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SYNTHESIS AND CRYSTALLOGRAPHY OF A DIMERIZED CHALCONE DERIVATIVE

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ABSTRACT

The chalcone derivative, [3-(4-Chlorobenzoyl)-2,4-bis((4-propan-2-yl)phenyl)cyclobutyl](4-chlorophenyl)methanone ($C_{36}H_{34}Cl_2O_2$), crystallizes in the monoclinic crystal system with space group $P2_1/c$ and unit cell parameters: a = 18.4793(1)Å, b = 14.0239(7)Å, c = 11.8370(1)Å, β = 99.904(8)° and Z = 4. The crystal structure was solved using direct methods and refined by full matrix least squares procédures to a final R-factor of 0.0969 for 2319 observed reflections. In the crystal, C–H···O contacts connect the molecule into a three-dimensional network. The molecule also contains two C–H···O intramolecular interactions which stabilizes the crystal structure.

Keywords: Chalcone, Chlorobenzoyl, Direct methods, Crystallogrophy, Intramolecular interactions.

INTRODUCTION

Chalcones comprise one of the most commonly occurring classes of medicinally important natural compounds as they possess various biological activities.[1,2] Cyclobutane-containing natural products have, *e.g.*, been reported for Combretum albopunctatum[3] and Goniothalamus thwaitesii.[4] Because of various biological activities of these natural compounds, the synthesis of cyclobutane-derived compounds is one of the most intensively studied photochemical reactions of chalcone derivatives. The nonlinear optical properties of the different chalcone derivatives have also been reported.[5-8] These α, β-unsaturated ketones possess a wide variety of biological activities, including anti-leishmanial[9], anti-invasive[10], anti-tuberculosis[11], anti-fungal[12], anti-malarial.[13,14]

The crystal structures of some dimerized chalcones such as *r*-1,*c*-2,*t*-3,*t*-4- 1,3-bis(4-methoxyphenyl)-2,4-bis(5-phenyl-1,3,4-oxadiazol-2-yl)cyclobutane 1,4-dioxane solvate[15] and *r*-1,*c*-2,*t*-3,*t*-4–1,2-bis(4-methoxyphenyl)-3,4-bis(5-phenyl-1,3,4-oxadiazol-2-yl) cyclobutane[16] exist in the literature. In view of the pharmacological importance and potential of chalcone derivatives, the synthesis of such a compound was attempted and its molecular structure validated X-ray crystallographically.

EXPERIMENTAL

Synthesis

To a mixture of cuminaldehyde (1.5 mL, 0.01 mol) and 4-chloroacetophenone (1.2mL, 0.01 mol) in ethanol (50mL), 15 mL of 10% sodium hydroxide solution was added and stirred at 0–5°C for 3 hours. The precipitate formed was collected by filtration and purified by recrystallization from ethanol. Single crystals suitable for X-ray diffraction study was grown by slow evaporation method and was dimerized during crystallization (M.P.: 467-469 K). The synthetic route for the preparation of the compounds is given in Scheme-1.

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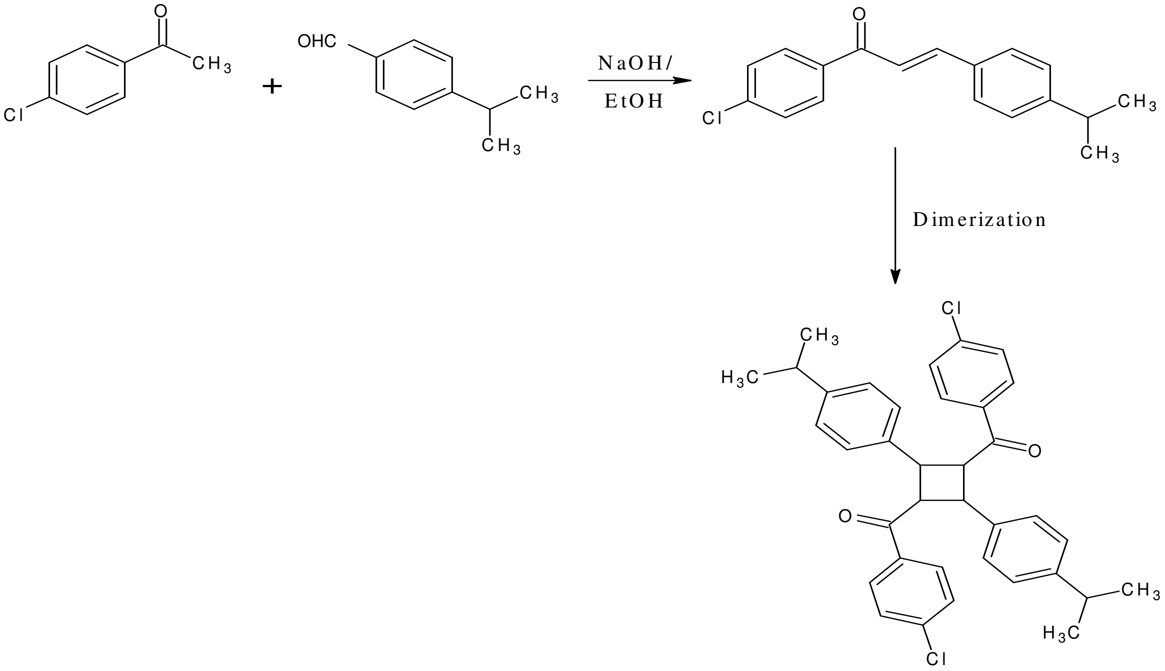

Scheme-1: Synthesis of [3-(4-Chlorobenzoyl)-2,4-bis((4-propan-2-yl)phenyl)cyclobutyl](4-chlorophenyl)methanone.

Crystal structure determination

X-ray intensity data of the crystal of dimensions 0.30 * 0.20 * 0.20 mm^3 having well defined morphology was collected on *X'calibur* CCD area-detector diffractometer equipped with graphite monochromated Mo*Kα* radiation (λ = 0.71073 Å). The intensities were measured by employing ω scan mode for the diffraction angle ranging from 3.39 to 25°. X-ray intensity data of 10623 reflections were collected at 293(2) K and out of these reflections 5176 were found unique. 2319 reflections were treated as observed by employing the criterion $I>2\sigma$ (I). Data was corrected for Lorentz-polarization and absorption factors. The structure was solved by direct methods using SHELXS97[17] and was refined using SHELXL97.[17] All non-hydrogen atoms of the molecule were located in the best E-map. All the hydrogen atoms were geometrically fixed and allowed to ride on the corresponding carbon with C-H= 0.93-0.97Å and U_{iso}= 1.2 U_{eq}(C), except for the methyl groups where $U_{iso}(H) = 1.5\ U_{eq}(C)$. The final refinement cycles converged to an R-factor of 0.0969 [$wR(F^2) = 0.1554$] for 2319 observed reflections. A relatively large value of R-factor could be due to poor quality crystallization of this material. Residual electron densities ranges from -0.239 to 0.229eÅ^{-3}. Geometrical calculations of the molecule were done using the WinGX[18], PARST[19] and PLATON[20] software.

Crystallographic information has been deposited at the Cambridge Crystallographic Data Centre with CCDC number 1530154. This data can be accessed free of charge at Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The crystallographic and refinement data of the crystal is given in Table-1.

Table-1: Crystallographic characteristic, the X-ray data collection and structure-refinement parameters for $C_{36}H_{34}Cl_2O_2$.

CCDC Number	1530154
System, Space group, Z	Monoclinic, $P2_1/c$, 4
a, *b*, *c* Å	18.4793(15), 14.0239(7), 11.8370(1)
β, deg	99.904(8)
V, Å^3	3021.9(4)
D_x g.cm^{-3}	1.252
Radiation, λ, Å	0.71073
μ, mm^{-1}	0.246

T, K	293(2)
Sample size, mm^3	0.30 * 0.20 * 0.20
Diffractometer	*X'calibur* Sapphire3 CCD area-detector
Scan mode	ω scan
Absorption correction	multi-scan
T_{min}, T_{max}	0.63965, 1.00000
θ range, deg	3.39→25
h, k, l ranges	$h = -21 \rightarrow 15$, $k = -16 \rightarrow 16$, $l = -14 \rightarrow 13$
Reflections total/unique	10623/ 5176
Reflections observed [$I > 2\sigma(I)$]	2319
R_{int}	0.0681
R_{sigma}	0.1338
F(000)	1200
R	0.0969
$wR(F^2)$	0.1554
$(\Delta/\sigma)_{max}$	0.00
Number of refined parameters	366
S	1.020
$\Delta\rho_{max}/\Delta\rho_{min}$, e/Å^3	0.229/-0.239
Programs used	SHELXS97, SHELXL97, PARST, PLATON, ORTEP

RESULTS AND DISCUSSION

The molecular structureis shown in Figure-1(ORTEP).[21] It comprises of dimerized chalcone derivative around a cyclobutane. The cyclobutane moiety bears one aromatic substituent on each carbon atom. The structural parameters, including bond distances and bond angles (Table-2) show normal geometry.[22]

Table-2: Selected bond distances and bond angles.

Bond Distances (Å)		Bond Distances (Å)	
C1–C2	1.441(1)	C16–CL1	1.728(7)
C2–C3	1.428(9)	C19–C20	1.505(6)
C2–C4	1.531(8)	C19–C29	1.572(7)
C7–C10	1.489(6)	C23–C26	1.527(9)
C10–H10	0.9800	C26–C27	1.307(1)
C10–C11	1.566(7)	C26–C28	1.395(1)
C10–C29	1.548(6)	C28–H28A	0.9600
C11–C12	1.498(7)	C29–C30	1.498(6)
C11–C19	1.523(6)	C30–O2	1.220(5)
C12–O1	1.217(6)	C30–C31	1.484(7)
C12–C13	1.482(7)	C34–CL2	1.724(6)
Bond Angles(˚)		Bond Angles(˚)	
C1–C2–C3	113.2(8)	C19–C20–C21	122.9(5)
C3–C2–C4	115.2(7)	C19–C29–C30	116.2(4)
C6–C7–C10	120.8(5)	C20–C19–C29	120.2(4)
C10–C11–C19	90.4(4)	C23–C26–C27	119.2(8)
C10–C29–C19	89.3(4)	C27–C26–C28	124.5(8)
C11–C19–C29	89.0(4)	C29–C10–C11	88.4(3)
C13–C12–O1	120.1(6)	C29–C30–C31	118.3(5)
C15–C16–CL1	119.2(7)	C33–C34–CL2	119.1(5)

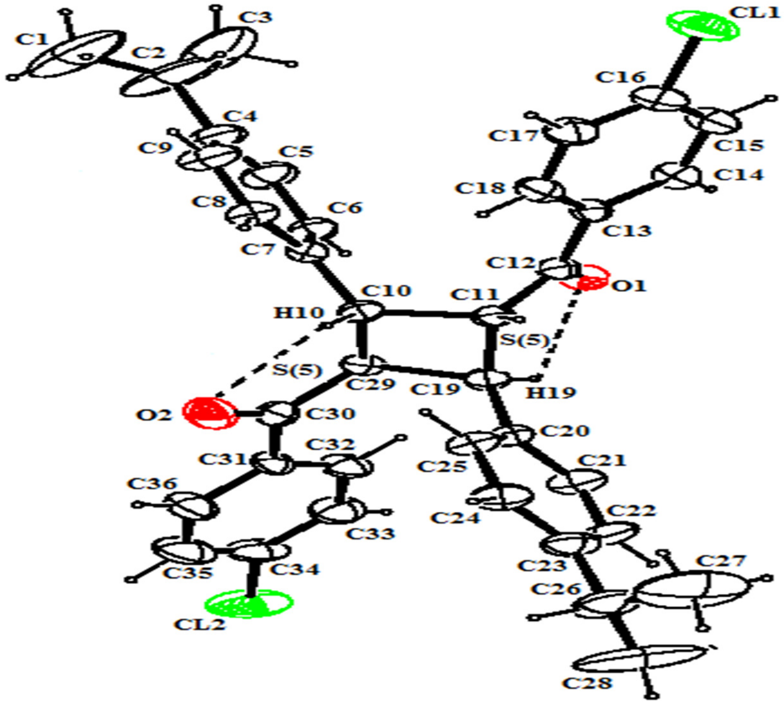

Fig.-1: ORTEP view of the molecule. Displacement ellipsoids are shown at the 40% probability level along with atomic labeling scheme. Hydrogen atoms are drawn at arbitrary radii and are not labeled for clarity. The graph-set motifs are also shown (dotted lines).

The length of the bonds C10-C11, C10-C29 and C7-C10, C11-C12 is similar to the corresponding distances as observed in case of some other tetra-aryl substituted cyclobutanes.[23,24] The distances of the bonds opposite to each other in the cyclobutane have nearly the same value and the endocyclic bond angles being very close to 90°; thus assume the shape of a rectangle. The propan-2-yl group and the phenyl rings lying on both sides of cyclobutane are not coplanar [torsion angle being C1–C2–C4–C5 (108.0(1)°) and C24–C23–C26–C27 (150.8(1)°), respectively (Table-3)].

The two chlorobenzoyl rings (the dihedral angle between them being 3.22(2)°) and the two phenyl rings (the dihedral angle between them being 8.95(2)°) are close to being planar. The dihedral angle between cyclobutane and each phenyl ring is 81.23(2)° and 75.87(2)°, respectively, while the dihedral angle between the cyclobutane ring and each of the chlorobenzoyl ring is 50.74(2)° and 53.29(2)°, respectively. The C11 and C19 atoms of the cyclobutane are deviated significantly (deviations being 0.0893(5) Å and -0.0889(5) Å respectively). The relative orientation of all the four aromatic substituents attached to central cyclobutane ring corresponds to *cis-trans-cis-trans* and this may be due to molecular centrosymmetry.

In the crystal structure, there exists C10-H10…O2 and C19-H19…O1 intramolecular interactions, both resulting in the formation of S(5) graph-set motifs. Only one intermolecular hydrogen bond C22-H22…O1 is observed that links molecule into infinite chains along the *y*-direction (Figure-2). Details of intra/inter-molecular hydrogen bonds are given in Table-4.

Table-3: Selected torsion angles

Torsion Angles(°)		Torsion Angles(°)	
C1–C2–C4–C5	108.0(1)	C14–C15–C16–CL1	-179.6(5)
C1–C2–C4–C9	-70.2(1)	C18–C13–C12–O1	-177.2(6)

C6–C7–C10–C11	119.5(6)	C19–C11–C10–C29	-13.1(4)
C7–C10–C11–C12	-14.6(7)	C19–C20–C25–C24	175.8(6)
C7–C10–C29–C30	132.9(5)	C20–C19–C29–C30	-21.2(7)
C8–C7–C10–C29	39.7(8)	C22–C23–C26–C28	150.5(1)
C11–C12–C13–C14	-176.0(5)	C24–C23–C26–C27	150.8(1)
C12–C11–C10–C29	-134.7(5)	O2–C30–C31–C32	162.2(5)
C12–C11–C19–C20	-99.3(6)	C36–C35–C34–CL2	-179.3(5)

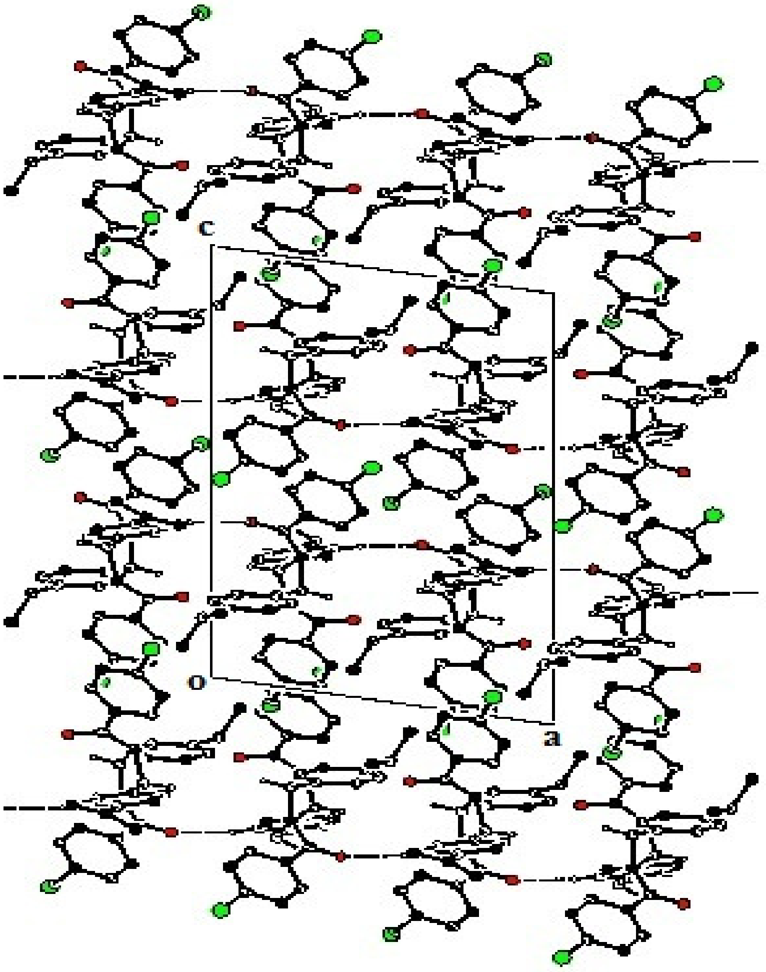

Fig.-2: Packing of the molecule along *b-axis*.

Table-4: Hydrogen bonding geometry (e.s.d.'s in parentheses)

D–H...A	D–H(Å)	H...A(Å)	D...A(Å)	D–H...A(°)
C10–H10...O2	0.98	2.38	2.821(6)	106
C19–H19...O1	0.98	2.44	2.833(7)	103
C22–H22...O1^{i}	0.93	2.53	3.203(7)	130

Symmetry code: (i) x, 3/2 - y, 1/2 + z

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