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Hydrogen-bonding and C—H···π interactions in 1,7-bis(4-hydroxy-3-methoxyphenyl)heptane-3,5-dione (tetrahydrocurcumin)

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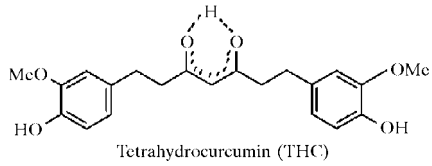
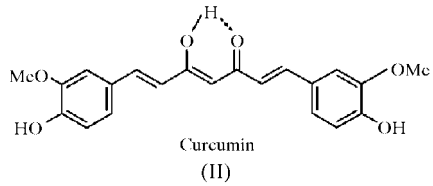
The title compound, $C_{21}H_{24}O_6$, is the reduced form of curcumin, and exhibits important cosmoceutical properties. The molecule is non-planar and the benzene rings positioned at the ends of the heptane chain are orthogonally placed, with a dihedral angle of 84.09 (7)° between them. The molecular geometry and H-atom locations reveal that the 'heptane-3,5-dione' moiety exists in the keto–enol form, with the hydroxy H atom disordered over two adjacent sites. The packing of the molecules in the lattice is directed by strong O—H···O intermolecular hydrogen bonds, which generate two-dimensional sheets. These sheets are linked by C—H···O hydrogen bonds and weak C—H···π interactions to develop a three-dimensional network.

Comment

Tetrahydrocurcuminoids, such as the title compound, (I), are derived from curcuminoids, such as (II), and may be extracted from the roots of *Curcuma longa*, commonly called turmeric root (Govindarajan, 1980). Tetrahydrocurcuminoids are colourless, unlike the yellow curcuminoids. They may therefore be used in colour-free foods and cosmetic products, which currently employ conventional synthetic antioxidants such as butylated hydroxytoluene (BHT). An antioxidant used in a cosmetic application should have the capability of efficiently quenching any radicals on the surface of the skin. In this context, compound (I) displays a superior free-radical scavenging ability and also exhibits antioxidant, anti-inflammatory and skin-lightening actions (Sugiyama *et al.*, 1996; Srihari Rao *et al.*, 1982) and anticancer activity (Huang *et al.*, 1995). It is thought that the *p*-hydroxy functional groups in (I) are responsible for the antioxidant and chemopreventive action of the compound (Rao *et al.*, 1995; Halliwell & Gutteridge, 1985). We have established the crystal structure of (I) with the intention that it will assist in pharmocological studies of the compound.



Tetrahydrocurcumin (THC)
(I)



Curcumin
(II)

Electron delocalization and intramolecular hydrogen bonding in the keto-enol moiety —CO—HC═C—OH have been studied in a number of molecules (Semmingsen, 1976) and in curcuminoid structures (Mostad, 1994; Arrieta *et al.*, 2000; Tonnesen *et al.*, 1982). Of the possible tautomeric forms, it appears that, in the crystal phase, *β*-diketones prefer the *cis*-enol arrangement stabilized by a strong intramolecular hydrogen bond.

A view of (I) with the labelling scheme is shown in Fig. 1 and the principal geometry details of the keto–enol function are

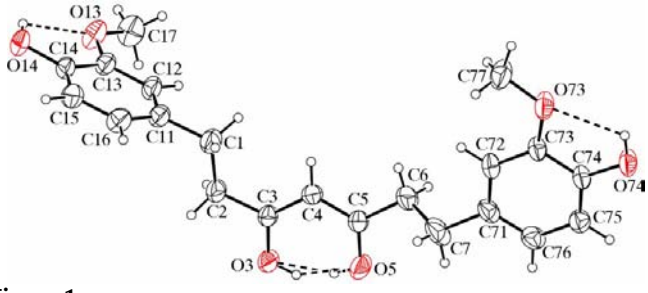


Figure 1
The structure of (I), showing the atom-numbering scheme and 30% probability displacement ellipsoids. H atoms are shown as small spheres of arbitrary radii.

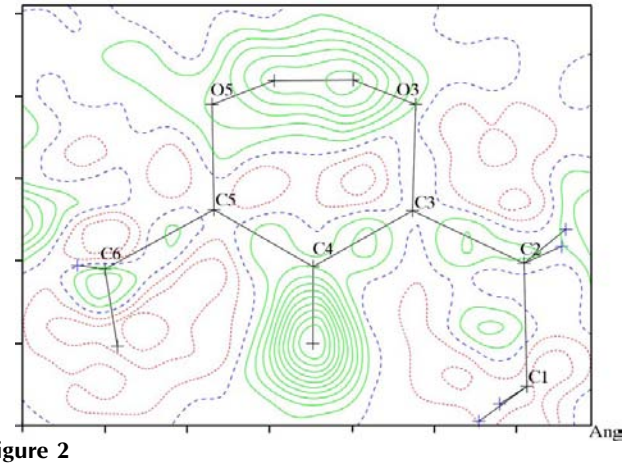


Figure 2
A difference map in the plane of the keto–enol system, showing the hydroxy H-atom disorder at O3 and O5 and the single H atom at C4. Contours are drawn at 0.05 e Å^{-3}.

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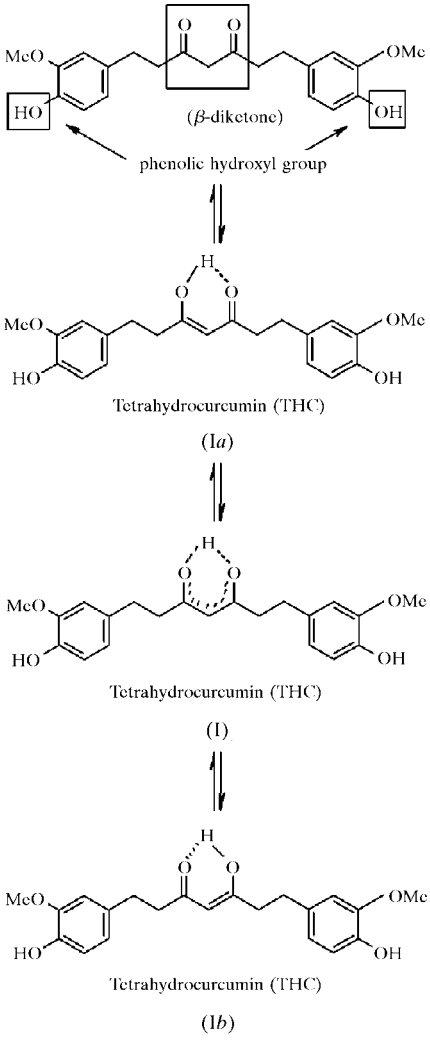
given in Table 1. A difference map (Fig. 2) clearly established that there is only one H atom at C4 and that the 'dione' adopts the expected keto–enol form, but with the hydroxy H atom essentially equally disordered between atoms O3 and O5 [respective hydroxy-atom occupancies = 0.54 (4) and 0.46 (4)], corresponding to structures (I*a*) and (I*b*) (see scheme below). The key bond lengths (Table 1) are entirely consistent with this disorder model and with strong intramolecular O3—H···O5 and O5—H···O3 hydrogen bonds (Table 2). The keto–enol moiety C3–C5/O3/O5 is planar [deviations in the range −0.012 (1) to 0.015 (1) Å]. The aromatic rings C11–C16 and C71–C76 form interplanar angles of 88.4 (1) and 9.9 (1)°, respectively, with the keto–enol plane, and an angle of 88.4 (1)° with one another.



The unit-occupancy hydroxy groups O14—H14 and O74—H74 both take part in strong bifurcated intra- and intermolecular O—H···O hydrogen bonds which, together with a C—H···O hydrogen bond (Table 2), serve to link the molecules into sheets in the ($\bar{1}$10) plane entirely by simple translation, as shown in Fig. 3. In this way, large $R_5^5(42)$ rings (Bernstein *et al.*, 1995) are developed, utilizing five O—H···O hydrogen bonds.

The packing of (I) is further stabilized into a three-dimensional network by C—H···O and C—H···π intermolecular interactions, which serve to link inversion-related sheets. Fig. 4 shows an $R_2^2(30)$ ring generated by pairs of inversion-related C12—H12···O74($2-x$, $1-y$, $1-z$) hydrogen bonds (see Table 2). The hydrogen-bonded sheets are further linked by weak C—H···π interactions between inversion- and translation-related molecules, as shown in Fig. 5 (details are given in Table 2). A combination of aromatic C—H···π and C—H···O interactions generate different packing motifs with altered molecular conformations. This may have a significant impact on the biological activity of the compound.

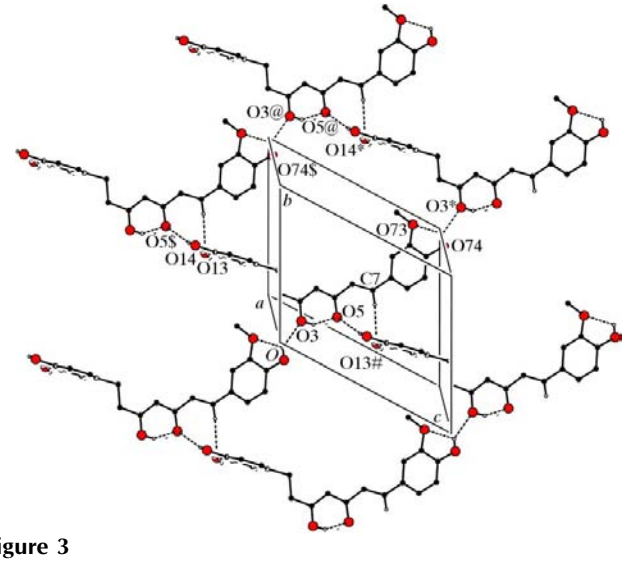


Figure 3
A packing diagram for (I), showing the hydrogen-bonded sheet of molecules. Atoms labelled with an asterisk (*), dollar sign ($), hash (#) or 'at' symbol (@) are at the symmetry positions ($1+x$, $1+y$, $1+z$), (x, y, $z-1$), (x, y, $1+z$) and (x, $1+y$, $1+z$), respectively.

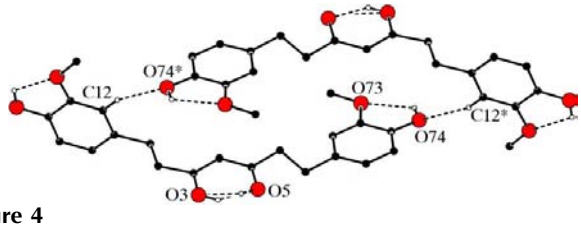


Figure 4
A diagram showing pairs of molecules about the inversion centre at (1, $\frac{1}{2}$, $\frac{1}{2}$), linked to form a dimer *via* C—H···O interactions. Atoms labelled with an asterisk (*) are at the symmetry position ($2-x$, $1-y$, $1-z$).

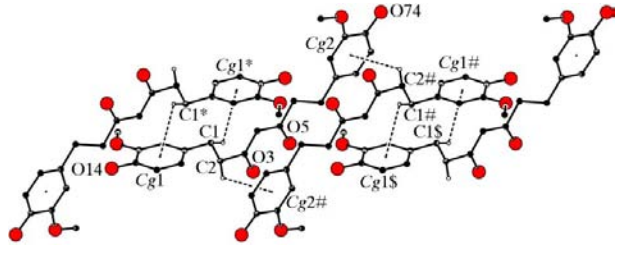


Figure 5
A diagram showing the development of a chain of molecules in the *c* direction *via* weak C—H···π interactions, with links generated by a combination of inversion and translation. Atoms labelled with an asterisk (*), dollar sign ($) or hash (#) are at the symmetry positions ($1-x$, $1-y$, $-z$), (x, y, $1+z$) and ($1-x$, $1-y$, $1-z$), respectively.

Experimental

Curcumin, (II), was converted to tetrahydrocurcumin, (I), by hydrogenation, with PtO_2 as catalyst, according to the method of Uehara *et al.* (1987). Single crystals of (I) were grown by slow evaporation of a solution in methanol.

Crystal data

$C_{21}H_{24}O_6$
M_r = 372.40
Triclinic, $P\overline{1}$
a = 7.981 (3) Å
b = 11.388 (3) Å
c = 12.497 (3) Å
α = 117.065 (3)°
β = 100.394 (10)°
γ = 94.856 (3)°
V = 976.7 (5) Å^3
Z = 2
D_x = 1.266 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 400 reflections
θ = 2.6–20.9°
μ = 0.09 mm^{-1}
T = 293 K
Prism, off-white
0.40 × 0.35 × 0.30 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.893, T_{max} = 0.981
10 125 measured reflections
3933 independent reflections
3244 reflections with $I > 2\sigma(I)$
R_{int} = 0.014
θ_{max} = 27.1°
$h = -9 \rightarrow 9$
$k = -14 \rightarrow 14$
$l = -15 \rightarrow 15$

Table 1
Selected geometric parameters (Å, °).

O3—C3	1.289 (2)	C3—C4	1.385 (2)
O5—C5	1.276 (2)	C4—C5	1.390 (2)
C1—C2	1.508 (3)	C5—C6	1.509 (2)
C1—C11	1.515 (2)	C6—C7	1.441 (3)
C2—C3	1.498 (2)	C7—C71	1.518 (2)
C1—C2—C3	116.56 (14)	C3—C4—C5	120.71 (16)
O3—C3—C2	113.52 (14)	O5—C5—C4	120.83 (15)
O3—C3—C4	121.12 (15)	O5—C5—C6	117.67 (17)
C2—C3—C4	125.36 (15)	C4—C5—C6	121.50 (17)

Table 2
Hydrogen-bonding geometry (Å, °).

*Cg*1 denotes the centroid of the C11–C16 ring and *Cg*2 the centroid of the C71–C76 ring.

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O5	0.82	1.74	2.472 (2)	147
O5—H5···O3	0.82	1.75	2.472 (2)	146
O14—H14···O5^{i}	0.82	2.18	2.934 (2)	153
O14—H14···O13	0.82	2.21	2.655 (2)	114
O74—H74···O3^{ii}	0.82	2.14	2.773 (2)	134
O74—H74···O73	0.82	2.23	2.678 (2)	115
C7—H7*A*···O13^{iii}	0.97	2.54	3.510 (3)	173
C12—H12···O74^{iv}	0.93	2.51	3.411 (2)	162
C1—H1*B*···*Cg*1^{v}	0.97	3.29	3.89	122
C2—H2*A*···*Cg*2^{vi}	0.97	3.20	3.82	123

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.171
S = 1.06
3933 reflections
251 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0943P)^2 + 0.1978P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

All H atoms were visible in difference maps. It was clear that there was H-atom disorder at the O3 and O5 sites, and this was allowed for by refinement of linked occupancy parameters for atoms H3 and H5 [final values = 0.54 (4) and 0.46 (4)]. All H atoms were treated as riding, with C—H = 0.93 Å for aromatic, 0.97 Å for CH_2 and 0.96 Å for CH_3 H atoms, and with U_{iso}(H) = 1.5U_{eq}(C) for methyl and 1.2U_{eq}(C) for all other H atoms.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1998); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003) and *ORTEP*-3 (Farrugia, 1977); software used to prepare material for publication: *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1755). Services for accessing these data are described at the back of the journal.

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