Structural Studies of Curcuminoids. II. Crystal Structure of 1,7-Bis(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione–Methanol Complex

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The crystal and molecular structure of the curcumin derivative 1,7-bis(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione-methanol complex (B4HPHDD) has been determined at 121 K by X-ray crystallographic methods using 2090 reflections observed by counter methods. The crystals are monoclinic, space group $P2_1/n$ with unit cell dimensions $a=6.781(2)$ Å, $b=7.606(1)$ Å, $c=33.024(5)$ Å, $\beta=93.73(2)°$. The structure was refined to a conventional R-factor of 0.033. Estimated standard deviations are 0.003 Å and 0.2° in interatomic distances and angles when hydrogen atoms are not involved. The enol-ring is found to be asymmetric.

Three diarylheptanoides have been isolated from the plant *Curcuma longa* L. (Fig. 1). These three compounds constitute the main coloured substances isolated from the plant material. Whereas the chromatographic analysis (HPLC) of the natural occurring diarylheptanoides will be published elsewhere,[1] we report here the X-ray crystallographic study of a synthetic compound found by HPLC/TLC to be equivalent to one of the compounds found in plant material, namely the one marked as III in Fig. 1. The crystal structure of the compound indicated as I has been reported previously.[2] These structure investigations are carried out in order to study the effect of the conjugation in curcuminoid molecules on the structure and stability of the 3,5-dione group as well as on the conformation of such molecules. By studying similar molecules in different crystalline environments it may also be possible to estimate the influence of molecular packing on the structure and conformation.

EXPERIMENTAL

The title compound is a natural product[3] and was prepared from 2,4-pentanedione and 4-hydroxybenzaldehyde.[4] The compound was recrystallized from a mixture of ethyl–acetate and methanol and deep orange coloured plate-formed crystals separated. A crystal of dimensions 0.6×0.5×0.1 mm was used for the collection of X-ray data through the procedure described under Experimental Conditions. Cell parameters were determined by a least squares fit to the diffractometer settings for 15 general reflections. The standard deviations in the measured intensities were calculated as $\delta(I)=[C_T+(0.02\ C_N)^2]^{1/2}$, where C_T is the total number of counts and C_N is the scan count minus the background count. The intensity data were
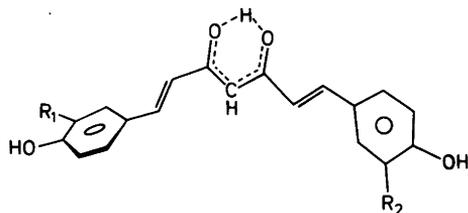

Fig. 1. Diaryl heptanoides isolated from *Curcuma longa* L. I, $R_1=R_2=OCH_3$: curcumin. II, $R_1=OCH_3$, $R_2=H$: demethoxycurcumin. III, $R_1=R_2=H$: bisdemethoxycurcumin.

Table 1. Fractional atomic coordinates and thermal parameters multiplied by 10^4. The anisotropic temperature factor is given by $-2\pi^2(U_{11}a^{+2}h^2+\ldots+2U_{12}a^+b^+hk+\ldots)$. Estimated standard deviations in parentheses.

Atom	X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	-4644(2)	4706(2)	6512(0)	318(9)	357(9)	228(8)	-1(8)	-80(7)	17(7)
O2	3083(2)	3189(2)	8549(0)	256(9)	313(9)	205(8)	-35(8)	6(7)	34(7)
O3	6180(2)	3615(2)	8999(0)	269(8)	280(8)	206(8)	-20(8)	5(7)	35(7)
O4	16870(2)	8605(2)	9738(0)	286(9)	424(10)	298(9)	11(9)	-64(7)	36(8)
O5	8611(2)	896(2)	9221(0)	275(9)	288(9)	254(8)	-25(8)	-70(7)	3(7)
C1	-3191(3)	4457(3)	6819(1)	314(13)	190(12)	185(11)	50(11)	39(10)	-55(9)
C2	-1261(3)	5057(3)	6783(1)	280(12)	197(12)	173(11)	-10(11)	20(10)	-9(9)
C3	122(3)	4815(3)	7104(1)	252(13)	192(12)	221(11)	-8(11)	20(10)	-18(9)
C4	-369(3)	3965(3)	7460(1)	245(12)	187(12)	180(10)	10(11)	17(9)	-19(9)
C5	-2306(3)	3321(3)	7472(1)	308(13)	214(12)	184(11)	-14(11)	39(10)	-2(9)
C6	-3694(3)	3560(3)	7154(1)	254(13)	252(12)	217(11)	-4(11)	13(10)	-29(9)
C7	961(3)	3767(3)	7823(1)	292(14)	202(12)	196(11)	7(12)	39(10)	-7(9)
C8	2717(3)	4532(3)	7903(1)	265(13)	219(12)	195(11)	-11(11)	14(10)	5(10)
C9	3882(3)	4246(3)	8281(1)	251(13)	199(11)	197(11)	15(11)	49(10)	-12(9)
C10	5707(3)	4990(3)	8364(1)	252(13)	229(12)	192(11)	-16(11)	38(10)	14(9)
C11	6833(3)	4661(3)	8734(1)	237(12)	208(11)	209(11)	24(11)	33(10)	-32(9)
C12	8742(3)	5519(3)	8810(1)	250(13)	232(12)	217(12)	6(11)	18(10)	11(10)
C13	9667(3)	5556(3)	9180(1)	256(13)	234(12)	224(12)	10(11)	39(10)	-4(10)
C14	11554(3)	6356(3)	9308(1)	228(13)	224(12)	231(11)	4(11)	14(10)	-21(9)
C15	12251(3)	6226(3)	9713(1)	315(14)	320(13)	194(11)	-51(13)	11(10)	13(10)
C16	14011(3)	6985(3)	9855(1)	350(15)	334(14)	181(12)	-26(12)	-31(11)	3(10)
C17	15137(3)	7891(3)	9589(1)	234(13)	251(12)	272(12)	-20(11)	-10(10)	-23(10)
C18	14490(3)	8020(3)	9181(1)	238(13)	271(13)	230(12)	15(12)	7(10)	26(10)
C19	12722(3)	7271(3)	9044(1)	258(13)	255(12)	187(11)	40(11)	-7(10)	-6(9)
C20	10446(4)	1248(4)	9457(1)	272(13)	332(15)	301(13)	-3(14)	-82(11)	-25(11)

Table 2. Fractional atomic coordinates and isotropic thermal parameters for the hydrogen atoms. Estimated standard deviations in parentheses.

Atom	X	Y	Z	B	Atom	X	Y	Z	B
HO1	-0.419(4)	0.515(4)	0.629(1)	6.2(8)	HO4	1.741(4)	.928(4)	0.954(1)	6.8(9)
HO5	0.789(4)	0.194(4)	0.917(1)	6.8(8)	HX	0.406(4)	0.317(3)	0.877(1)	4.5(7)
H2	-0.091(3)	0.569(3)	0.654(1)	1.8(4)	H3	0.150(3)	0.527(3)	0.708(1)	2.3(5)
H5	-0.266(3)	0.271(3)	0.771(1)	1.5(4)	H6	-0.503(3)	0.310(3)	0.717(1)	2.4(5)
H7	0.049(3)	0.299(3)	0.803(1)	1.9(4)	H8	0.331(3)	0.531(3)	0.772(1)	2.0(5)
H10	0.625(3)	0.573(3)	0.817(1)	1.7(4)	H12	0.929(3)	0.610(3)	0.858(1)	2.0(4)
H13	0.897(3)	0.497(3)	0.940(1)	1.8(4)	H15	1.152(3)	0.555(3)	0.991(1)	3.4(5)
H16	1.447(3)	0.689(3)	1.013(1)	2.1(4)	H18	1.533(3)	0.868(3)	0.900(1)	2.5(5)
H19	1.225(3)	0.741(3)	.875(1)	1.8(4)	H2O1	1.130(4)	0.201(3)	0.930(1)	3.8(6)
H2O2	1.110(4)	0.010(4)	0.951(1)	4.2(6)	H2O3	1.016(3)	0.181(3)	0.972(1)	3.6(5)

corrected for Lorentz and polarization effects. The variation in the intensities of the test reflections were less than 1.5 % and no corrections were made on this basis. Scattering factors used were those of Doyle and Turner[5] for O and C, and of Stewart, Davidson and Simpson[6] for H.

CRYSTAL DATA

1,7-Bis(4-hydroxyphenyl)-1,6-heptadien-3,5-dione-methanol. $C_{19}O_4H_{16} \cdot CH_3OH$, monoclinic, $a=6.781(2)$ Å, $b=7.606(1)$ Å, $c=33.024(5)$ Å, $\beta=93.73(2)°$, $V=1699.7$ Å^3, $FW=340.2$, $Z=4$, $F_{000}=720$, space group $P2_1/n$.

EXPERIMENTAL CONDITIONS

Instrument	SYNTEX P$\bar{1}$
Radiation	Graphite crystal monochromated Mo$K\alpha$ $\lambda=0.71069$ Å
Crystal dimensions/mm	0.6×0.5×0.1
Scanning mode	ω
Scan speed/° min^{-1}	2
Scan range/°	1.5
Background counts	For 0.35 of scan time at scan limits
Temperature/K	121
2θ range/°	2.5–45.0
Number of reflections meas.	2634
Number of reflections $I>2.5\sigma(I)$	2090
Number of standard reflections	3
Number of reflections between standard reflections	57

STRUCTURE DETERMINATION

The structure was solved by direct methods using the program assembly MULTAN.[7] Successive Fourier syntheses yielded the positions of all the non-hydrogen atoms, and revealed the existence of one molecule of methanol per asymmetric unit. After a least squares refinement with isotropic temperature factors, all the hydrogen atomic positions were found from difference syntheses. All positional parameters, anisotropic
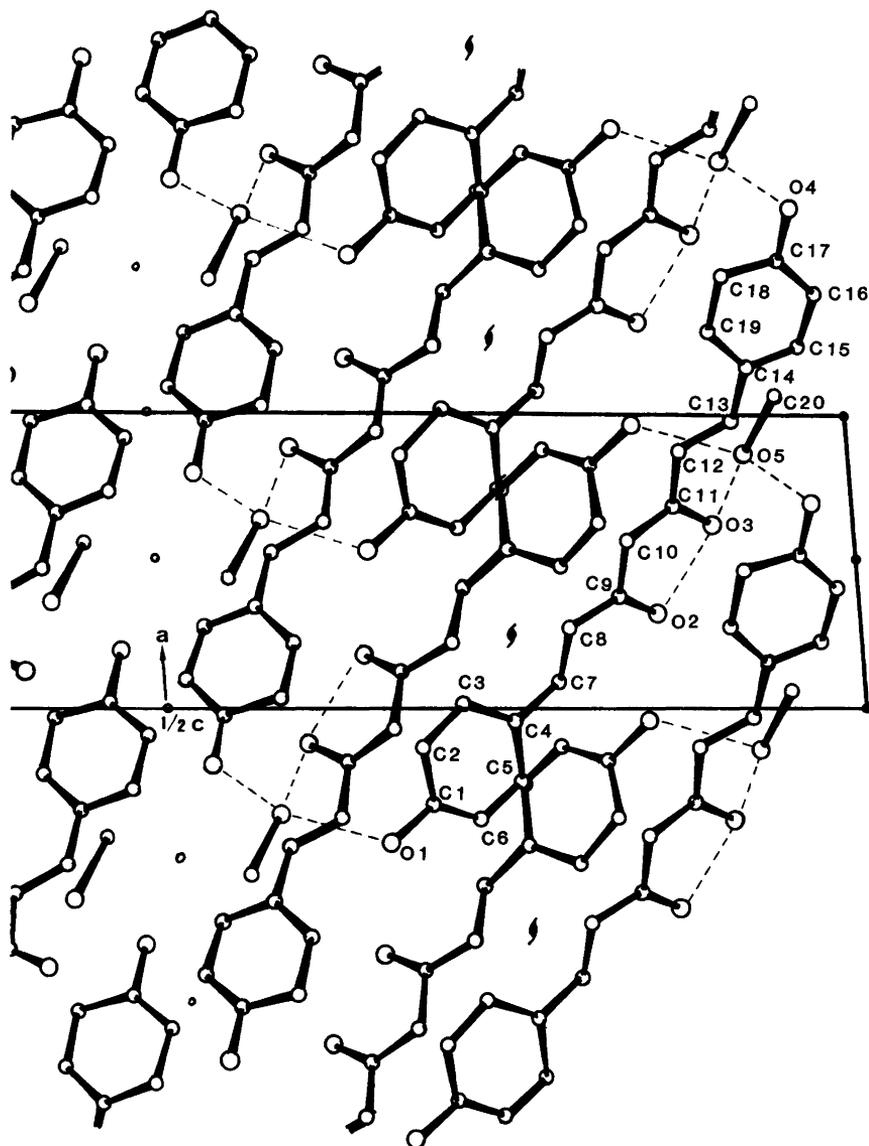
Fig. 2. Numbering of the atoms and the molecular packing in crystals of B4HPHDD·M as seen along the *b*-axis.

temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms were refined in the final least squares calculations giving an *R*-factor of 0.033 and a goodness of fit $S=[\Sigma w\Delta^2/(m-n)]^{1/2}=2.9$. The final parameters are given i Tables 1 and 2. Tables of observed and calculated structure factors are available from the authors.

DESCRIPTION AND DISCUSSION

The labelling of the atoms is given in Fig. 2, which also illustrates the molecular packing and the hydrogen bond system. Bond lengths and angles are given in Table 3 and some of the torsion angles in Table 4. The packing of the molecules in the present structure is different

Table 3. Bond lengths and angles. Estimated standard deviations are $(2–3)\times10^{-3}$ Å in bond lengths and 2×10^{-1} in angles.

Bond lengths (Å)		Bond angles (°)	
C1–O1	1.359	O1–C1–C2	123.2
C1–C2	1.394	O1–C1–C6	117.1
C2–C3	1.382	C1–C2–C3	120.1
C3–C4	1.401	C2–C3–C4	121.3
C4–C5	1.404	C3–C4–C5	117.3
C5–C6	1.377	C4–C5–C6	121.8
C6–C1	1.388	C5–C6–C1	119.9
C4–C7	1.459	C3–C4–C7	124.6
C7–C8	1.336	C5–C4–C7	118.0
C8–C9	1.448	C4–C7–C8	127.9
C9–O2	1.337	C7–C8–C9	122.4
C9–C10	1.372	C8–C9–C10	123.1
C10–C11	1.421	C8–C9–C2	116.0
C11–O3	1.283	O2–C9–C10	120.9
C11–C12	1.457	C9–C10–C11	121.8
C12–C13	1.337	C10–C11–C12	119.3
C13–C14	1.455	C10–C11–O3	120.4
C14–C15	1.395	C3–C11–C12	120.2
C15–C16	1.380	C11–C12–C13	121.6
C16–C17	1.386	C12–C13–C14	128.8
C17–O4	1.357	C13–C14–C15	119.1
C17–C18	1.394	C14–C15–C16	121.9
C18–C19	1.377	C15–C16–C17	119.5
C19–C14	1.400	C16–C17–C18	119.8
C20–O5	1.447	C16–C17–C4	118.0
		O4–C17–C18	122.2
		C17–C18–C19	120.1
Mean value of the X–H distances		C18–C19–C14	121.1
C–H	0.98(2)	C19–C14–C15	117.6
O–H	0.91(4)	C19–C14–C13	123.3

Table 4. Torsion angles in B4HPHDD.

Angle	
C3–C4–C7–C8	9.9
C4–C7–C8–C9	178.9
C7–C8–C9–C10	178.5
C7–C8–C9–O2	–1.1
C8–C9–C10–C11	–178.9
O2–C9–C10–C11	0.7
C9–C10–C11–O3	1.5
C9–C10–C11–C12	–178.7
C10–C11–C12–C13	165.8
O3–C11–C12–C13	–14.4
C11–C12–C13–C14	–179.6
C12–C13–C14–C15	–179.7

from that found for curcumin molecules.[2] The presence of the methanol molecules results in a

hydrogen bond system where there is no direct hydrogen bond between B4HPHDD molecules. The alcoholic oxygen atom is involved in three hydrogen bonds to three different B4HPHDD molecules, as donor to the O3 oxygen and to O1 and O4 as acceptor. In this way molecules related by screw axes are bonded together in layers parallel to, and separated by, (002) planes. Between these layers there appears to be only weak van der Waals forces, the closest contact being C16–C16' related by a center of symmetry (3.414 Å). (H16–C16':3.12 Å). Within the hydrogen bonded layers there also appears to be interactions between the aromatic parts of the molecules in a way often encountered in crystal structures of such molecules.[6] These contacts are illustrated in Fig. 3.
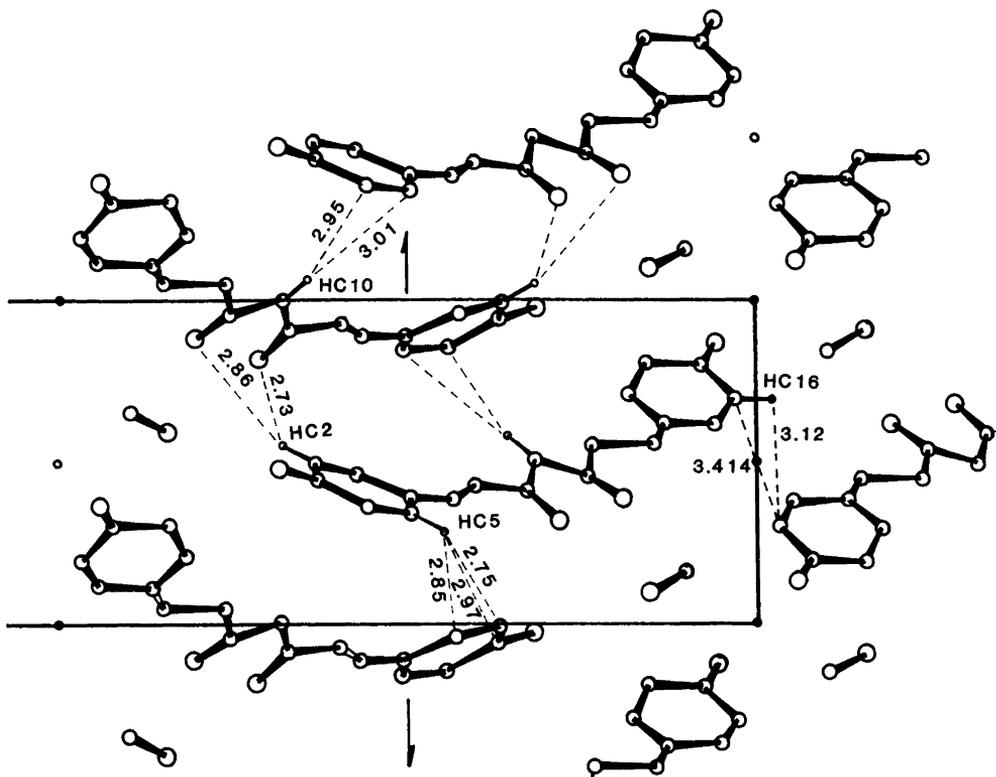
Only one of the oxygen atoms of the enol-ring

*Fig. 3.*Molecular packing of B4HPHDD·M units as seen along the *a*-axis, showing the distances between the aromatic moieties.

is engaged in an intermolecular hydrogen bond and in comparison with curcumin this introduces an element of asymmetry, which may explain the asymmetry of the entire enol-ring geometry in the present structure. Thus the two C–O bonds are significantly different as are the two bonds C9–C10 and C10–C11 signaling a localization of double bonding between C9–C10 and C11–O3. The intramolecular hydrogen bond between O2 and O3 is found to be established and the
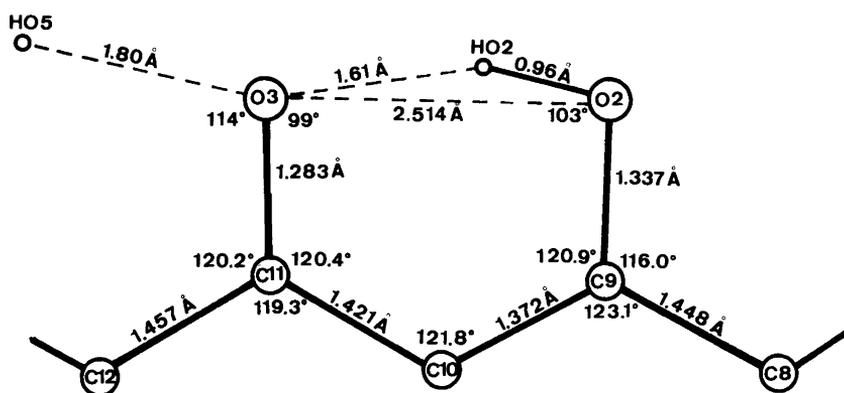

*Fig. 4.*The geometry of the enol ring and relevant hydrogen bonds.

geometry of the enol-ring and the relevant hydrogen atoms is shown in Fig. 4. The five atoms of the enol-ring are within 0.015 Å from a least squares plane through these atoms, whereas HO2 is not significantly (0.036 Å) out of that plane.

The O2–O3 distance of 2.514 Å is significantly longer than the corresponding distance found in the crystal structure of curcumin.

The overall conformation of the B4HPHDD molecules in the crystal of the methanol complex is also different from that found in the curcumin crystals. The torsion-angles about the C11–C12 and C13–C14 bonds are in the present study found to be –14.4 and –179.7°, respectively, as compared to –163.3 and 25.2° in curcumin. Thus the devition from coplanarity between the three groups connected through the C7–C8 and the C12–C13 bonds is less pronounced in the present crystals than in those of curcumin. The angles between the terminal phenyl groups are found to be 16.2° as compared to 47° in the curcumin crystals. The shortening of the C13–C14 bond which might be expected with a decrease of 25° in the torsion angle about C13–C14 appears also to be present, the C13–C14 bond being 1.455 Å as compared to 1.471 in curcumin and the C4–C7 and C13–C14 bonds are of equal lengths in the present study in contrast to the findings in the curcumin crystals. The C14–C19 ring is planar within the accuracy of the study, however, the C1–C6 ring appears to display a slight deviation from strict planarity as C1 and C4 is situated 0.015 Å above a least squares plane through the six ring atoms, whereas the other ring atoms lie about 0.008 Å beneath that plane. The angle between the planes C1–C2–C3–C4 and C4–C5–C6–C1 is found to be 2.2°.

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