Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# 4-Hydroxy-4,4-diphenylbutan-2-one

**Dennis P. Arnold and John C. McMurtrie***

School of Physical and Chemical Sciences, Queensland University of Technology, 2 George St, Brisbane, Queensland 4001, Australia
Correspondence e-mail: j.mcmurtrie@qut.edu.au

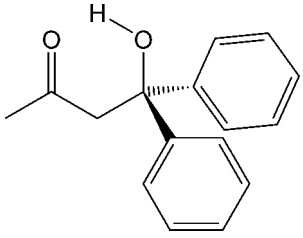
Received 3 July 2008; accepted 7 July 2008

Key indicators: single-crystal X-ray study; $T$ = 150 K; mean $\sigma$(C–C) = 0.002 Å; $R$ factor = 0.037; $wR$ factor = 0.066; data-to-parameter ratio = 17.6.

The molecules of the title compound, $C_{16}H_{16}O_2$, display an intramolecular O—H···O hydrogen bond between the hydroxyl donor and the ketone acceptor. Intermolecular C—H···$\pi$ interactions connect adjacent molecules into chains that propagate parallel to the *ac* diagonal. The chains are arranged in sheets, and molecules in adjacent sheets interact *via* intermolecular O—H···O hydrogen bonds.

## Related literature

For related literature, see: Rivett (1980); Paulson *et al.* (1973).




## Experimental

### Crystal data

$C_{16}H_{16}O_2$
$M_r$ = 240.29
Monoclinic, $P2_1/n$
$a$ = 9.8619 (2) Å
$b$ = 9.2015 (2) Å
$c$ = 14.3720 (3) Å
$\beta$ = 102.098 (2)°
$V$ = 1275.21 (5) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.08 mm$^{-1}$
$T$ = 150 (2) K
0.35 × 0.30 × 0.20 mm

### Data collection

Oxford Diffraction Gemini diffractometer
Absorption correction: multi-scan (*CrysAlis RED*; Oxford Diffraction, 2007)
$T_{min}$ = 0.933, $T_{max}$ = 0.984
7361 measured reflections
2935 independent reflections
2144 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.021

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.066
$S$ = 1.01
2935 reflections
167 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.22 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.20 e Å$^{-3}$

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O2—H2*O*···O1 | 0.910 (12) | 2.016 (12) | 2.7636 (12) | 138.5 (11) |
| O2—H2*O*···O1$^{i}$ | 0.910 (12) | 2.385 (13) | 3.0530 (12) | 130.3 (10) |

Symmetry code: (i) $-x+1, -y, -z+2$.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2007); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2007); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SIR97* (Altomare *et al.* 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *CrystalMaker* (CrystalMaker, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2008).

The authors gratefully acknowledge the Synthesis and Molecular Recognition Program, Faculty of Science, Queensland University of Technology, for financial support.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HG2422).

## References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
CrystalMaker (2006). *CrystalMaker*. CrystalMaker Software, Yarnton, Oxfordshire, UK.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Oxford Diffraction (2007). *CrysAlis CCD* and *CrysAlis RED*. Oxford Diffraction Ltd, Abingdon, Oxfordshire, England.
Paulson, D. R., Hartwig, A. L. & Moran, G. F. (1973). *J. Chem. Educ.* **50**, 216–217.
Rivett, E. E. A. (1980). *J. Chem. Educ.* **57**, 751.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Westrip, S. P. (2008). *publCIF*. In preparation.

# supplementary materials

*Acta Cryst.* (2008). E**64**, o1465 [ **doi:10.1107/S1600536808020886** ]

# 4-Hydroxy-4,4-diphenylbutan-2-one

**D. P. Arnold and J. C. McMurtrie**

## Comment

The molecular stucture of the title compound, (I), is illustrated in Fig. 1. There is an intramolecular hydrogen bond between the hydroxyl moiety and the ketone oxygen. The molecules are arranged in chains that propagate parallel to the *ac* diagonal *via* intermolecular CH···π interactions. There are two such interactions; the aromatic ring comprising C5—C10 is the CH donor and the ring comprising C11—C16 is the acceptor in both cases. Geometric parameters for the two interactions are as follows; C6—H6···C11—$C16_{plane}$ distance 2.731 Å with C5—$C10_{plane}$···C11—$C16_{plane}$ dihedral angle 78.67° and C8—H8···C11—$C16_{plane}$ distance 2.947 Å with C5—$C10_{plane}$···C11—$C16_{plane}$ dihedral angle 83.52°. The chains stack to form two-dimensional sheets in the crystal structure (Fig. 2). Intermolecular hydrogen bonds connect pairs of molecules from contiguous two-dimensional sheets. The pairwise intermolecular H-bond interactions and the intramolecular H-bond interactions are illustrated in Fig. 3.

## Experimental

The title compound was prepared according to the procedure described by Rivett (1980) which is an adaptation of the method reported earlier by Paulson *et al.* (1973). Large colourless prismatic crystals of the compound were obtained by crystallization from an evaporating dichloromethane/methanol solution.

## Refinement

C-bound H atoms were included in idealized positions and refined using a riding model approximation with methylene, methyl and aromatic bond lengths fixed at 0.99, 0.98 and 0.95 Å, respectively. $U_{iso}$(H) values were fixed at $1.2U_{eq}$ of the parent C atoms for methylene and aromatic H atoms and $1.5U_{eq}$ of the parent C atoms for methyl H atoms. The hydroxy H atom was located in a Fourier difference map and refined with an O—H bond length restraint of 0.98 Å and with $U_{iso}$ fixed at $1.5U_{eq}$ of the parent O atom.

## Figures

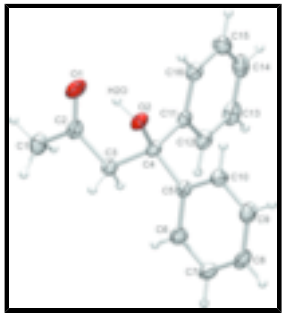


Fig. 1. *ORTEP* depiction of the molecular structure with atom numbering scheme. Ellipsoids are drawn at the 50% probability level.

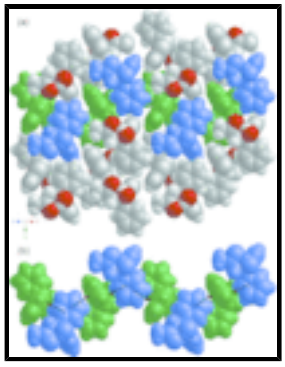


Fig. 2. (*a*) The molecules are arranged in sheets. Within the sheets the molecules are linked in one-dimensional chains by CH···π interactions between phenyl rings. Once such chain is highlighted with alternating molecules coloured green and blue. (*b*) Excerpt from (*a*) showing the propagation of the chain by CH···π interactions between phenyl rings of adjacent molecules.

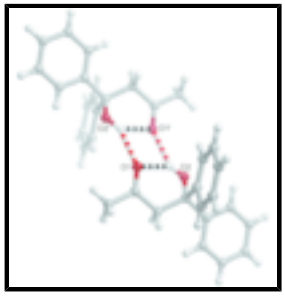


Fig. 3. Molecules in adjacent two-dimensional sheets are connected by intermolecular hydrogen bonds. The arrangement of these hydrogen bonds between a pair of molecules is illustrated (red/white dashed contact). The intramolecular hydrogen bonds are also shown (black/white dashed line). Symmetry code: (i) -*x* + 1, -*y*, -*z* + 2.

### 4-Hydroxy-4,4-diphenylbutan-2-one

*Crystal data*

| | |
|---|---|
| $C_{16}H_{16}O_2$ | $F_{000}$ = 512 |
| $M_r$ = 240.29 | $D_x$ = 1.252 Mg m$^{-3}$ |
| Monoclinic, $P2_1/n$ | Mo $K\alpha$ radiation<br>λ = 0.71073 Å |
| Hall symbol: -P 2yn | Cell parameters from 3618 reflections |
| *a* = 9.8619 (2) Å | θ = 2.9–28.7º |
| *b* = 9.2015 (2) Å | μ = 0.08 mm$^{-1}$ |
| *c* = 14.3720 (3) Å | *T* = 150 (2) K |
| β = 102.098 (2)º | Prism, colourless |
| *V* = 1275.21 (5) Å$^3$ | 0.35 × 0.30 × 0.20 mm |
| *Z* = 4 | |

*Data collection*

| | |
|---|---|
| Oxford Diffraction Gemini diffractometer | 2935 independent reflections |
| Radiation source: Enhance (Mo) X-ray Source | 2144 reflections with $I > 2\sigma(I)$ |
| Monochromator: graphite | $R_{int}$ = 0.021 |
| Detector resolution: 16.0774 pixels mm$^{-1}$ | $\theta_{max}$ = 28.8º |
| *T* = 150(2) K | $\theta_{min}$ = 2.9º |
| ω scans | *h* = −11→12 |
| Absorption correction: multi-scan (CrysAlis RED; Oxford Diffraction, 2007) | *k* = −12→12 |
| $T_{min}$ = 0.933, $T_{max}$ = 0.984 | *l* = −19→19 |

7361 measured reflections

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | Secondary atom site location: difference Fourier map |
| Least-squares matrix: full | Hydrogen site location: inferred from neighbouring sites |
| $R[F^2 > 2\sigma(F^2)] = 0.036$ | H atoms treated by a mixture of independent and constrained refinement |
| $wR(F^2) = 0.066$ | $w = 1/[\sigma^2(F_o^2) + (0.01P)^2 + 0.4P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $S = 1.01$ | $(\Delta/\sigma)_{max} = 0.001$ |
| 2935 reflections | $\Delta\rho_{max} = 0.22$ e Å$^{-3}$ |
| 167 parameters | $\Delta\rho_{min} = -0.20$ e Å$^{-3}$ |
| 1 restraint | Extinction correction: none |
| Primary atom site location: structure-invariant direct methods | |

*Special details*

**Experimental**. Crystal cleaved from larger prism.

Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

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

**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on $F^2$, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative $F^2$. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on $F^2$ are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| C1 | 0.55546 (14) | 0.14657 (15) | 0.76771 (9) | 0.0373 (3) |
| H1A | 0.6047 | 0.0538 | 0.7694 | 0.056* |
| H1B | 0.6224 | 0.2266 | 0.7750 | 0.056* |
| H1C | 0.4896 | 0.1562 | 0.7067 | 0.056* |
| C2 | 0.47849 (12) | 0.15136 (14) | 0.84736 (8) | 0.0276 (3) |
| C3 | 0.42255 (12) | 0.29752 (13) | 0.86860 (8) | 0.0256 (3) |
| H3A | 0.3802 | 0.3449 | 0.8076 | 0.031* |
| H3B | 0.5012 | 0.3589 | 0.9004 | 0.031* |
| C4 | 0.31411 (11) | 0.29285 (13) | 0.93164 (7) | 0.0224 (2) |
| C5 | 0.27448 (11) | 0.44508 (13) | 0.95954 (8) | 0.0227 (2) |
| C6 | 0.30596 (13) | 0.57091 (14) | 0.91585 (8) | 0.0294 (3) |
| H6 | 0.3561 | 0.5648 | 0.8663 | 0.035* |

| | | | | |
|---|---|---|---|---|
| C7 | 0.26527 (13) | 0.70651 (14) | 0.94343 (9) | 0.0328 (3) |
| H7 | 0.2875 | 0.7920 | 0.9127 | 0.039* |
| C8 | 0.19261 (12) | 0.71662 (14) | 1.01542 (8) | 0.0311 (3) |
| H8 | 0.1649 | 0.8089 | 1.0345 | 0.037* |
| C9 | 0.16028 (13) | 0.59169 (15) | 1.05965 (9) | 0.0330 (3) |
| H9 | 0.1100 | 0.5983 | 1.1091 | 0.040* |
| C10 | 0.20081 (13) | 0.45708 (14) | 1.03224 (8) | 0.0291 (3) |
| H10 | 0.1783 | 0.3719 | 1.0632 | 0.035* |
| C11 | 0.18229 (11) | 0.21520 (13) | 0.87881 (7) | 0.0221 (2) |
| C12 | 0.10703 (12) | 0.27142 (14) | 0.79318 (8) | 0.0282 (3) |
| H12 | 0.1379 | 0.3576 | 0.7677 | 0.034* |
| C13 | −0.01221 (13) | 0.20283 (15) | 0.74497 (8) | 0.0336 (3) |
| H13 | −0.0627 | 0.2423 | 0.6869 | 0.040* |
| C14 | −0.05786 (13) | 0.07704 (15) | 0.78118 (9) | 0.0344 (3) |
| H14 | −0.1390 | 0.0294 | 0.7477 | 0.041* |
| C15 | 0.01500 (13) | 0.02096 (15) | 0.86617 (9) | 0.0341 (3) |
| H15 | −0.0165 | −0.0650 | 0.8915 | 0.041* |
| C16 | 0.13418 (12) | 0.08994 (14) | 0.91473 (8) | 0.0281 (3) |
| H16 | 0.1834 | 0.0508 | 0.9733 | 0.034* |
| O1 | 0.46398 (10) | 0.04232 (10) | 0.89213 (6) | 0.0388 (2) |
| O2 | 0.37110 (8) | 0.22230 (9) | 1.01953 (5) | 0.02635 (19) |
| H2O | 0.4104 (14) | 0.1379 (14) | 1.0054 (9) | 0.040* |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C1 | 0.0371 (8) | 0.0363 (8) | 0.0426 (7) | 0.0045 (6) | 0.0178 (6) | −0.0073 (6) |
| C2 | 0.0246 (6) | 0.0290 (7) | 0.0283 (6) | 0.0047 (5) | 0.0030 (5) | −0.0038 (5) |
| C3 | 0.0260 (6) | 0.0247 (6) | 0.0271 (6) | 0.0035 (5) | 0.0077 (5) | −0.0001 (5) |
| C4 | 0.0258 (6) | 0.0221 (6) | 0.0196 (5) | 0.0044 (5) | 0.0057 (4) | 0.0023 (5) |
| C5 | 0.0219 (6) | 0.0225 (6) | 0.0230 (5) | 0.0026 (5) | 0.0032 (4) | −0.0014 (5) |
| C6 | 0.0337 (7) | 0.0256 (7) | 0.0315 (6) | 0.0036 (5) | 0.0127 (5) | 0.0010 (6) |
| C7 | 0.0379 (7) | 0.0221 (6) | 0.0391 (7) | 0.0039 (6) | 0.0099 (6) | 0.0023 (6) |
| C8 | 0.0316 (7) | 0.0245 (7) | 0.0360 (6) | 0.0080 (6) | 0.0042 (5) | −0.0057 (6) |
| C9 | 0.0348 (7) | 0.0341 (7) | 0.0331 (6) | 0.0062 (6) | 0.0141 (5) | −0.0043 (6) |
| C10 | 0.0336 (7) | 0.0259 (7) | 0.0304 (6) | 0.0016 (5) | 0.0126 (5) | 0.0008 (5) |
| C11 | 0.0247 (6) | 0.0227 (6) | 0.0200 (5) | 0.0055 (5) | 0.0074 (4) | −0.0024 (5) |
| C12 | 0.0318 (6) | 0.0310 (7) | 0.0227 (6) | 0.0070 (6) | 0.0078 (5) | 0.0012 (5) |
| C13 | 0.0318 (7) | 0.0444 (8) | 0.0230 (6) | 0.0105 (6) | 0.0018 (5) | −0.0046 (6) |
| C14 | 0.0257 (6) | 0.0414 (8) | 0.0354 (7) | 0.0009 (6) | 0.0049 (5) | −0.0143 (6) |
| C15 | 0.0333 (7) | 0.0308 (7) | 0.0396 (7) | −0.0031 (6) | 0.0110 (6) | −0.0035 (6) |
| C16 | 0.0307 (7) | 0.0270 (7) | 0.0268 (6) | 0.0027 (5) | 0.0063 (5) | 0.0007 (5) |
| O1 | 0.0515 (6) | 0.0275 (5) | 0.0405 (5) | 0.0123 (4) | 0.0166 (4) | 0.0030 (4) |
| O2 | 0.0320 (5) | 0.0241 (5) | 0.0214 (4) | 0.0077 (4) | 0.0021 (3) | 0.0016 (4) |

*Geometric parameters (Å, °)*

| | | | |
|---|---|---|---|
| C1—C2 | 1.5009 (16) | C8—C9 | 1.3828 (18) |
| C1—H1A | 0.9800 | C8—H8 | 0.9500 |

| | | | |
|---|---|---|---|
| C1—H1B | 0.9800 | C9—C10 | 1.3839 (17) |
| C1—H1C | 0.9800 | C9—H9 | 0.9500 |
| C2—O1 | 1.2165 (15) | C10—H10 | 0.9500 |
| C2—C3 | 1.5089 (16) | C11—C16 | 1.3866 (16) |
| C3—C4 | 1.5403 (15) | C11—C12 | 1.3965 (15) |
| C3—H3A | 0.9900 | C12—C13 | 1.3855 (17) |
| C3—H3B | 0.9900 | C12—H12 | 0.9500 |
| C4—O2 | 1.4266 (13) | C13—C14 | 1.3826 (19) |
| C4—C5 | 1.5301 (16) | C13—H13 | 0.9500 |
| C4—C11 | 1.5373 (16) | C14—C15 | 1.3808 (18) |
| C5—C6 | 1.3830 (16) | C14—H14 | 0.9500 |
| C5—C10 | 1.3964 (15) | C15—C16 | 1.3884 (17) |
| C6—C7 | 1.3934 (17) | C15—H15 | 0.9500 |
| C6—H6 | 0.9500 | C16—H16 | 0.9500 |
| C7—C8 | 1.3795 (17) | O2—H2O | 0.910 (12) |
| C7—H7 | 0.9500 | | |
| C2—C1—H1A | 109.5 | C6—C7—H7 | 120.0 |
| C2—C1—H1B | 109.5 | C7—C8—C9 | 119.65 (12) |
| H1A—C1—H1B | 109.5 | C7—C8—H8 | 120.2 |
| C2—C1—H1C | 109.5 | C9—C8—H8 | 120.2 |
| H1A—C1—H1C | 109.5 | C8—C9—C10 | 120.33 (11) |
| H1B—C1—H1C | 109.5 | C8—C9—H9 | 119.8 |
| O1—C2—C1 | 120.90 (12) | C10—C9—H9 | 119.8 |
| O1—C2—C3 | 122.65 (11) | C9—C10—C5 | 120.69 (12) |
| C1—C2—C3 | 116.44 (11) | C9—C10—H10 | 119.7 |
| C2—C3—C4 | 114.99 (10) | C5—C10—H10 | 119.7 |
| C2—C3—H3A | 108.5 | C16—C11—C12 | 118.42 (11) |
| C4—C3—H3A | 108.5 | C16—C11—C4 | 121.49 (10) |
| C2—C3—H3B | 108.5 | C12—C11—C4 | 120.09 (11) |
| C4—C3—H3B | 108.5 | C13—C12—C11 | 120.70 (12) |
| H3A—C3—H3B | 107.5 | C13—C12—H12 | 119.6 |
| O2—C4—C5 | 105.04 (8) | C11—C12—H12 | 119.6 |
| O2—C4—C11 | 111.18 (9) | C14—C13—C12 | 120.15 (11) |
| C5—C4—C11 | 108.60 (9) | C14—C13—H13 | 119.9 |
| O2—C4—C3 | 109.89 (9) | C12—C13—H13 | 119.9 |
| C5—C4—C3 | 112.06 (10) | C15—C14—C13 | 119.72 (12) |
| C11—C4—C3 | 110.00 (9) | C15—C14—H14 | 120.1 |
| C6—C5—C10 | 118.35 (11) | C13—C14—H14 | 120.1 |
| C6—C5—C4 | 123.61 (10) | C14—C15—C16 | 120.17 (12) |
| C10—C5—C4 | 118.03 (10) | C14—C15—H15 | 119.9 |
| C5—C6—C7 | 121.00 (11) | C16—C15—H15 | 119.9 |
| C5—C6—H6 | 119.5 | C11—C16—C15 | 120.84 (11) |
| C7—C6—H6 | 119.5 | C11—C16—H16 | 119.6 |
| C8—C7—C6 | 119.97 (12) | C15—C16—H16 | 119.6 |
| C8—C7—H7 | 120.0 | C4—O2—H2O | 107.4 (8) |
| O1—C2—C3—C4 | −15.52 (17) | C6—C5—C10—C9 | 0.08 (18) |
| C1—C2—C3—C4 | 165.07 (10) | C4—C5—C10—C9 | −179.04 (11) |
| C2—C3—C4—O2 | 57.09 (13) | O2—C4—C11—C16 | −2.22 (14) |

| | | | |
|---|---|---|---|
| C2—C3—C4—C5 | 173.47 (9) | C5—C4—C11—C16 | −117.30 (11) |
| C2—C3—C4—C11 | −65.63 (12) | C3—C4—C11—C16 | 119.73 (11) |
| O2—C4—C5—C6 | 133.63 (11) | O2—C4—C11—C12 | 177.02 (10) |
| C11—C4—C5—C6 | −107.35 (12) | C5—C4—C11—C12 | 61.94 (13) |
| C3—C4—C5—C6 | 14.36 (15) | C3—C4—C11—C12 | −61.03 (13) |
| O2—C4—C5—C10 | −47.29 (13) | C16—C11—C12—C13 | −0.53 (17) |
| C11—C4—C5—C10 | 71.72 (12) | C4—C11—C12—C13 | −179.79 (11) |
| C3—C4—C5—C10 | −166.56 (10) | C11—C12—C13—C14 | −0.24 (18) |
| C10—C5—C6—C7 | −0.05 (18) | C12—C13—C14—C15 | 0.74 (18) |
| C4—C5—C6—C7 | 179.02 (11) | C13—C14—C15—C16 | −0.48 (19) |
| C5—C6—C7—C8 | 0.10 (19) | C12—C11—C16—C15 | 0.79 (17) |
| C6—C7—C8—C9 | −0.17 (19) | C4—C11—C16—C15 | −179.96 (11) |
| C7—C8—C9—C10 | 0.21 (19) | C14—C15—C16—C11 | −0.29 (18) |
| C8—C9—C10—C5 | −0.16 (19) | | |

*Hydrogen-bond geometry (Å, °)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O2—H2O···O1 | 0.910 (12) | 2.016 (12) | 2.7636 (12) | 138.5 (11) |
| O2—H2O···O1$^{i}$ | 0.910 (12) | 2.385 (13) | 3.0530 (12) | 130.3 (10) |

Symmetry codes: (i) −*x*+1, −*y*, −*z*+2.

**Fig. 1**

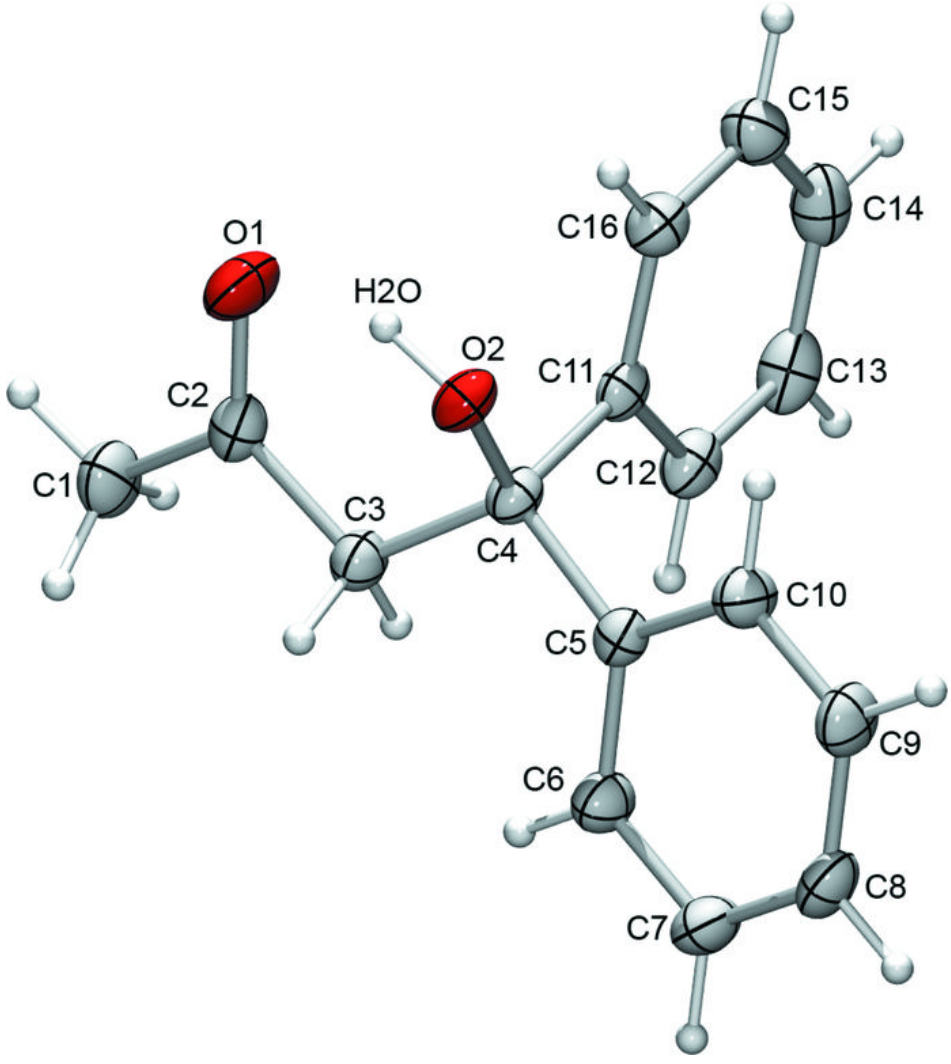


**Fig. 2**

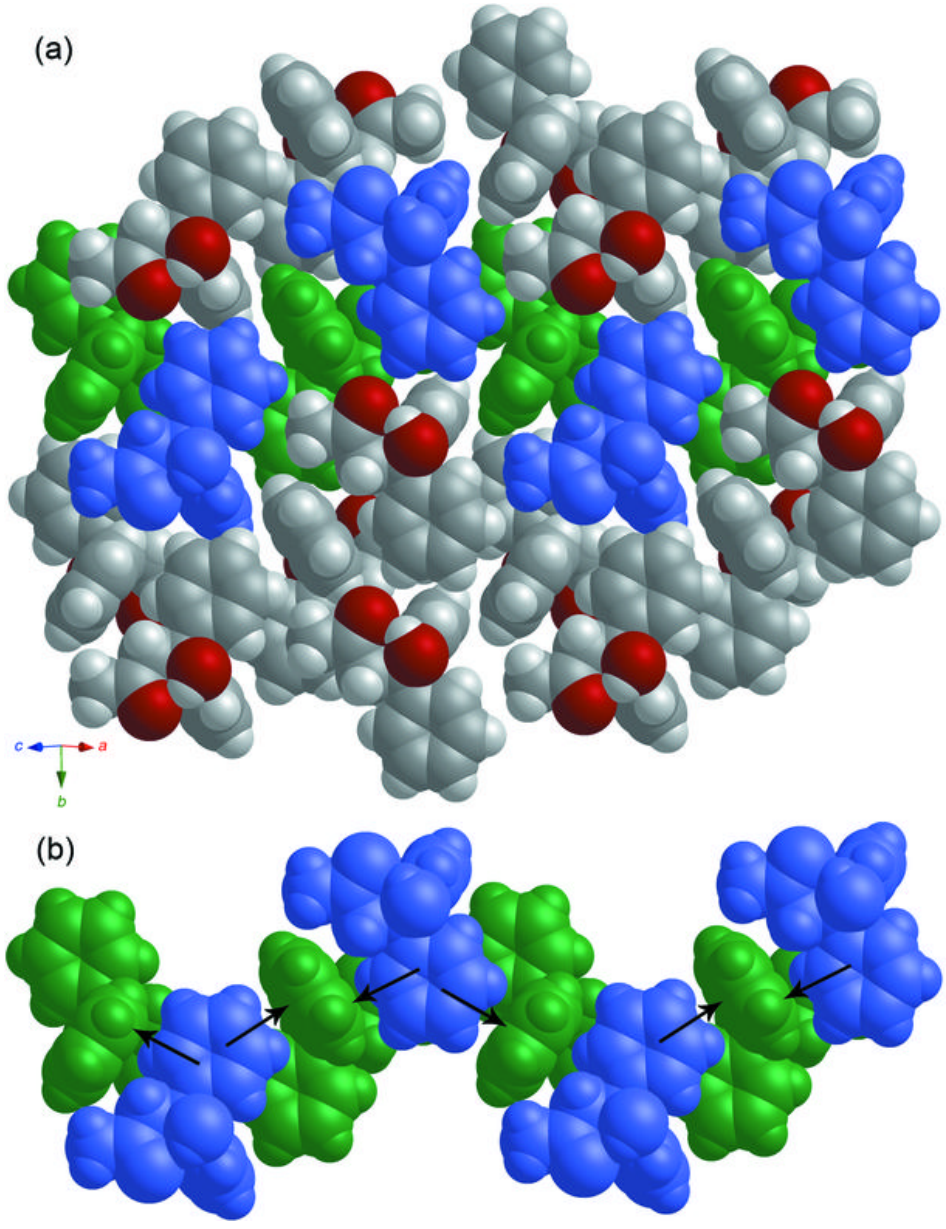


**Fig. 3**