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ORIGINAL PAPER

Crystal Structure of 1,7-Bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione

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Abstract The synthesis and crystal structure of 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione is described. This compound is a curcuminoid analogue, configurationally symmetric about the C4–C5 atoms and also retains the two fold axis in the crystal phase. This compound crystallizes in the space group C2/c with unit cell parameters $a = 19.203(1)$ Å, $b = 13.147(1)$ Å, $c = 8.801(1)$ Å, $\beta = 112.99(1)°$, with half a molecule in the asymmetric unit. The ketenedithioacetal functionality present between the carbonyl groups prevents the possibility of keto-enol tautomerization in this compound. The push-pull nature of the ketenedithioacetal functionality organizes the cinnamoyl groups parallel to each other.

Keywords Crystal structure · 1,7-Bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione · Curcumin analogue · X-ray diffraction

Introduction

The title compound 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione is a derivative of curcumin, 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione, a natural food dye used in traditional cooking in Asia. Curcuminoids (1,7-diaryl-1,6-heptadiene-3,5-diones) constitute the most important active chemical components in the herbaceous medicinal plant Curcuma longa Linn(turmeric). Natural and synthetic curcuminoid analogues are reported to possess antitumour, antioxidant, antimutagenic and anti-inflammatory activities [1–6]. The synthetic curcuminoid analogue 1,7-bis(2-chlorophenyl)-1,6-heptadiene-3,5-dione which also shows antitumour activity is closely related to the title compound except for the substitution at the C(4) position [7]. The structure investigation of the title compound gains considerable attention in this context.

Curcumin and its analogues usually exist in the completely enolized form as shown by their crystal structures [8, 9]. In the crystal structure of Curcumin, the substituted cinnamoyl groups are far apart (5.015 Å) [8]. The compound 1,6-hexadiene-3,5-dione having an unsubstituted methylene group between the carbonyl groups and 1,7-diphenyl-4-butyl-1,6-heptadiene-3,5-dione having a butyl group between the carbonyl groups do have linear structures [10]. The extended conjugation resulting from the enolization contributes to the stability of their linear structure. In bis(cinnamoyl) ketenedithioacetal, the ketenedithioacetal functionality present between the carbonyl groups prevent the possibility of keto-enol tautomerization observed in enolizable 1,3-carbonyl compounds [11–13]. The crystal structure of the title compound shows that the two cinnamoyl groups are parallel to each other and the double bonds are very close to each other. The push-pull

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nature of the ketenedithioacetal functionality organizes the cinnamoyl groups parallel to each other.

Experimental

Synthesis

Sodium metal (0.45 g, 20 mmol) was dissolved in ethanol (20 mL) to which cyclic diacetyl ketenedithioacetal (1.01 g, 5 mmol) was added followed by para-chloro benzaldehyde (10 mmol). The reaction mixture was stirred at 0–5 °C for 4 h. The solid obtained was filtered, washed in ethanol and recrystallized from a mixture of hexane and ethyl acetate to give the title compound.

Crystallography

Needle shaped yellow crystals of the title compound were obtained from a solution of methanol–chloroform by slow evaporation. The dimension of the crystal used for data collection was 0.2 mm × 0.2 mm × 0.1 mm. The crystals of this compound belong to the monoclinic space group C2/c with unit cell parameters $a = 19.203(1)$ Å, $b = 13.147(1)$ Å, $c = 8.801(1)$ Å, $\beta = 112.99(1)°$. The intensity data were collected upto 2θ max of 139.8° by an Enraf-Nonius CAD-4 diffractometer using crystal monochromated CuKα radiation ($\lambda = 1.5418$ Å). The ω-2θ scan mode was used. The usual precaution of checking the consistency of the intensities of three strong reflections periodically (every one hour) for monitoring the stability of the crystal during X-ray exposure was observed. The intensities were corrected for Lorentz, polarization and absorption.

The structure was solved by direct methods using SHELXS-97 [14] and all the non-hydrogen atoms were located from the E-map. The structure was refined using SHELXL-97 [14]. The ideal hydrogen atom coordinates were calculated by the program and were made to ride on the coordinates and temperature factors of the respective carbon atoms. The refinement was continued until the maximum shift/e.s.d was zero. The final difference map was featureless with maximum and minimum electron densities at 0.305 and −0.315 e Å^{-3} respectively. The crystal data, intensity collection conditions and refinement parameters are presented in Table 1.

Table 1 Crystal data, intensity collection conditions and refinement parameters for 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione

CCDC No.	273894
Empirical formula	$C_{22} H_{16} Cl_2 O_2 S_2$
Formula weight	447.36
Temperature (K)	293 (2)
Wavelength (Å)	1.54180
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions (Å, °)	$a = 19.203$ (1), $b = 13.147$ (1), $c = 8.801$ (1), $\beta = 112.99$ (1)
Volume (Å^3)	2045.4 (3)
Z, Calculated density (Mg/m^3)	4, 1.453
Absorption coefficient (mm^{-1})	4.892
Absorption correction	Psi-scan [17]
Max. and min. transmission	0.65 and 0.26
Crystal size (mm)	0.2 × 0.2 × 0.1
F(000)	920
θ range for data collection (°)	4.19–69.94
Index ranges	$-23 \le h \le 21, 0 \le k \le 16, 0 \le l \le 10$
Reflections collected/unique	1871/1871 (R(int) = 0.0)
Completeness to $2\theta = 70$	98.4%
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1.037
Data/parameters	1871/153
Final R indices ($I > 2\sigma(I)$)	$R1 = 0.0483$, w$R2 = 0.1321$
R indices (all data)	$R1 = 0.0547$, w$R2 = 0.1430$
Extinction coefficient	0.00039 (17)
Largest diff. peak and hole (e Å^{-3})	0.305 and −0.315

Results and Discussion

The title compound shows perfect symmetry in its crystalline form. In the crystal phase, it retained the two fold axis passing through the middle atoms C(4)–C(5) (Fig. 1). The asymmetric unit is half a molecule of the compound.

The parallel alignment of the cinnamoyl groups in the title compound apparently results from the push-pull nature of the ketene dithioacetal moiety [15]. The carbon atoms α to the carbonyl groups (C(2) and C(2a)) are separated by 2.968(2) Å. Due to the electron releasing nature of the ketene dithioacetal functionality, the oxygen atoms of the carbonyl groups develop partial negative charges while the sulphur atoms develop partial positive charges. This would bring the ketene dithioacetal group and the carbonyl groups into the same plane, forming a relatively more stable conformation. The sulphur atoms S(1) & S(1a) are close to the oxygen atoms O(1) & O(1a) respectively. The non-bonded distances between S(1)···O(1) = 2.569(2) Å. Thus the ketene dithioacetal functionality organizes the cinnamoyl groups parallel and close to each other. Bond lengths and angles in this compound are comparable with those reported for other curcumin analogues [9, 10, 15, 16] (Table 2).

The phenyl plane (C(7)–C(8)–C(9)–C(10)–C(11)–C(12)) and the dithiolan plane (S(1)–C(5)–S(1)a–C(6)a–C(6))

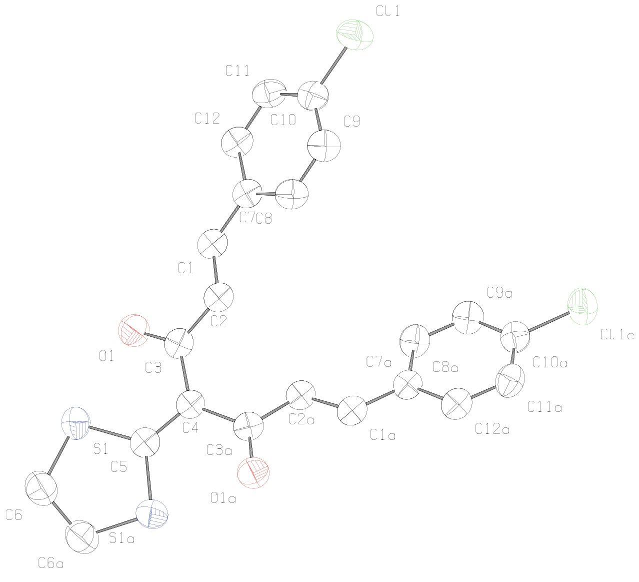

Fig. 1 ORTEP drawing of 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione [18]

Table 2 Bond lengths (Å) and angles (deg.) for 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione

Bond length (Å)		Angle (deg.)	
S(1)–C(5)	1.739(2)	C(5)–S(1)–C(6)	95.8(2)
S(1)–C(6)	1.813(3)	C(2)–C(1)–C(7)	127.5(2)
Cl(1)–C(10)	1.737(3)	C(1)–C(2)–C(3)	120.0(2)
O(1)–C(3)	1.231(3)	O(1)–C(3)–C(4)	119.4(2)
C(1)–C(2)	1.332(3)	O(1)–C(3)–C(2)	119.5(2)
C(1)–C(7)	1.452(3)	C(4)–C(3)–C(2)	121.0(2)
C(2)–C(3)	1.476(3)	C(5)–C(4)–C(3)	118.5(1)
C(3)–C(4)	1.473(3)	C(5)–C(4)–C(3)#1	118.5(1)
C(4)–C(5)	1.379(5)	C(3)–C(4)–C(3)#1	123.1(3)
C(4)–C(3)#1	1.473(3)	C(4)–C(5)–S(1)#1	122.8(1)
C(5)–S(1)#1	1.739(2)	C(4)–C(5)–S(1)	122.8(1)
C(6)–C(6)#1	1.487(6)	S(1)#1–C(5)–S(1)	114.5(2)
C(7)–C(8)	1.397(3)	C(6)#1–C(6)–S(1)	107.6(2)
C(7)–C(12)	1.400(3)	C(8)–C(7)–C(12)	117.7(2)
C(8)–C(9)	1.373(4)	C(8)–C(7)–C(1)	123.2(2)
C(9)–C(10)	1.382(4)	C(12)–C(7)–C(1)	119.0(2)
C(10)–C(11)	1.381(4)	C(9)–C(8)–C(7)	121.2(2)
C(11)–C(12)	1.370(4)	C(8)–C(9)–C(10)	119.3(2)
		C(11)–C(10)–C(9)	121.2(2)
		C(11)–C(10)–Cl(1)	119.3(2)
		C(9)–C(10)–Cl(1)	119.5(2)
		C(12)–C(11)–C(10)	119.0(2)
		C(11)–C(12)–C(7)	121.6(2)

make an angle of 32.07(2)°. The chlorine atom lies in the plane of the phenyl ring as seen from the torsion angle C(8)–C(9)–C(10)–Cl [178.4(2)°] (Table 3).

Table 3 Torsion angles (deg.) for 1,7-bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)-1,6-heptadiene-3,5-dione

C(7)–C(1)–C(2)–C(3)	179.4(2)
C(1)–C(2)–C(3)–O(1)	14.2(3)
C(1)–C(2)–C(3)–C(4)	−169.7(2)
O(1)–C(3)–C(4)–C(5)	18.4(2)
C(2)–C(3)–C(4)–C(5)	−157.8(2)
O(1)–C(3)–C(4)–C(3)#1	−161.6(2)
C(2)–C(3)–C(4)–C(3)#1	22.2(2)
C(3)–C(4)–C(5)–S(1)#1	174.4(1)
C(3)#1–C(4)–C(5)–S(1)#1	−5.6(1)
C(3)–C(4)–C(5)–S(1)	−5.6(1)
C(3)#1–C(4)–C(5)–S(1)	174.4(1)
C(6)–S(1)–C(5)–C(4)	168.9(1)
C(6)–S(1)–C(5)–S(1)#1	−11.1(1)
C(5)–S(1)–C(6)–C(6)#1	35.3(4)
C(2)–C(1)–C(7)–C(8)	5.0(4)
C(2)–C(1)–C(7)–C(12)	−174.6(2)
C(12)–C(7)–C(8)–C(9)	0.0(4)
C(1)–C(7)–C(8)–C(9)	−179.7(2)
C(7)–C(8)–C(9)–C(10)	0.9(4)
C(8)–C(9)–C(10)–C(11)	−1.4(4)
C(8)–C(9)–C(10)–Cl(1)	178.4(2)
C(9)–C(10)–C(11)–C(12)	0.9(4)
Cl(1)–C(10)–C(11)–C(12)	−178.9(2)
C(10)–C(11)–C(12)–C(7)	0.1(4)
C(8)–C(7)–C(12)–C(11)	−0.5(4)
C(1)–C(7)–C(12)–C(11)	179.2(2)

The five member ring S1–C(5)–S(1)a–C(6)a–C(6) is in a distorted half chair conformation which is twisted on C(6)–C(6)a bond [19, 20]. A similar conformation is also observed for other compounds with a dithiolane ring substitution [15, 21].

The molecules related by the c-glide are arranged to form a layer of molecules almost parallel to the bc-plane (Fig. 2) [22]. The molecules related by the C-centering form another layer separated by ∼9 Å from this layer. There is a probable hydrogen bonding between the carbon atom in the chlorophenyl ring and carbonyl oxygen at $x, -y, z - 1/2$ position within a layer. The hydrogen bonding parameters are:

D–H···A	Symm	H···A	D···A	D–H···A
C(8)–H(8)···O(1)	$x, -y, z - 1/2$	2.4085 Å	3.3272 Å	169.44°

Symmetry transformations used to generate equivalent atoms: #1 $-x + 1, y, -z + 1/2$

Conclusion

The title compound crystallized in the space group C2/c with the two-fold axis passing through C(4)–C(5) atoms so

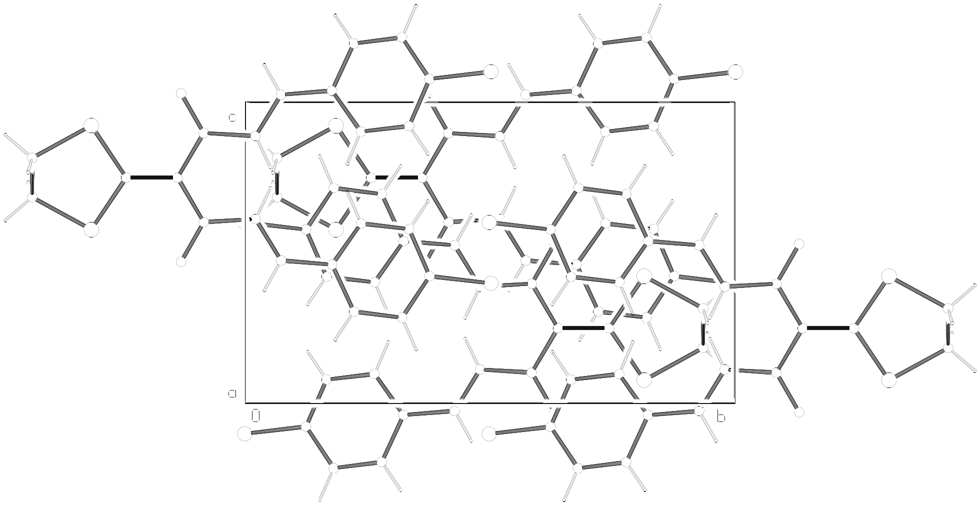

Fig. 2 Packing of molecules down *a*-axis

that there is only half a molecule in the asymmetric unit. The ketene dithioacetal functionality present in the compound organizes the cinnamoyl groups close and parallel to each other. The five member ring S1–C(5)–S(1)a–C(6)a–C(6) is in a distorted half chair conformation.

Supplementary Material

All crystallographic data for this paper are deposited with the Cambridge Crystallographic Data Centre (CCDC-273894). The data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0) 1223-336033; e-mail:deposit@ccdc.cam.ac.uk].

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