Synthesis and crystal structure of 2-chloro-1-(3-hydroxyphenyl)ethanone

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The structure of 2-chloro-1-(3-hydroxyphenyl)ethanone, C₈H₇ClO₂, an α-haloketone is described. The molecule is planar (r.m.s. deviation = 0.0164 Å) and in the crystal, inversion-symmetric dimers are formed as a result of pairs of strong O—H···O and weak C—H···O hydrogen bonds. A brief comparison is made with structurally related compounds deposited in the CSD. In addition, the synthesis and some spectroscopic details are presented.

1. Chemical context

α-Haloketones have proven to be useful building blocks for the preparation of compounds of various classes because of their high reactivity and selective transformations with a variety of reagents (Erian et al., 2003). Chlorinated acetophenones are widely used in organic synthesis as intermediates for the manufacture of active pharmaceutical ingredients (Ott-Dombrowski et al., 2019). For example, 2-chloro-1-(4-hydroxyphenyl)ethanone is a reagent that is used in the preparation of hydroxypyrimidine derivatives for their HDAC (histone deacetylase) inhibitory activity (Kemp et al., 2011). In light of the importance of α-haloketones, this paper reports the synthesis, crystal structure, and some spectroscopic details for the title compound, C₈H₇O₂Cl, (I).

2. Structural commentary

The molecule of I (Fig. 1) is planar (r.m.s. deviation = 0.0164 Å), with the largest deviation being for Cl1, which is 0.0346 (5) Å from the mean plane through all non-H atoms due to the O2—C7—C8—Cl1 torsion angle of −2.07 (14)°. The hydroxyl hydrogen atom, H1O, which was refined freely, lies 0.045 (16) Å out of the mean plane, with a C2—C3—O1—H1O torsion angle of 1.8 (12)°, its position being mandated by intermolecular hydrogen bonding (see section 3, Supramolecular details). All bond lengths and angles fall within the expected ranges for organic structures.
3. Supramolecular features

The main supramolecular feature is an inversion dimer resulting from a pair of symmetrically equivalent hydrogen bonds, O1—H1O···O2 and O1i—H1O···O2 [symmetry code: (i) x + 1, y + 1, z + 1], giving an R22(14) motif. The cohesion of this dimer is augmented by a pair of weak hydrogen bonds, C2—H2O2i and C2i—H2O2 (Table 1).

It also, however, brings inversion-related H2 atoms into unfavourably close proximity [H2H2i = 2.22 (3) Å]. These interactions are all illustrated in Fig. 2. Other noteworthy intermolecular contacts are weak C8—H8O1ii [symmetry code: (ii) x + 3, y, z + 3] interactions between 21 screw-related molecules, which loosely connect the dimers into layers parallel to (101). Almost all of the atom–atom contact coverages quantified in a Hirshfeld-surface analysis using CrystalExplorer (Spackman et al., 2021) involve hydrogen (H-H = 26.6%, H-O/O···H = 23.7%, H-Cl/Cl···H = 21.2%, H-C/C···H = 15.8%), with all other contact types being <5%. Further details are given in individual Hirshfeld-surface fingerprint plots (Fig. 3).

4. Database survey

A search of the Cambridge Structure Database (v5.43 with updates as of June 2022; Groom et al., 2016) for a search fragment consisting of the structure of I but with the OH and Cl groups replaced by ‘any non-H’ gave 71 hits. If the Cl site is specified as ‘any halogen’, there are just four hits, only three of which are unique, and all have Br as the halogen. Structure AWOCAS (Aldeborgh et al., 2014) is chemically a Br analogue of I, but its crystal structure is quite different (triclinic P1 vs P21/n for I). QAJNAS (Jasinski et al., 2011) [and QAJNAS01 (Mounir et al., 2013)] has NO2 in place of the hydroxyl. Lastly,

Table 1
Hydrogen-bond geometry (Å, °).

| D—H···A | D—H | H···A | D···A | D—H···A |
|---------|------|-------|-------|---------|
| O1—H1O···O2' | 0.803 (17) | 2.004 (18) | 2.8029 (12) | 173.4 (16) |
| C2—H2···O2' | 0.945 (15) | 2.547 (15) | 3.2633 (14) | 132.7 (11) |
| C8—H8A···O1i | 0.99 | 2.36 | 3.3485 (14) | 176 |

Symmetry codes: (i) x + 1, y + 1, z + 1; (ii) x + 3, y, z + 3.

**Figure 1**
An ellipsoid plot (50% probability) of I. Hydrogen atoms are drawn as small circles.

**Figure 2**
A partial packing plot showing the main supramolecular motif in I: a hydrogen-bonded dimer between inversion-related [symmetry code: (i) x + 1, y + 1, z + 1] molecules. Strong O—H···O hydrogen bonds are shown as thick dashed lines, weaker C—H···O interactions as open dashed lines, and an unfavourable, forced close contact between hydrogen atoms as a dotted line.

**Figure 3**
Hirshfeld surface fingerprint plots showing the relative contributions of various atom–atom contacts in the packing of I. (a) All contacts, (b) H···H (26.6%), (c) H···O/O···H (23.7%), (d) H···Cl/Cl···H (21.2%), (e) H···C/C···H (15.7%), (f) C···Cl/Cl···C (4.5%), (g) C···O/O···C (3.6%), (h) C···C (3.0%), (i) O···O (1.2%). All other contact types are <1%.
MEXCOJ (Ambekar et al., 2013) has OC—OPh in place of the OH in I. Other similar structures in the literature include: LEFNASN (Fun et al., 2012), which is the 4-hydroxyphenyl analogue of I and crystalizes with the symmetry of P21/c; FUHHOG (Qing & Zhang, 2009), which is the bromo analogue of LEFNASN; and CUYDOR (Mei et al., 2015), which has 4-fluorophenyl in place of the halogen of LEFNASN and FUHHOG.

5. Synthesis, crystallization and spectroscopic details

Synthesis and crystallization: For the synthesis of I, sulfuryl chloride (150 mg, 1.1 mmol) was added dropwise to a stirred mixture of 3-hydroxyacetophenone (100 mg, 0.74 mmol) in 5 ml of methanol and 10 ml of ethyl acetate/dichloromethane at 293–303 K. After completion of the addition, it was allowed to return to RT with stirring for 1 h. The reaction was monitored by TLC. Then the solvent was removed under reduced pressure by rotary evaporation to give the desired product in 95% yield. An overall reaction scheme is depicted in Fig. 4.

X-ray quality crystals were obtained by crystallization from ethanol (m.p. 352–354 K).

Spectroscopic data: Infrared and NMR spectroscopic details are as follows.

FTIR (ν in cm⁻¹): 3400 (Ar—OH, broad), 2987 (C—H stretching), 1694 (C=O stretching), 1789 (s, C=O stretching), 832 (s, Ar-C—H bending).

¹H NMR: CDCl₃ (400 MHz, δ ppm): 4.7 (s, 2H, —CH₂), 5.671 (s, 1H, —OH), 7.14 (d, 1H, Ar—H, J = 4.8 Hz), 7.36–7.4 (t, 2H, Ar—H, J = 16 Hz), 7.493–7.51 (m, 1H, Ar—H, J = 6.4 Hz).

6. Refinement

Crystal data, data collection, and structure refinement details are given in Table 2. All hydrogen atoms were found in difference-Fourier maps, but subsequently, the carbon-bound hydrogens were included using riding models, with constrained distances set to 0.95 Å (C—H) and 0.99 Å (R₂CH₂). The hydroxyl hydrogen atom coordinates were refined freely. In all cases, Uiso(H) values were set to 1.2Ueq of the attached atom.

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Computing details

Data collection: APEX3 (Bruker, 2016); cell refinement: APEX3 (Bruker, 2016); data reduction: APEX3 (Bruker, 2016); program(s) used to solve structure: SHELXT (Sheldrick, 2015a); program(s) used to refine structure: SHELXL2019/2 (Sheldrick, 2015b); molecular graphics: XP in SHELXTL (Sheldrick, 2008); software used to prepare material for publication: SHELX (Sheldrick, 2008) and publCIF (Westrip, 2010).

2-Chloro-1-(3-hydroxyphenyl)ethanone

Crystal data

| C_{8}H_{7}ClO_{2} | F(000) = 352 |
|-------------------|--------------|
| Mr = 170.59       | D_{x} = 1.539 Mg m^{-3} |
| Monoclinic, P2_{1}/n | Mo Kα radiation, λ = 0.71073 Å |
| a = 4.9172 (2) Å | Cell parameters from 9994 reflections |
| b = 12.7016 (4) Å | θ = 2.4–27.5° |
| c = 11.8573 (3) Å | μ = 0.46 mm^{-1} |
| β = 96.294 (1)° | T = 90 K |
| V = 736.10 (4) Å^{3} | Cut block, colourless |
| Z = 4            | 0.25 × 0.22 × 0.19 mm |

Data collection

| Bruker D8 Venture dual source diffractometer | 12264 measured reflections |
| Radiation source: microsource | 1685 independent reflections |
| Detector resolution: 7.41 pixels mm^{-1} | 1569 reflections with I > 2σ(I) |
| ϕ and σ scans | R_{min} = 0.028 |
| Absorption correction: multi-scan | θ_{max} = 27.5°, θ_{min} = 2.4° |
| (SADABS; Krause et al., 2015) | h = −6→6 |
| T_{min} = 0.855, T_{max} = 0.971 | k = −15→16 |
|                               | l = −15→15 |

Refinement

| Refinement on F^2 | Secondary atom site location: difference Fourier map |
|                   | Hydrogen site location: mixed |
| Least-squares matrix: full | H atoms treated by a mixture of independent and constrained refinement |
| R[F^2 > 2σ(F^2)] = 0.024 | w = 1/[(σ(Fo)^2) + 0.0323P]^{1/2} + 0.366P] |
| wR(F^2) = 0.067 | where P = (Fo^2 + 2Fc^2)/3 |
| S = 1.04 | (Δ/σ)_{max} < 0.001 |
| 1685 reflections | Δρ_{max} = 0.35 e Å^{-3} |
| 106 parameters | Δρ_{min} = −0.18 e Å^{-3} |
| 0 restraints |  

Primary atom site location: structure-invariant direct methods
Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

|    | x     | y     | z     | Uiso or Ueq (Å²) |
|----|-------|-------|-------|------------------|
| O1 | 1.05641 (18) | 0.59830 (6) | 0.66167 (7) | 0.01786 (19) |
| H1O| 0.938 (3) | 0.6217 (12) | 0.6166 (14) | 0.021* |
| O2 | 0.38728 (17) | 0.32908 (6) | 0.48648 (7) | 0.01810 (19) |
| C1 | 0.22134 (5) | 0.10971 (2) | 0.48449 (2) | 0.01719 (10) |
| C | 0.7757 (2) | 0.33060 (8) | 0.62318 (9) | 0.0131 (2) |
| C2 | 0.8093 (2) | 0.43878 (9) | 0.60814 (9) | 0.014 (2) |
| C3 | 1.0190 (2) | 0.49212 (9) | 0.67174 (9) | 0.0139 (2) |
| C4 | 1.1997 (2) | 0.43790 (9) | 0.74969 (9) | 0.0151 (2) |
| H4 | 1.345037 | 0.474217 | 0.792591 | 0.018* |
| C5 | 1.1662 (2) | 0.33023 (9) | 0.76434 (9) | 0.0157 (2) |
| H5 | 1.289511 | 0.293235 | 0.817524 | 0.019* |
| C6 | 0.9546 (2) | 0.27607 (9) | 0.70220 (9) | 0.0147 (2) |
| C7 | 0.931888 | 0.202668 | 0.713351 | 0.018* |
| C8 | 0.5426 (2) | 0.27915 (8) | 0.55286 (9) | 0.0133 (2) |
| H8A| 0.5108 (2) | 0.16148 (9) | 0.56861 (10) | 0.0148 (2) |
| H8B| 0.493730 | 0.146717 | 0.649517 | 0.018* |

Atomic displacement parameters (Å²)

|    | U₁₁  | U₂₂  | U₃₃  | U₁₂  | U₁₃  | U₂₃  |
|----|------|------|------|------|------|------|
| O1 | 0.0212 (4) | 0.0116 (4) | 0.0191 (4) | −0.0027 (3) | −0.0048 (3) | 0.0006 (3) |
| O2 | 0.0185 (4) | 0.0146 (4) | 0.0198 (4) | −0.0007 (3) | −0.0042 (3) | 0.0025 (3) |
| Cl | 0.01466 (15) | 0.01477 (15) | 0.02144 (16) | −0.00314 (9) | −0.00114 (11) | −0.00204 (10) |
| C1 | 0.0128 (5) | 0.0137 (5) | 0.0137 (5) | −0.0003 (4) | 0.0021 (4) | −0.0001 (4) |
| C2 | 0.0143 (5) | 0.0135 (5) | 0.0141 (5) | 0.0006 (4) | −0.0001 (4) | 0.0008 (4) |
| C3 | 0.0160 (5) | 0.0120 (5) | 0.0141 (5) | −0.0006 (4) | 0.0030 (4) | −0.0012 (4) |
| C4 | 0.0142 (5) | 0.0162 (5) | 0.0146 (5) | −0.0004 (4) | −0.0004 (4) | −0.0032 (4) |
| C5 | 0.0159 (5) | 0.0157 (5) | 0.0150 (5) | 0.0033 (4) | −0.0006 (4) | −0.0001 (4) |
| C6 | 0.0161 (5) | 0.0121 (5) | 0.0159 (5) | 0.0010 (4) | 0.0020 (4) | 0.0000 (4) |
| C7 | 0.0136 (5) | 0.0129 (5) | 0.0138 (5) | 0.0000 (4) | 0.0029 (4) | −0.0006 (4) |
| C8 | 0.0125 (5) | 0.0126 (5) | 0.0184 (5) | −0.0011 (4) | −0.0020 (4) | 0.0005 (4) |

Geometric parameters (Å, °)

|    | O1—C3 | O1—H1O | O2—C7 | C3—C4 | C4—C5 | C4—H4 |
|----|-------|--------|-------|-------|-------|-------|
| O1—C3 | 1.3682 (13) | 0.803 (17) | 1.2138 (14) | 1.3922 (16) |
| O1—H1O | 1.3906 (16) | 0.9500 | | | | |
|            |          |          |          |          |
|------------|----------|----------|----------|----------|
| C1—C8      | 1.7725 (11) | C5—C6    | 1.3892 (16) |
| C1—C6      | 1.3967 (15)  | C5—H5    | 0.9500    |
| C1—C2      | 1.3978 (15)  | C6—H6    | 0.9500    |
| C1—C7      | 1.4921 (15)  | C7—C8    | 1.5164 (15) |
| C2—C3      | 1.3857 (15)  | C8—H8A   | 0.9900    |
| C2—H2      | 0.945 (15)   | C8—H8B   | 0.9900    |
| C3—O1—H1O  | 109.2 (11)   | C6—C5—H5 | 119.6     |
| C6—C1—C2   | 119.91 (10)  | C4—C5—H5 | 119.6     |
| C6—C1—C7   | 123.12 (10)  | C5—C6—C1 | 119.35 (10) |
| C2—C1—C7   | 116.97 (10)  | C5—C6—H6 | 120.3     |
| C3—C2—C1   | 120.16 (10)  | C1—C6—H6 | 120.3     |
| C3—C2—H2   | 120.1 (9)    | O2—C7—C1 | 121.59 (10)|
| C1—C2—H2   | 119.7 (9)    | O2—C7—C8 | 121.91 (10)|
| O1—C3—C2   | 122.25 (10)  | C1—C7—C8 | 116.50 (9)|
| O1—C3—C4   | 117.6 (1)    | C7—C8—C11 | 112.57 (8)|
| C2—C3—C4   | 120.15 (10)  | C7—C8—H8A | 109.1    |
| C5—C4—C3   | 119.57 (10)  | C11—C8—H8A | 109.1    |
| C5—C4—H4   | 120.2        | C7—C8—H8B | 109.1    |
| C3—C4—H4   | 120.2        | C11—C8—H8B | 109.1    |
| C6—C5—C4   | 120.86 (10)  | H8A—C8—H8B | 107.8    |
| C6—C1—C2—C3 | −0.24 (16)    | C2—C1—C6—C5 | −0.61 (16)|
| C7—C1—C2—C3 | 179.06 (10)  | C7—C1—C6—C5 | −179.86 (10)|
| C1—C2—C3—O1 | −178.62 (10) | C6—C1—C7—O2 | 178.50 (11)|
| C1—C2—C3—C4 | 0.97 (16)    | C2—C1—C7—O2 | 0.77 (15)|
| O1—C3—C4—C5 | 178.75 (10)  | C6—C1—C7—C8 | −1.61 (15)|
| C2—C3—C4—C5 | −0.85 (16)   | C2—C1—C7—C8 | 179.11 (9)|
| C3—C4—C5—C6 | 0.00 (17)    | O2—C7—C8—C11 | −2.07 (14)|
| C4—C5—C6—C1 | 0.73 (17)    | C1—C7—C8—C11 | 178.05 (7)|

**Hydrogen-bond geometry (Å, °)**

| D—H:···A   | D—H   | H···A   | D···A   | D—H···A   |
|------------|--------|---------|---------|-----------|
| O1—H1O···O2i | 0.803 (17) | 2.004 (18) | 2.8029 (12) | 173.4 (16) |
| C2—H2···O2i  | 0.945 (15)  | 2.547 (15) | 3.2633 (14) | 132.7 (11) |
| C8—H8A···O1ii | 0.99    | 2.36     | 3.3485 (14) | 176       |

Symmetry codes: (i) −x+1, −y+1, −z+1; (ii) −x+3/2, y−1/2, −z+3/2.