

3-[(*R*)-3,3-Dichloro-2-hydroxypropyl]-8-hydroxy-6-methoxy-1*H*-isochromen-1-one

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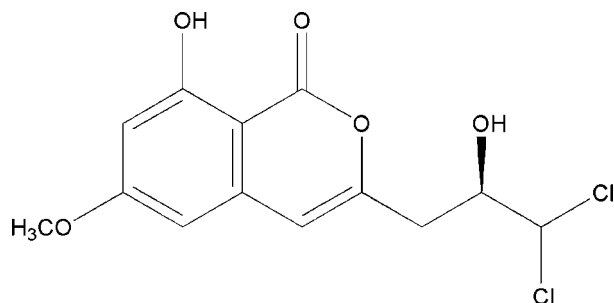
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Key indicators: single-crystal X-ray study; $T = 293$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.035; wR factor = 0.096; data-to-parameter ratio = 13.7.

The title compound, $\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{O}_5$, is an isocoumarin compound which has been isolated from the ethyl acetate extract of the fermentation broth of actinomycete *Streptomyces* sp. (V_4) from the South China Sea. There are intra- and intermolecular hydrogen bonds and halogen bonds [$\text{Cl}\cdots\text{Cl} = 3.434$ (2) Å; $\text{C}-\text{Cl}\cdots\text{Cl} = 121.6^\circ$]. The intermolecular $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonds link molecules into chains along the b axis.

Related literature

For related literature, see: Larsen & Breinholt (1999).



Experimental

Crystal data

$\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{O}_5$	$V = 667.1$ (4) Å ³
$M_r = 319.13$	$Z = 2$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 9.483$ (3) Å	$\mu = 0.50$ mm ⁻¹
$b = 6.757$ (2) Å	$T = 293$ (2) K
$c = 10.548$ (3) Å	$0.50 \times 0.34 \times 0.21$ mm
$\beta = 99.217$ (5)°	

Data collection

Bruker SMART 1K area-detector diffractometer	4190 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)	2524 independent reflections
$T_{\min} = 0.787$, $T_{\max} = 0.902$	2320 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.019$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.035$	H-atom parameters constrained
$wR(F^2) = 0.095$	$\Delta\rho_{\text{max}} = 0.26$ e Å ⁻³
$S = 1.07$	$\Delta\rho_{\text{min}} = -0.39$ e Å ⁻³
2524 reflections	Absolute structure: Flack (1983),
184 parameters	931 Friedel pairs
1 restraint	Flack parameter: 0.06 (8)

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{O5}-\text{H5}\cdots\text{O3}^i$	0.82	2.18	2.913 (3)	149
$\text{O3}-\text{H3}\cdots\text{O2}$	0.82	1.91	2.624 (2)	145

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

Data collection: SMART (Bruker, 1999); cell refinement: SAINT-Plus (Bruker, 1999); data reduction: SAINT-Plus; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: SHELXTL (Sheldrick, 2008); software used to prepare material for publication: SHELXTL.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: WW2128).

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3-[(*R*)-3,3-Dichloro-2-hydroxypropyl]-8-hydroxy-6-methoxy-1*H*-isochromen-1-one

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Comment

As a kind of natural products from marine microorganisms, 3-((*R*)-3,3-dichloro-2-hydroxypropyl)-8-hydroxy-6-methoxy-1*H*-isochromen-1-one, is a isocoumarin-related dihydrodiaportin compound, from the fermentation broth of *actinomyces Streptomyces sp.* (V4). In the primary biotest, the title compound showed weak activity inhibiting AchE *in vitro* (IC₅₀ = 3.9 μM/ml).

Larsen *et al.* also reported dichlorodiaportin (Larsen & Breinholt, 1999), but it was isolated from quite different microorganism, the typical cheese-associated isolates of *Penicillium nalgiovense*, and its structure was only elucidated based on spectral analysis, and the absolute configuration was depicted *S* by comparison with the optical rotation of those reported for several analogues of known absolute configuration. However, according to the optical rotation and our crystal structure, it is clear that Larsen's compound is the same compound as our dichlorodiaportin.

We report here the crystal structure of (I). Compound (I) crystallizes in space group *P* 2₁, and the 8-hydroxy-isochromen-1-one core rings in (I) is a planar conjugated ring system (Fig.1). In the crystal structure, there is an intra- molecular hydrogen bond [O...O = 2.624 (2) Å, and O—H...O = 144.6°] of O—H...O type between O3 and O5 hydroxyl groups in (I), and adjacent molecules form an infinite one-dimensional chain along *b* axis *via* O—H...O intermolecular hydrogen bonds [O...O = 2.913 (3) Å, and O—H...O = 149.0°] between the O3 and O5 hydroxyl groups (Fig.1 and Table 2).

Experimental

A strain of *streptomyces sp.* (V4) was isolated from the South China Sea, has been deposited in the School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou, P. R. China.

Culture conditions: soluble starch 10 g l⁻¹, Ca carbonate 2 g l⁻¹, ammonium sulfate 2 g l⁻¹, dipotassium hydrogen phosphate 1 g l⁻¹, magnesium sulfate hydrated 1 g l⁻¹, sodium chloride 1 g l⁻¹, yeast extract 10 g l⁻¹, pH 7.2 and incubation at 298 K for 6 d. For the extraction and separation of the metabolite, the cultures (100 L) of (I) were filtered through cheesecloth. The filtrate was concentrated to 5L below 323 K, then extracted three times by shaking with an equal volume of ethyl acetate. The extract was evaporated under reduced pressure. The combined organic extracts were subjected to silica-gel column chromatography, eluting with petroleum ether/ethyl (1:1 v/v) acetate, to yield (I).

Colorless block crystals of (I) were obtained by evaporation of a methanol solution.

The compound identity was confirmed by NMR spectroscopy, Elemental Analysis, IR, FAB-MS, melting point and optical rotation.

¹H-NMR in CDCl₃ (500 MHz): 6.59 (s, 1H), 6.57 (d, *J* = 2.0 1H), 3.01 (m, 1H), 2.95 (m, 1H), 4.42 (m, 1H), 6.20 (d, *J* = 3.0 1H), 3.92 (s, 3H), 11.10 (s, OH) and 5.20 (d, *J* = 6.0, OH).

supplementary materials

^{13}C -NMR in CDCl_3 (125 MHz): 166.8 (C), 154 (C), 107.4 (CH), 140.4 (C), 102.1 (CH), 168.0 (C), 101.2 (CH), 164.3 (C), 111.4 (C), 37.3 (CH_2), 73.1 (CH), 77.2 (CH) and 56.3 (CH_3).

Elemental Analysis: C 48.91, H 3.97, calc. (for $\text{C}_{13}\text{H}_{12}\text{O}_5\text{Cl}_2$): C 48.93, H 3.79%.

IR (KBr): 3474, 3032, 2986, 1693, 1643, 1568, 1465, 1356, 1237, 1197, 1096, 853, 790, 690.

FAB-MS: 319 $[M]^+$, 321 $[M+2]^+$, 235 $[M-\text{CHCl}_2]^+$, 107, 77.

M.p. 419–420 K.

$[\alpha]_{\text{D}}^{20} = +7.8$ ($c = 0.05$, MeOH).

Refinement

The H atoms were positioned geometrically and were treated as riding on their parent C atoms, with C—H distances in the range of 0.93–0.98 Å, with U_{iso} (H) = 1.2–1.5 times U_{eq} of the parent atom. H atoms attached to O3 and O5 (hydroxyl oxygen atoms) were located in difference Fourier maps and refined initially with distance restraints of 0.82 Å with U_{iso} (H) = 1.5 times U_{eq} (O).

Figures

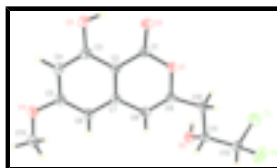


Figure 1 View of the molecules in the asymmetric unit of (I), with anisotropic displacement parameters drawn at the 50% probability level.

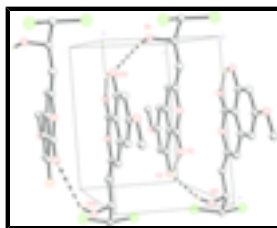
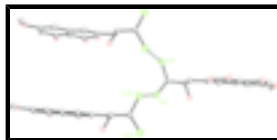


Figure 2 A view of the hydrogen-bonded molecular chains (Dashed lines). The chains are aligned parallel to the crystallographic b axis. H atoms not involved in H-bonding have been omitted for clarity. Symmetry codes: (I) $1 - x, y - 1/2, -z$; (II) $1 - x, 1/2 + y, -z$.



3-[(*R*)-3,3-Dichloro-2-hydroxypropyl]-8-hydroxy-6-methoxy-1*H*-isochromen-1-one

Crystal data

$\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{O}_5$

$M_r = 319.13$

Monoclinic, $P2_1$

$F_{000} = 328$

$D_x = 1.589 \text{ Mg m}^{-3}$

Melting point: 420 K

Hall symbol: P 2yb

$a = 9.483$ (3) Å

$b = 6.757$ (2) Å

$c = 10.548$ (3) Å

$\beta = 99.217$ (5)°

$V = 667.1$ (4) Å³

$Z = 2$

Mo $K\alpha$ radiation

$\lambda = 0.71073$ Å

Cell parameters from 1002 reflections

$\theta = 2.7\text{--}27.0^\circ$

$\mu = 0.50$ mm⁻¹

$T = 293$ (2) K

Block, colorless

$0.50 \times 0.34 \times 0.21$ mm

Data collection

Bruker SMART 1K area-detector
diffractometer

Radiation source: fine-focus sealed tube

Monochromator: graphite

$T = 293$ (2) K

φ and ω scans

Absorption correction: multi-scan
(SADABS; Sheldrick, 1996)

$T_{\min} = 0.787$, $T_{\max} = 0.902$

4190 measured reflections

2524 independent reflections

2320 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.019$

$\theta_{\max} = 27.1^\circ$

$\theta_{\min} = 2.0^\circ$

$h = -12 \rightarrow 11$

$k = -8 \rightarrow 7$

$l = -13 \rightarrow 11$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.035$

$wR(F^2) = 0.095$

$S = 1.07$

2524 reflections

184 parameters

1 restraint

Primary atom site location: structure-invariant direct
methods

Secondary atom site location: difference Fourier map

Hydrogen site location: difference Fourier map

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0525P)^2 + 0.1606P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.26$ e Å⁻³

$\Delta\rho_{\min} = -0.39$ e Å⁻³

Extinction correction: none

Absolute structure: Flack (1983), 931 Friedel pairs

Flack parameter: 0.06 (8)

Special details

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.

supplementary materials

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.54937 (19)	0.4698 (4)	-0.06308 (18)	0.0334 (4)
C2	0.55042 (19)	0.4661 (4)	0.07326 (17)	0.0317 (4)
C3	0.6821 (2)	0.4688 (4)	0.15853 (18)	0.0356 (4)
C4	0.6830 (2)	0.4614 (4)	0.28857 (19)	0.0387 (4)
H4	0.7694	0.4607	0.3446	0.046*
C5	0.5540 (2)	0.4548 (4)	0.33695 (18)	0.0361 (4)
C6	0.4234 (2)	0.4543 (4)	0.25529 (18)	0.0369 (4)
H6	0.3383	0.4501	0.2884	0.044*
C7	0.42213 (19)	0.4602 (4)	0.12326 (17)	0.0332 (4)
C8	0.29092 (19)	0.4610 (4)	0.03216 (18)	0.0358 (4)
H8	0.2038	0.4583	0.0619	0.043*
C9	0.29283 (18)	0.4657 (4)	-0.09298 (17)	0.0332 (4)
C10	0.17165 (19)	0.4676 (5)	-0.20293 (17)	0.0356 (4)
H10A	0.1783	0.3505	-0.2548	0.043*
H10B	0.1821	0.5820	-0.2562	0.043*
C11	0.02418 (19)	0.4735 (5)	-0.16418 (17)	0.0393 (5)
H11	0.0161	0.3586	-0.1091	0.047*
C12	-0.0964 (2)	0.4600 (5)	-0.2789 (2)	0.0471 (5)
H12	-0.1876	0.4740	-0.2473	0.057*
C13	0.4413 (3)	0.4492 (5)	0.5247 (2)	0.0502 (5)
H13A	0.3875	0.5677	0.5015	0.075*
H13B	0.4673	0.4429	0.6163	0.075*
H13C	0.3843	0.3359	0.4950	0.075*
C11	-0.08373 (8)	0.65243 (17)	-0.39091 (7)	0.0803 (3)
C12	-0.09425 (9)	0.22660 (16)	-0.35406 (9)	0.0829 (3)
O1	0.42041 (13)	0.4685 (3)	-0.14183 (12)	0.0349 (3)
O2	0.65509 (15)	0.4724 (3)	-0.11589 (14)	0.0452 (4)
O3	0.80850 (14)	0.4768 (3)	0.11445 (14)	0.0459 (4)
H3	0.7939	0.4940	0.0365	0.069*
O4	0.56832 (17)	0.4506 (3)	0.46640 (14)	0.0463 (4)
O5	0.00051 (18)	0.6449 (3)	-0.09336 (15)	0.0524 (5)
H5	0.0323	0.7420	-0.1259	0.079*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0317 (8)	0.0335 (10)	0.0355 (9)	0.0005 (10)	0.0067 (7)	-0.0017 (10)
C2	0.0315 (8)	0.0309 (9)	0.0325 (9)	0.0027 (10)	0.0044 (7)	0.0009 (9)
C3	0.0321 (9)	0.0324 (10)	0.0414 (10)	0.0010 (11)	0.0034 (7)	-0.0001 (10)
C4	0.0363 (9)	0.0401 (10)	0.0367 (10)	0.0003 (11)	-0.0033 (7)	-0.0017 (11)
C5	0.0442 (10)	0.0323 (10)	0.0305 (9)	-0.0006 (11)	0.0016 (7)	-0.0008 (10)
C6	0.0364 (9)	0.0434 (11)	0.0316 (9)	0.0011 (11)	0.0072 (7)	0.0010 (10)
C7	0.0323 (9)	0.0363 (10)	0.0309 (9)	-0.0008 (11)	0.0046 (7)	-0.0008 (10)
C8	0.0287 (8)	0.0461 (11)	0.0330 (9)	0.0007 (11)	0.0067 (7)	0.0016 (11)

C9	0.0297 (8)	0.0352 (10)	0.0354 (9)	-0.0024 (10)	0.0070 (7)	-0.0031 (10)
C10	0.0330 (8)	0.0470 (11)	0.0271 (8)	0.0013 (11)	0.0058 (6)	-0.0018 (10)
C11	0.0333 (9)	0.0568 (13)	0.0281 (9)	-0.0076 (11)	0.0060 (7)	-0.0016 (11)
C12	0.0311 (9)	0.0760 (16)	0.0349 (10)	-0.0087 (14)	0.0074 (7)	-0.0079 (13)
C13	0.0613 (13)	0.0601 (15)	0.0300 (10)	0.0009 (15)	0.0095 (9)	0.0023 (11)
Cl1	0.0525 (4)	0.1251 (9)	0.0574 (4)	-0.0046 (4)	-0.0090 (3)	0.0333 (5)
Cl2	0.0561 (4)	0.1063 (7)	0.0842 (5)	-0.0205 (4)	0.0046 (4)	-0.0486 (5)
O1	0.0296 (6)	0.0467 (8)	0.0291 (6)	0.0006 (8)	0.0062 (5)	-0.0002 (7)
O2	0.0332 (7)	0.0632 (10)	0.0413 (7)	0.0014 (9)	0.0126 (6)	0.0000 (9)
O3	0.0313 (6)	0.0623 (10)	0.0434 (8)	0.0011 (9)	0.0038 (5)	0.0036 (9)
O4	0.0511 (8)	0.0562 (9)	0.0298 (7)	0.0021 (10)	0.0011 (6)	0.0012 (8)
O5	0.0412 (8)	0.0737 (13)	0.0441 (8)	0.0008 (9)	0.0120 (6)	-0.0175 (9)

Geometric parameters (Å, °)

C1—O2	1.223 (2)	C9—C10	1.496 (2)
C1—O1	1.364 (2)	C10—C11	1.519 (2)
C1—C2	1.437 (3)	C10—H10A	0.9700
C2—C7	1.402 (2)	C10—H10B	0.9700
C2—C3	1.417 (2)	C11—O5	1.415 (3)
C3—O3	1.354 (2)	C11—C12	1.529 (3)
C3—C4	1.371 (3)	C11—H11	0.9800
C4—C5	1.400 (3)	C12—Cl2	1.766 (3)
C4—H4	0.9300	C12—Cl1	1.774 (3)
C5—O4	1.351 (2)	C12—H12	0.9800
C5—C6	1.390 (3)	C13—O4	1.437 (3)
C6—C7	1.391 (3)	C13—H13A	0.9600
C6—H6	0.9300	C13—H13B	0.9600
C7—C8	1.445 (2)	C13—H13C	0.9600
C8—C9	1.323 (3)	O3—H3	0.8200
C8—H8	0.9300	O5—H5	0.8200
C9—O1	1.389 (2)		
O2—C1—O1	116.32 (17)	C9—C10—H10A	108.6
O2—C1—C2	125.56 (17)	C11—C10—H10A	108.6
O1—C1—C2	118.12 (16)	C9—C10—H10B	108.6
C7—C2—C3	119.41 (16)	C11—C10—H10B	108.6
C7—C2—C1	120.64 (16)	H10A—C10—H10B	107.6
C3—C2—C1	119.94 (16)	O5—C11—C10	113.2 (2)
O3—C3—C4	118.72 (17)	O5—C11—C12	107.8 (2)
O3—C3—C2	121.39 (17)	C10—C11—C12	112.93 (15)
C4—C3—C2	119.89 (17)	O5—C11—H11	107.6
C3—C4—C5	119.98 (17)	C10—C11—H11	107.6
C3—C4—H4	120.0	C12—C11—H11	107.6
C5—C4—H4	120.0	C11—C12—Cl2	110.3 (2)
O4—C5—C6	124.15 (19)	C11—C12—Cl1	111.17 (19)
O4—C5—C4	114.65 (17)	Cl2—C12—Cl1	110.42 (12)
C6—C5—C4	121.19 (17)	C11—C12—H12	108.3
C5—C6—C7	118.97 (18)	Cl2—C12—H12	108.3
C5—C6—H6	120.5	Cl1—C12—H12	108.3

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C7—C6—H6	120.5	O4—C13—H13A	109.5
C6—C7—C2	120.54 (17)	O4—C13—H13B	109.5
C6—C7—C8	122.30 (17)	H13A—C13—H13B	109.5
C2—C7—C8	117.15 (16)	O4—C13—H13C	109.5
C9—C8—C7	121.02 (17)	H13A—C13—H13C	109.5
C9—C8—H8	119.5	H13B—C13—H13C	109.5
C7—C8—H8	119.5	C1—O1—C9	121.57 (14)
C8—C9—O1	121.48 (16)	C3—O3—H3	109.5
C8—C9—C10	129.93 (17)	C5—O4—C13	118.50 (15)
O1—C9—C10	108.59 (15)	C11—O5—H5	109.5
C9—C10—C11	114.68 (15)		
O2—C1—C2—C7	-179.0 (3)	C1—C2—C7—C8	-0.9 (4)
O1—C1—C2—C7	0.4 (4)	C6—C7—C8—C9	-179.7 (3)
O2—C1—C2—C3	1.1 (4)	C2—C7—C8—C9	0.5 (4)
O1—C1—C2—C3	-179.5 (2)	C7—C8—C9—O1	0.4 (4)
C7—C2—C3—O3	-179.2 (2)	C7—C8—C9—C10	-179.9 (3)
C1—C2—C3—O3	0.7 (4)	C8—C9—C10—C11	2.8 (5)
C7—C2—C3—C4	1.4 (4)	O1—C9—C10—C11	-177.6 (2)
C1—C2—C3—C4	-178.7 (2)	C9—C10—C11—O5	61.4 (3)
O3—C3—C4—C5	179.4 (2)	C9—C10—C11—C12	-175.8 (3)
C2—C3—C4—C5	-1.2 (4)	O5—C11—C12—C12	-168.62 (15)
C3—C4—C5—O4	-179.1 (3)	C10—C11—C12—C12	65.6 (3)
C3—C4—C5—C6	0.4 (4)	O5—C11—C12—C11	68.5 (2)
O4—C5—C6—C7	179.6 (2)	C10—C11—C12—C11	-57.3 (3)
C4—C5—C6—C7	0.1 (4)	O2—C1—O1—C9	-180.0 (2)
C5—C6—C7—C2	0.1 (4)	C2—C1—O1—C9	0.6 (4)
C5—C6—C7—C8	-179.7 (3)	C8—C9—O1—C1	-1.0 (4)
C3—C2—C7—C6	-0.8 (4)	C10—C9—O1—C1	179.3 (2)
C1—C2—C7—C6	179.3 (3)	C6—C5—O4—C13	-1.2 (4)
C3—C2—C7—C8	179.0 (2)	C4—C5—O4—C13	178.3 (3)

Hydrogen-bond geometry (\AA , $^\circ$)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
O5—H5 \cdots O3 ⁱ	0.82	2.18	2.913 (3)	149
O3—H3 \cdots O2	0.82	1.91	2.624 (2)	145

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

Fig. 1

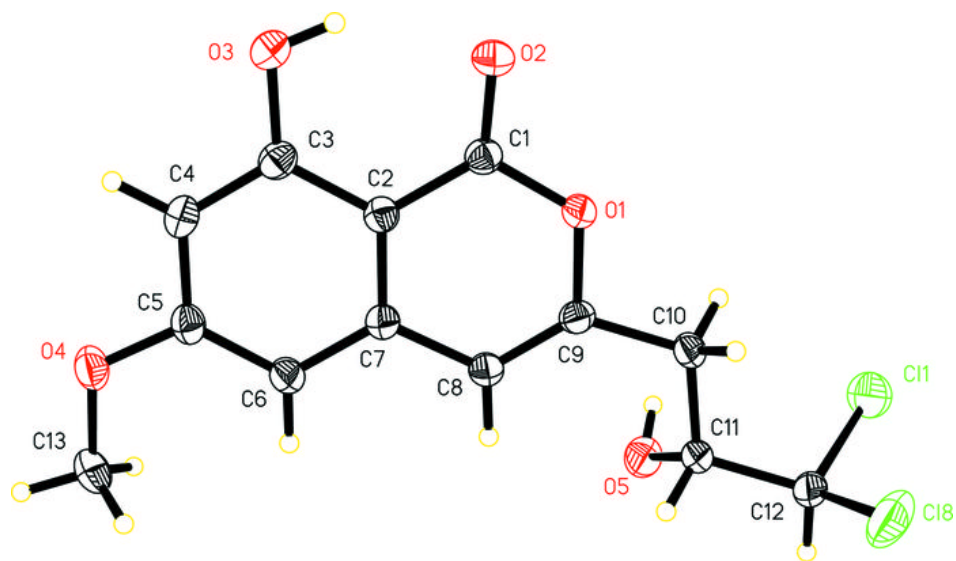


Fig. 2

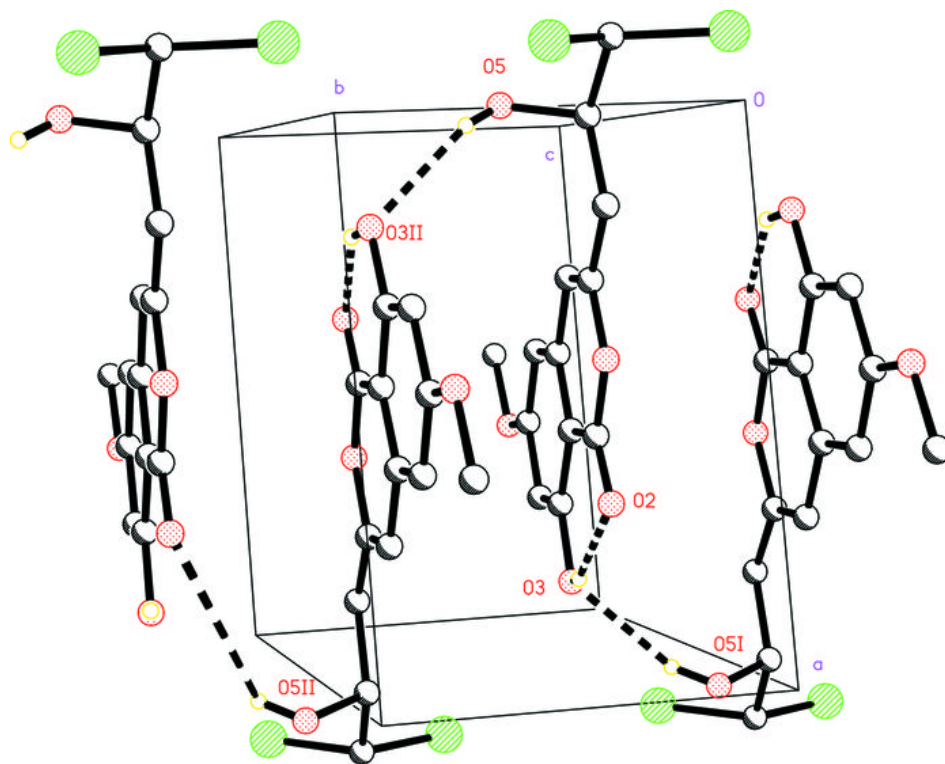


Fig. 3

