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1-[2-(2,4-Dichlorophenoxy)acetyl]-4-cyclohexylthiosemicarbazide

Ghulam Qadeer,[a] Nasim Hasan Rama,[a]* Mohammad Azad Malik,[b] Javeed Akhtar[b] and James Raftery[b]

[a]Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan, and [b]School of Chemistry and Materials Science Centre, University of Manchester, Oxford Road, Manchester M13 9PL, England
Correspondence e-mail: nasimhrama@yahoo.com

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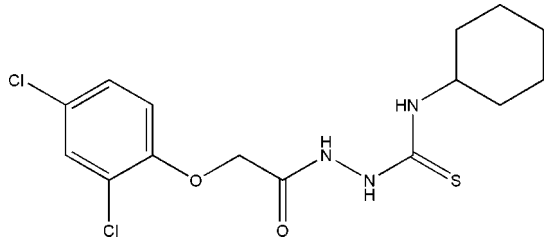
Key indicators: single-crystal X-ray study; T = 100 K; mean σ(C–C) = 0.004 Å; R factor = 0.040; wR factor = 0.107; data-to-parameter ratio = 19.0.

The title compound, $C_{15}H_{19}Cl_2N_3O_2S$, is an important intermediate for the synthesis of biologically active heterocyclic compounds. The thiosemicarbazide group is approximately planar and forms a dihedral angle of 88.03 (5)° with the benzene ring. The structure is stabilized by intermolecular N—H···O and N—H···S hydrogen-bond interactions.

Related literature

For general background, see: Antholine & Taketa (1982); Mao *et al.* (1999); Shen *et al.* (1998). For a related structure, see Ji *et al.* (2002).



Experimental

Crystal data

$C_{15}H_{19}Cl_2N_3O_2S$
M_r = 376.29
Monoclinic, $P2_1/c$
a = 15.4180 (16) Å
b = 12.1530 (13) Å
c = 9.285 (1) Å
β = 103.299 (2)°
V = 1693.1 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.52 mm^{-1}
T = 100 (2) K
0.25 × 0.20 × 0.15 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)
T_{min} = 0.881, T_{max} = 0.926
10375 measured reflections
3957 independent reflections
2789 reflections with $I > 2\sigma(I)$
R_{int} = 0.048

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.107
S = 0.96
3957 reflections
208 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.40 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2A···O2^{i}	0.88	2.06	2.926 (3)	166
N3—H3A···S1^{ii}	0.88	2.60	3.430 (2)	157

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

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 1999); data reduction: *SAINT*; program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1999); 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: XU2290).

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supplementary materials

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1-[2-(2,4-Dichlorophenoxy)acetyl]-4-cyclohexylthiosemicarbazide

G. Qadeer, N. H. Rama, M. A. Malik, J. Akhtar and J. Raftery

Comment

Thiosemicarbazide is interesting because of the formation of complexes with biological activities (Shen *et al.*, 1998). Some substituted thiourea derivatives have shown interesting biological effects, including anti-HIV properties (Mao *et al.*, 1999), and thiourea derivatives have also been successfully screened for various biological actions (Antholine & Taketa, 1982). As a ligand with potential S– and N-atom donors, thiosemicarbazide is interesting because of the structural chemistry of its multifunctional coordination modes (N-monodentate, S-monodentate or N:*S*-bidentate). In order to investigate further this kind of ligand, we synthesized the title compound and describe its structure here.

In the molecule of the title compound (Fig. 1), the bond lengths and angles are in normal ranges (Ji *et al.*, 2002). The thiosemicabazide group is approximately planar and forms a dihedral angles of 88.03 (5)° with the benzene ring. The crystal structure is stabilized by intermolecular N—-H···O and N—H··· S hydrogen bonding (Table 1). Dipole–dipole and van der Waals interactions are also effective in the molecular packing in the crystal structure.

Experimental

The title compound was prepared by the reaction of 2-(2,4-dichlorophenoxy) acetohydrazide (4.7 g, 20 mmol) and cyclohexylisothiocyanate (2.82 g, 20 mmol) in an ethanol solution (Fig. 3). Single crystals suitable for X-ray measurements were obtained by recrystallization from a water-ethanol solution at room temperature (yield: 80%).

Refinement

H atoms were included in calculated positions with C—H = 0.95 (CH), 0.99 (CH_2) and N—H = 0.88 Å, and refined in riding mode with U_{iso}(H) = 1.2U_{eq}(C,*N*).

Figures

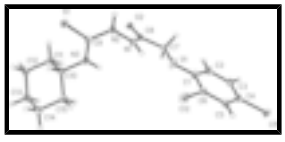


Fig. 1. The molecular structure of (I) with 50% probability displacement ellipsoids (arbitrary spheres for H atoms).

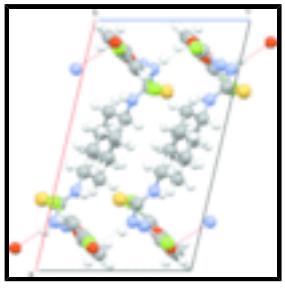


Fig. 2. Crystal packing of (I), along *b* axis.

Fig. 3. The reaction scheme.

1-[2-(2,4-Dichlorophenoxy)acetyl]-4-cyclohexylthiosemicarbazide

Crystal data

$C_{15}H_{19}Cl_2N_3O_2S$	F_{000} = 784
	D_x = 1.476 Mg m^{-3}
M_r = 376.29	D_m = 1.429 Mg m^{-3}
	D_m measured by not measured
Monoclinic, $P2_1/c$	Melting point: 462(1) K
Hall symbol: -P 2ybc	Mo $K\alpha$ radiation
	λ = 0.71073 Å
a = 15.4180 (16) Å	Cell parameters from 2164 reflections
b = 12.1530 (13) Å	θ = 2.1–27.5º
c = 9.285 (1) Å	μ = 0.52 mm^{-1}
β = 103.299 (2)º	T = 100 (2) K
V = 1693.1 (3) Å^3	Block, colorless
Z = 4	0.25 × 0.20 × 0.15 mm

Data collection

Bruker SMART CCD area-detector diffractometer	3957 independent reflections
Radiation source: fine-focus sealed tube	2789 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.048
T = 100(2) K	θ_{max} = 28.3º
φ and ω scans	θ_{min} = 1.3º
Absorption correction: multi-scan (SADABS; Sheldrick, 2002)	h = −18→20
T_{min} = 0.881, T_{max} = 0.926	k = −15→14
10375 measured reflections	l = −12→10

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)]$ = 0.040	H-atom parameters constrained
$wR(F^2)$ = 0.107	$w = 1/[\sigma^2(F_o^2) + (0.0451P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 0.96	$(\Delta/\sigma)_{max}$ = 0.001
3957 reflections	$\Delta\rho_{max}$ = 0.40 e Å^{-3}
208 parameters	$\Delta\rho_{min}$ = −0.31 e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

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 $F^2 > 2\text{sigma}(F^2)$ 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	0.13846 (17)	0.6689 (2)	0.7485 (3)	0.0166 (6)
C2	0.07493 (17)	0.7128 (2)	0.6323 (3)	0.0181 (6)
H2	0.0368	0.6653	0.5648	0.022*
C3	0.06700 (17)	0.8258 (2)	0.6143 (3)	0.0172 (6)
H3	0.0239	0.8561	0.5342	0.021*
C4	0.12233 (17)	0.8939 (2)	0.7139 (3)	0.0162 (6)
C5	0.18637 (17)	0.8522 (2)	0.8310 (3)	0.0159 (6)
H5	0.2237	0.9000	0.8992	0.019*
C6	0.19441 (17)	0.7396 (2)	0.8458 (3)	0.0154 (6)
C7	0.09777 (17)	0.4823 (2)	0.6805 (3)	0.0159 (6)
H7A	0.1085	0.4896	0.5799	0.019*
H7B	0.0339	0.4967	0.6750	0.019*
C8	0.12191 (16)	0.3672 (2)	0.7391 (3)	0.0143 (6)
C9	0.26704 (17)	0.1994 (2)	0.9505 (3)	0.0142 (6)
C10	0.39401 (16)	0.1555 (2)	0.8427 (3)	0.0153 (6)
H10	0.4187	0.1192	0.9401	0.018*
C11	0.36496 (17)	0.0664 (2)	0.7282 (3)	0.0187 (6)
H11A	0.3397	0.1004	0.6307	0.022*
H11B	0.3180	0.0210	0.7556	0.022*
C12	0.44379 (17)	−0.0063 (2)	0.7176 (3)	0.0209 (6)
H12A	0.4660	−0.0447	0.8130	0.025*
H12B	0.4241	−0.0626	0.6400	0.025*
C13	0.51860 (17)	0.0618 (2)	0.6807 (3)	0.0200 (6)
H13A	0.4984	0.0935	0.5804	0.024*
H13B	0.5704	0.0137	0.6808	0.024*
C14	0.54661 (18)	0.1542 (2)	0.7923 (3)	0.0219 (6)
H14A	0.5922	0.2002	0.7617	0.026*
H14B	0.5737	0.1223	0.8904	0.026*
C15	0.46748 (17)	0.2262 (2)	0.8046 (3)	0.0209 (6)
H15A	0.4870	0.2824	0.8825	0.025*
H15B	0.4442	0.2647	0.7096	0.025*
Cl1	0.11146 (4)	1.03696 (5)	0.69465 (8)	0.01992 (17)
Cl2	0.27468 (5)	0.68394 (6)	0.98848 (8)	0.02279 (18)

N1	0.17825 (14)	0.36264 (18)	0.8738 (2)	0.0151 (5)
H1	0.2046	0.4233	0.9134	0.018*
N2	0.19546 (14)	0.26475 (17)	0.9509 (3)	0.0161 (5)
H2A	0.1578	0.2434	1.0035	0.019*
N3	0.31812 (14)	0.22479 (18)	0.8581 (2)	0.0153 (5)
H3A	0.3063	0.2849	0.8043	0.018*
O1	0.15121 (12)	0.55908 (14)	0.7776 (2)	0.0207 (5)
O2	0.08986 (11)	0.28700 (14)	0.6667 (2)	0.0160 (4)
S1	0.28518 (4)	0.09197 (5)	1.06962 (8)	0.01578 (17)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0196 (14)	0.0135 (14)	0.0166 (15)	0.0021 (11)	0.0043 (12)	0.0014 (11)
C2	0.0175 (13)	0.0156 (14)	0.0192 (16)	−0.0001 (11)	0.0005 (12)	−0.0002 (12)
C3	0.0166 (13)	0.0164 (14)	0.0179 (15)	0.0020 (11)	0.0027 (11)	0.0035 (12)
C4	0.0204 (14)	0.0100 (13)	0.0201 (15)	0.0015 (11)	0.0085 (12)	0.0006 (11)
C5	0.0178 (13)	0.0150 (14)	0.0157 (14)	−0.0020 (11)	0.0054 (11)	−0.0013 (11)
C6	0.0162 (13)	0.0175 (14)	0.0121 (14)	0.0023 (11)	0.0024 (11)	0.0027 (11)
C7	0.0192 (14)	0.0112 (13)	0.0167 (15)	0.0001 (10)	0.0030 (11)	−0.0006 (11)
C8	0.0122 (13)	0.0159 (14)	0.0166 (15)	0.0018 (10)	0.0071 (11)	0.0011 (12)
C9	0.0172 (13)	0.0128 (13)	0.0122 (14)	−0.0016 (10)	0.0025 (11)	−0.0023 (11)
C10	0.0146 (13)	0.0151 (14)	0.0173 (15)	0.0035 (10)	0.0056 (11)	0.0025 (11)
C11	0.0167 (14)	0.0186 (15)	0.0218 (16)	0.0005 (11)	0.0065 (12)	−0.0014 (12)
C12	0.0200 (14)	0.0165 (14)	0.0266 (17)	0.0017 (11)	0.0063 (13)	−0.0040 (12)
C13	0.0177 (14)	0.0222 (16)	0.0214 (16)	0.0036 (11)	0.0071 (12)	−0.0035 (12)
C14	0.0156 (14)	0.0252 (16)	0.0260 (17)	−0.0038 (11)	0.0070 (12)	−0.0037 (13)
C15	0.0215 (14)	0.0170 (15)	0.0270 (17)	−0.0033 (11)	0.0112 (13)	−0.0039 (13)
Cl1	0.0222 (4)	0.0109 (3)	0.0265 (4)	0.0006 (3)	0.0052 (3)	0.0030 (3)
Cl2	0.0248 (4)	0.0185 (4)	0.0204 (4)	0.0000 (3)	−0.0043 (3)	0.0030 (3)
N1	0.0213 (12)	0.0097 (11)	0.0154 (12)	0.0000 (9)	0.0061 (10)	0.0012 (9)
N2	0.0204 (12)	0.0133 (12)	0.0173 (13)	0.0039 (9)	0.0094 (10)	0.0050 (10)
N3	0.0193 (12)	0.0125 (11)	0.0162 (13)	0.0026 (9)	0.0081 (10)	0.0038 (9)
O1	0.0265 (11)	0.0093 (10)	0.0212 (11)	0.0006 (8)	−0.0052 (9)	0.0000 (8)
O2	0.0196 (9)	0.0125 (10)	0.0171 (10)	−0.0026 (7)	0.0069 (8)	−0.0024 (8)
S1	0.0204 (3)	0.0133 (3)	0.0143 (4)	0.0018 (3)	0.0053 (3)	0.0020 (3)

Geometric parameters (Å, °)

C1—O1	1.367 (3)	C10—C11	1.511 (4)
C1—C2	1.387 (4)	C10—C15	1.527 (4)
C1—C6	1.393 (4)	C10—H10	1.0000
C2—C3	1.386 (4)	C11—C12	1.524 (4)
C2—H2	0.9500	C11—H11A	0.9900
C3—C4	1.381 (4)	C11—H11B	0.9900
C3—H3	0.9500	C12—C13	1.521 (4)
C4—C5	1.385 (4)	C12—H12A	0.9900
C4—Cl1	1.752 (3)	C12—H12B	0.9900
C5—C6	1.378 (4)	C13—C14	1.521 (4)

C5—H5	0.9500	C13—H13A	0.9900
C6—Cl2	1.729 (3)	C13—H13B	0.9900
C7—O1	1.421 (3)	C14—C15	1.527 (4)
C7—C8	1.516 (4)	C14—H14A	0.9900
C7—H7A	0.9900	C14—H14B	0.9900
C7—H7B	0.9900	C15—H15A	0.9900
C8—O2	1.222 (3)	C15—H15B	0.9900
C8—N1	1.350 (3)	N1—N2	1.382 (3)
C9—N3	1.327 (3)	N1—H1	0.8800
C9—N2	1.360 (3)	N2—H2A	0.8800
C9—S1	1.693 (3)	N3—H3A	0.8800
C10—N3	1.475 (3)		
O1—C1—C2	125.0 (2)	C12—C11—H11A	109.6
O1—C1—C6	115.8 (2)	C10—C11—H11B	109.6
C2—C1—C6	119.2 (2)	C12—C11—H11B	109.6
C3—C2—C1	120.1 (3)	H11A—C11—H11B	108.1
C3—C2—H2	119.9	C13—C12—C11	110.9 (2)
C1—C2—H2	119.9	C13—C12—H12A	109.5
C4—C3—C2	119.3 (3)	C11—C12—H12A	109.5
C4—C3—H3	120.3	C13—C12—H12B	109.5
C2—C3—H3	120.3	C11—C12—H12B	109.5
C3—C4—C5	121.7 (2)	H12A—C12—H12B	108.1
C3—C4—Cl1	119.8 (2)	C12—C13—C14	111.1 (2)
C5—C4—Cl1	118.5 (2)	C12—C13—H13A	109.4
C6—C5—C4	118.2 (3)	C14—C13—H13A	109.4
C6—C5—H5	120.9	C12—C13—H13B	109.4
C4—C5—H5	120.9	C14—C13—H13B	109.4
C5—C6—C1	121.3 (2)	H13A—C13—H13B	108.0
C5—C6—Cl2	119.8 (2)	C13—C14—C15	111.6 (2)
C1—C6—Cl2	118.9 (2)	C13—C14—H14A	109.3
O1—C7—C8	108.7 (2)	C15—C14—H14A	109.3
O1—C7—H7A	110.0	C13—C14—H14B	109.3
C8—C7—H7A	110.0	C15—C14—H14B	109.3
O1—C7—H7B	110.0	H14A—C14—H14B	108.0
C8—C7—H7B	110.0	C10—C15—C14	110.1 (2)
H7A—C7—H7B	108.3	C10—C15—H15A	109.6
O2—C8—N1	124.7 (2)	C14—C15—H15A	109.6
O2—C8—C7	120.2 (2)	C10—C15—H15B	109.6
N1—C8—C7	115.0 (2)	C14—C15—H15B	109.6
N3—C9—N2	118.0 (2)	H15A—C15—H15B	108.2
N3—C9—S1	124.60 (19)	C8—N1—N2	121.4 (2)
N2—C9—S1	117.4 (2)	C8—N1—H1	119.3
N3—C10—C11	111.3 (2)	N2—N1—H1	119.3
N3—C10—C15	110.4 (2)	C9—N2—N1	124.1 (2)
C11—C10—C15	110.9 (2)	C9—N2—H2A	118.0
N3—C10—H10	108.0	N1—N2—H2A	118.0
C11—C10—H10	108.0	C9—N3—C10	122.2 (2)
C15—C10—H10	108.0	C9—N3—H3A	118.9
C10—C11—C12	110.4 (2)	C10—N3—H3A	118.9

C10—C11—H11A	109.6	C1—O1—C7	118.7 (2)
O1—C1—C2—C3	179.1 (2)	C11—C12—C13—C14	55.5 (3)
C6—C1—C2—C3	−0.5 (4)	C12—C13—C14—C15	−55.0 (3)
C1—C2—C3—C4	−0.6 (4)	N3—C10—C15—C14	178.7 (2)
C2—C3—C4—C5	0.6 (4)	C11—C10—C15—C14	−57.4 (3)
C2—C3—C4—Cl1	−178.7 (2)	C13—C14—C15—C10	55.6 (3)
C3—C4—C5—C6	0.5 (4)	O2—C8—N1—N2	−8.8 (4)
Cl1—C4—C5—C6	179.8 (2)	C7—C8—N1—N2	170.0 (2)
C4—C5—C6—C1	−1.6 (4)	N3—C9—N2—N1	−7.7 (4)
C4—C5—C6—Cl2	178.93 (19)	S1—C9—N2—N1	171.72 (19)
O1—C1—C6—C5	−178.0 (2)	C8—N1—N2—C9	96.4 (3)
C2—C1—C6—C5	1.7 (4)	N2—C9—N3—C10	−176.2 (2)
O1—C1—C6—Cl2	1.4 (3)	S1—C9—N3—C10	4.4 (4)
C2—C1—C6—Cl2	−178.9 (2)	C11—C10—N3—C9	87.9 (3)
O1—C7—C8—O2	−173.6 (2)	C15—C10—N3—C9	−148.5 (2)
O1—C7—C8—N1	7.5 (3)	C2—C1—O1—C7	1.8 (4)
N3—C10—C11—C12	−178.2 (2)	C6—C1—O1—C7	−178.5 (2)
C15—C10—C11—C12	58.5 (3)	C8—C7—O1—C1	−177.9 (2)
C10—C11—C12—C13	−57.3 (3)		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2A···O2^{i}	0.88	2.06	2.926 (3)	166
N3—H3A···S1^{ii}	0.88	2.60	3.430 (2)	157

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

Fig. 1

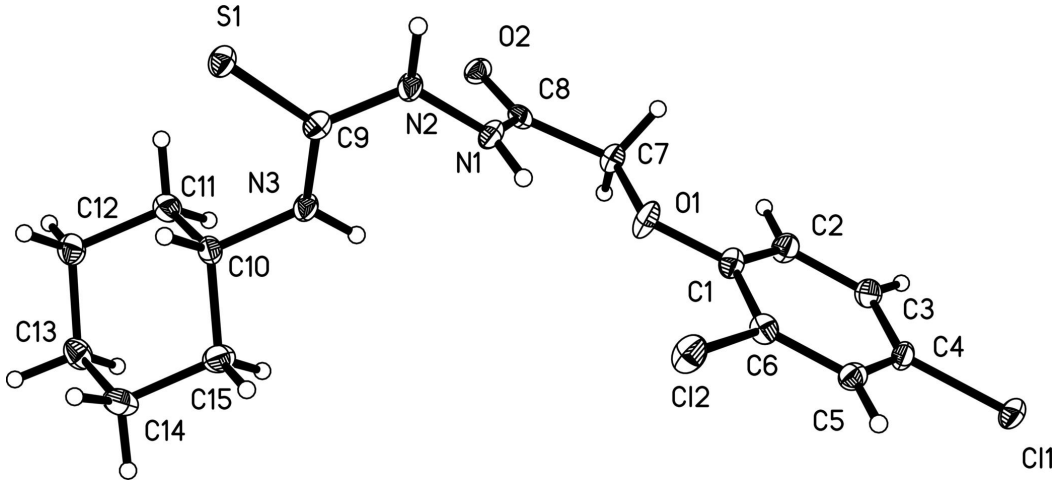

S1
O2
C8
C9
N2
N1
C7
C11
N3
O1
C12
C2
C10
C1
C3
C13
C4
C6
Cl2
C15
C5
C14
Cl1

Fig. 2

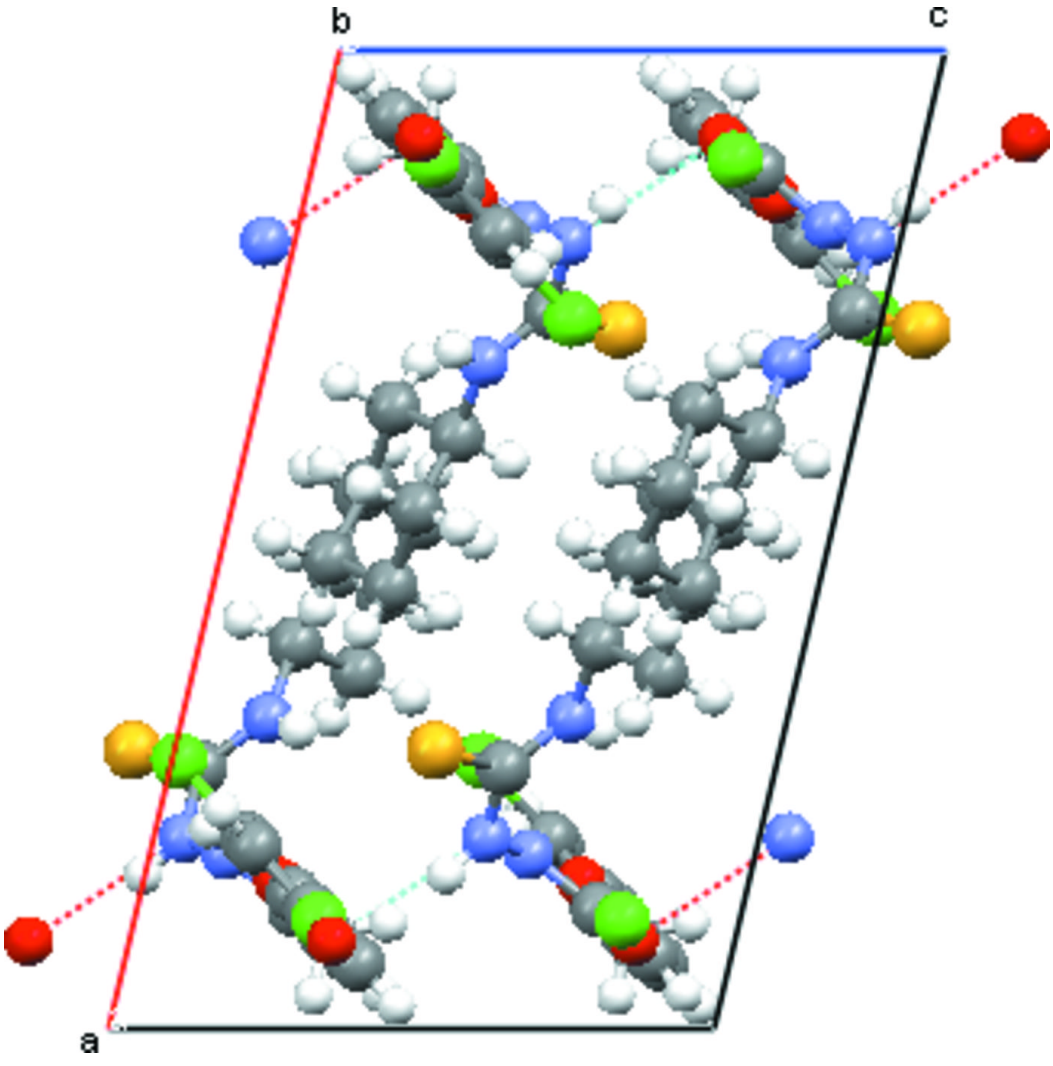
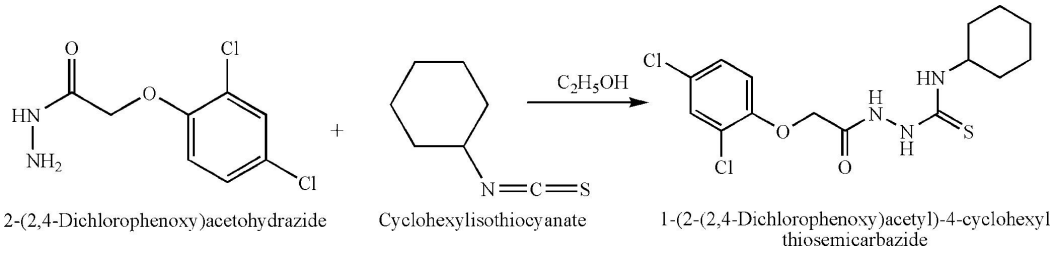


Fig. 3



2-(2,4-Dichlorophenoxy)acetohydrazide Cyclohexylisothiocyanate 1-(2-(2,4-Dichlorophenoxy)acetyl)-4-cyclohexyl thiosemicarbazide