Acta Cryst E CRYSTALLOGRAPHIC COMMUNICATIONS

ISSN 2056-9890

Crystal structure of the pharmaceutical impurity 2-(4-chlorobenzoyl)pyridine

Karan J. Singh and Joseph M. Tanski*

Department of Chemistry, Vassar College, Poughkeepsie, NY 12604, USA. *Correspondence e-mail: jotanski@vassar.edu

Received 31 August 2026
Accepted 1 September 2026

Edited by W. T. A. Harrison, University of Aberdeen, United Kingdom

Keywords: crystal structure; π-stacking; pharmaceutical impurity; benzophenone derivative.

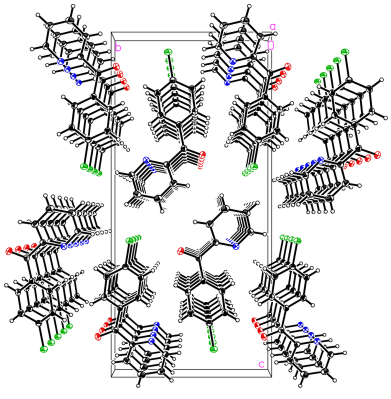
CCDC reference: 2584887

Supporting information: this article has supporting information at journals.iucr.org/e

The title compound, $C_{12}H_8ClNO$, is a pharmaceutical impurity and possible intermediate in the synthesis of carbinoxamine. The aromatic rings of the molecule twist relative to one another resulting in an interplanar angle of 38.1 (1)°. In the extended structure, the molecules are packed into rippled sheets with offset face-to-face stacking of each aromatic ring with the equivalent ring in the neighboring molecule.

1. Chemical context

2-(4-Chlorobenzoyl)pyridine, $C_{12}H_8ClNO$ (**I**), also known as carbinoxamine related compound A, is a known manufacturing impurity of the pharmaceutical ingredient carbinoxamine, 2-[(4-chlorophenyl)-pyridin-2-yl-methoxy]-*N*,*N*-dimethyl-ethanamine ($C_{16}H_{19}ClN_2O$). The compound may be used to synthesize enantiopure alcohols, such as (*S*)-(4-chlorophenyl)(pyridin-2-yl)methanol, as precursors for the synthesis of carbinoxamine in the fungus *Geotrichum candidum* using a mutated acetophenone reductase enzyme that catalyzes the reduction of ketones to alcohols (Tang *et al.*, 2024). This enzyme belongs to the alcohol dehydrogenase (ADH) class, which catalyzes the reversible interconversion between ketones and alcohols. Carbinoxamine maleate, the maleic acid salt of carbinoxamine, is a first-generation H_1-antihistamine used to treat allergy symptoms and may be synthesized *via* a Grignard reaction: *para*-chlorophenylmagnesium bromide, formed by the addition of *para*-bromochlorobenzene to magnesium in anhydrous ether, is treated with 2-pyridinealdehyde and subsequently with sodium and 2-dimethylaminoethyl chloride to produce an approximate 65% yield of the medication (Mansukhbhai & Das, 2021). Carbinoxamine maleate performs by binding to inactive H_1 receptors belonging to G-protein-coupled receptors (GPCRs) found in cells and stabilizing them to remain inactive. This mechanism prevents the binding of the chemical signal histamine to the receptors and inhibits signal transduction pathways leading to allergic reactions (Leurs *et al.*, 2002). As part of our studies in this area, we now describe the crystal structure of (**I**).



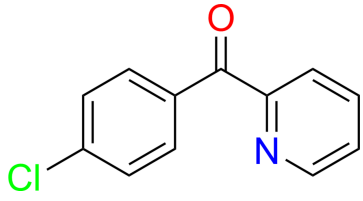


Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2A···Cl1^{i}	0.95	2.96	3.633 (4)	129
C11—H11A···O1^{ii}	0.95	2.46	3.406 (5)	173

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

2. Structural commentary

Compound (**I**) crystallizes in space group $P2_1/c$ with one molecule in the asymmetric unit. The molecular structure of (**I**) (Fig. 1) reveals a 4-chlorobenzoyl group, consisting of a benzene ring bearing a chlorine-atom substituent at the *para* position relative to the carbonyl group, which is attached to the carbon atom *meta* to the nitrogen atom of the pyridine ring. Individual molecules of (**I**) adopt a twisted conformation that minimizes intramolecular repulsion between the benzene and pyridine rings with an interplanar angle of 38.1 (1)° between the C1–C5/N1 and C7–C12 rings. The C5—C6 [1.506 (5) Å] and C6—C7 [1.506 (5) Å] bond lengths are almost identical and the N1—C5—C6—O1 torsion angle is −152.6 (4)°.

3. Supramolecular features

In the extended structure, molecules of (**I**) assemble into rippled (100) sheets *via* weak C—H···O and C—H···Cl interactions (Fig. 2, Table 1). As expected, the C11—H11A···O1 interaction with a donor–acceptor distance of 3.406 (5) Å is shorter than the C2—H2A···Cl1 interaction with a corresponding distance of 3.633 (4) Å. The shortest Cl···Cl contact of 3.894 (6) Å is much longer than the sum of the van der Waals radii for chlorine (3.50 Å; Bondi, 1964). The sheets stack in such a manner that a slipped face-to-face π-stacking geometrical arrangement of the rings is present between equivalent rings within the molecules (Fig. 3). The π-stacking of the chlorobenzoyl rings is characterized by a centroid–centroid distance of 3.8943 (6) Å (the a unit-cell dimension) and a plane-to-centroid separation of 3.402 (3) Å, resulting in a ring shift of 1.895 (6) Å. The very similar π-stacking of the pyridine rings is characterized by the same centroid–centroid separation and a plane-to-centroid separation of 3.419 (3) Å, resulting in a ring shift of 1.865 (6) Å. In the overall packing (Fig. 4) there is also a longer C—H···N interaction (not shown) that interconnects the π-stacked sheets formed by the C—H···O and C—H···Cl interactions, with a C9—H9A···N1 donor–acceptor distance of 3.686 (5) Å.

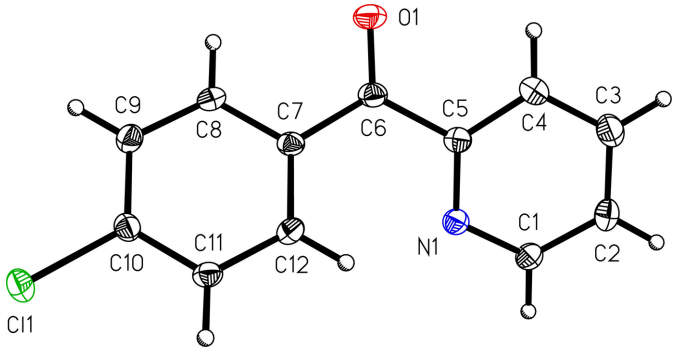


Figure 1
The molecular structure of (**I**) with displacement ellipsoids shown at the 50% probability level.

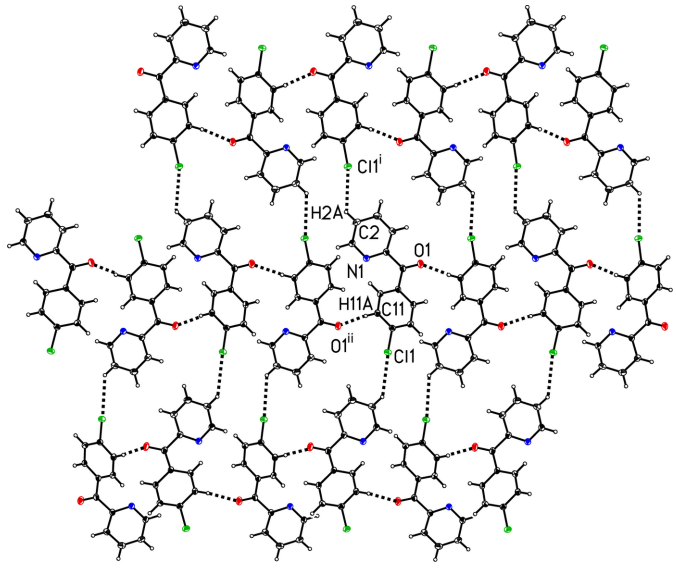


Figure 2
A view of the weak hydrogen-bonded sheets in (**I**). Displacement ellipsoids are shown at the 50% probability level. Symmetry codes: (i) $x+1, -y+\frac{1}{2}, z-1/2$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.

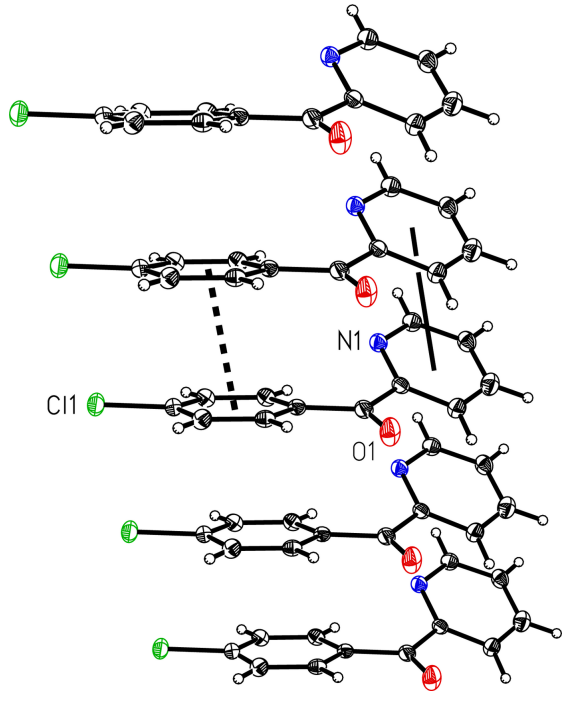


Figure 3
A view of the face-to-face π-stacking geometrical arrangement in (**I**) with a dashed line indicating the chlorobenzoyl interaction and a solid line indicating the pyridine interaction.

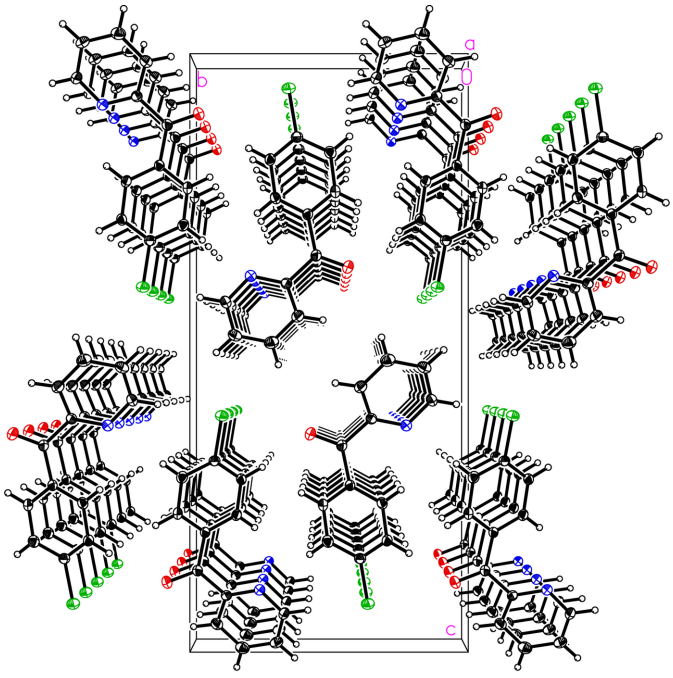


Figure 4
The packing in (**I**) viewed down [100].

4. Database survey

One similar compound to (**I**) was found in the CSD version 6.00, April 2025.; Groom *et al.*, 2016) with the CSD refcode CEYWOS (Syed *et al.*, 1984), which consists of a 4-chlorobenzoyl group attached to a pyridine ring. However, in contrast to (**I**), the 4-chlorobenzoyl group in CEYWOS is attached to the carbon atom *para* to the nitrogen atom of the pyridine ring instead of the *meta* carbon atom. Both CEYWOS (space group $P2_1$) and (**I**) display similar weak intermolecular hydrogen bonding as well as π–π stacking interactions between the benzene and pyridine rings in parallel molecules. However, CEYWOS exhibits a greater twist angle of the benzoyl and pyridine rings relative to one another, resulting in an interplanar angle of 52.41° and a shortest Cl···Cl contact distance of 3.630 Å that is much closer to the sum of the van der Waals radii for chlorine.

5. Synthesis and crystallization

2-(4-Chlorobenzoyl)pyridine (95%) was purchased from Enamine, USA, and recrystallized by slow evaporation over 48 h at room temperature using a 1:1 solvent mixture of ethyl acetate/hexane.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. Hydrogen atoms were included in calculated positions and refined using a riding model with C—H = 0.95 Å and U_{iso}(H) = 1.2U_{eq}(C).

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_8ClNO$
M_r	217.64
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	125
a, b, c (Å)	3.8943 (6), 10.8402 (15), 23.307 (3)
β (°)	90.573 (2)
V (Å^3)	983.9 (2)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.36
Crystal size (mm)	0.30 × 0.17 × 0.04
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.87, 0.99
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	22981, 3018, 2627
R_{int}	0.047
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.715
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.087, 0.234, 1.19
No. of reflections	3018
No. of parameters	136
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.63, −0.92

Computer programs: *SAINT* and *SPEX3* (Bruker, 2013), *SHELXT2018/2* (Sheldrick, 2015*a*), *SHELXL2017/1* (Sheldrick, 2015*b*), *SHELXTL2014* (Sheldrick, 2008), *OLEX2* (Dolomanov *et al.*, 2009) and *Mercury* (Macrae *et al.*, 2020).

Acknowledgements

This work was supported by Vassar College. X-ray facilities were provided by the US National Science Foundation (grant Nos. 0521237 and 0911324 to JT).

Funding information

Funding for this research was provided by: National Science Foundation, Directorate for Mathematical and Physical Sciences (grant No. 0521237 to Joseph M. Tanski; award No. 0911324 to Joseph M. Tanski).

References

Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.
Bruker (2013). *SAINT* and *APEX3*. Bruker AXS Inc., Madison, Wisconsin, USA.
Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.
Krause, L., Herbst-Irmer, R., Sheldrick, G. M. & Stalke, D. (2015). *J. Appl. Cryst.* **48**, 3–10.
Leurs, R., Church, M. K. & Taglialatela, M. (2002). *Clin. Exp. Allergy* **32**, 489–498.
Macrae, C. F., Sovago, I., Cottrell, S. J., Galek, P. T. A., McCabe, P., Pidcock, E., Platings, M., Shields, G. P., Stevens, J. S., Towler, M. & Wood, P. A. (2020). *J. Appl. Cryst.* **53**, 226–235.
Mansukhbhai, S. A. & Das, A. K. (2021). *J. Pharm. Res.* **20**, 21–26.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.
Syed, A., Foss, L. I. & Stevens, E. D. (1984). *Acta Cryst.* C**40**, 834–836.
Tang, Z., Takagi, Y., Koesoema, A. A. & Matsuda, T. (2024). *Appl. Microbiol. Biotechnol.* **108**, 545.

supporting information

Acta Cryst. (2026). E**82** [https://doi.org/10.1107/S2056989026009175]

Crystal structure of the pharmaceutical impurity 2-(4-chlorobenzoyl)pyridine

Karan J. Singh and Joseph M. Tanski

Computing details

2-[(4-Chlorophenyl)carbonyl]pyridine

Crystal data

$C_{12}H_8ClNO$
$M_r = 217.64$
Monoclinic, $P2_1/c$
$a = 3.8943$ (6) Å
$b = 10.8402$ (15) Å
$c = 23.307$ (3) Å
$\beta = 90.573$ (2)°
$V = 983.9$ (2) Å^3
$Z = 4$
$F(000) = 448$
$D_x = 1.469$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 9976 reflections
$\theta = 2.6$–30.5°
$\mu = 0.36$ mm^{-1}
$T = 125$ K
Plate, colourless
0.30 × 0.17 × 0.04 mm

Data collection

Bruker APEXII CCD diffractometer
Radiation source: sealed X-ray tube, Bruker APEXII CCD
Graphite monochromator
Detector resolution: 8.3333 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan (SADABS; Krause *et al.*, 2015)
$T_{min} = 0.87$, $T_{max} = 0.99$
22981 measured reflections
3018 independent reflections
2627 reflections with $I > 2\sigma(I)$
$R_{int} = 0.047$
$\theta_{max} = 30.6°$, $\theta_{min} = 2.1°$
$h = -5 \rightarrow 5$
$k = -15 \rightarrow 15$
$l = -33 \rightarrow 33$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.087$
$wR(F^2) = 0.234$
$S = 1.19$
3018 reflections
136 parameters
0 restraints
Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0373P)^2 + 7.3622P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.63$ e Å^{-3}
$\Delta\rho_{min} = -0.91$ e Å^{-3}

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	0.1218 (3)	0.36829 (10)	0.89790 (4)	0.0240 (3)
O1	0.3127 (10)	0.5625 (3)	0.62865 (14)	0.0306 (8)
N1	0.3630 (9)	0.2415 (3)	0.61545 (14)	0.0182 (6)
C1	0.4401 (11)	0.1573 (4)	0.57571 (17)	0.0209 (8)
H1B	0.375692	0.074018	0.582413	0.025*
C2	0.6100 (11)	0.1851 (4)	0.52497 (18)	0.0220 (8)
H2A	0.66341	0.121867	0.498278	0.026*
C3	0.6995 (11)	0.3065 (4)	0.51413 (19)	0.0247 (8)
H3A	0.810253	0.328332	0.47945	0.03*
C4	0.6246 (11)	0.3954 (4)	0.55481 (17)	0.0209 (8)
H4A	0.687546	0.479185	0.549092	0.025*
C5	0.4537 (10)	0.3588 (4)	0.60456 (16)	0.0167 (7)
C6	0.3522 (11)	0.4574 (4)	0.64667 (17)	0.0186 (7)
C7	0.3001 (10)	0.4297 (3)	0.70928 (16)	0.0159 (7)
C8	0.1338 (10)	0.5204 (3)	0.74168 (17)	0.0165 (7)
H8A	0.055346	0.593758	0.723501	0.02*
C9	0.0826 (10)	0.5041 (4)	0.79999 (17)	0.0193 (7)
H9A	−0.027204	0.566012	0.82209	0.023*
C10	0.1959 (10)	0.3951 (4)	0.82540 (16)	0.0172 (7)
C11	0.3722 (10)	0.3054 (4)	0.79449 (17)	0.0174 (7)
H11A	0.458215	0.233698	0.813115	0.021*
C12	0.4203 (10)	0.3227 (4)	0.73593 (17)	0.0174 (7)
H12A	0.534994	0.261473	0.714114	0.021*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0307 (5)	0.0248 (5)	0.0165 (4)	−0.0023 (4)	0.0050 (3)	0.0009 (4)
O1	0.054 (2)	0.0156 (14)	0.0218 (15)	0.0020 (14)	0.0022 (14)	0.0033 (12)
N1	0.0213 (16)	0.0166 (15)	0.0168 (15)	−0.0006 (12)	−0.0001 (12)	−0.0006 (12)
C1	0.0264 (19)	0.0161 (17)	0.0201 (18)	−0.0016 (15)	0.0015 (15)	−0.0030 (14)
C2	0.0225 (19)	0.025 (2)	0.0184 (18)	0.0022 (16)	0.0024 (14)	−0.0043 (15)
C3	0.024 (2)	0.029 (2)	0.0208 (19)	0.0014 (17)	0.0040 (15)	0.0023 (16)
C4	0.0223 (18)	0.0207 (19)	0.0198 (18)	−0.0013 (15)	0.0011 (14)	0.0029 (15)
C5	0.0184 (16)	0.0159 (16)	0.0156 (16)	−0.0017 (13)	−0.0031 (13)	−0.0002 (13)
C6	0.0233 (18)	0.0147 (16)	0.0176 (17)	−0.0021 (14)	−0.0022 (14)	0.0005 (13)
C7	0.0181 (16)	0.0132 (16)	0.0163 (16)	−0.0027 (13)	−0.0016 (13)	0.0002 (13)
C8	0.0163 (16)	0.0123 (16)	0.0210 (17)	−0.0001 (13)	−0.0007 (13)	−0.0003 (13)
C9	0.0200 (18)	0.0177 (17)	0.0204 (18)	0.0012 (14)	0.0038 (14)	−0.0018 (14)

C10	0.0190 (17)	0.0178 (17)	0.0149 (16)	−0.0024 (13)	0.0004 (13)	−0.0001 (13)
C11	0.0198 (17)	0.0142 (16)	0.0181 (17)	0.0015 (13)	−0.0030 (13)	0.0008 (13)
C12	0.0189 (17)	0.0144 (17)	0.0188 (17)	0.0014 (13)	−0.0004 (13)	−0.0022 (13)

Geometric parameters (Å, º)

Cl1—C10	1.741 (4)	C5—C6	1.506 (5)
O1—C6	1.224 (5)	C6—C7	1.506 (5)
N1—C1	1.337 (5)	C7—C12	1.394 (5)
N1—C5	1.345 (5)	C7—C8	1.403 (5)
C1—C2	1.394 (6)	C8—C9	1.387 (5)
C1—H1B	0.95	C8—H8A	0.95
C2—C3	1.385 (6)	C9—C10	1.392 (6)
C2—H2A	0.95	C9—H9A	0.95
C3—C4	1.386 (6)	C10—C11	1.395 (5)
C3—H3A	0.95	C11—C12	1.392 (5)
C4—C5	1.400 (5)	C11—H11A	0.95
C4—H4A	0.95	C12—H12A	0.95
C1—N1—C5	117.0 (3)	C12—C7—C8	119.9 (3)
N1—C1—C2	123.5 (4)	C12—C7—C6	123.3 (3)
N1—C1—H1B	118.3	C8—C7—C6	116.7 (3)
C2—C1—H1B	118.3	C9—C8—C7	120.7 (4)
C3—C2—C1	118.9 (4)	C9—C8—H8A	119.7
C3—C2—H2A	120.6	C7—C8—H8A	119.7
C1—C2—H2A	120.6	C8—C9—C10	118.5 (4)
C2—C3—C4	118.8 (4)	C8—C9—H9A	120.8
C2—C3—H3A	120.6	C10—C9—H9A	120.8
C4—C3—H3A	120.6	C9—C10—C11	121.8 (4)
C3—C4—C5	118.3 (4)	C9—C10—Cl1	120.0 (3)
C3—C4—H4A	120.8	C11—C10—Cl1	118.2 (3)
C5—C4—H4A	120.8	C12—C11—C10	119.0 (4)
N1—C5—C4	123.5 (4)	C12—C11—H11A	120.5
N1—C5—C6	118.5 (3)	C10—C11—H11A	120.5
C4—C5—C6	117.9 (4)	C11—C12—C7	120.0 (4)
O1—C6—C7	120.0 (4)	C11—C12—H12A	120.0
O1—C6—C5	118.0 (4)	C7—C12—H12A	120.0
C7—C6—C5	121.9 (3)		
C5—N1—C1—C2	0.7 (6)	C5—C6—C7—C12	16.5 (6)
N1—C1—C2—C3	−1.2 (7)	O1—C6—C7—C8	13.9 (6)
C1—C2—C3—C4	1.6 (7)	C5—C6—C7—C8	−166.2 (4)
C2—C3—C4—C5	−1.5 (6)	C12—C7—C8—C9	−1.0 (6)
C1—N1—C5—C4	−0.7 (6)	C6—C7—C8—C9	−178.4 (4)
C1—N1—C5—C6	176.4 (4)	C7—C8—C9—C10	−0.9 (6)
C3—C4—C5—N1	1.1 (6)	C8—C9—C10—C11	3.1 (6)
C3—C4—C5—C6	−176.0 (4)	C8—C9—C10—Cl1	−177.5 (3)
N1—C5—C6—O1	−152.6 (4)	C9—C10—C11—C12	−3.4 (6)

C4—C5—C6—O1	24.6 (6)	Cl1—C10—C11—C12	177.1 (3)
N1—C5—C6—C7	27.5 (6)	C10—C11—C12—C7	1.5 (6)
C4—C5—C6—C7	−155.3 (4)	C8—C7—C12—C11	0.6 (6)
O1—C6—C7—C12	−163.4 (4)	C6—C7—C12—C11	177.8 (4)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2*A*···Cl1^{i}	0.95	2.96	3.633 (4)	129
C11—H11*A*···O1^{ii}	0.95	2.46	3.406 (5)	173

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