Journal of Chemical Crystallography, Vol. 35, No. 6, June 2005 (© 2005)
DOI: 10.1007/s10870-005-2221-9

Synthesis and crystal structure of 2-benzoyl-4-methyl phenyl benzoate

M. Mahendra,[1] B. H. Doreswamy,[1] M. A. Sridhar,[1] J. Shashidhara Prasad,[1]*
S. A. Khanum,[2] S. Shashikanth,[2] and T. D. Venu[2]

Received October 15, 2004; accepted December 21, 2004

The crystal structure of the title compound, $C_{21}H_{16}O_3$, has been determined. The compound crystallizes in triclinic space group $P\bar{1}$ with cell parameters $a = 9.2240(9)$ Å, $b = 9.8050(8)$ Å, $c = 10.1610(11)$ Å, $\alpha = 94.749(6)^\circ$, $\beta = 112.544(4)^\circ$, $\gamma = 102.145(6)^\circ$ and $Z = 2$. The structure exhibits both intra and intermolecular interactions of the type C−H···O. The intermolecular interaction between the molecules form centrosymmetric dimers.

KEY WORDS: Benzophenone analogues; synthesis; crystal structure; C−H···O.

Introduction

Compounds containing the benzophenone moiety find a unique place in medicinal chemistry and play a significant role as they are associated with immense biological activities.[1–4] In recent years, it has been shown that benzophenone analogues exhibit antiallergic,[5,6] anticancer,[2,7–9] antiinflammatory,[10–12] antiasthmatic,[5,6] antimalarial,[13,14] antimicrobial,[15,16] antimitotic[17] and antianaphylactic activities.[5,6] These compounds inhibit the release of leukutrienes (LT) C4 & D4 in vitro from sensitized guinea pig chopped lung. Some of the compounds inhibited the release of leukutrienes from passively sensitized human chopped lungs. These compounds are evaluated as inhibitors of HIV reverse transcriptase (RT) and the growth of HIV in MT-4 cells. According to structural activity relationships, the interactions of these compounds with the RT enzyme are through hydrogen bonding of the amide and benzophenones carbonyls and pi-orbital interactions with the benzophenones nucleus and an aromatic function separated from the benzophenones by a suitable spacer group.[1] In addition, they find place in industrial chemistry.[18–21]

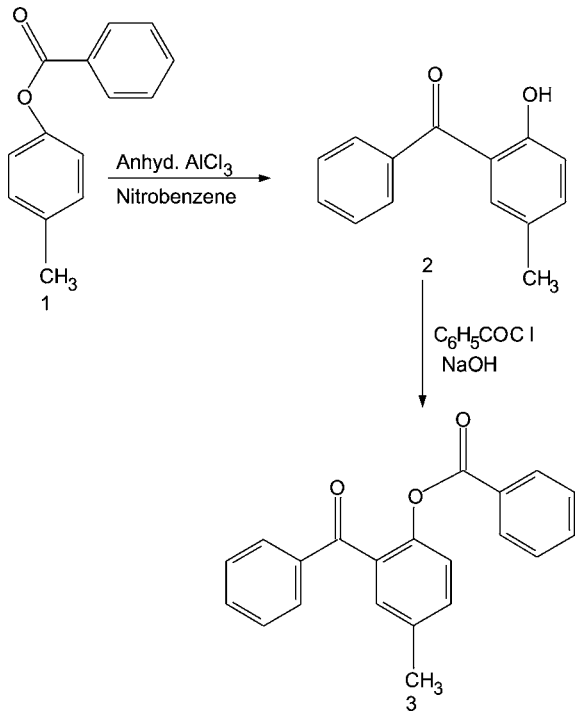
Literature survey revealed that no efforts were directed towards the study of the crystal structure of (2-benzoyl-4-methyl phenyl benzoate). Encouraged by the above information, it was considered valuable to synthesize compound **3** as outlined in Scheme 1 and characterised by X-ray studies.

Synthesis and characterisation

*(2-Hydroxy-5-methyl phenyl)phenyl methanone (**2**)*

A solution of anhydrous aluminum chloride (3.2 g, 0.02 mol) in dry nitrobenzene (25 ml) was added to 4-methyl phenyl benzoate (**1**, 5 g,

[1] Department of Studies in Physics, University of Mysore, Manasagangotri, Mysore 570006, India.
[2] Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570006, India.
* To whom correspondence should be addressed; e-mail: jsp@uomphysics.net.



Scheme 1.

0.02 mol) dissolved in nitrobenzene (10 ml), the mixture being protected from moisture by a calcium chloride guard tube and refluxed with stirring for 30 min. At the end of this period the solution was cooled and decomposed by acidulated ice-cold water. The nitrobenzene was removed by steam distillation. The residual solid was crushed into powder, extracted with 10% sodium hydroxide (3 × 50 ml) and the basic aqueous solution was neutralized with 10% hydrochloric acid. The product was extracted into ether and the ether layer was washed well with saturated sodium chloride solution. Evaporation of the ether after drying over anhydrous sodium sulphate followed by recrystallization from alcohol giving (2-hydroxy-5-methyl phenyl) phenyl methanone (**2**)in 85% (4.2 g) yield. M.P. 82°C.

IR (Nujol): 1670.2 (C=O), 3545–3649.1 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.3(s, 3H, CH_3), 7.1–7.7 (m, 8H, Ar−H), 9.8 (bs, 1H, OH); MS: m/z 212 (M^+, 87), 211 (100), 135 (60), 105 (35), 77 (56), 51(15); Anal. Cal. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.08; H, 5.64%.

*2-Benzoyl-4-methyl phenyl benzoate (**3**)*

To a well-stirred ice cold solution of **2** (3 g, 0.014 mol) in 10% sodium hydroxide (20 ml), benzoyl chloride (1.96 g, 0.014 mol) was added dropwise and stirring was continued for about 15 min. The mixture was made alkaline by adding 10% sodium hydroxide. A white solid separated, which was filtered and washed with water. On recrystallization with alcohol this gave **3** in 75% (3.35 g) yield. M.P. 90°C.

IR (Nujol): 1670.2 (C=O), 1760 cm^{-1} (COO); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.2 (s, 3H, CH_3), 7.0–7.8 (m, 13H, Ar−H); MS: m/z 316 (M^+, 80), 239 (55), 211 (100), 105 (30), 77 (50); Anal. Cal. for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.68; H, 5.07%.

*Crystal structure determination of **3***

A single crystal of **3** of dimensions 0.2 mm × 0.3 mm × 0.25 mm was chosen for X-ray diffraction studies. The measurements were made on a DIPLabo Image Plate system with graphite monochromated radiation (MoK_α). Thirty six frames of data were collected by oscillation method. Successive frames were scanned in steps of 3° per min with an oscillation range of 5°. Image processing and data reduction were done by using Denzo.[22] All frames could be indexed with a triclinic primitive lattice. The structure was solved by direct methods using SHELXS-97.[23] All the non-hydrogen atoms were revealed in the first map. Full-matrix least-squares refinement (using SHELXL-97[24]) based on 3305 observed reflections ($I > 2\sigma(I)$) with isotropic temperature factors for all the atoms converged residual to $R_1 = 0.1421$. Refinement of non-hydrogen atoms with anisotropic thermal parameters was started at this stage. After eight cycles of refinement the residuals saturated at $R_1 = 0.0543$. The hydrogen atoms were placed at chemically

Table 1. Crystal Data and Experimental Crystallographic Details

Empirical formula	$C_{21}H_{16}O_3$
Formula weight	316.34
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system	Triclinic
Space group	$P\bar{1}$
Cell dimensions	
a (Å)	9.2240(9)
b (Å)	9.8050(8)
c (Å)	10.1610(11)
α (°)	94.749(6)
β (°)	112.544(4)
γ (°)	102.145(6)
Volume (Å^3)	816.05(14)
Z	2
Density(calculated) (Mg/m^3)	1.287
Absorption coefficient (mm^{-1})	0.086
F_{000}	332
Crystal size	0.2 mm × 0.3 mm × 0.25 mm
θ range for data collection	2.55–32.50°
Index ranges	$-13 \le h \le 13$ $-14 \le k \le 14$ $-15 \le l \le 15$
Reflections collected	7723
Independent reflections	4824 [$R_{int} = 0.0310$]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4824/0/218
Goodness-of-fit on F^2	1.067
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0515$, $wR_2 = 0.1487$
R indices (all data)	$R_1 = 0.0823$, $wR_2 = 0.1836$
Largest diff. peak and hole (eÅ^{-3})	0.351 and −0.344
CCDC deposit no.	213702

Table 2. Bond Lengths (Å) and Bond angles (°)

Bond length			
C1−C2	1.384(3)	C12−C13	1.385(2)
C1−C6	1.390(2)	C13−C14	1.379(2)
C2−C3	1.369(3)	C14−C15	1.380(2)
C3−C4	1.373(3)	C15−O16	1.401(2)
C4−C5	1.381(2)	O16−C18	1.360(2)
C5−C6	1.386(2)	O17−C18	1.200(2)
C6−C8	1.486(2)	C18−C19	1.483(2)
O7−C8	1.218(2)	C19−C24	1.385(2)
C8−C9	1.497(2)	C19−C20	1.389(2)
C9−C15	1.389(2)	C20−C21	1.386(2)
C9−C10	1.397(2)	C21−C22	1.375(3)
C10−C12	1.387(2)	C22−C23	1.372(3)
C11−C12	1.503(2)	C23−C24	1.388(2)
Bond angle			
C2−C1−C6	119.7(2)	C14−C13−C12	121.2(1)
C3−C2−C1	120.5(2)	C15−C14−C13	119.1(1)
C2−C3−C4	120.2(2)	C14−C15−C9	120.9(1)
C3−C4−C5	119.9(2)	C14−C15−O16	115.4(1)
C6−C5−C4	120.4(2)	C9−C15−O16	123.6(1)
C5−C6−C1	119.2(1)	C18−O16−C15	120.3(1)
C5−C6−C8	121.6(1)	O17−C18−O16	123.3(1)
C1−C6−C8	119.1(1)	O17−C18−C19	125.4(1)
O7−C8−C6	121.3(1)	O16−C18−C19	111.3(1)
O7−C8−C9	120.4(1)	C24−C19−C20	119.5(1)
C6−C8−C9	118.3(1)	C24−C19−C18	121.9(1)
C15−C9−C10	117.7(1)	C20−C19−C18	118.6(1)
C15−C9−C8	123.2(1)	C21−C20−C19	120.0(2)
C10−C9−C8	118.1(1)	C22−C21−C20	120.1(2)
C12−C10−C9	122.4(2)	C23−C22−C21	120.5(2)
C13−C12−C10	117.8(1)	C22−C23−C24	119.9(2)
C13−C12−C11	121.2(2)	C19−C24−C23	120.0(2)
C10−C12−C11	121.0(2)		

acceptable positions and were not refined. The details of crystal data and refinement are given in Table 1.

Results and discussion

Table 2 gives the bond distances and angles of non-hydrogen atoms respectively. The bond distances and bond angles are in good agreement with the standard values. Figure 1 represents the ORTEP[25] diagram of the molecule **3** with thermal ellipsoids at 50% probability. The title compound has independent planar phenyl ring systems, which are bridged via −CO− and −OCO− groups, and inturn rotated away from their coplanarity by 68.95(9)°, 80.85(10)° and 54.98(9)°, respectively. The maximum deviation is 0.013(2) Å for C14. The structure exhibits both intra and intermolecular interactions of the type C−H···O. The intermolecular interaction between atoms is as follows: C20−H20···O7 has length 3.459(2) Å and an angle of 172.14°, with symmetry code $1-x$, $1-y$, $-z$, respectively. The interaction with a neighbouring molecule is related to the other by a centre of inversion and form hydrogen bonded dimer units. Each unit is independently stacked when viewed down a axis (Fig. 2). The crystal structure shows intermolecular interactions (C−H···O type) through hydrogen bonding of the carbonyl (benzophenone moiety) and ester substituent. There appears to be an

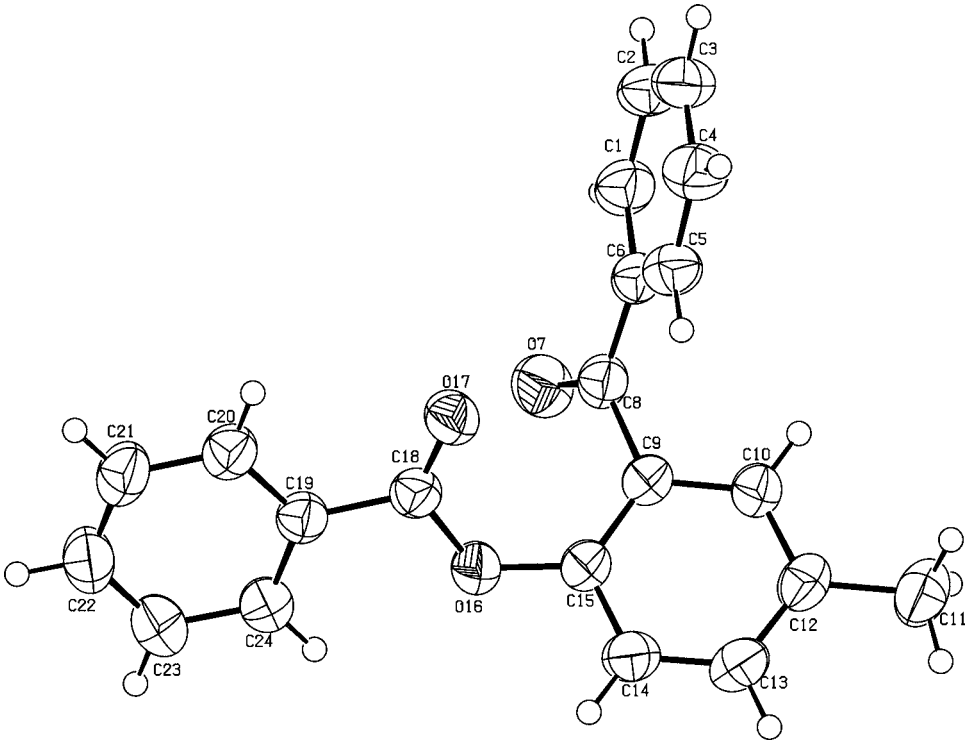


Fig. 1. ORTEP of the molecule at 50% probability.

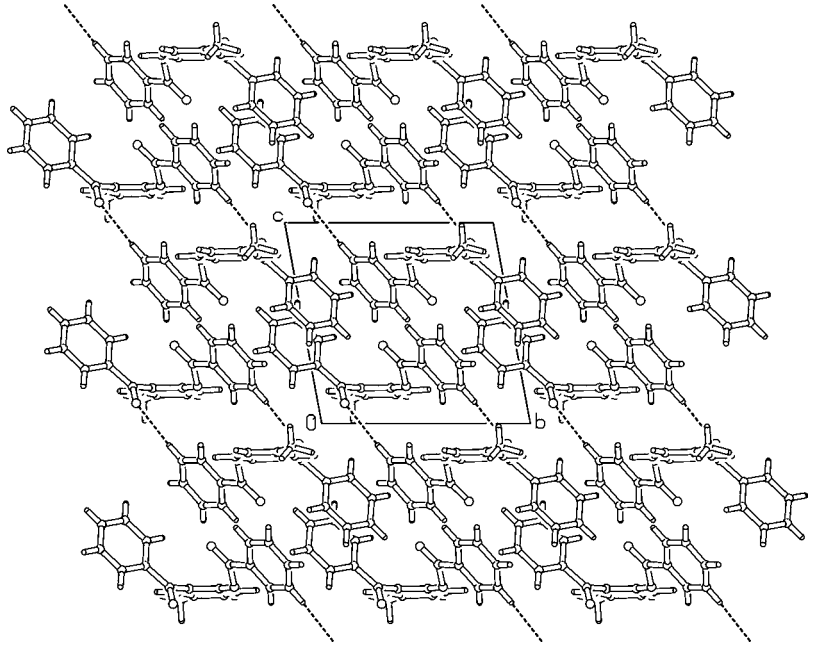


Fig. 2. Packing of the molecules down *a* axis. Dashed lines represent the hydrogen bonds.

unusual discrepancy between the carbonyl group bond lengths of ketone (C8−O7:1.218(2) Å) and ester (C18−O17:1.200(2) Å) group. This change can be attributed due to strong resonance of keto carbonyl group. The keto and ester groups in the structure are important determinants for some potent biological activities.[5,6,11,12]

Supplementary material CCDC-213702 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk.

Acknowledgments

The authors would like to express their thanks to DST, Government of India for financial assistance under the project SP/I2/FOO/93. Also the author Mahendra, would like to thank CSIR, Government of India, for awarding Senior Research Fellowship.

References

1. Wyatt, P.G.; Bethell, R.C.; Cammack, N.; Charon, D.; Dodie, N.; Dumaitre, B.; Evans, D.N.; Darren, V.; Green, S.; Hopwell, P.L.; Humber, D.C.; Lamont, R.B.; Orr, D.C.; Plested, S.J.; Ryan, D.M.; Sollis, S.L.; Storer, R.; Weingarten, G.G. *J. Med. Chem.* **1995**, *38,* 1657–1665.
2. Hsieh, H.P.; Liou, J.P.; Lin, Y.T.; Mahindroo, N.; Chang, J.Y.; Yang, Y.N.; Chern, S.S.; Tan, U.K.; Chang, C.W.; Chen, T.W.; Lin, C.H.; Chang, Y.Y.; Wang, C.C. *Bioorg. Med. Chem. Lett.* **2003**, *13,* 101.
3. Wiesner, J.; Kettler, K.; Jomaa, H.; Schlitzer, M. *Bioorg. Med. Chem. Lett.* **2002**, *12,* 543.
4. Palaska, E.; Sahin, G.; Kelicen, P.; Durllu, N.T.; Altinok, G. *IL Farmaco* **2002**, *57,* 101.
5. Evans, D.; Cracknell, M.E.; Saunders, J.C.; Smith; C.E.; Nigel, W.R.; Willamson, N.W.R.; Dowson, W.; John, F.; Sweatman, W. *J. Med. Chem.* **1987**, *30,* 1321–1327.
6. Brancaccio, G.; Angelo; Larizza; Lettier, G. *J. Med. Chem.* **1981**, *24,* 998–1000.
7. Schlitzer, M.; Bohm, M.; Sattler, I. *Bioorg. Med. Chem.* **2002**, *10,* 615.
8. Sakowski, J.; Bohm, M.; Sattler, I.; Dahse, H.M.; Schlitzer, M. *J. Med. Chem.* **2001**, *44,* 2086.
9. Leonard, D.M. *J. Med. Chem.* **1997**, *40,* 2971; Williams, T.M.; Dinsmore, C.J. *Adv. Med. Chem.* **1999**, *4,* 273.
10. Palomer, A.; Pascual, J.; Cabre, M.; Borras, L.; Gonzalez, G.; Aparici, M.; Carabaza, A.; Cabre, F.; Garcia, M.L.; Mauleon, D. *Bioorg. Med. Chem. Lett.* **2002**, *12,* 533.
11. Khanum, S.A.; Shashikanth, S.; Deepak, A.V. *Bioorg. Chem.* **2004**, *32,* 211.
12. Khanum, S.A.; Venu, T.D.; Shashikanth, S.; Firdouse, A. *Bioorg. Med. Chem. Lett.* **2004**, *14,* 5351.
13. Wiesner, J.; Mitsch, A.; Wibner, P.; Jomaa, H.; Schlitzer, M. *Bioorg. Med. Chem. Lett.* **2001**, *9,* 785.
14. Wiesner, J.; Kettler, K.; Jomaa, H.; Schlitzer, M. *Bioorg. Med. Chem. Lett.* **2002**, *12,* 543.
15. Thomas, G.; Andreas, G.; Joachim, R.; Ingo, R.; Peter, S.; Frank, S.; Norbert, G.; Karl, E.; Eberhard, A.; Siegfried, S.; Gisela, L.; Reinhard, S. *Chem. Abstr.* **2002**, *137,* 232443.
16. Ke, L.; Wannian, Z.; Wu, Z.; Xiaoyan, W. *Zhongguo Yiyao Gongye Zazhi* **2001**, *32,* 115.
17. Liou, G.P.; Chang, C.W.; Song, J.S.; Yang, Y.N.; Yeh, C.F.; Tseng, H.Y.; Lo, Y.K.; Chang, Y.L.; Chang, C.M.; Hsieh, H.P. *J. Med. Chem.* **2002**, *45,* 2556.
18. Nakagawa, Y.; Suzuki, T.; Tayama, S. *Toxicology* **2000**, *156,* 27.
19. Qianghua, W.; Baojun, Q. *J. Appl. Polym. Sci.* **2002**, *85,* 1581.
20. Lajos, A.; Rene, B.; Victor, S. *PCT Int. WO 2002064580 A1*, 2002. Through *Chem. Abstr.* **2002**, *137,* 187276.
21. Kadry, A.M.; Okereke, C.S.; Abdel-Rahman, M.S.; Friedman, M.A.; Davis, R.A. *J. Appl. Toxicol.* **1995**, *15,* 97.
22. Sheldrick, G.M. *SHELXS-97*; University of Göttingen: Germany, 1997.
23. Sheldrick, G.M. *SHELXL-97*; University of Göttingen: Germany, 1997.
24. Otwinowski, Z.; Minor, W. Processing of X-ray Diffraction Data Collected in Oscillation mode. In *Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A*; Carter, C.W. Jr.; Sweet, R.M., Eds.; Academic Press: New York, 1997; pp. 307–326
25. Johnson, C.K. *ORTEP-II. A Fortran Thermal-Ellipsoid Plot Program*. Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, Tennessee, USA, 1976.