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Structure of 2,2-Dichloro-2′-hydroxy-4′-methoxyacetophenone, $C_9H_8Cl_2O_3$

By D. Chattopadhyay, T. Banerjee and S. K. Mazumdar

Crystallography and Molecular Biology Division, Saha Institute of Nuclear Physics, Block 'AF', Sector I, Bidhannagar, Calcutta-700 064, *India*

and G. Podder

School of Tropical Medicine, Calcutta, India

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Abstract. $M_r = 235{\cdot}08$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}981\,(1)$, $b = 11{\cdot}901\,(3)$, $c = 12{\cdot}061\,(3)$ Å, $V = 1002{\cdot}0\,(3)$ Å^3, $Z = 4$, $D_m = 1{\cdot}553$, $D_x = 1{\cdot}557$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0{\cdot}7107$ Å, $\mu = 6{\cdot}24$ cm^{-1}, $F(000) = 480$, $T = 297$ K, final $R = 0{\cdot}042$ for 946 observed reflections. The molecule is approximately planar and is in the *endo* conformation. An intramolecular O—H···O(keto) hydrogen bond stabilizes the conformation. The π-acceptor and π-donor substituents take part in conjugation with the phenyl ring. The geometry of the $-CHCl_2$ moiety of the dichloroacetyl group resembles that in the chloramphenicol molecule.

Introduction. A thorough study of the relationship between molecular structure and pharmacological activity of the well known broad-spectrum antibiotic chloramphenicol has stressed the importance of the dichloroacetyl moiety present in the compound (Dennis & Berberian, 1954). It has been shown that the biological activity of chloramphenicol is decreased to a marked degree if the dichloroacetyl group is changed (Podder, 1976). Also the compounds containing the dichloroacetamido group, $-NHCOCHCl_2$, have found wide applications as antiamoebic and antifungal agents (Khaskin, Shomova & Stolper, 1967).

The title compound was synthesized with the aid of Friedel–Crafts condensation of dimethylresorcinol and dichloroacetyl chloride under the catalytic influence of anhydrous aluminium chloride. The present structure determination has been undertaken as a part of our programme of studies on 2,2-dichloroacetophenone derivatives with a view to observing the conformation of the molecules containing the dichloroacetyl group.

Experimental. Pale-yellow rod-shaped crystals (from ethanol), density by flotation (benzene–bromoform), crystal size: 0·32 × 0·22 × 0·20 mm, symmetry from oscillation and Weissenberg photographs, $P2_12_12_1$ (systematic absences: $h00$, h odd; $0k0$, k odd and $00l$, l odd), Enraf–Nonius CAD-4 diffractometer, graphite-monochromatized Mo $K\alpha$, cell parameters refined from setting angles of 25 reflections ($13 \leq \theta \leq 18°$), 1057 unique reflections ($0 \leq h \leq 8$, $0 \leq k \leq 14$, $0 \leq l \leq 14$, $2 \leq \theta \leq 25°$), 946 observed [$I \geq 3\sigma(I)$], correction for Lp, absorption ignored, three orientation-control reflections (372, $\bar{4}\bar{4}5$, 338) monitored every 50 reflections and three intensity-control reflections (335, $\bar{2}8\bar{4}$, 175) monitored every hour of exposure, intensity variation (< 2%) corrected for, direct methods (*MULTAN*78; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), anisotropic full-matrix refinement based on F (*ORFLS*; Busing, Martin & Levy, 1962), H (from ΔF synthesis) refined isotropically, $R = 0{\cdot}042$, $R_w = 0{\cdot}038$, $S = 1{\cdot}41$, $w = 1/\sigma^2(|F_o|)$, max. shift–error $< 0{\cdot}05$, residual $\Delta\rho$ excursions $-0{\cdot}18$ to $0{\cdot}21$ e Å^{-3} in final ΔF synthesis, scattering factors for non-H atoms from Cromer & Waber (1965), for H from Stewart, Davidson & Simpson (1965), anomalous-dispersion corrections for non-H atoms from *International Tables for X-ray Crystallography* (1974).

Discussion. Fig. 1 shows a perspective view of the molecule together with the atomic-labelling scheme. The fractional coordinates together with their isotropic thermal parameters are listed in Table 1.* Bond distances, bond angles and some selected torsion angles are given in Table 2.

The molecule is nearly planar; the dihedral angle between the phenyl ring and the plane defined by C(7), C(1), C(8) is 3·8 (6)°. Such planarity has also been observed in acetophenone and *p*-aminoacetophenone (Tanimoto, Kobayashi, Nagakura & Saito, 1973; Haisa, Kashino, Yuasa & Akigawa, 1976).

The Cl(1)—C(8)—Cl(2) bond angle and the Cl(1)—C(8) and Cl(2)—C(8) bond lengths are similar to the corresponding values in chloramphenicol [110·2 (6)°, 1·789 (11) and 1·753 (11) Å] (Ravindra Acharya,

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* Lists of structure factors, anisotropic thermal parameters, bond distances and angles involving H atoms, deviations from least-squares planes and net charges on individual atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39823 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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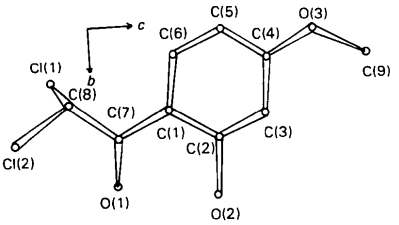

Fig. 1. Perspective view of 2,2-dichloro-2'-hydroxy-4'-methoxyacetophenone.

Table 1. *Fractional coordinates of the atoms and their isotropic temperature factors* (Å^2) *with e.s.d.'s in parentheses*

$$B_{\rm eq} = \tfrac{4}{3}\textstyle\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$B_{\rm eq}/B$
Cl(1)	0·8157 (3)	0·1078 (1)	0·6666 (1)	5·0
Cl(2)	1·1300 (3)	0·2385 (1)	0·5775 (1)	4·8
O(1)	1·0247 (8)	0·3384 (3)	0·7849 (3)	4·4
O(2)	1·0380 (8)	0·3605 (3)	0·9983 (4)	4·4
O(3)	1·0766 (7)	0·0253 (3)	1·2118 (3)	3·8
C(1)	1·0438 (9)	0·1812 (4)	0·9046 (4)	2·7
C(2)	1·0448 (9)	0·2460 (6)	1·0016 (5)	2·8
C(3)	1·0520 (9)	0·1977 (5)	1·1063 (5)	3·0
C(4)	1·0644 (9)	0·0827 (5)	1·1147 (5)	3·1
C(5)	1·061 (1)	0·0155 (5)	1·0192 (5)	3·1
C(6)	1·051 (1)	0·0640 (5)	0·9182 (5)	3·3
C(7)	1·0374 (9)	0·2361 (5)	0·7970 (4)	3·2
C(8)	1·051 (1)	0·1630 (5)	0·6933 (5)	3·5
C(9)	1·044 (1)	0·0851 (3)	1·3130 (6)	5·2
H(O2)	1·08 (1)	0·383 (6)	0·917 (6)	17 (3)
H(C3)	1·095 (8)	0·250 (4)	1·165 (4)	4 (1)
H(C5)	1·101 (8)	−0·065 (4)	1·028 (4)	3 (1)
H(C6)	1·094 (8)	0·025 (3)	0·855 (4)	3 (1)
H(C8)	1·148 (7)	0·100 (4)	0·701 (3)	2 (1)
H(C9)1	1·148 (9)	0·154 (5)	1·334 (4)	5 (2)
H(C9)2	0·896 (8)	0·116 (5)	1·304 (4)	4 (1)
H(C9)3	1·071 (9)	0·031 (5)	1·368 (5)	6 (2)

Table 2. *Bond distances* (Å), *bond angles* (°) *and some selected torsion angles* (°) *with e.s.d.'s in parentheses*

Cl(1)—C(8)	1·798 (7)	C(2)—C(3)	1·388 (9)
Cl(2)—C(8)	1·750 (6)	C(3)—C(4)	1·375 (8)
O(1)—C(7)	1·229 (7)	C(4)—C(5)	1·402 (8)
O(2)—C(2)	1·364 (8)	C(5)—C(6)	1·350 (8)
O(3)—C(4)	1·358 (7)	C(6)—C(1)	1·405 (8)
O(3)—C(9)	1·431 (7)	C(7)—C(1)	1·454 (7)
C(1)—C(2)	1·401 (8)	C(7)—C(8)	1·526 (8)
Cl(1)—C(8)—Cl(2)	109·4 (4)	C(2)—C(1)—C(7)	119·9 (5)
Cl(1)—C(8)—C(7)	107·3 (4)	C(6)—C(1)—C(7)	123·5 (5)
Cl(2)—C(8)—C(7)	112·4 (4)	C(1)—C(2)—C(3)	122·1 (6)
O(1)—C(7)—C(1)	123·6 (5)	C(2)—C(3)—C(4)	118·8 (6)
O(1)—C(7)—C(8)	118·1 (5)	C(3)—C(4)—C(5)	120·4 (6)
O(2)—C(2)—C(1)	121·7 (6)	C(4)—C(5)—C(6)	119·9 (6)
O(2)—C(2)—C(3)	116·2 (6)	C(5)—C(6)—C(1)	122·1 (5)
O(3)—C(4)—C(3)	124·6 (5)	C(1)—C(7)—C(8)	118·3 (5)
O(3)—C(4)—C(5)	115·0 (5)	C(4)—O(3)—C(9)	118·4 (4)
C(2)—C(1)—C(6)	116·6 (5)		
C(9)—O(3)—C(4)—C(3)	10·5 (8)	Cl(2)—C(8)—C(7)—C(1)	−157·7 (4)
Cl(1)—C(8)—C(7)—O(1)	−99·2 (6)	C(7)—C(1)—C(2)—O(2)	0·7 (9)
Cl(1)—C(8)—C(7)—C(1)	82·0 (6)	C(2)—C(1)—C(7)—O(1)	−3·1 (9)
Cl(2)—C(8)—C(7)—O(1)	21·2 (7)		

Sake Gowda & Post, 1979). However, the O(1)—C(7) and C(7)—C(8) bond distances and the angle at the keto carbon, O(1)—C(7)—C(8), differ from the corresponding values in chloramphenicol [1·244 (1), 1·571 (13) Å and 120·9 (8)°] (Ravindra Acharya *et al.*, 1979). The O(1)—C(7) bond is slightly longer than the keto bonds in 4'-chloro-5'-(dichloroacetyl)-2'-methylacetanilide [1·187 (3) Å] (Banerjee, 1983) and *p*-aminoacetophenone [1·215 (5) Å] (Haisa *et al.*, 1976). This lengthening may be attributed to the delocalization of the π-electron cloud of the keto bond as is evidenced by a negative charge on O(1) and a positive charge on the C(7) atom calculated by the CNDO/2 method (Pople & Beveridge, 1970).

The C(1)—C(7) bond is considerably shorter than the similar bond in *p*-hydroxyacetophenone (1·49 Å) (Vainshtein, Lobanova & Gurskaya, 1974) and 4'-chloro-5'-(dichloroacetyl)-2'-methylacetanilide [1·495 (3) Å] (Banerjee, 1983) and is slightly shorter than those in *p*-aminoacetophenone [1·468 (5) Å] (Haisa *et al.,* 1976) and 4'-amino-2,2,3'-trichloroacetophenone [1·467 (9) Å] (De, 1984). This, together with the narrowing of the endocyclic bond angle at C(1) from the sp^2 value, indicates conjugation between the phenyl ring and the dichloroacetyl group (Domenicano, Vaciago & Coulson, 1975). The hydroxy and methoxy substituents, having $+R$ effects, at the positions *ortho* and *para,* respectively, to the dichloroacetyl group favour this conjugation; shortening of the two C(sp^2)—O bonds, namely C(2)—O(2) and C(4)—O(3), as compared to those in *p*-hydroxyacetophenone (1·37 Å) (Vainshtein *et al.,* 1974) and *p*-hydroxyacetanilide [1·380 (5) Å] (Haisa, Kashino & Maeda, 1974) suggests the involvement of the hydroxy and the methoxy group in conjugation.

The C(9)—O(3)—C(4)—C(3) torsion angle indicates a near coplanarity of the methoxy carbon, C(9), with the phenyl ring. Such planar arrangements have been observed in a large number of structures containing methoxy groups. The C(4)—O(3) bond length agrees well with the average, 1·36 Å, calculated for similar bonds (Eliopoulos, Sheldrick & Hamodrakas, 1983). The observed dissymmetry in the exocyclic angles at C(4) may be attributed to the steric interaction between the methyl group and H(C3) [H(C9)···H(C3) = 2·36 (7) Å], resulting from the coplanarity of the methoxy group and the phenyl ring. A similar situation has been observed in ethyl 3-[4,5-dimethoxy-2-(3-methyl-2-pyridylsulphamoyl)phenyl]propionate (Eliopoulos *et al.*, 1983).

Four of the endocyclic bond angles in the present structure agree well with the respective angles in *p*-aminoacetophenone (Haisa *et al.*, 1976) but the angle at C(4) is larger and that at C(3) is smaller in the present structure. This difference in the distribution of the angles may be due to the different effects of the substituent groups.

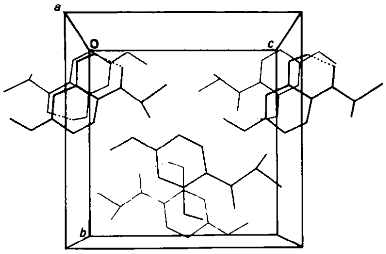

Fig. 2. Perspective view of the molecular packing of 2,2-dichloro-2′-hydroxy-4′-methoxyacetophenone.

A positive charge on H(O2) and a negative charge on O(1) and the geometry O(2)···O(1) = 2·589 (6), O(2)—H(O2) = 1·05 (7), O(1)···H(O2) = 1·72 (7) Å, O(2)—H(O2)···O(1) = 136 (6)° indicate that the conformation of the molecule is stabilized by an intramolecular 'O—H···O(keto)' hydrogen bond.

The *endo* conformation of the carbonyl group, as shown by the C(2)—C(1)—C(7)—O(1) torsion angle, favours this intramolecular hydrogen bonding which results in the formation of a six-membered ring. The O(1)···H(O2) and O(2)···O(1) distances are shorter than the mean values [1·818 (9) and 2·76 (7) Å] observed by Ceccarelli, Jeffrey & Taylor (1981). A corresponding increase in the O(2)—H(O2) distance compared to the mean O(donor)—H distance [0·969 (1) Å] indicates that the hydrogen bond is a strong one (Ceccarelli *et al.*, 1981). The molecules are packed in three dimensions through van der Waals forces. A perspective view of the molecular packing is shown in Fig. 2.

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rel-Methyl (3*R*,3a*R*,4a*S*,5*S*,7*R*,8*R*,8a*S*,9a*S*)-5-Bromododecahydro-3-isopropyl-8,9a-dimethyl-10-oxo-4a,8-(epoxymethano)-4a*H*-benz[*f*]indene-7-carboxylate (1) and *rel*-Methyl (3*R*,3a*S*,4a*S*,5*S*,7*R*,8*R*,8a*S*,9a*S*)-5-Bromododecahydro-3-isopropyl-8,9a-dimethyl-10-oxo-4a,8-(epoxymethano)-4a*H*-benz[*f*]indene-7-carboxylate (2), $C_{21}H_{31}BrO_4$

By E. J. Corey, T. A. Engler and Jeremy M. Berg

Department of Chemistry, Harvard University, 12 *Oxford Street, Cambridge, Massachusetts* 02138, *USA*

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Abstract. (1) M_r = 427·43, triclinic, $P\bar{1}$, a = 7·042 (2), b = 11·760 (2), c = 13·160 (2) Å, α = 102·21 (1), β = 96·25 (2), γ = 95·20 (2)°, V = 1051·1 (4) Å^3, Z = 2, D_x = 1·35 g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ = 19·48 cm^{-1}, F(000) = 448, T = 296 K, final R = 3·38% for 2110 unique reflections. (2) M_r = 427·43, monoclinic, $P2_1/c$, a = 11·855 (4), b = 7·190 (3), c = 24·571 (6) Å, β = 97·59 (3)°, V = 2076 (1) Å^3, Z = 4, D_x = 1·37 g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ = 19·80 cm^{-1}, F(000) = 896, T = 296 K, final R = 3·62% for 1922 unique reflections. Ring B in (1) has a chair conformation and in (2) has a twist-boat conformation. Largest bond-angle differences involve the ring-junction C atoms.

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