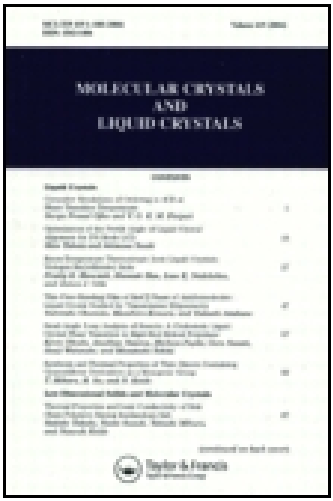

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Synthesis and Crystal Structure of [5-Chloro-2-(4-nitro-benzyloxy)-phenyl]-(4-chloro-phenyl) Methanone

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Synthesis and Crystal Structure of [5-Chloro-2-(4-nitro-benzyloxy)-phenyl]-(4-chloro-phenyl) Methanone

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The title compound, $C_{20}H_{13}Cl_2NO_4$, crystallizes in the monoclinic crystal system and space group $P2_1/n$ with cell parameters $a = 9.434(2)$ Å, $b = 13.167(3)$ Å, $c = 15.087(4)$ Å, $\beta = 105.289(8)^\circ$, $V = 1807.7(7)$ Å^3 for $Z = 4$. The structure exhibits inter-molecular hydrogen bonds of the type C-H···O.

Keywords: benzophenone; crystal structure; hydrogen bond

INTRODUCTION

Benzophenone is a prototypical aromatic carbonyl compound that has been extensively studied [1] and are usually obtained from natural products and by synthetic methods. The great importance of these substances is fundamentally due to the diverse biological and chemical properties that they possess [2–11]. Subsequently, benzophenones are frequently used in medicine and industry [12–17]. The proficiency of benzophenone analogues as chemotherapeutic agent especially as anti-inflammatory is well documented [18]. Several scientist have reported benzophenon analogues as an effective anti-inflammatory agents [19–22]. Recently, synthesis and structural activity relationship of benzophenones as a novel class of p38 MAP kinase inhibitors with high anti-inflammatory activity has been reported [23].

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Functionalized phenols, such as 2-hydroxy benzophenones, represent important building blocks in organic and medicinal chemistry [24–25]. The in vitro and in vivo studies of novel nitro and amino-substituted benzophenones have been investigated as potential anticancer agents with low cytotoxicity [26]. The search for new molecules with anti-inflammatory activity encouraged us to integrate p-nitro phenyl moiety in benzophenone framework, which possess well-documented anti-inflammatory activity.

SYNTHESIS AND METHOD OF CRYSTALLIZATION

4-Chloro-benzoic acid 4-chloro-phenyl ester (3) was synthesized by benzoylation of 4-chloro-phenol (1) with 4-chloro benzoyl chloride (2) using 10% sodium hydroxide solution. (5-Chloro-2-hydroxy-phenyl)-(4-chloro-phenyl)-methanone (4) was synthesized by Fries rearrangement of the above ester in presence of anhydrous aluminium chloride. A mixture of 4 (1 g, 4.41 mmol) and 4-nitro benzyl bromide (0.95 g, 4.41 mmol) was refluxed in dry acetone for 5 h, in the presence of anhydrous potassium carbonate (1.83 g, 13.25 mmol). The reaction mass was cooled, and the solvent was removed under reduced pressure. The residual mass was triturated with ice-cold water to remove

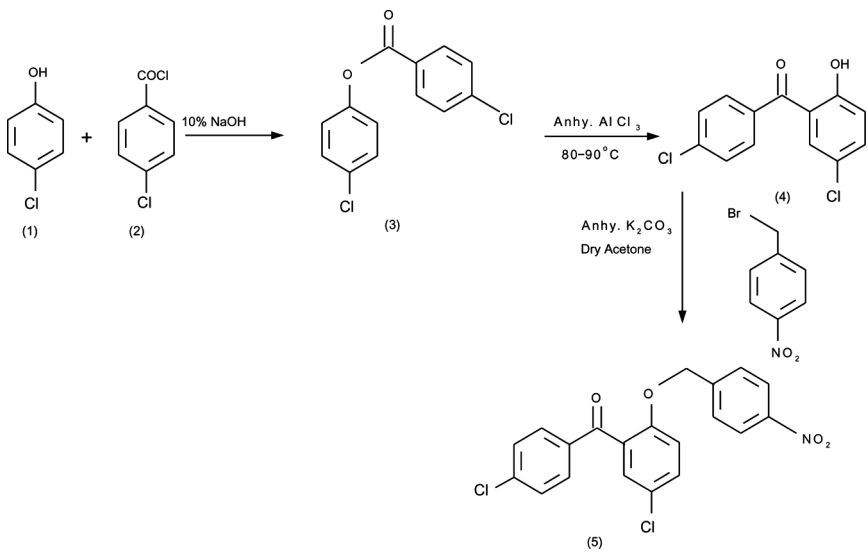

FIGURE 1 Schematic diagram.

TABLE 1 Crystal Data and Structure Refinement Table

CCDC	702891
Empirical formula	$C_{20}H_{13}Cl_2NO_4$
Formula weight	402.21
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/n$
Cell dimensions	$a = 9.434(2)$ Å
	$b = 13.167(3)$ Å
	$c = 15.087(4)$ Å
	$\beta = 105.289(8)^\circ$
Volume	1807.7(7) Å^3
Z	4
Density (calculated)	1.478 Mg/m^3
Absorption coefficient	0.386 mm^{-1}
F_{000}	824
Crystal size	$0.3 \times 0.25 \times 0.25$ mm
Theta range for data collection	2.09° to 25.00°
Index ranges	$-11 \le h \le 11$
	$-15 \le k \le 15$
	$-17 \le l \le 17$
Reflections collected	3918
Independent reflections	2672 [R(int) = 0.0450]
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2672/0/245
Goodness-of-fit on F^2	1.063
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0737$, $wR2 = 0.1945$
R indices (all data)	$R1 = 0.0900$, $wR2 = 0.2206$
Extinction coefficient	0.001(9)
Largest diff. peak and hole	0.255 and −0.257 eÅ^{-3}

potassium carbonate and then extracted with dichloromethane (3×20 ml). The organic layer was washed with 10% sodium hydroxide solution (3×10 ml) followed with water wash (3×15 ml) and then dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure to obtain the crude solid, which recrystallization with ethanol yielded [5-chloro-2-(4-nitro-benzyloxy)-phenyl]-(4-chloro-phenyl) methanone (5) as pale yellow crystals, the yield was good. Figure 1 gives the schematic diagram of the molecule.

C,H,N analysis: Calculated %: C: (73.12), H: (5.30), N: (3.88). Found %: C: (73.06), H: (5.28), N: (3.80). ^{1}H NMR($CDCl_3$): δ 2.31 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 4.9 (s, 2 H, CH_2), 7.17–7.36 ppm (m, 11 H, Ar-H). IR (Nujol): 1716 cm^{-1} (C = 0). M.P.: 167°C. Yield: 88% (1.40 g).

TABLE 2 Atomic Coordinates and Equivalent Thermal Parameters of the Non-Hydrogen Atoms

Atom	x	y	z	U_{eq}
O1	0.6628(3)	1.0642(2)	0.2896(2)	0.0989(8)
N2	0.5750(3)	1.0337(3)	0.3287(2)	0.0903(9)
O3	0.5187(5)	1.0898(3)	0.3732(4)	0.1572(2)
C4	0.5374(4)	0.9251(3)	0.3247(2)	0.0783(9)
C5	0.4516(4)	0.8897(3)	0.3795(3)	0.0883(1)
C6	0.4219(4)	0.7872(3)	0.3770(3)	0.0863(1)
C7	0.4732(3)	0.7207(3)	0.3218(2)	0.0742(8)
C8	0.5578(4)	0.7601(3)	0.2677(2)	0.0820(9)
C9	0.5903(4)	0.8623(3)	0.2684(3)	0.0815(9)
C10	0.4394(4)	0.6094(3)	0.3173(2)	0.0769(8)
O11	0.3801(3)	0.5828(2)	0.39123(2)	0.0847(7)
C12	0.3398(3)	0.4841(3)	0.3983(2)	0.0739(8)
C13	0.2678(3)	0.4634(3)	0.4668(2)	0.0754(8)
C14	0.2314(3)	0.3636(3)	0.4818(2)	0.0784(9)
C15	0.2635(4)	0.2864(3)	0.4285(2)	0.0789(9)
C16	0.3326(4)	0.3061(3)	0.3607(3)	0.0812(9)
C17	0.3705(4)	0.4048(3)	0.3463(3)	0.0810(9)
Cl18	0.21317(1)	0.16180(8)	0.44568(8)	0.0959(4)
C19	0.2326(4)	0.5449(3)	0.5271(3)	0.0799(9)
O20	0.2537(4)	0.5290(3)	0.60891(2)	0.1060(9)
C21	0.1665(3)	0.6427(3)	0.4868(2)	0.0743(8)
C22	0.0763(4)	0.6476(3)	0.3970(3)	0.0799(9)
C23	0.0127(4)	0.7385(3)	0.3611(2)	0.0827(9)
C24	0.0439(4)	0.8249(3)	0.4145(3)	0.0798(9)
C25	0.1336(4)	0.8232(3)	0.5039(3)	0.0842(9)
C26	0.1927(4)	0.7313(3)	0.5391(3)	0.0841(1)
Cl27	−0.03151(1)	0.94037(8)	0.36776(8)	0.1009(5)

$U_{eq} = (1/3)\sum_i \sum_j U_{ij}\left(a_i^* a_j^*\right)(a_i \cdot a_j)$.

CRYSTAL STRUCTURE DETERMINATION

A single crystal of the title compound with the dimensions $0.30 \times 0.25 \times 0.25$ mm was chosen for the X-ray diffraction study. The data were collected on a DIPLabo Image Plate system equipped with a normal focus, 3 kW sealed X-ray source (graphite monochromated Mok_α). The crystal to detector distance was fixed at 120 mm with the detector area of $441 \times 240\,mm^2$. Thirty-six frames of data were collected at room temperature by the oscillation method. Each exposure of the image plate was set to 400 s. Successive frames were scanned in steps of 5° per minute with an oscillation range of 5°. Image processing and data reduction were done using Denzo [27]. The reflections were merged with Scalepack [28]. All the frames

TABLE 3 Bond Lengths (Å)

Atoms	Length	Atoms	Length
O1-N2	1.207(4)	C13-C19	1.500(5)
N2-O3	1.211(5)	C14-C15	1.379(5)
N2-C4	1.470(5)	C15-C16	1.375(5)
C4-C9	1.371(5)	C15-Cl18	1.746(4)
C4-C5	1.381(5)	C16-C17	1.381(5)
C5-C6	1.376(6)	C19-O20	1.215(4)
C6-C7	1.381(5)	C19-C21	1.488(5)
C7-C8	1.383(5)	C21-C26	1.394(5)
C7-C10	1.498(5)	C21-C22	1.399(5)
C8-C9	1.380(5)	C22-C23	1.383(5)
C10-O11	1.417(4)	C23-C24	1.381(6)
O11-C12	1.366(4)	C24-C25	1.391(6)
C12-C17	1.382(5)	C24-Cl27	1.747(4)
C12-C13	1.405(4)	C25-C26	1.379(6)
C13-C14	1.392(5)		

could be indexed using a primitive monoclinic lattice. Absorption correction was not applied. The structure was solved by direct methods using SHELXS-97 [29]. Least-squares refinement using SHELXL-97 [29] with isotropic temperature factors for all the non-hydrogen atoms converged the residual $R1$ to 0.1595. Subsequent refinements were carried out with anisotropic thermal parameters for non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms which were placed at chemically acceptable positions. The hydrogen atoms were allowed to ride on their parent atoms. After eight cycles of refinement the residual converged to 0.0737. The details of crystal data and refinement are given in Table 1.[1] Table 2 gives the atomic coordinates and equivalent thermal parameters of the non-hydrogen atoms. Tables 3 and 4 give the list of bond lengths and bond angles respectively which are in good agreement with the standard values. The ORTEP of the molecule with thermal ellipsoids drawn at 50% probability is shown in Fig. 2.

The title compound has independent planar phenyl ring system. The dihedral angle between the two, 4-chloro-phenyl rings, bridged by carbonyl group is 64.51(17) Å. The atom C23 deviate from the Cremer and Pople plane [30] C21/C22/C24/C25/C26 by 0.0123(39) Å. Torsion

[1]CCDC 702891 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(0)1223–336033. E-mail: deposit@ccdc.cam.ac.uk

TABLE 4 Bond Angles (°)

Atoms	Angle	Atoms	Angle
O1-N2-O3	121.7(4)	C12-C13-C19	122.4(3)
O1-N2-C4	119.6(3)	C15-C14-C13	120.0(3)
O3-N2-C4	118.7(4)	C16-C15-C14	121.0(3)
C9-C4-C5	122.3(3)	C16-C15-Cl18	119.3(3)
C9-C4-N2	119.3(3)	C14-C15-Cl18	119.7(3)
C5-C4-N2	118.5(3)	C15-C16-C17	119.3(3)
C6-C5-C4	117.5(3)	C16-C17-C12	121.3(3)
C5-C6-C7	122.4(3)	O20-C19-C21	120.2(3)
C6-C7-C8	117.8(3)	O20-C19-C13	119.3(4)
C6-C7-C10	122.9(3)	C21-C19-C13	120.4(3)
C8-C7-C10	119.3(3)	C26-C21-C22	118.8(3)
C9-C8-C7	121.6(3)	C26-C21-C19	120.0(3)
C4-C9-C8	118.4(3)	C22-C21-C19	121.3(3)
O11-C10-C7	109.3(3)	C23-C22-C21	120.7(3)
C12-O11-C10	118.2(3)	C24-C23-C22	118.7(3)
O11-C12-C17	124.7(3)	C23-C24-C25	122.4(4)
O11-C12-C13	116.1(3)	C23-C24-Cl27	118.7(3)
C17-C12-C13	119.1(3)	C25-C24-Cl27	119.0(3)
C14-C13-C12	119.4(3)	C26-C25-C24	117.9(4)
C14-C13-C19	118.2(3)	C25-C26-C21	121.6(3)

angle values of −136.23(33)° and 41.16(51)° for C14-C13-C19-C21 and C14-C13-C19-C20, respectively, gives *−anti-clinal* and *+syn-clinal* conformation. The torsion angle about C12/C11/C10/C7 being 179.01(27) Å reflects *+anti-periplanar* conformation w.r.t chlorophenyl and nitroxy phenyl ring, respectively. The keto group in the structure plays a vital role in the determination of some potent biological

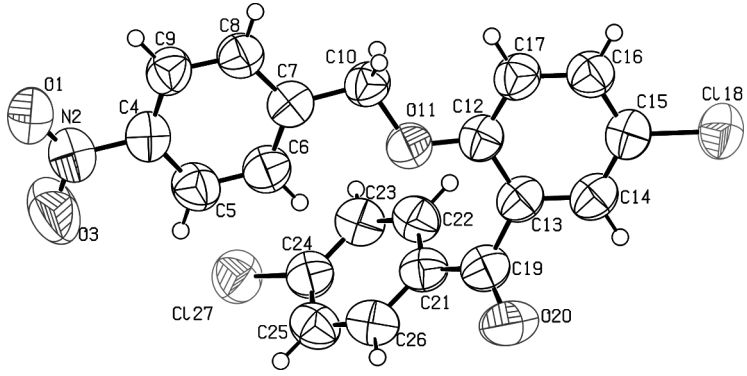

FIGURE 2 ORTEP of the molecule at 50% probability.

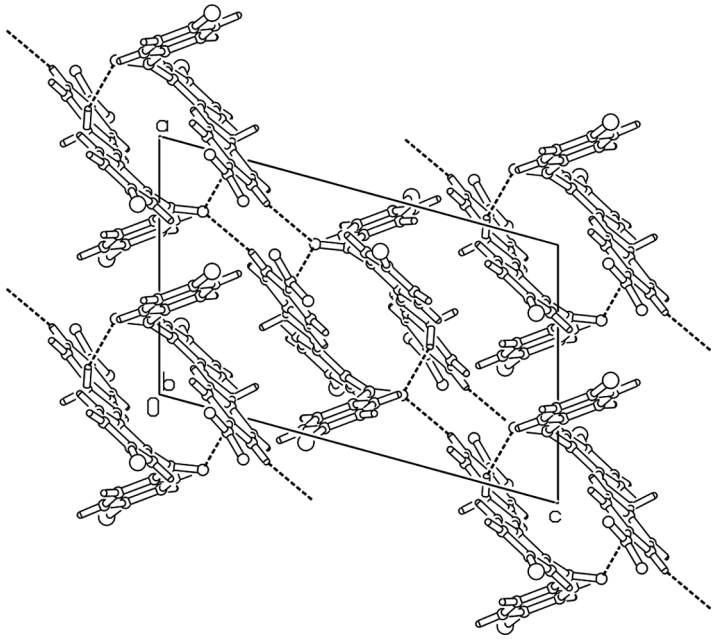

FIGURE 3 Packing of the molecules down the *b* axis. The dashed lines represent the hydrogen bonds.

activities [20]. The structure exhibits intermolecular hydrogen bonds of the type C–H···O. C9–H9···O20 has a length of 3.489(5) Å with an angle of 168° and C10–H10B···O20 which has a length of 3.353(5) Å and an angle of 158° with symmetry codes $1/2+x$, $3/2-y$, $-1/2+z$, and $1-x$, $1-y$, $1-z$, respectively. The stability of the crystal structure can be accounted for by these hydrogen bonds. Packing of the molecules down b axis is shown in Fig. 3.

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