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Different interaction motifs of dipolar S═O···C═O contacts that associate diastereomers of 2,4(6)-di-*O*-benzoyl-6(4)-*O*-{[(1*S*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-ylmethyl]sulfonyl}-*myo*-inositol 1,3,5-orthoacetate

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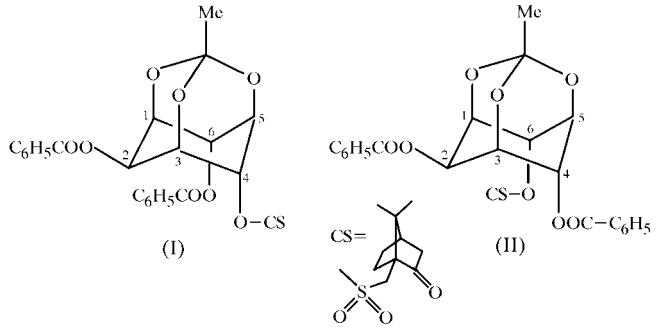
Diastereomeric mixtures of 2,4(6)-di-*O*-benzoyl-6(4)-*O*-[(1*S*)-10-camphorsulfonyl]-*myo*-inositol 1,3,5-orthoesters associate in their crystal structures *via* different geometries of S═O···C═O short contacts, depending upon the substitution. A comparison of the dimeric association in the orthoacetate and orthoformate (solvated) derivatives shows a sheared parallel motif of dipolar S═O···C═O contacts bridging the former, whereas perpendicular S═O···C═O contacts occur in the latter. The title compound, $C_{32}H_{34}O_{11}S$, is chiral, owing to the presence of the camphor moiety.

Comment

The importance of noncovalent intermolecular interactions is being increasingly recognized because of their role in crystal engineering, host–guest complexes, enzyme–substrate binding and drug design (Desiraju & Steiner, 1999). The understanding of weak interactions in molecular crystals can be utilized for the design and synthesis of functional supramolecular assemblies (Desiraju, 1989). Amongst these, dipolar contacts are of considerable interest because of their involvement in the conformational stabilization of proteins (Maccallum *et al.*, 1995) and the structure-based design of drugs (Hof & Diedrich, 2004). The geometrical preferences of S═O···C═O contacts and their role in the formation of inclusion crystals of 2,4(6)-di-*O*-benzoyl-6(4)-*O*-[(1*S*)-10-camphorsulfonyl]-*myo*-inositol 1,3,5-orthoformate were first recognized by us (Manoj *et al.*, 2005, 2006). In order to explore the dipolar association of this framework, a diastereomeric mixture, (I) and (II), of the orthoacetate derivative was prepared. Suitable single crystals containing a 1:1 mixture of (I) and (II) were obtained from a dichloromethane–methanol mixture. We did not observe any (pseudo)polymorphic modifications using different crystallization methods or solvents. Synthetically protected *myo*-inositol 1,3,5-orthoester derivatives also serve as key intermediates (Sureshan *et al.*, 2003) for the preparation of biologically relevant *myo*-inositol phosphates, which play a significant role in cellular signal transduction (Potter & Lampe, 1995).



The crystal structure of the title compound shows short intramolecular C—H···O interactions (Fig. 1) between atom H23*A* (H23*D*) of the camphorsulfonyl methylene group and atom O7 (O7′) of the equatorial benzoyl group in both diastereomers (Table 1). Compared with the conformation of the orthoformate derivative (Manoj *et al.*, 2005, 2006), the orthoacetate shows a significant orientational change in the camphorsulfonate group (see supplementary figures for molecular overlapping), which could be due to this intramolecular C—H···O interaction.

In the absence of conventional hydrogen bonding, diastereomers (I) and (II) are associated *via* dipolar S═O···C═O short contacts and weak hydrogen bonds. The crystal structure shows dimeric bridging (Fig. 1) and the contacts between the diastereomers are asymmetric. The (S═)O···C(═O) distances are 3.144 (5) and 3.556 (5) Å [O9···C16′ = 3.144 (5) Å, O9···C16′═O8′ = 92.2 (1)° and S1═O9···C16′ = 123.6 (1)°; O9′···C16^{i} = 3.556 (5) Å, O9′···C16═O8 = 94.7 (1)° and S1′═O9′···C16 = 103.6 (1)°], with complementary C—H···O contacts of 2.63 and 2.41 Å, respectively (Table 1). These complementary interactions (the shorter of the S═O···C═O contacts is accompanied by a longer C—H···O interaction and *vice versa*) between diastereomers were also seen in the solvates of the orthoformate derivative (Manoj *et al.*, 2005, 2006).

The basic difference in the association of the diastereomers in the title compound and its orthoformate analogue (Manoj *et al.*, 2005, 2006) is in the geometry of the dipolar S═O···C═O contacts. We have classified the S═O···C═O interaction motifs as Types I, II and III (Fig. 2*a*), similar to carbonyl–carbonyl interactions (Allen *et al.*, 1998). In all the crystalline solvates of orthoformate (Manoj *et al.*, 2005, 2006), the contacts were of Type I (Fig. 2*b*), whereas in the orthoacetate crystals they are of Type III (Fig. 2*c*). In the case of

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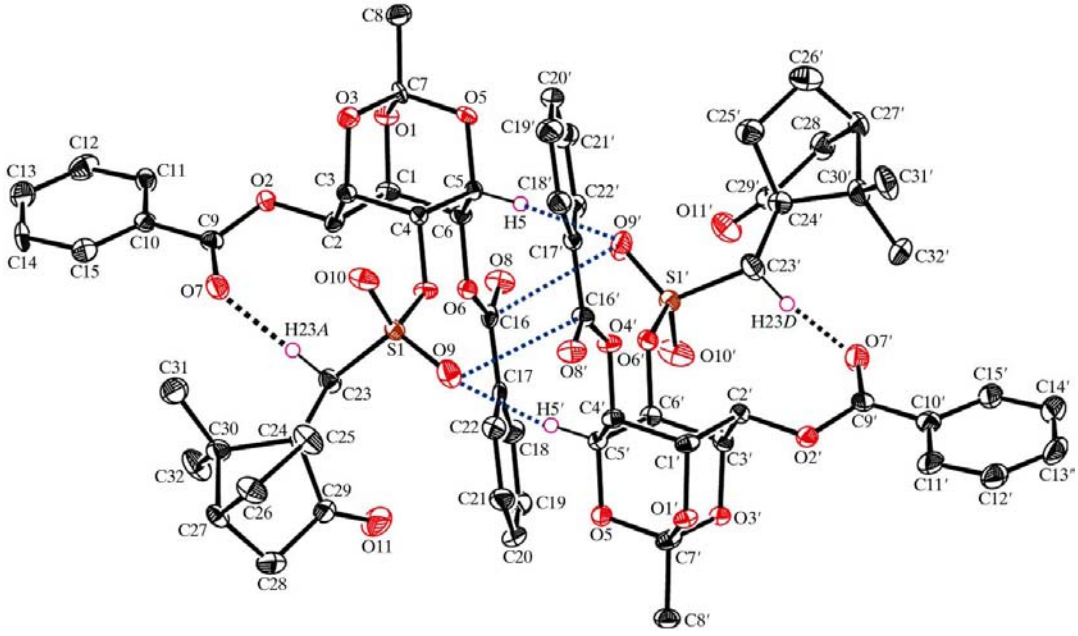

Figure 1
A view of the associated diastereomers of the title compound, showing the atom-labelleing scheme; diastereomer (I) is unprimed and diastereomer (II) is primed. Displacement ellipsoids are drawn at the 30% probability level. Intermolecular S═O···C═O and C—H···O contacts and intramolecular C—H···O interactions are shown as dashed lines. Only H atoms involved in these interactions are shown.

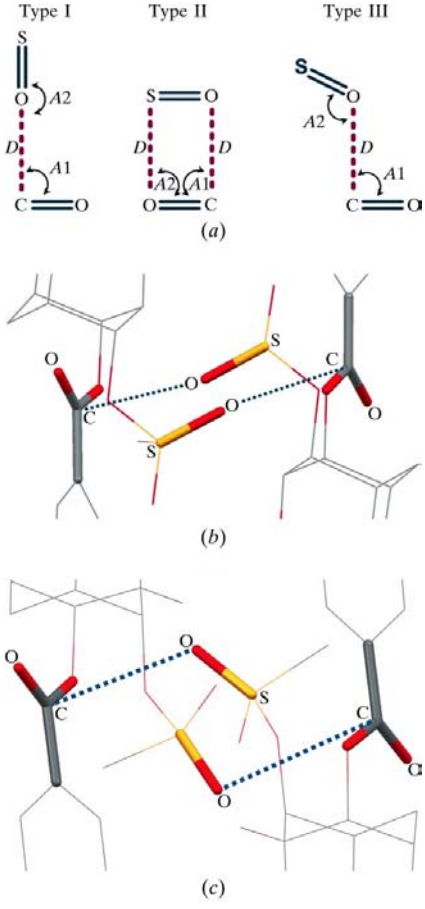

Figure 2
(*a*) Three possible interaction motifs of S═O···C═O dipolar contacts, (*b*) Type I contacts in orthoformate crystals (Manoj *et al.*, 2005, 2006) and (*c*) Type III contacts in orthoacetate crystals.

C═O···C═O contacts, the frequency of occurrence of the various motifs is of the order Type II > Type III > Type I (Allen *et al.*, 1998). A survey of the Cambridge Structural Database (CSD, Version 5.28; Allen, 2002) was carried out to see how S═O···C═O contacts are distributed amongst these three types. The CSD was used for the geometric analysis of noncovalent intermolecular interactions with a distance (*D*) cut-off of 3.6 Å (twice the van der Waals radius of carbon, with a tolerance of 0.2 Å). The angle criteria for Type I were $A1 = 90\pm10^\circ$ and $A2 = 160\pm20^\circ$, for Type II they were $A1 = 90\pm10^\circ$ and $A2 = 90\pm20^\circ$, and for Type III they were $A1 = 90\pm10^\circ$ and $A2 = 120\pm20^\circ$. All searches were carried out with error-free coordinates and restricted entries of disordered, ionic, polymeric and powdered structures. Interestingly, the maximum number of hits (235) was found for Type III, followed by Type I (111 hits) and Type II contacts (21 hits). The preferred Type III motif (and also the less preferred Type II) in S═O···C═O contacts may be due to the heterodipoles having different van der Waals radii for S and C atoms. The Type III dipolar S═O···C═O interaction motif is indeed observed in the binding of *N*-tosyl-D-proline (ligand) to thymidylate synthase (from *Escherichia coli*), an essential enzyme in pyrimidine metabolism with therapeutic applications in cancer and infectious diseases (Erlanson *et al.*, 2000).

Diastereomers (I) and (II), associated *via* S═O···C═O (and C—H···O) interactions, are packed in the crystal structure only *via* weak intermolecular interactions such as C—H···π and C—H···O by translation. These dimeric units, translated along the diagonal to the *a* and *c* axes, form somewhat off-centred C—H···π interactions between the methyl H atoms (H31*E* and H31*C*) of the camphor moiety and the phenyl ring of the axial benzoyl groups, as shown in Fig. 3;

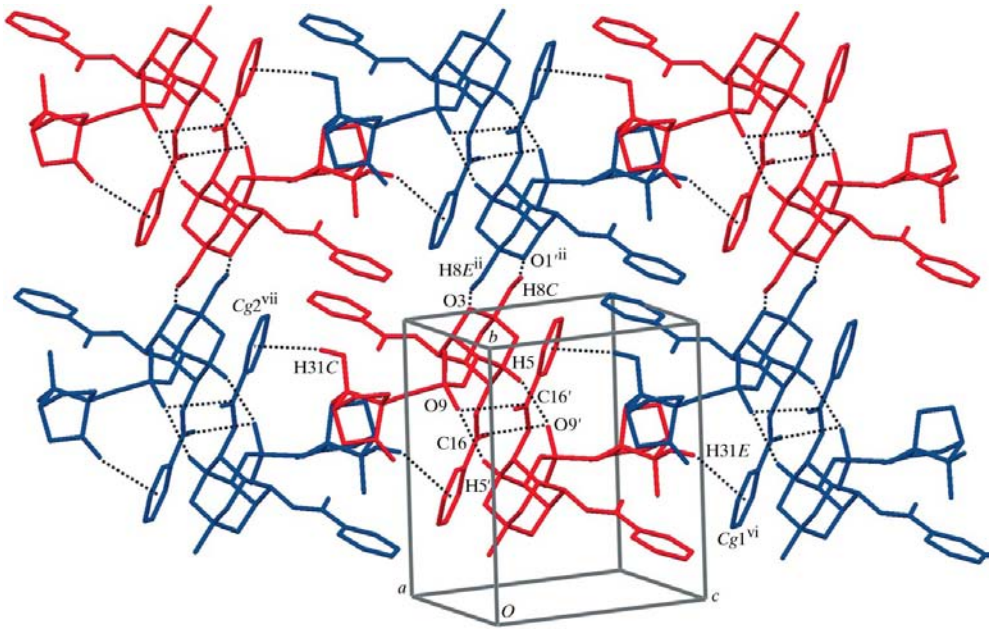

Figure 3
A layer of dimers linked *via* C—H···π (along the diagonal) and C—H···O (along the *b* axis) interactions, both shown as dashed lines. *Cg*1 and *Cg*2 are the centroids of the C17–C22 and C17′–C22′ rings, respectively. [Symmetry codes: (i) $x, y-1, z$; (ii) $x, y+1, z$; (vi) $x-1, y, z+1$; (vii) $x+1, y, z-1$.]

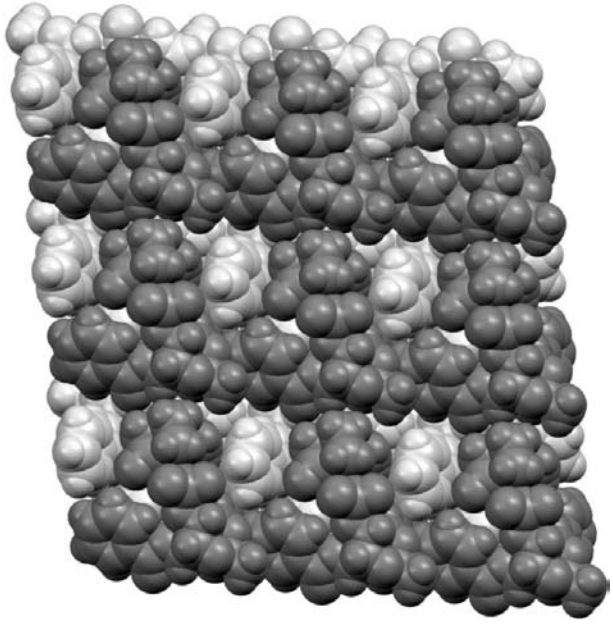

Figure 4
Interlocked grids of diastereomers (I) (dark grey) and (II) (light grey), viewed down the *a* axis.

details are given in Table 1. These molecular rows are linked to unit-translated ones along the *b* axis by very weak head-to-head C—H···O contacts, forming layers as shown in Fig. 3; details are given in Table 1. These layers are linked along the third dimension *via* symmetric C—H···O contacts (Table 1) between the axial benzoyl atoms O8 and O8′, and inositol ring atoms H3′ and H1, respectively (see supplementary figures). Additionally, they are also linked *via* C18′—H18′···O1 and C12—H12···O10 contacts (Table 1) along the *b* axis.

The rectangular net of each of the diastereomers interlocks into the other *via* the equatorial benzoyl groups (Fig. 4), leaving no possibility of any guest inclusion, whereas the orthoformate derivative (Manoj *et al.*, 2005, 2006) had the diastereomers organized in such a way that they created voids for the guests (see supplementary figures).

In conclusion, different motifs of association of S═O and C═O were observed in the crystals of 2,4(6)-di-*O*-benzoyl-6(4)-*O*-[(1*S*)-10-camphorsulfonyl]-*myo*-inositol 1,3,5-orthoformate and its orthoacetate analogue. The experimentally observed motifs of these S═O···C═O contacts are expected to be of considerable interest in the context of improved binding of drug molecules containing S═O groups to their receptors (Erlanson *et al.*, 2000).

Experimental

The preparation of 2,4(6)-di-*O*-benzoyl-6(4)-*O*-[(1*S*)-10-camphorsulfonyl]-*myo*-inositol 1,3,5-orthoacetate, a mixture of diastereomers (I) and (II), was carried out as follows. A mixture of pyridine (10 ml), racemic 2,4-di-*O*-benzoyl-*myo*-inositol 1,3,5-orthoacetate (0.412 g, 1 mmol) and (1*S*)-10-camphorsulfonyl chloride (0.751 g, 3 mmol) was stirred at room temperature for 24 h. Pyridine was evaporated under reduced pressure and the residue obtained was worked up with chloroform. The crude product was purified (yield 0.451 g, 72%) by flash column chromatography over silica (eluent: ethyl acetate–petroleum ether, 1:9 *v*/*v*). The mixture of diastereomers (I) and (II) was crystallized from a mixture of dichloromethane and methanol (4:1 *v*/*v*) in a closed container at room temperature (m.p. 426–427 K). IR ($CHCl_3$, ν, cm^{-1}): 1718, 1733; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.71–0.77 (2*s*, 3H), 0.92–1.02 (2*s*, 3H), 1.43 (*s*, 1H), 1.62 (*s*, 3H), 1.64–1.73 (*m*, 1H), 1.88–2.10 (*m*, 3H), 2.26–2.42 (*m*, 2H), 2.81–2.98 (*m*, 1H), 3.46–3.59 (2*d*, 1H), 4.61–4.76 (*m*, 2H), 4.76–4.83 (*m*, 1H), 5.47–5.59 (*m*, 2H), 5.78–5.86 (*m*, 1H), 7.43–7.63 (*m*, 6H), 8.10–8.18 (*m*, 4H); ^{13}C

NMR ($CDCl_3$, 50 MHz): δ 19.4, 19.5, 23.9, 24.7, 26.7, 26.8, 42.2, 42.6, 47.9, 48.0, 48.1, 57.7, 57.8, 62.3, 67.3, 67.4, 67.5, 69.8, 70.0, 70.3, 72.4, 72.6, 109.2, 128.4, 128.6, 128.8, 129.3, 129.9, 130.0, 133.5, 133.6, 165.1, 165.9, 213.9. Analysis calculated for $C_{32}H_{34}O_{11}S$: C 61.33, H 5.47%; found: C 61.49, H 5.42%.

Crystal data

$C_{32}H_{34}O_{11}S$
M_r = 626.65
Triclinic, $P\overline{1}$
a = 11.5241 (16) Å
b = 11.6958 (16) Å
c = 12.453 (2) Å
α = 80.499 (3)°
β = 62.449 (2)°
γ = 75.937 (2)°
V = 1440.8 (4) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.18 mm^{-1}
T = 298 (2) K
0.68 × 0.25 × 0.14 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2000)
T_{min} = 0.889, T_{max} = 0.976
9388 measured reflections
7596 independent reflections
7284 reflections with $I > 2\sigma(I)$
R_{int} = 0.039

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.052
$wR(F^2)$ = 0.136
S = 1.09
7596 reflections
799 parameters
3 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.54 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Absolute structure: Flack (1983), with 2944 Friedel pairs
Flack parameter: 0.00 (8)

Table 1
Details of intermolecular contacts (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C5—H5···O9′	0.98	2.41	3.153 (5)	132
C23—H23A···O7	0.97	2.43	3.347 (5)	158
C5′—H5′···O9	0.98	2.63	3.351 (5)	130
C23′—H23D···O7′	0.97	2.63	3.252 (5)	122
C8′—H8E···O3^{i}	0.96	2.76	3.658 (6)	155
C8—H8C···O1′^{ii}	0.96	2.75	3.644 (5)	155
C12—H12···O10^{iii}	0.93	2.72	3.495 (6)	142
C1—H1···O8′^{iii}	0.98	2.33	3.275 (5)	161
C28—H28B···O11′^{iv}	0.97	2.45	3.297 (6)	146
C18′—H18′···O1^{v}	0.93	2.71	3.485 (6)	142
C3′—H3′···O8^{v}	0.98	2.35	3.310 (5)	167
C31′—H31E···$Cg1^{vi}$	0.96	2.86	3.724	151
C31—H31C···$Cg2^{vii}$	0.96	3.06	3.943	153

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

All H atoms were placed in idealized positions, with C—H = 0.98 Å for atoms H27 and H27′ and inositol ring H atoms, 0.93 Å for phenyl H atoms, 0.97 Å for methylene H atoms and 0.96 Å for methyl H atoms, and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Version 1.5; Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* (Sheldrick, 1997), *PLATON* (Spek, 2003) and *publCIF* (Westrip, 2007).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3047). Services for accessing these data are described at the back of the journal.

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