table 2), without leaving voids either for solvent inclusion or for conformational flexibility. In conclusion, the molecular association *via* S═O···C═O contacts observed in (II) is of considerable interest and could have relevance in the binding of sulfa drugs to their receptor proteins. Further work on the theoretical energy calculation of dipolar associations and their packing motifs is underway.

Experimental

For the preparation of (I), 2-*O*-tosyl-*myo*-inositol 1,3,5-orthoformate (0.172 g, 0.5 mmol; Sureshan *et al.*, 2003) and acetic anhydride (0.2 ml, 2.10 mmol) were dissolved in pyridine (6 ml) and the mixture was stirred at room temperature for 8 h. The solvent was evaporated from the reaction mixture under reduced pressure and the residue worked up with ethyl acetate. The product was purified by flash column chromatography to obtain 2-*O*-tosyl-4,6-di-*O*-acetyl-*myo*-inositol 1,3,5-orthoformate, (I), as a colourless solid (yield 0.205 g, 96%; m.p. 448–449 K). IR ($CHCl_3$, ν, cm^{-1}): 1751; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.09 (*s*, 6H, MeCO), 2.47 (*s*, 3H, ArMe), 4.25–4.31 (*m*, 2H, Ins H), 4.52–4.58 (*m*, 1H, Ins H), 4.94–4.98 (*m*, 1H, Ins H), 5.46 (*t*, *J* = 3.9 Hz, 2H, Ins H), 5.52 (*d*, 1H, *J* = 1.5 Hz, O_3CH), 7.34–7.42 (*m*, 2H, ArH), 7.82–7.89 (*m*, 2H, ArH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.5, 21.6, 65.8, 67.5, 68.8, 69.1, 71.8, 102.7, 127.7, 129.9, 133.3, 145.5, 168.7. Analysis calculated for $C_{18}H_{20}O_{10}S$: C 50.47, H 4.71%; found: C 50.23, H 4.55%.

Fot the preparation of (II), a mixture of *myo*-inositol 1,3,5-orthobenzoate (0.266 g, 1 mmol; Murali *et al.*, 2007), tosyl chloride (0.200 g, 1.05 mmol) and pyridine (8 ml) was heated at 353 K for 48 h. The reaction mixture was concentrated under reduced pressure and the residue worked up as usual. The product was purified by column chromatography to obtain 2-*O*-tosyl-*myo*-inositol 1,3,5-orthobenzoate (yield 0.264 g, 63%; m.p. 429–430 K). The 2-*O*-tosyl derivative (0.211 g, 0.5 mmol) and acetic anhydride (0.2 ml, 4 mmol) were dissolved in pyridine (6 ml) and the mixture stirred at room temperature for 8 h. The solvent was evaporated from the reaction mixture under reduced pressure and the residue worked up as usual. The product was purified by flash column chromatography to obtain the diacetate, (II), as a colourless solid (yield 0.459 g, 91%; m.p. 461–462 K). IR ($CHCl_3$, ν, cm^{-1}): 1755; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.11 (*s*, 6H, MeCO), 2.46 (*s*, 3H, ArMe), 4.43–4.50 (*m*, 2H, Ins H), 4.65–4.73 (*m*, 1H, Ins H), 5.01 (*t*, *J* = 1.9 Hz, 1H, Ins H), 5.58 (*m*, 2H, Ins H), 7.31–7.41 (*m*, 5H, ArH), 7.54–7.62 (*m*, 2H, ArH), 7.82–7.90 (*m*, 2H, ArH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.6, 21.6, 66.8, 67.7, 68.2, 70.5, 107.8, 125.3, 127.7, 128.0, 129.8, 129.9, 133.6, 135.8, 145.4, 168.8. Analysis calculated for $C_{24}H_{24}O_{10}S$: C 57.14, H 4.79%; found: C 57.23, H 4.97%.

Crystallization was carried out by the slow evaporation of a solution of (I) or (II) in organic solvents such as acetonitrile, chloroform, dichloromethane, ethyl acetate and nitromethane at ambient temperature, and yielded plate-like crystals in the case of each solvent.

Compound (I)

Crystal data

$C_{18}H_{20}O_{10}S$
M_r = 428.40
Triclinic, $P\overline{1}$
a = 8.5756 (6) Å
b = 11.0381 (8) Å
c = 11.2005 (8) Å
α = 100.4260 (10)°
β = 103.1230 (10)°
γ = 99.6600 (10)°
V = 991.04 (12) Å^3
Z = 2
Mo *K*α radiation
μ = 0.22 mm^{-1}
T = 298 K
0.49 × 0.29 × 0.13 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2003)
T_{min} = 0.901, T_{max} = 0.972
9864 measured reflections
3581 independent reflections
3179 reflections with $I > 2\sigma(I)$
R_{int} = 0.020

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.115
S = 1.03
3581 reflections
294 parameters
29 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Compound (II)

Crystal data

$C_{24}H_{24}O_{10}S$
M_r = 504.49
Monoclinic, $P2_1/c$
a = 12.3019 (14) Å
b = 8.2155 (10) Å
c = 23.551 (3) Å
β = 91.306 (2)°
V = 2379.6 (5) Å^3
Z = 4
Mo *K*α radiation
μ = 0.19 mm^{-1}
T = 298 K
0.59 × 0.17 × 0.07 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2003)
T_{min} = 0.878, T_{max} = 0.987
11497 measured reflections
4179 independent reflections
3082 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.123
S = 1.08
4179 reflections
319 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

All H atoms were placed in idealized positions (C—H = 0.98 Å for atom H7 and inositol ring H atoms, C—H = 0.93 Å for phenyl H atoms and C—H = 0.96 Å for methyl H atoms) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(methyl C). In compound (I), the anisotropic displacement parameters for carbonyl atom O10 were too large, indicating orientational disorder. However, a reasonable model was obtained by splitting the acetyl

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1···O9^{i}	0.98	2.64	3.344 (2)	129
C4—H4···O5^{ii}	0.98	2.49	3.370 (2)	149
C7—H7···O1^{iii}	0.98	2.47	3.221 (2)	133
C7—H7···O9^{ii}	0.98	2.60	3.391 (2)	138
C9—H9···O8^{iv}	0.93	2.41	3.329 (2)	171
C14—H14*C*···O5^{v}	0.96	2.63	3.443 (3)	142
C16—H16*B*···O8^{iv}	0.96	2.64	3.551 (3)	158
C16—H16*A*···O10^{vi}	0.96	2.60	3.444 (5)	146
C18—H18*A*···O9^{vi}	0.96	2.50	3.437 (15)	165

Symmetry codes: (i) $x+1, y, z$; (ii) $-x+1, -y, -z$; (iii) $-x+2, -y, -z$; (iv) $-x+2, -y+1, -z+1$; (v) $x, y, z+1$; (vi) $-x+1, -y+1, -z$.

Table 2
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1···O8^{i}	0.98	2.56	3.490 (3)	159
C5—H5···O10^{ii}	0.98	2.58	3.153 (3)	117
C22—H22*C*···O10^{iii}	0.96	2.63	3.435 (4)	142
C24—H24*B*···O9^{iv}	0.96	2.46	3.360 (4)	156

Symmetry codes: (i) $-x+2, -y+2, -z+1$; (ii) $-x+1, -y+2, -z+1$; (iii) $x, y-1, z$; (iv) $-x+1, -y+1, -z+1$.

group into two components (C18—C17═O10 and C18′—C17′═O10′), with the sum of the site-occupancy factors for the disordered atoms constrained to unity. The geometries of the two disordered conformations of the acetyl group were restrained to be similar using the SAME and FLAT instructions (s.u. value = 0.005 Å) in *SHELXL97* (Sheldrick, 2008), while the anisotropic displacement parameters of these atoms were restrained to be similar (SIMU instruction; s.u. value = 0.005 Å). The final site-occupation factor of the major conformation was 0.581 (15).

For both compounds, data collection: *SMART* (Bruker, 2003); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2009).

We thank the Department of Science and Technology, New Delhi, India, for financial support. KM is the recipient of a Senior Research Fellowship from the University Grants Commission, New Delhi, India.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SF3106). Services for accessing these data are described at the back of the journal.

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