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Chlorothiazide formic acid solvate (1/2)

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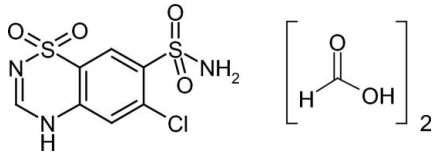
Key indicators: single-crystal X-ray study; T = 123 K; mean σ(C–C) = 0.006 Å; R factor = 0.052; wR factor = 0.114; data-to-parameter ratio = 11.6.

Chlorothiazide forms a 1:2 solvate with formic acid (systematic name: 6-chloro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide methanoic acid disolvate), $C_7H_6ClN_3O_4S_2{\cdot}2CH_2O_2$. The compound crystallizes with one chlorothiazide molecule and two solvent molecules in the asymmetric unit and displays an extensive hydrogen-bonding network.

Related literature

For details on experimental methods used to obtain this form, see: Florence *et al.* (2003, 2006). For previous studies on the anhydrous form of the title compound, see: Dupont & Dideberg (1970); Shankland *et al.* (1997); for solvated forms, see: Johnston *et al.* (2007*a*,*b*). Intermolecular interactions in polymorphs and solvates of the related thiazide diuretic hydrochlorothiazide have also been studied (Johnston *et al.*, 2007).



Experimental

Crystal data

$C_7H_6ClN_3O_4S_2{\cdot}2CH_2O_2$
M_r = 387.77
Monoclinic, $P2_1/c$
a = 8.2985 (5) Å
b = 21.5271 (14) Å
c = 8.3676 (5) Å
β = 105.580 (3)°
V = 1439.89 (15) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.60 mm^{-1}
T = 123 (2) K
0.30 × 0.12 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: none
8698 measured reflections
2650 independent reflections
1872 reflections with $I > 2\sigma(I)$
R_{int} = 0.079

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.052
$wR(F^2)$ = 0.114
S = 1.07
2650 reflections
228 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.53 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O5—H1H···O7	0.95 (6)	1.64 (6)	2.593 (5)	175 (6)
N2—H1N···O6^{i}	0.88 (4)	1.83 (4)	2.690 (4)	166 (5)
O8—H2H···O3	1.10 (6)	2.02 (5)	3.027 (5)	152 (4)
N3—H2N···N1^{ii}	0.94 (5)	2.09 (5)	3.022 (5)	171 (4)
N3—H3N···O7^{iii}	0.76 (5)	2.13 (5)	2.890 (5)	178 (6)

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

Data collection: *COLLECT* (Hooft, 1988) and *DENZO* (Otwinowski & Minor, 1997); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *PLATON*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: WN2197).

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supplementary materials

Acta Cryst. (2007). E**63**, o4021 [**doi:10.1107/S1600536807042845**]

Chlorothiazide formic acid solvate (1/2)

A. Johnston, A. J. Florence and A. R. Kennedy

Comment

Chlorothiazide (CT) is a thiazide diuretic drug that is known to crystallize in at least one non-solvated form (Dupont & Dideberg, 1970; Shankland *et al.*, 1997). The title compound was produced as part of an automated parallel crystallization study (Florence *et al.*, 2006) of CT as part of a wider investigation that couples automated parallel crystallization with crystal structure prediction to investigate the basic science underlying the solid-state diversity of CT and the related thiazide diuretic, hydrochlorothiazide (Johnston *et al.*, 2007). The sample was identified as a novel form using multi-sample foil transmission X-ray powder diffraction analysis (Florence *et al.*, 2003). Subsequent manual recrystallization from a saturated formic acid solution by slow evaporation at 278 K yielded a sample suitable for single-crystal *x*-ray diffraction (Fig. 1).

The molecules crystallize in space group (*P*21/c) with one chlorothiazide (CT) and two solvent molecules in the asymmetric unit. The structure contains one N—H···N contact between CT molecules that forms an infinite chain of CT extending in the [101] direction. Molecules of CT also stack in the direction of the *c* axis with a further two N—H···O contacts between CT and each solvent molecule (residues B and C). In addition, two O—H···O interactions connect residue C with residues A and B (Table 1).

The contacts combine to form a layered structure (Fig. 2) comprising alternating layes of CT molecules (residue A) and solvent molecules (residues B and C) in the [010] direction.

Experimental

A single-crystal sample of the title compound was recrystallized from a saturated formic acid solution by isothermal solvent evaporation at 278 ^{o}K.

Refinement

The H-atoms attached to O or N-atoms were located by difference synthesis and refined isotropically. All other H-atoms were constrained to idealized geometries using a riding model with U_{iso}(H)=1.2U_{eq}(C) and C—H=0.95 Å.

Figures

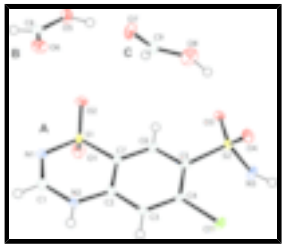

Fig. 1. Molecular structure of title compound, showing 50% probablility displacement ellipsoids.

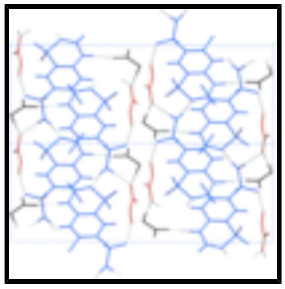

Fig. 2. Crystal packing of the title compound, viewed down the *a*-axis·Residues A, B and C (Fig. 1) are coloured red, blue and green, respectively. Hydrogen bonds are shown as grey dashed lines.

6-chloro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide methanoic acid disolvate

Crystal data

$C_7H_6ClN_3O_4S_2·2CH_2O_2$	F_{000} = 792
M_r = 387.77	D_x = 1.789 Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation λ = 0.71073 Å
a = 8.2985 (5) Å	Cell parameters from 2389 reflections
b = 21.5271 (14) Å	θ = 1.0–27.5º
c = 8.3676 (5) Å	μ = 0.60 mm^{-1}
β = 105.580 (3)º	T = 123 (2) K
V = 1439.89 (15) Å^3	Block, colourless
Z = 4	0.30 × 0.12 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer	1872 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	R_{int} = 0.079
Monochromator: graphite	θ_{max} = 26.0º
T = 123(2) K	θ_{min} = 1.9º
phi and ω scans	h = −10→10
Absorption correction: none	k = −26→26
8698 measured reflections	l = −10→10
2650 independent reflections	

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0295P)^2 + 2.9523P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.052	$(\Delta/\sigma)_{max}$ = 0.002
$wR(F^2)$ = 0.114	$\Delta\rho_{max}$ = 0.49 e Å^{-3}
S = 1.07	$\Delta\rho_{min}$ = −0.53 e Å^{-3}
2650 reflections	Extinction correction: none
228 parameters	

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}
Cl1	0.58237 (12)	0.27340 (4)	0.40275 (12)	0.0165 (3)
S1	1.15604 (12)	0.13926 (4)	0.92688 (12)	0.0142 (3)
S2	0.57857 (12)	0.12000 (4)	0.43857 (12)	0.0132 (3)
O1	1.2736 (3)	0.11880 (14)	0.8414 (4)	0.0241 (7)
O2	1.0919 (4)	0.09369 (13)	1.0152 (4)	0.0231 (7)
O3	0.6350 (3)	0.05729 (12)	0.4813 (3)	0.0160 (7)
O4	0.4262 (3)	0.14023 (13)	0.4706 (3)	0.0188 (7)
O5	0.9981 (4)	0.00567 (13)	1.2892 (4)	0.0218 (7)
O6	1.0024 (4)	0.10413 (12)	1.3725 (4)	0.0227 (7)
O7	0.7176 (4)	0.03970 (14)	1.0859 (4)	0.0232 (7)
O8	0.5671 (5)	0.04283 (17)	0.8172 (5)	0.0418 (10)
N1	1.2463 (4)	0.19341 (15)	1.0552 (4)	0.0154 (8)
N2	1.1002 (4)	0.27635 (16)	0.8923 (4)	0.0137 (7)
N3	0.5668 (5)	0.13232 (18)	0.2500 (4)	0.0165 (8)
C1	1.2150 (5)	0.25210 (19)	1.0209 (5)	0.0142 (9)
H1	1.2817	0.2810	1.0963	0.017*
C2	0.9839 (5)	0.24083 (17)	0.7773 (5)	0.0124 (9)
C3	0.8579 (5)	0.27031 (17)	0.6553 (5)	0.0125 (9)
H3	0.8550	0.3143	0.6462	0.015*
C4	0.7382 (5)	0.23454 (17)	0.5490 (5)	0.0113 (8)
C5	0.7398 (5)	0.16901 (18)	0.5576 (5)	0.0122 (8)
C6	0.8692 (5)	0.14063 (18)	0.6763 (5)	0.0128 (8)
H6	0.8744	0.0966	0.6837	0.015*
C7	0.9906 (5)	0.17624 (17)	0.7838 (5)	0.0126 (9)
C8	1.0677 (5)	0.05427 (18)	1.3764 (5)	0.0187 (10)
H8	1.1774	0.0495	1.4475	0.022*
C9	0.7036 (5)	0.03154 (18)	0.9384 (5)	0.0173 (9)
H9	0.7983	0.0158	0.9081	0.021*
H1H	0.898 (7)	0.018 (3)	1.210 (7)	0.058 (18)*
H2H	0.562 (6)	0.036 (2)	0.686 (7)	0.045 (15)*
H1N	1.086 (6)	0.317 (2)	0.887 (6)	0.040 (15)*
H2N	0.470 (6)	0.155 (2)	0.197 (6)	0.032 (13)*
H3N	0.608 (6)	0.108 (2)	0.209 (6)	0.034 (17)*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0158 (5)	0.0160 (5)	0.0156 (5)	0.0048 (4)	0.0004 (4)	0.0034 (4)
S1	0.0124 (5)	0.0133 (5)	0.0146 (6)	0.0017 (4)	−0.0005 (4)	0.0012 (4)
S2	0.0125 (5)	0.0133 (5)	0.0130 (5)	0.0001 (4)	0.0019 (4)	−0.0009 (4)
O1	0.0166 (16)	0.0281 (17)	0.0267 (18)	0.0082 (13)	0.0041 (13)	−0.0070 (14)
O2	0.0241 (17)	0.0187 (15)	0.0228 (17)	−0.0064 (13)	−0.0001 (14)	0.0077 (13)
O3	0.0177 (16)	0.0113 (14)	0.0173 (15)	−0.0035 (12)	0.0015 (12)	0.0002 (11)
O4	0.0122 (15)	0.0221 (15)	0.0225 (17)	0.0012 (12)	0.0053 (13)	−0.0026 (12)
O5	0.0236 (17)	0.0136 (15)	0.0238 (18)	0.0023 (13)	−0.0012 (14)	−0.0027 (13)
O6	0.0251 (17)	0.0120 (15)	0.0317 (19)	0.0034 (13)	0.0089 (14)	0.0009 (13)
O7	0.0238 (17)	0.0293 (17)	0.0147 (17)	0.0054 (14)	0.0020 (13)	−0.0046 (13)
O8	0.045 (2)	0.048 (2)	0.030 (2)	−0.0025 (18)	0.0073 (18)	0.0041 (17)
N1	0.0148 (18)	0.0161 (18)	0.0143 (18)	−0.0032 (15)	0.0021 (15)	0.0022 (14)
N2	0.0159 (18)	0.0123 (16)	0.0123 (18)	−0.0028 (15)	0.0025 (15)	0.0016 (14)
N3	0.016 (2)	0.020 (2)	0.0119 (19)	0.0079 (16)	0.0007 (16)	−0.0011 (16)
C1	0.015 (2)	0.018 (2)	0.012 (2)	0.0004 (17)	0.0061 (17)	−0.0007 (17)
C2	0.012 (2)	0.015 (2)	0.012 (2)	−0.0029 (16)	0.0063 (17)	−0.0028 (16)
C3	0.014 (2)	0.0087 (18)	0.015 (2)	−0.0008 (16)	0.0048 (17)	0.0007 (16)
C4	0.012 (2)	0.016 (2)	0.008 (2)	0.0043 (16)	0.0079 (16)	0.0038 (15)
C5	0.016 (2)	0.015 (2)	0.007 (2)	0.0024 (17)	0.0066 (17)	−0.0019 (16)
C6	0.016 (2)	0.014 (2)	0.009 (2)	0.0023 (17)	0.0058 (16)	0.0007 (16)
C7	0.011 (2)	0.015 (2)	0.012 (2)	−0.0010 (16)	0.0038 (17)	−0.0002 (16)
C8	0.019 (2)	0.018 (2)	0.019 (2)	−0.0020 (18)	0.0045 (19)	−0.0012 (18)
C9	0.015 (2)	0.011 (2)	0.024 (3)	0.0017 (16)	0.0021 (19)	0.0002 (17)

Geometric parameters (Å, °)

Cl1—C4	1.738 (4)	N2—C1	1.337 (5)
S1—O2	1.415 (3)	N2—C2	1.394 (5)
S1—O1	1.425 (3)	N2—H1N	0.89 (5)
S1—N1	1.625 (3)	N3—H2N	0.95 (5)
S1—C7	1.752 (4)	N3—H3N	0.75 (5)
S2—O4	1.429 (3)	C1—H1	0.9500
S2—O3	1.442 (3)	C2—C7	1.392 (5)
S2—N3	1.577 (4)	C2—C3	1.402 (5)
S2—C5	1.783 (4)	C3—C4	1.377 (5)
O5—C8	1.317 (5)	C3—H3	0.9500
O5—H1H	0.95 (6)	C4—C5	1.413 (5)
O6—C8	1.199 (5)	C5—C6	1.393 (5)
O7—C9	1.221 (5)	C6—C7	1.387 (5)
O8—C9	1.324 (5)	C6—H6	0.9500
O8—H2H	1.10 (5)	C8—H8	0.9500
N1—C1	1.306 (5)	C9—H9	0.9500
?···?	?		
O2—S1—O1	116.85 (19)	C7—C2—N2	120.5 (3)

O2—S1—N1	108.88 (18)	C7—C2—C3	119.7 (3)
O1—S1—N1	107.28 (18)	N2—C2—C3	119.8 (3)
O2—S1—C7	109.66 (18)	C4—C3—C2	119.0 (3)
O1—S1—C7	108.27 (19)	C4—C3—H3	120.5
N1—S1—C7	105.26 (18)	C2—C3—H3	120.5
O4—S2—O3	118.90 (18)	C3—C4—C5	122.0 (3)
O4—S2—N3	108.45 (19)	C3—C4—Cl1	117.2 (3)
O3—S2—N3	109.52 (19)	C5—C4—Cl1	120.8 (3)
O4—S2—C5	106.48 (17)	C6—C5—C4	118.0 (3)
O3—S2—C5	105.71 (17)	C6—C5—S2	117.3 (3)
N3—S2—C5	107.16 (19)	C4—C5—S2	124.6 (3)
C8—O5—H1H	109 (3)	C7—C6—C5	120.4 (4)
C9—O8—H2H	122 (3)	C7—C6—H6	119.8
C1—N1—S1	121.3 (3)	C5—C6—H6	119.8
C1—N2—C2	123.6 (4)	C6—C7—C2	120.8 (3)
C1—N2—H1N	119 (3)	C6—C7—S1	119.4 (3)
C2—N2—H1N	117 (3)	C2—C7—S1	119.8 (3)
S2—N3—H2N	112 (3)	O6—C8—O5	124.6 (4)
S2—N3—H3N	116 (4)	O6—C8—H8	117.7
H2N—N3—H3N	125 (5)	O5—C8—H8	117.7
N1—C1—N2	127.7 (4)	O7—C9—O8	125.2 (4)
N1—C1—H1	116.2	O7—C9—H9	117.4
N2—C1—H1	116.2	O8—C9—H9	117.4
O2—S1—N1—C1	−131.6 (3)	O4—S2—C5—C4	−55.1 (4)
O1—S1—N1—C1	101.1 (4)	O3—S2—C5—C4	177.6 (3)
C7—S1—N1—C1	−14.1 (4)	N3—S2—C5—C4	60.8 (4)
S1—N1—C1—N2	6.7 (6)	C4—C5—C6—C7	1.0 (6)
C2—N2—C1—N1	5.0 (7)	S2—C5—C6—C7	−174.1 (3)
C1—N2—C2—C7	−5.2 (6)	C5—C6—C7—C2	1.2 (6)
C1—N2—C2—C3	174.0 (4)	C5—C6—C7—S1	−177.7 (3)
C7—C2—C3—C4	3.0 (6)	N2—C2—C7—C6	175.9 (4)
N2—C2—C3—C4	−176.2 (4)	C3—C2—C7—C6	−3.3 (6)
C2—C3—C4—C5	−0.8 (6)	N2—C2—C7—S1	−5.1 (6)
C2—C3—C4—Cl1	178.8 (3)	C3—C2—C7—S1	175.7 (3)
C3—C4—C5—C6	−1.2 (6)	O2—S1—C7—C6	−50.7 (4)
Cl1—C4—C5—C6	179.3 (3)	O1—S1—C7—C6	77.8 (4)
C3—C4—C5—S2	173.5 (3)	N1—S1—C7—C6	−167.7 (3)
Cl1—C4—C5—S2	−6.1 (5)	O2—S1—C7—C2	130.3 (3)
O4—S2—C5—C6	119.6 (3)	O1—S1—C7—C2	−101.1 (4)
O3—S2—C5—C6	−7.7 (4)	N1—S1—C7—C2	13.3 (4)
N3—S2—C5—C6	−124.5 (3)		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H1H···O7	0.95 (6)	1.64 (6)	2.593 (5)	175 (6)
N2—H1N···O6^{i}	0.88 (4)	1.83 (4)	2.690 (4)	166 (5)
O8—H2H···O3	1.10 (6)	2.02 (5)	3.027 (5)	152 (4)

N3—H2N···N1^{ii}	0.94 (5)	2.09 (5)	3.022 (5)	171 (4)
N3—H3N···O7^{iii}	0.76 (5)	2.13 (5)	2.890 (5)	178 (6)

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

Fig. 1

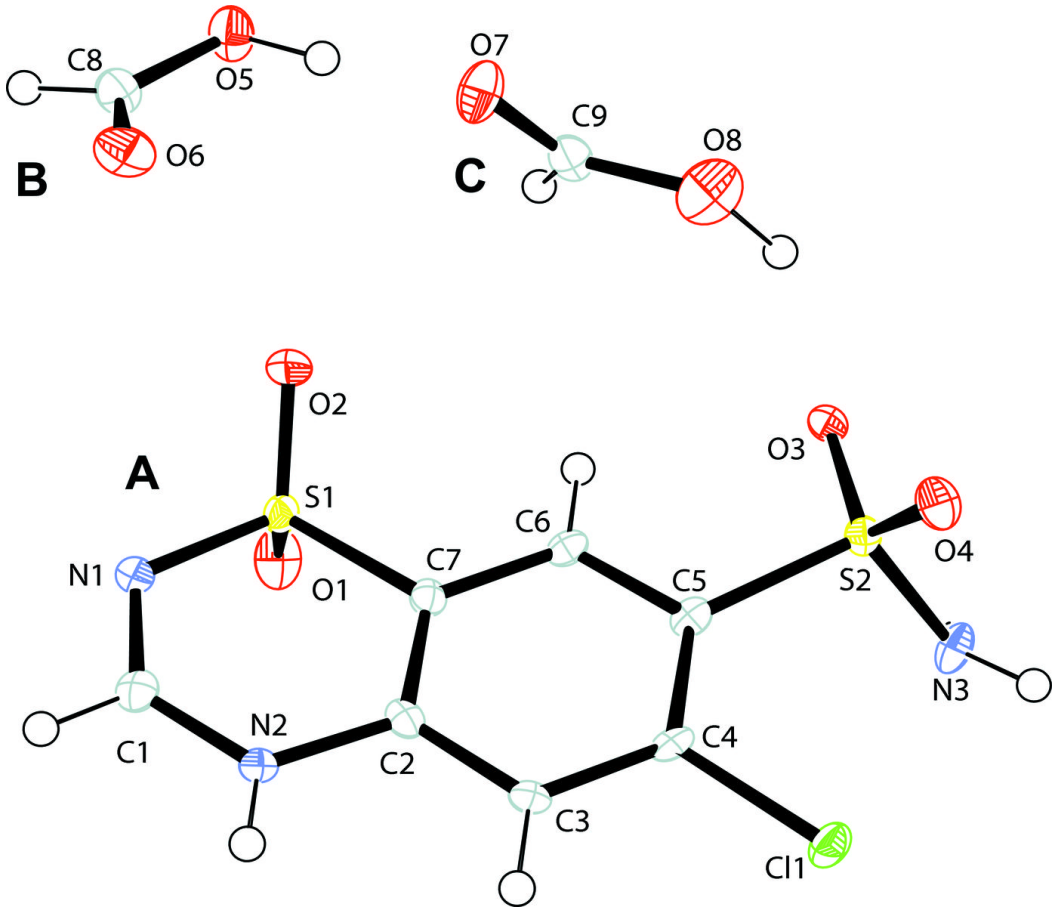
C8
O5
O6
B
O7
C9
O8
C
O2
A
S1
O1
N1
C7
C6
O3
S2
O4
C5
N3
C1
N2
C2
C4
C3
Cl1

Fig. 2