research communications

Crystal structure of anabolic steroid metabolite 4-chloroandrost-4-ene-3,17-dione

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The title compound, NorClAD, $C_{18}H_{23}ClO_2$, a metabolite of an anabolic steroid norchlorotestosterone acetate (NClTA), was successfully synthesized. Its molecular structure was characterized by ^1H NMR and ^{13}C NMR spectroscopy and single-crystal X-ray diffraction. The positions of the chlorine substituent, carbonyl groups and the double bond, as well as the absolute configuration of the molecule, were established. A Hirshfeld surface analysis was performed.

1. Chemical context

Anabolic steroids have been reported to be used as growth-accelerating agents (Schanzer, 1996). Norchlorotestosterone acetate (NClTA), one of the synthetic anabolic steroids, is applied by athletes as a testosterone mimetic for an improvement of their performance. The use of testosterone derivatives has therefore been banned by the World Anti-Doping Agency (WADA) (Wood & Stanton, 2012). The metabolism of anabolic steroids is divided into two phases. In phase I, the functional group of anabolic steroids is converted into a more polar functional group. In phase II, the metabolite of anabolic steroids is transformed to glucuronic acid or a sulfate derivative that may easily be eliminated from the human body. Knowledge of its metabolic pathway is therefore necessary to prove the illegal administration of NClTA.

The metabolism of NClTA has been investigated successfully in invertebrates (*Neomysis integer*) and vertebrates (bovine) through oral and subcutaneous administration (Leyssens *et al.*, 1994; Hendriks *et al.*, 1994; Bizec *et al.*, 1998). Mass spectrometry results indicate that one of the most abundant metabolites, found in both invertebrates and vertebrates (after subcutaneous injection), is 4-chloroandrost-4-ene-3,17-dione (NorClAD), the oxidized form of NClTA (see Fig. 1). NorClAD was synthesized through hydrolysis of NClTA followed by an oxidation (Hoof *et al.*, 2004). However,
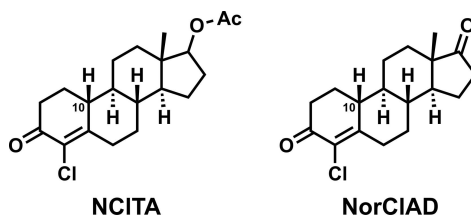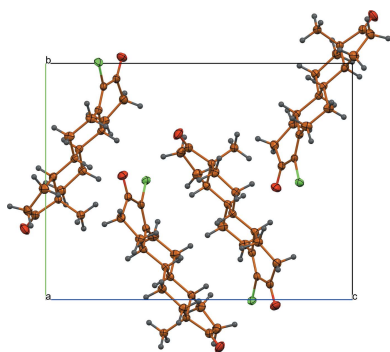

Figure 1
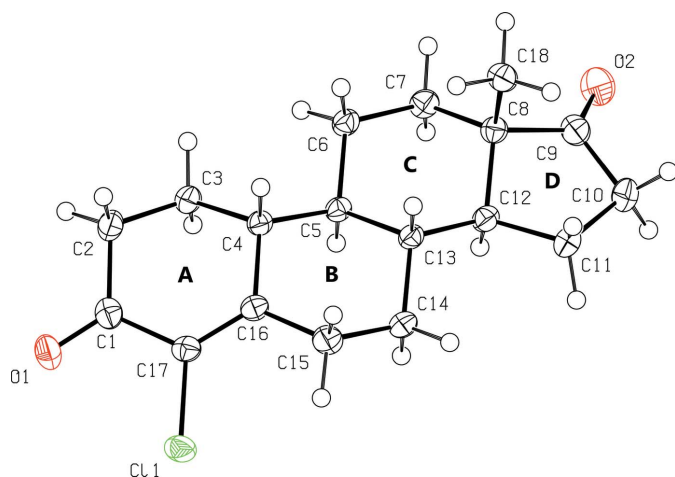The structures of NClTA and NorClAD.

Figure 2
The molecular structure of the title compound, NorClAD. Displacement ellipsoids are drawn at the 50% probability level.

elucidation of its crystal and molecular structures and its absolute stereochemistry were required. In this work, NorClAD was successfully synthesized in two steps according to the given scheme (Ringold *et al.*, 1956), and its X-ray structure and absolute stereochemistry were determined.
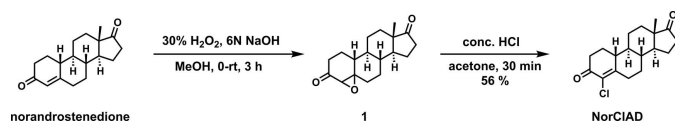
2. Structural commentary

The molecular structure of the title compound is represented in Fig. 2. The compound consists of three six-membered rings *A*(C1–C4/C16/C17), *B*(C4/C5/C13–C16), *C*(C5–C8/C12/C13)
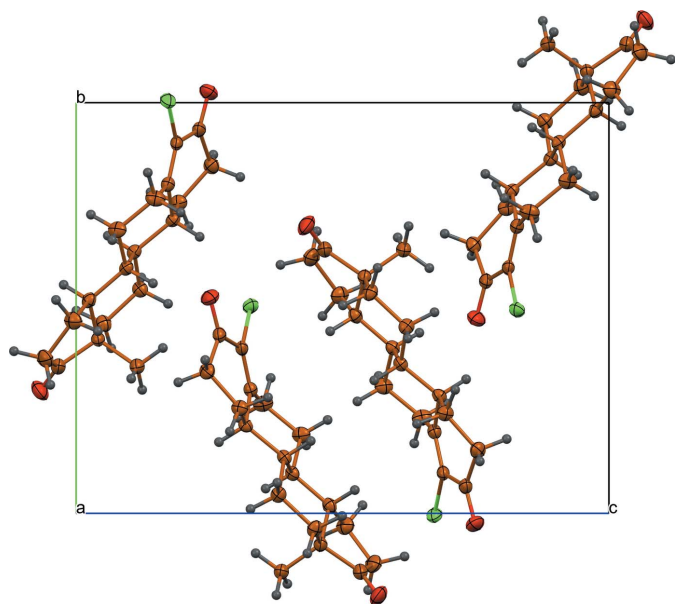
Table 1
Hydrogen-bond geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
C2—H2*A*$\cdots$O2[i]	0.99	2.60	3.563 (2)	165
C10—H10*A*$\cdots$O2[ii]	0.99	2.57	3.398 (3)	141
C18—H18*B*$\cdots$O2[ii]	0.98	2.56	3.507 (3)	163
C10—H10*B*$\cdots$O1[iii]	0.99	2.48	3.443 (3)	164
C4—H4$\cdots$Cl1[iv]	1.00	2.88	3.8202 (18)	158

Symmetry codes: (i) $-x + \frac{1}{2}, -y + 1, z + \frac{1}{2}$; (ii) $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$; (iii) $x + \frac{1}{2}, -y + \frac{1}{2}, -z + 1$; (iv) $-x + 1, y + \frac{1}{2}, -z + \frac{3}{2}$.

and one five-membered ring *D* (C8–C12). Cyclohexenone ring *A* adopts a half-chair conformation while cyclohexane rings *B* and *C* adopt chair conformations. Cyclopentanone ring *D* adopts an envelope conformation with C12 as the flap. It is evident from the bond dimensions that the chlorine atom lies at C17, C1 and C9 are involved in carbonyl groups, and that the C16—C17 bond has double-bond character. The title compound adopts an all-*trans* ring junction and the absolute stereochemistry of atoms C4(*R*), C5(*S*) C8(*S*) C12(*S*) and C13(*R*) were properly determined using Cu *K*α radiation and confirmed by the Flack parameter of 0.029 (4) (Parsons *et al.*, 2013).

3. Supramolecular features and Hirshfeld surface analysis

A view of the unit-cell content of the title compound is presented in Fig. 3. There are several C—H$\cdots$O and C—H$\cdots$Cl contacts that can be considered as weak hydrogen bonds (see Table 1). In order to better understand the importance of these contacts, a Hirshfeld surface (Hirshfeld, 1977) was performed and the two-dimensional fingerprint plots were generated with *Crystal Explorer 21.0* (Spackman *et al.*, 2021). The Hirshfeld surface mapped over d_{norm} (see Fig. 4) is scaled between −0.1622 to 1.3540 a.u. The bright-red spots indicate the positions of the respective H-atom donors and H-atom acceptors (Venkatesan *et al.*, 2016). Fig. 5 shows how these red spots correspond to short intermolecular contacts. The overall two-dimensional fingerprint plot and those deli-
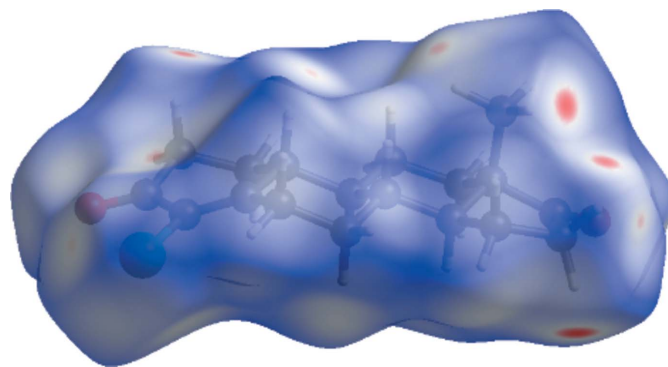

Figure 3
The packing of the title compound viewed down the *a* axis.

Figure 4
The three-dimensional Hirshfeld surface of the title compound plotted over d_{norm}.

Table 2
Percentage contributions of the most relevant atom–atom contacts to the Hirshfeld surface in the title structure.

Atom-atom interaction	Percentage
H···H	56.2
H···O/O···H	22.8
H···Cl/Cl···H	13.7
H···C/C···H	5.6
Cl···O/O···Cl	1.6
Cl···C/C···Cl	0.2

neated into H···H, H···Cl/Cl···H, H···O/O···H, H···C/C···H, Cl···C/C···Cl, and Cl···O/O···Cl contacts (McKinnon *et al.*, 2007) are presented in Fig. 6*a–g*, respectively, together with their relative contributions to the Hirshfeld surface. The most abundant interaction is H···H, contributing 56.2% to the overall crystal packing, which is reflected in Fig. 6*b* as widely scattered points of high density owing to the large hydrogen content of the molecule. The blue region fingerprint plot of H···O/O···H interaction represents a symmetric distribution of points (22.8% contribution, Fig. 6*d*). While, the contribution of H···Cl/Cl···H contacts (Fig. 6*c*) is 13.7%. Percentages of other types of contacts are given in Table 2. The large number of H···H interactions indicate that van der Waals interactions play a major role in the crystal packing (Hathwar *et al.*, 2015).

4. Database survey

A search of Cambridge Structure Database (CSD, version 5.42, update of May 2021; Groom *et al.*, 2016) found four structures that are closely related to the title compound and which play significant roles in the biological mechanisms. For
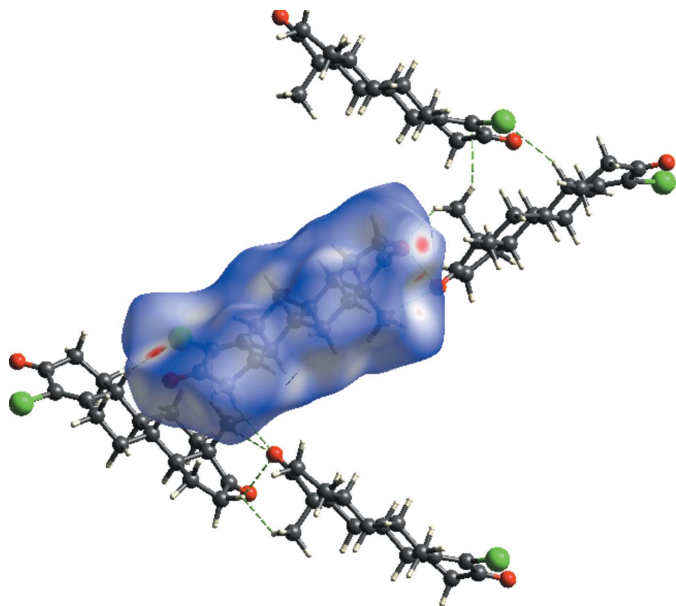
Figure 5
View of the three-dimensional Hirshfeld surface of the title compound together with the hydrogen-bonding (dashed lines) between adjacent molecules.
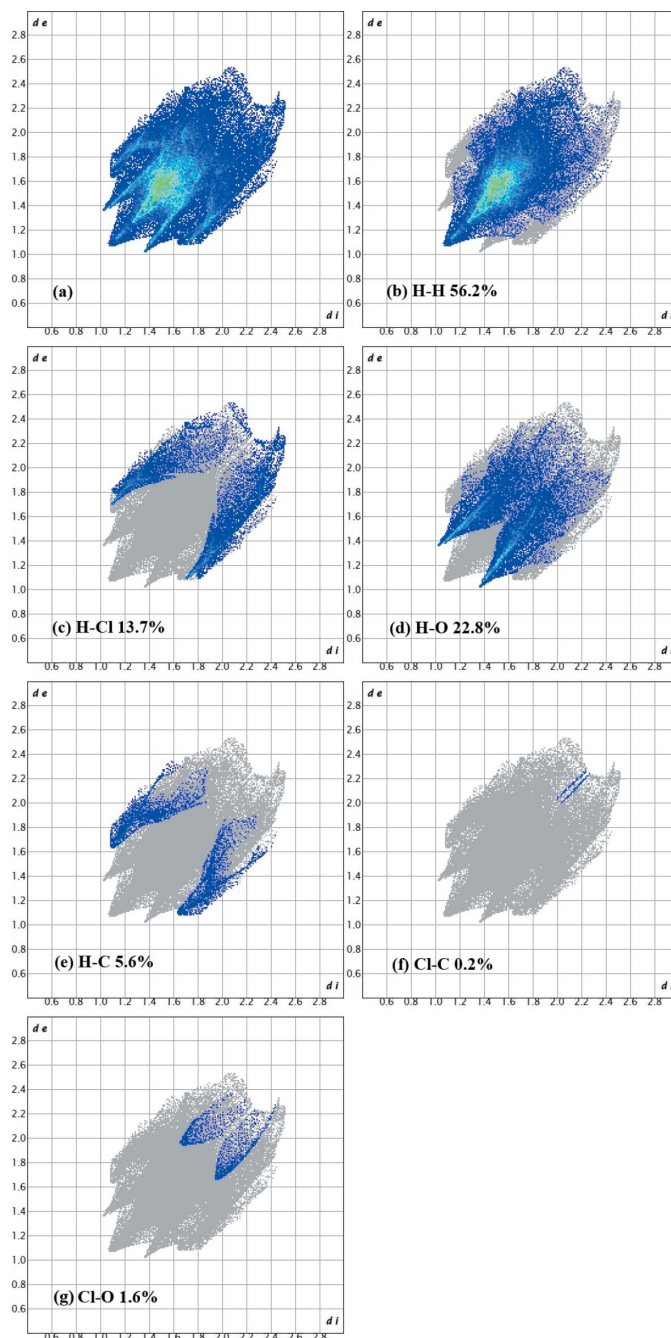
Figure 6
The two-dimensional fingerprint plots for the title compound, showing all interactions (*a*), and those delineated into H···H (*b*), H···Cl/Cl···H (*c*), H···O/O···H (*d*), H···C/C···H (*e*), Cl···C/C···Cl (*f*) and Cl···O/O···Cl (*g*) interactions.

the disordered structure of cortisol (11*b*,17*a*,21-trihydroxy-4-pregnene-3,20-dione), see CORTSL (Castellano, 1980). For dexamethasone at 119 K, see DEXMET11 (Raynor *et al.*, 2007). For 17*β*-hydroxy-17*a*-methylandrostano[3,2-*c*]pyrazole, stanozolol, see AVENUL (Karpinska *et al.*, 2011). For the crystal structure, Hirshfeld surface analysis, interaction energies, and DFT studies of cholesteryl heptanoate, see ZZZBIP01 (Akduran *et al.*, 2021).

5. Synthesis and crystallization

The target compound was synthesized in two steps as shown in the scheme.

To a solution of norandrostenedione (5.00 g, 18.36 mmol) in methanol (100 mL) at 273 K were slowly added 30% H_2O_2 (4.5 mL, 57.55 mmol) and 6N NaOH (1.5 mL, 9.0 mmol). The mixture was then stirred at 273 K for 1 h. After that, the reaction solution was warmed up to room temperature and stirring continued for 2 h. After completion, water was added to the reaction mixture and the solvent was evaporated. The aqueous residue was extracted three times with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and then concentrated to dryness *in vacuo* to provide epoxide **1**, which was used in the next step without further purification.

A solution of epoxide **1** (4.13 g) in acetone (100 mL) was treated with conc. HCl (1.5 mL) and the mixture was stirred at room temperature for 30 min. After that, water was added to the reaction mixture and it was extracted three times with dichloromethane. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. The solid product was recrystallized from MeOH:CH_2Cl_2 (3:1) at room temperature to provide 3.19 g of 4-chloroandrost-4-ene-3,17-dione (NorClAD) (56% yield).

Compound characterization: ^{1}H NMR (400 MHz, chloroform-*d*) δ 3.42 (*ddd*, *J* = 15.0, 4.1, 2.4 Hz, 1H), 2.66 (*dt*, *J* = 16.2, 4.4 Hz, 1H), 2.55–2.36 (*m*, 2H), 2.36–2.25 (*m*, 2H), 2.19–2.08 (*m*, 2H), 2.07–1.92 (*m*, 3H), 1.88 (*dt*, *J* = 9.3, 2.7 Hz, 1H), 1.65–1.49 (*m*, 3H), 1.39–1.30 (*m*, 3H), 1.20 (*tdd*, *J* = 13.3, 11.7, 4.0 Hz, 1H), 1.05 0.97 (*m*, 1H), 0.95 (*s*, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 220.3, 191.1, 159.6, 127.9, 50.1, 49.4, 47.7, 44.8, 39.7, 36.6, 35.8, 31.9, 31.3, 29.3, 25.7, 25.5, 21.7, 13.9.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. All H atoms were positioned geometrically, with C—H = 0.98, 0.99 and 1.00 Å for methyl, methylene and methine protons, respectively, and refined as riding with $U_{iso}(H) = 1.2$ or $1.5U_{eq}(C)$. In addition, the absolute configuration of this compound was confirmed by the Flack parameter of 0.029 (4) (Parsons *et al.*, 2013).

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{18}H_{23}ClO_2$
M_r	306.81
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
a, b, c (Å)	7.4379 (4), 12.7142 (6), 16.4790 (8)
V (Å^3)	1558.37 (13)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	2.18
Crystal size (mm)	$0.05 \times 0.01 \times 0.01$
Data collection	
Diffractometer	Bruker D8 VENTURE
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.678, 0.753
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	18469, 2907, 2787
R_{int}	0.031
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.024, 0.065, 1.04
No. of reflections	2907
No. of parameters	191
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.17, −0.18
Absolute structure	Flack x determined using 1150 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.029 (4)

Computer programs: *APEX3* and *SAINT* (Bruker, 2016), *SHELXT* (Sheldrick, 2015), *SHELXL* (Sheldrick, 2008) and *OLEX2* (Dolomanov *et al.*, 2009).

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Crystal structure of anabolic steroid metabolite 4-chloroandrost-4-ene-3,17-dione

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Computing details

Data collection: *APEX3* (Bruker, 2016); cell refinement: *SAINT* (Bruker, 2016); data reduction: *SAINT* (Bruker, 2016); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015); program(s) used to refine structure: *SHELXL* (Sheldrick, 2008); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

4-Chloroandrost-4-ene-3,17-dione

Crystal data

$C_{18}H_{23}ClO_2$	$D_x = 1.308$ Mg m^{-3}
$M_r = 306.81$	Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Orthorhombic, $P2_12_12_1$	Cell parameters from 9974 reflections
$a = 7.4379$ (4) Å	$\theta = 4.4$–70.2°
$b = 12.7142$ (6) Å	$\mu = 2.18$ mm^{-1}
$c = 16.4790$ (8) Å	$T = 100$ K
$V = 1558.37$ (13) Å^3	Block, clear light colourless
$Z = 4$	$0.05 \times 0.01 \times 0.01$ mm
$F(000) = 656$	

Data collection

BRUKER D8 VENTURE diffractometer	18469 measured reflections
Radiation source: X-ray tube, Micro focus tube	2907 independent reflections
Graphite monochromator	2787 reflections with $I > 2\sigma(I)$
Detector resolution: 10.4167 pixels mm^{-1}	$R_{int} = 0.031$
ω and φ scans	$\theta_{max} = 70.1°$, $\theta_{min} = 4.4°$
Absorption correction: multi-scan (*SADABS*; Krause *et al.*, 2015)	$h = -9 \rightarrow 9$
	$k = -15 \rightarrow 15$
$T_{min} = 0.678$, $T_{max} = 0.753$	$l = -20 \rightarrow 19$

Refinement

Refinement on F^2	Primary atom site location: dual
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.024$	H-atom parameters constrained
$wR(F^2) = 0.065$	$w = 1/[\sigma^2(F_o^2) + (0.0383P)^2 + 0.2052P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.04$	
2907 reflections	$(\Delta/\sigma)_{max} = 0.001$
191 parameters	$\Delta\rho_{max} = 0.17$ e Å^{-3}
0 restraints	

$\Delta\rho_{min} = -0.18$ e Å^{-3}

Absolute structure: Flack x determined using 1150 quotients $[(I^+)-(I)]/[(I^+)+(I)]$ (Parsons *et al.*, 2013)

Absolute structure parameter: 0.029 (4)

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*	U_{iso}*/U_{eq}
Cl1	0.53413 (6)	−0.00451 (3)	0.67248 (3)	0.02851 (13)
O1	0.1878 (2)	−0.02569 (11)	0.74872 (9)	0.0345 (3)
O2	0.3004 (2)	0.70098 (13)	0.43229 (10)	0.0401 (4)
C1	0.2157 (3)	0.06557 (15)	0.73085 (11)	0.0242 (4)
C5	0.2976 (2)	0.36358 (14)	0.60909 (11)	0.0191 (3)
H5	0.259997	0.323792	0.559582	0.023*
C6	0.1640 (2)	0.45474 (14)	0.62010 (12)	0.0228 (4)
H6A	0.188454	0.489661	0.672646	0.027*
H6B	0.040622	0.425670	0.622443	0.027*
C17	0.3824 (2)	0.09845 (14)	0.68886 (11)	0.0214 (4)
C3	0.0974 (2)	0.24336 (14)	0.69275 (11)	0.0234 (4)
H3A	0.017607	0.300838	0.711313	0.028*
H3B	0.051866	0.217948	0.639818	0.028*
C7	0.1726 (2)	0.53763 (15)	0.55206 (12)	0.0243 (4)
H7A	0.128879	0.506525	0.500636	0.029*
H7B	0.093792	0.597774	0.565909	0.029*
C4	0.2882 (2)	0.28617 (13)	0.68182 (11)	0.0193 (3)
H4	0.319484	0.326567	0.731938	0.023*
C16	0.4260 (2)	0.19893 (13)	0.67251 (11)	0.0206 (3)
C13	0.4912 (2)	0.40302 (14)	0.59430 (11)	0.0197 (4)
H13	0.534533	0.439779	0.644250	0.024*
C9	0.4042 (3)	0.64247 (15)	0.46663 (12)	0.0278 (4)
C15	0.6121 (3)	0.23322 (15)	0.64898 (13)	0.0277 (4)
H15A	0.684117	0.170390	0.634705	0.033*
H15B	0.670068	0.267385	0.696210	0.033*
C2	0.0914 (3)	0.15384 (15)	0.75394 (12)	0.0263 (4)
H2A	0.125680	0.180934	0.808097	0.032*
H2B	−0.033061	0.126618	0.757601	0.032*
C8	0.3650 (2)	0.57594 (14)	0.54125 (11)	0.0215 (4)
C18	0.4268 (3)	0.64214 (15)	0.61467 (12)	0.0255 (4)
H18A	0.340763	0.699209	0.624110	0.038*
H18B	0.545813	0.671945	0.603545	0.038*
H18C	0.433172	0.597296	0.662951	0.038*
C14	0.6134 (2)	0.30946 (15)	0.57747 (12)	0.0262 (4)
H14A	0.737587	0.334569	0.567856	0.031*

H14B	0.572060	0.272622	0.527940	0.031*
C12	0.4880 (2)	0.48125 (14)	0.52440 (11)	0.0221 (4)
H12	0.435207	0.443399	0.476847	0.027*
C10	0.5982 (3)	0.62344 (17)	0.44187 (13)	0.0336 (5)
H10A	0.671889	0.687004	0.451795	0.040*
H10B	0.605681	0.605168	0.383565	0.040*
C11	0.6645 (3)	0.53098 (16)	0.49478 (13)	0.0302 (4)
H11A	0.735925	0.480383	0.462438	0.036*
H11B	0.738045	0.556310	0.540879	0.036*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0383 (2)	0.0235 (2)	0.0237 (2)	0.00946 (18)	0.00264 (17)	0.00324 (19)
O1	0.0444 (8)	0.0246 (7)	0.0345 (8)	−0.0055 (6)	0.0073 (7)	0.0060 (6)
O2	0.0503 (9)	0.0395 (8)	0.0305 (8)	0.0078 (8)	0.0007 (7)	0.0141 (7)
C1	0.0307 (9)	0.0246 (9)	0.0173 (9)	−0.0043 (8)	−0.0020 (7)	−0.0001 (7)
C5	0.0164 (8)	0.0212 (8)	0.0198 (8)	−0.0009 (7)	0.0004 (7)	−0.0029 (7)
C6	0.0190 (8)	0.0252 (9)	0.0241 (10)	0.0023 (7)	0.0021 (7)	0.0019 (7)
C17	0.0263 (9)	0.0229 (8)	0.0151 (8)	0.0034 (7)	−0.0013 (7)	−0.0013 (7)
C3	0.0189 (8)	0.0237 (9)	0.0275 (10)	−0.0015 (7)	0.0027 (7)	−0.0004 (7)
C7	0.0212 (8)	0.0279 (9)	0.0237 (9)	0.0042 (7)	−0.0011 (7)	0.0033 (7)
C4	0.0176 (7)	0.0199 (8)	0.0203 (8)	−0.0011 (6)	0.0008 (7)	−0.0025 (7)
C16	0.0206 (8)	0.0229 (8)	0.0183 (8)	0.0011 (6)	−0.0004 (7)	−0.0018 (7)
C13	0.0171 (8)	0.0208 (8)	0.0212 (9)	−0.0008 (7)	0.0026 (6)	−0.0022 (7)
C9	0.0387 (10)	0.0246 (9)	0.0202 (9)	−0.0019 (8)	0.0012 (8)	−0.0007 (8)
C15	0.0186 (8)	0.0259 (9)	0.0386 (11)	0.0029 (7)	0.0001 (8)	0.0025 (8)
C2	0.0260 (9)	0.0277 (9)	0.0253 (9)	−0.0046 (7)	0.0060 (7)	0.0006 (8)
C8	0.0241 (9)	0.0224 (8)	0.0179 (8)	0.0016 (7)	0.0004 (7)	0.0008 (7)
C18	0.0320 (10)	0.0232 (9)	0.0211 (9)	0.0018 (7)	−0.0011 (7)	0.0001 (7)
C14	0.0192 (8)	0.0261 (9)	0.0332 (10)	0.0025 (7)	0.0069 (8)	−0.0001 (8)
C12	0.0214 (8)	0.0242 (9)	0.0207 (9)	−0.0007 (7)	0.0031 (6)	−0.0026 (7)
C10	0.0411 (11)	0.0313 (11)	0.0285 (10)	−0.0027 (9)	0.0117 (9)	0.0048 (8)
C11	0.0281 (9)	0.0302 (10)	0.0323 (11)	−0.0007 (8)	0.0109 (8)	0.0021 (8)

Geometric parameters (Å, º)

Cl1—C17	1.7493 (17)	C13—C14	1.523 (2)
O1—C1	1.215 (2)	C13—C12	1.522 (3)
O2—C9	1.212 (3)	C9—C8	1.521 (3)
C1—C17	1.480 (3)	C9—C10	1.519 (3)
C1—C2	1.503 (3)	C15—H15A	0.9900
C5—H5	1.0000	C15—H15B	0.9900
C5—C6	1.538 (2)	C15—C14	1.526 (3)
C5—C4	1.552 (2)	C2—H2A	0.9900
C5—C13	1.544 (2)	C2—H2B	0.9900
C6—H6A	0.9900	C8—C18	1.544 (3)
C6—H6B	0.9900	C8—C12	1.538 (2)

C6—C7	1.540 (3)	C18—H18A	0.9800
C17—C16	1.345 (2)	C18—H18B	0.9800
C3—H3A	0.9900	C18—H18C	0.9800
C3—H3B	0.9900	C14—H14A	0.9900
C3—C4	1.530 (2)	C14—H14B	0.9900
C3—C2	1.521 (3)	C12—H12	1.0000
C7—H7A	0.9900	C12—C11	1.537 (2)
C7—H7B	0.9900	C10—H10A	0.9900
C7—C8	1.522 (3)	C10—H10B	0.9900
C4—H4	1.0000	C10—C11	1.544 (3)
C4—C16	1.518 (2)	C11—H11A	0.9900
C16—C15	1.502 (3)	C11—H11B	0.9900
C13—H13	1.0000		
O1—C1—C17	121.74 (18)	C16—C15—H15A	109.0
O1—C1—C2	123.14 (18)	C16—C15—H15B	109.0
C17—C1—C2	115.01 (15)	C16—C15—C14	112.91 (15)
C6—C5—H5	107.2	H15A—C15—H15B	107.8
C6—C5—C4	110.95 (14)	C14—C15—H15A	109.0
C6—C5—C13	112.12 (14)	C14—C15—H15B	109.0
C4—C5—H5	107.2	C1—C2—C3	111.88 (15)
C13—C5—H5	107.2	C1—C2—H2A	109.2
C13—C5—C4	111.73 (14)	C1—C2—H2B	109.2
C5—C6—H6A	108.8	C3—C2—H2A	109.2
C5—C6—H6B	108.8	C3—C2—H2B	109.2
C5—C6—C7	113.78 (15)	H2A—C2—H2B	107.9
H6A—C6—H6B	107.7	C7—C8—C18	111.28 (15)
C7—C6—H6A	108.8	C7—C8—C12	109.28 (15)
C7—C6—H6B	108.8	C9—C8—C7	116.95 (16)
C1—C17—Cl1	113.65 (13)	C9—C8—C18	105.85 (15)
C16—C17—Cl1	121.62 (14)	C9—C8—C12	100.08 (14)
C16—C17—C1	124.31 (16)	C12—C8—C18	113.01 (15)
H3A—C3—H3B	107.9	C8—C18—H18A	109.5
C4—C3—H3A	109.3	C8—C18—H18B	109.5
C4—C3—H3B	109.3	C8—C18—H18C	109.5
C2—C3—H3A	109.3	H18A—C18—H18B	109.5
C2—C3—H3B	109.3	H18A—C18—H18C	109.5
C2—C3—C4	111.81 (15)	H18B—C18—H18C	109.5
C6—C7—H7A	109.6	C13—C14—C15	110.60 (15)
C6—C7—H7B	109.6	C13—C14—H14A	109.5
H7A—C7—H7B	108.2	C13—C14—H14B	109.5
C8—C7—C6	110.07 (15)	C15—C14—H14A	109.5
C8—C7—H7A	109.6	C15—C14—H14B	109.5
C8—C7—H7B	109.6	H14A—C14—H14B	108.1
C5—C4—H4	107.5	C13—C12—C8	112.60 (14)
C3—C4—C5	111.00 (14)	C13—C12—H12	106.5
C3—C4—H4	107.5	C13—C12—C11	119.74 (15)
C16—C4—C5	110.76 (14)	C8—C12—H12	106.5

C16—C4—C3	112.21 (14)	C11—C12—C8	104.11 (14)
C16—C4—H4	107.5	C11—C12—H12	106.5
C17—C16—C4	120.72 (15)	C9—C10—H10A	110.6
C17—C16—C15	123.32 (16)	C9—C10—H10B	110.6
C15—C16—C4	115.87 (14)	C9—C10—C11	105.83 (16)
C5—C13—H13	108.8	H10A—C10—H10B	108.7
C14—C13—C5	109.38 (14)	C11—C10—H10A	110.6
C14—C13—H13	108.8	C11—C10—H10B	110.6
C12—C13—C5	108.50 (14)	C12—C11—C10	102.70 (16)
C12—C13—H13	108.8	C12—C11—H11A	111.2
C12—C13—C14	112.45 (15)	C12—C11—H11B	111.2
O2—C9—C8	126.60 (18)	C10—C11—H11A	111.2
O2—C9—C10	125.27 (19)	C10—C11—H11B	111.2
C10—C9—C8	108.13 (16)	H11A—C11—H11B	109.1

Cl1—C17—C16—C4	175.86 (13)	C7—C8—C12—C11	166.87 (15)
Cl1—C17—C16—C15	−7.7 (3)	C4—C5—C6—C7	177.20 (14)
O1—C1—C17—Cl1	−2.6 (2)	C4—C5—C13—C14	59.07 (19)
O1—C1—C17—C16	−175.31 (19)	C4—C5—C13—C12	−177.92 (14)
O1—C1—C2—C3	−150.53 (19)	C4—C3—C2—C1	−56.7 (2)
O2—C9—C8—C7	30.3 (3)	C4—C16—C15—C14	−48.3 (2)
O2—C9—C8—C18	−94.3 (2)	C16—C15—C14—C13	53.9 (2)
O2—C9—C8—C12	148.1 (2)	C13—C5—C6—C7	51.5 (2)
O2—C9—C10—C11	−171.2 (2)	C13—C5—C4—C3	−176.96 (14)
C1—C17—C16—C4	−12.0 (3)	C13—C5—C4—C16	−51.60 (19)
C1—C17—C16—C15	164.43 (18)	C13—C12—C11—C10	−165.63 (16)
C5—C6—C7—C8	−52.9 (2)	C9—C8—C12—C13	174.71 (15)
C5—C4—C16—C17	−136.86 (17)	C9—C8—C12—C11	43.51 (18)
C5—C4—C16—C15	46.5 (2)	C9—C10—C11—C12	18.2 (2)
C5—C13—C14—C15	−59.3 (2)	C2—C1—C17—Cl1	173.68 (13)
C5—C13—C12—C8	58.98 (19)	C2—C1—C17—C16	1.0 (3)
C5—C13—C12—C11	−178.21 (16)	C2—C3—C4—C5	170.25 (14)
C6—C5—C4—C3	57.13 (18)	C2—C3—C4—C16	45.7 (2)
C6—C5—C4—C16	−177.52 (14)	C8—C9—C10—C11	8.9 (2)
C6—C5—C13—C14	−175.66 (15)	C8—C12—C11—C10	−38.77 (19)
C6—C5—C13—C12	−52.7 (2)	C18—C8—C12—C13	62.56 (19)
C6—C7—C8—C9	168.92 (15)	C18—C8—C12—C11	−68.63 (19)
C6—C7—C8—C18	−69.28 (19)	C14—C13—C12—C8	−179.90 (15)
C6—C7—C8—C12	56.2 (2)	C14—C13—C12—C11	−57.1 (2)
C17—C1—C2—C3	33.2 (2)	C12—C13—C14—C15	−179.92 (15)
C17—C16—C15—C14	135.14 (19)	C10—C9—C8—C7	−149.86 (17)
C3—C4—C16—C17	−12.2 (2)	C10—C9—C8—C18	85.56 (18)
C3—C4—C16—C15	171.12 (16)	C10—C9—C8—C12	−32.04 (19)
C7—C8—C12—C13	−61.93 (19)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2*A*···O2[i]	0.99	2.60	3.563 (2)	165
C10—H10*A*···O2[ii]	0.99	2.57	3.398 (3)	141
C18—H18*B*···O2[ii]	0.98	2.56	3.507 (3)	163
C10—H10*B*···O1[iii]	0.99	2.48	3.443 (3)	164
C4—H4···Cl1[iv]	1.00	2.88	3.8202 (18)	158

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