

Acta Crystallographica Section E

Structure Reports

Online

ISSN 1600-5368

Chlordiazepoxide dichloromethane monosolvate

Andreas Fischer

 Division of Applied Physical Chemistry, School of Chemical Science and Engineering, 100 44 Stockholm, Sweden
 Correspondence e-mail: afischer@kth.se

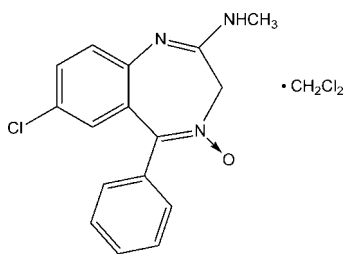
Received 4 March 2012; accepted 5 March 2012

 Key indicators: single-crystal X-ray study; $T = 173$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.040; wR factor = 0.104; data-to-parameter ratio = 18.3.

In the title compound (systematic name: 7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide dichloromethane monosolvate), $\text{C}_{16}\text{H}_{14}\text{ClN}_3\text{O}\cdot\text{CH}_2\text{Cl}_2$, the seven-membered ring adopts a boat conformation with the CH_2 group as the prow and the two aromatic C atoms as the stern. The dihedral angle between the benzene rings is 75.25 (6)°. The crystal structure features centrosymmetric pairs of chlordiazepoxide molecules linked by pairs of $\text{N}-\text{H}\cdots\text{O}$ hydrogen bonds, which generate $R_2^2(12)$ loops.

Related literature

For the synthesis of chlordiazepoxide, see: Sternbach *et al.* (1961). For the structure of chlordiazepoxide, see: Bertolasi *et al.* (1982). For the structure of a second polymorph of chlordiazepoxide, see: Singh *et al.* (1998). For the structure of chlordiazepoxide hydrochloride, see: Herrnstadt *et al.* (1979). For the early history of benzodiazepines, see: Sternbach (1979).



Experimental

Crystal data

 $\text{C}_{16}\text{H}_{14}\text{ClN}_3\text{O}\cdot\text{CH}_2\text{Cl}_2$
 $M_r = 384.69$

 Triclinic, $P\bar{1}$
 $a = 7.8310$ (12) Å

 $b = 9.461$ (2) Å
 $c = 12.6947$ (5) Å
 $\alpha = 94.284$ (11)°
 $\beta = 93.821$ (9)°
 $\gamma = 108.499$ (13)°
 $V = 885.4$ (2) Å³
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.53$ mm⁻¹
 $T = 173$ K
 $0.60 \times 0.33 \times 0.04$ mm

Data collection

 Bruker–Nonius KappaCCD
 diffractometer
 Absorption correction: multi-scan
 SADABS (Sheldrick, 2003)
 $T_{\min} = 0.763$, $T_{\max} = 0.979$

 20348 measured reflections
 4040 independent reflections
 3124 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.034$

Refinement

 $R[F^2 > 2\sigma(F^2)] = 0.040$
 $wR(F^2) = 0.104$
 $S = 1.03$
 4040 reflections
 221 parameters
 1 restraint

 H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\text{max}} = 0.76$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.52$ e Å⁻³
Table 1

Hydrogen-bond geometry (Å, °).

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
$\text{N3}-\text{H3A}\cdots\text{O1}^i$	0.85 (2)	2.08 (2)	2.916 (2)	166 (2)

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

Data collection: COLLECT (Nonius, 1999); cell refinement: DIRAX (Duisenberg, 1992); data reduction: EVALCCD (Duisenberg *et al.*, 2003); program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: DIAMOND (Brandenburg, 2007).; software used to prepare material for publication: publCIF (Westrip, 2010).

The Swedish Research Council is acknowledged for providing funding for the single-crystal diffractometer.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HB6668).

References

- Bertolasi, V., Sacerdoti, M., Gilli, G. & Borea, P. A. (1982). *Acta Cryst.* **B38**, 1768–1772.
- Brandenburg, K. (2007). *DIAMOND*. Crystal Impact GbR, Bonn, Germany.
- Duisenberg, A. J. M. (1992). *J. Appl. Cryst.* **25**, 92–96.
- Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.
- Herrnstadt, C., Mootz, D., Wunderlich, H. & Möhrle, H. (1979). *J. Chem. Soc. Perkin Trans. 2*, pp. 735–740.
- Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
- Sheldrick, G. M. (2003). *SADABS*. University of Göttingen, Germany.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Singh, D., Marshall, P. V., Shields, L. & York, P. (1998). *J. Pharm. Sci.* **87**, 655–662.
- Sternbach, L. H. (1979). *J. Med. Chem.* **22**, 1–7.
- Sternbach, L. H., Reeder, E., Keller, O. & Metlesics, W. (1961). *J. Org. Chem.* **26**, 4488–4497.
- Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.

supplementary materials

Acta Cryst. (2012). E68, o1011 [doi:10.1107/S1600536812009695]

Chlordiazepoxide dichloromethane monosolvate

Andreas Fischer

Comment

Chlordiazepoxide (7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide) was the first benzodiazepine to enter the market as member of a new class of powerful tranquilizers. The crystal structure of the hydrochloride was determined in 1979 (Herrnstadt *et al.*, 1979), the structure of the pure compound in 1982 (Bertolasi *et al.*, 1982). The reason for the study of chlordiazepoxide salts was the presence of three potential protonation sites (Herrnstadt *et al.*, 1979). In order to study a number of different chlordiazepoxide salts, we synthesized the compound according to the description by Sternbach *et al.* (1961). The final step in this synthesis is the crystallization from dichloromethane. It turned out that the crystallization product that forms initially is a chlordiazepoxide dichloromethane solvate, whose structure is described here. The title compound (Fig. 1) features pairs of chlordiazepoxide molecules, which are hydrogen-bonded *via* two symmetry-equivalent N–H \cdots O bonds across an inversion centre (Fig. 2). The same pattern could be found in the hydrochloride (Herrnstadt *et al.*, 1979). In the structure of pure chlordiazepoxide, pairs of molecules of the same chirality (due to the high energy barrier of ring inversion, benzodiazepines are chiral) were observed and it was argued that this arrangement might be more stable than dimers of two different enantiomers. However, this effect must be quite subtle since the only interactions between the chlordiazepoxide and dichloromethane molecules are due to van der Waals forces. The dihedral angle between the two phenyl groups is 75.25 (6) $^\circ$.

Experimental

Chlordiazepoxide was synthesized according to the procedure described by Sternbach *et al.* (1961), starting from commercial 2-amino-5-chlorobenzophenone. Slow evaporation of the solution of the final product in dichloromethane yielded colourless, block-shaped crystals of the title compound. Once removed from the mother liquor, the crystals decomposed slowly (within days), yielding solvent-free chlordiazepoxide.

Refinement

All H atoms except that attached to N were placed at calculated positions and refined riding. The N–H atom was located from the Fourier map and refined with the N–H distance restrained to 0.88 (2) Å.

Computing details

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX* (Duisenberg, 1992); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg, 2007).; software used to prepare material for publication: *pubCIF* (Westrip, 2010).

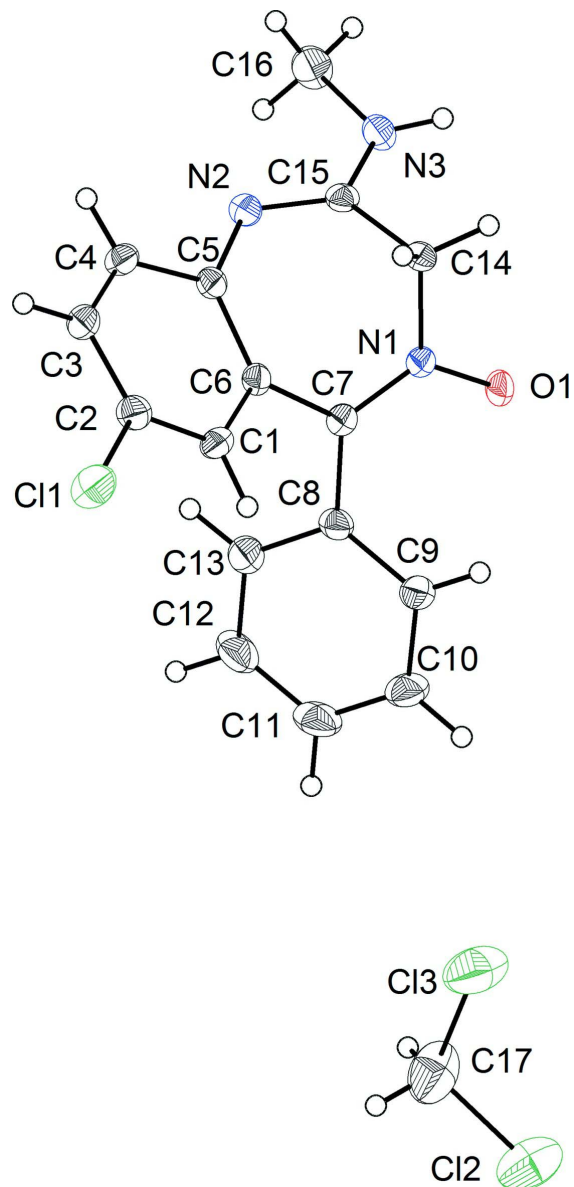
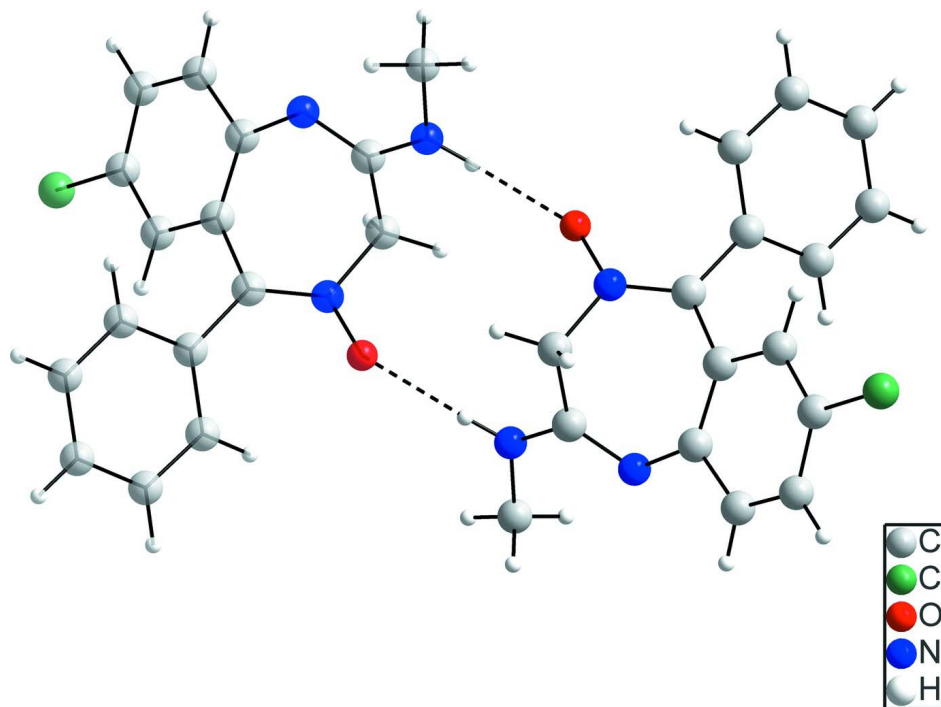


Figure 1

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

**Figure 2**

The centrosymmetric chlordiazepoxide dimers in the title compound. The half-transparent moiety is generated by (i)– $x+1$, $-y+1$, $-z+2$.

7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide dichloromethane monosolvate

Crystal data

$C_{16}H_{14}ClN_3O \cdot CH_2Cl_2$

$M_r = 384.69$

Triclinic, $P\bar{1}$

Hall symbol: $-P\ 1$

$a = 7.8310$ (12) Å

$b = 9.461$ (2) Å

$c = 12.6947$ (5) Å

$\alpha = 94.284$ (11)°

$\beta = 93.821$ (9)°

$\gamma = 108.499$ (13)°

$V = 885.4$ (2) Å³

$Z = 2$

$F(000) = 396$

$D_x = 1.443$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 38 reflections

$\theta = 8.7$ – 19.5 °

$\mu = 0.53$ mm⁻¹

$T = 173$ K

Plate, colourless

$0.60 \times 0.33 \times 0.04$ mm

Data collection

Bruker–Nonius KappaCCD

diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

φ & ω scans

Absorption correction: multi-scan

SADABS (Sheldrick, 2003)

$T_{\min} = 0.763$, $T_{\max} = 0.979$

20348 measured reflections

4040 independent reflections

3124 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.034$

$\theta_{\text{max}} = 27.5$ °, $\theta_{\text{min}} = 4.5$ °

$h = -10 \rightarrow 10$

$k = -12 \rightarrow 12$

$l = -15 \rightarrow 16$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.040$

$wR(F^2) = 0.104$

$S = 1.03$

4040 reflections

221 parameters

1 restraint

Primary atom site location: structure-invariant
direct methods

Secondary atom site location: difference Fourier
map

H atoms treated by a mixture of independent
and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0409P)^2 + 0.7625P]$

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

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

$\Delta\rho_{\max} = 0.76 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.52 \text{ e } \text{\AA}^{-3}$

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.

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

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.4054 (3)	0.0142 (2)	0.68015 (14)	0.0228 (4)
C2	0.4147 (3)	-0.1283 (2)	0.67919 (15)	0.0233 (4)
C3	0.3620 (3)	-0.2137 (2)	0.76314 (15)	0.0229 (4)
C4	0.3110 (2)	-0.1489 (2)	0.85106 (14)	0.0219 (4)
C5	0.3146 (2)	0.00119 (19)	0.85985 (14)	0.0183 (3)
C6	0.3543 (2)	0.08072 (19)	0.76981 (14)	0.0188 (4)
C7	0.3392 (2)	0.23116 (19)	0.76213 (14)	0.0193 (4)
C8	0.2418 (3)	0.2605 (2)	0.66676 (14)	0.0213 (4)
C9	0.3090 (3)	0.3890 (2)	0.61483 (15)	0.0251 (4)
C10	0.2113 (3)	0.4097 (2)	0.52552 (16)	0.0335 (5)
C11	0.0461 (3)	0.3048 (3)	0.48835 (17)	0.0375 (5)
C12	-0.0217 (3)	0.1780 (3)	0.53961 (18)	0.0374 (5)
C13	0.0762 (3)	0.1547 (2)	0.62793 (16)	0.0300 (4)
C14	0.4974 (2)	0.2983 (2)	0.93612 (13)	0.0189 (4)
C15	0.3509 (2)	0.1940 (2)	0.99178 (13)	0.0186 (4)
C16	0.1763 (3)	0.1635 (2)	1.14472 (17)	0.0334 (5)
C17	0.0152 (4)	0.5580 (3)	0.1687 (3)	0.0561 (7)
Cl1	0.50033 (8)	-0.20239 (6)	0.57295 (4)	0.03756 (16)
Cl2	0.04988 (9)	0.72192 (8)	0.10404 (6)	0.0542 (2)
Cl3	0.19167 (10)	0.57040 (9)	0.26233 (6)	0.0620 (2)
O1	0.39853 (18)	0.47104 (13)	0.84472 (10)	0.0218 (3)
N1	0.4092 (2)	0.33547 (16)	0.84073 (11)	0.0176 (3)
N2	0.2700 (2)	0.05504 (17)	0.95575 (12)	0.0203 (3)
N3	0.3075 (2)	0.25397 (18)	1.08078 (12)	0.0227 (3)
H1	0.4336	0.0679	0.6199	0.027*
H3	0.3613	-0.3145	0.7599	0.027*

H4	0.2720	-0.2076	0.9078	0.026*
H9	0.4214	0.4621	0.6407	0.030*
H10	0.2581	0.4963	0.4896	0.040*
H11	-0.0206	0.3202	0.4275	0.045*
H12	-0.1357	0.1066	0.5144	0.045*
H13	0.0303	0.0662	0.6621	0.036*
H14A	0.5617	0.3906	0.9836	0.023*
H14B	0.5862	0.2490	0.9159	0.023*
H16A	0.0613	0.1156	1.1011	0.050*
H16B	0.1578	0.2274	1.2043	0.050*
H16C	0.2211	0.0863	1.1720	0.050*
H17A	-0.0980	0.5380	0.2038	0.067*
H17B	0.0001	0.4723	0.1151	0.067*
H3A	0.379 (3)	0.3395 (19)	1.1074 (17)	0.027*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0312 (10)	0.0182 (9)	0.0194 (9)	0.0079 (8)	0.0027 (7)	0.0051 (7)
C2	0.0296 (10)	0.0209 (9)	0.0205 (9)	0.0104 (8)	0.0026 (7)	0.0002 (7)
C3	0.0275 (10)	0.0175 (9)	0.0247 (9)	0.0094 (8)	-0.0012 (8)	0.0030 (7)
C4	0.0233 (9)	0.0206 (9)	0.0214 (9)	0.0059 (7)	0.0006 (7)	0.0067 (7)
C5	0.0156 (8)	0.0184 (8)	0.0192 (8)	0.0037 (7)	-0.0011 (7)	0.0015 (6)
C6	0.0206 (9)	0.0148 (8)	0.0200 (9)	0.0049 (7)	-0.0020 (7)	0.0013 (6)
C7	0.0209 (9)	0.0169 (8)	0.0197 (9)	0.0055 (7)	0.0009 (7)	0.0028 (6)
C8	0.0288 (10)	0.0192 (9)	0.0178 (9)	0.0117 (8)	-0.0014 (7)	-0.0008 (7)
C9	0.0343 (11)	0.0206 (9)	0.0209 (9)	0.0100 (8)	0.0001 (8)	0.0017 (7)
C10	0.0522 (14)	0.0285 (10)	0.0247 (10)	0.0199 (10)	-0.0009 (9)	0.0070 (8)
C11	0.0535 (15)	0.0380 (12)	0.0262 (11)	0.0260 (11)	-0.0128 (10)	0.0004 (9)
C12	0.0385 (13)	0.0344 (12)	0.0349 (12)	0.0114 (10)	-0.0164 (10)	-0.0044 (9)
C13	0.0361 (12)	0.0227 (10)	0.0292 (10)	0.0087 (9)	-0.0062 (9)	0.0024 (8)
C14	0.0175 (9)	0.0201 (9)	0.0175 (8)	0.0044 (7)	-0.0028 (7)	0.0023 (7)
C15	0.0166 (8)	0.0221 (9)	0.0165 (8)	0.0058 (7)	-0.0015 (7)	0.0038 (7)
C16	0.0309 (11)	0.0362 (11)	0.0273 (11)	0.0018 (9)	0.0105 (9)	-0.0007 (8)
C17	0.0338 (14)	0.0492 (15)	0.085 (2)	0.0101 (12)	0.0003 (13)	0.0207 (14)
Cl1	0.0618 (4)	0.0276 (3)	0.0305 (3)	0.0216 (2)	0.0185 (2)	0.00376 (19)
Cl2	0.0412 (3)	0.0717 (5)	0.0646 (4)	0.0315 (3)	0.0154 (3)	0.0322 (3)
Cl3	0.0553 (4)	0.0777 (5)	0.0559 (4)	0.0205 (4)	0.0033 (3)	0.0317 (4)
O1	0.0268 (7)	0.0131 (6)	0.0243 (7)	0.0060 (5)	-0.0019 (5)	-0.0003 (5)
N1	0.0189 (7)	0.0153 (7)	0.0183 (7)	0.0051 (6)	0.0001 (6)	0.0026 (5)
N2	0.0203 (8)	0.0206 (8)	0.0185 (7)	0.0048 (6)	0.0013 (6)	0.0018 (6)
N3	0.0214 (8)	0.0231 (8)	0.0203 (8)	0.0036 (7)	0.0013 (6)	-0.0015 (6)

Geometric parameters (\AA , $^\circ$)

C1—C2	1.372 (3)	C16—N3	1.451 (3)
C1—C6	1.402 (2)	C17—Cl3	1.730 (3)
C2—C3	1.391 (3)	C17—Cl2	1.762 (3)
C2—Cl1	1.7428 (19)	O1—N1	1.3090 (18)
C3—C4	1.376 (3)	C1—H1	0.9500

C4—C5	1.407 (2)	C3—H3	0.9500
C5—N2	1.393 (2)	C4—H4	0.9500
C5—C6	1.413 (2)	C9—H9	0.9500
C6—C7	1.475 (2)	C10—H10	0.9500
C7—N1	1.306 (2)	C11—H11	0.9500
C7—C8	1.478 (2)	C12—H12	0.9500
C8—C13	1.394 (3)	C13—H13	0.9500
C8—C9	1.396 (3)	C14—H14A	0.9900
C9—C10	1.386 (3)	C14—H14B	0.9900
C10—C11	1.384 (3)	C16—H16A	0.9800
C11—C12	1.380 (3)	C16—H16B	0.9800
C12—C13	1.387 (3)	C16—H16C	0.9800
C14—N1	1.474 (2)	C17—H17A	0.9900
C14—C15	1.511 (2)	C17—H17B	0.9900
C15—N2	1.297 (2)	N3—H3A	0.854 (16)
C15—N3	1.338 (2)		
C2—C1—C6	120.20 (16)	C6—C1—H1	119.9
C1—C2—C3	121.22 (17)	C4—C3—H3	120.7
C1—C2—C11	119.68 (14)	C2—C3—H3	120.7
C3—C2—C11	119.07 (14)	C3—C4—H4	118.8
C4—C3—C2	118.55 (16)	C5—C4—H4	118.8
C3—C4—C5	122.33 (16)	C10—C9—H9	120.1
N2—C5—C4	116.32 (15)	C8—C9—H9	120.1
N2—C5—C6	126.13 (16)	C11—C10—H10	119.8
C4—C5—C6	117.48 (16)	C9—C10—H10	119.8
C1—C6—C5	119.75 (16)	C12—C11—H11	120.0
C1—C6—C7	116.61 (15)	C10—C11—H11	120.0
C5—C6—C7	123.60 (16)	C11—C12—H12	120.0
N1—C7—C6	119.34 (16)	C13—C12—H12	120.0
N1—C7—C8	121.14 (15)	C12—C13—H13	119.8
C6—C7—C8	119.51 (15)	C8—C13—H13	119.8
C13—C8—C9	119.24 (17)	N1—C14—H14A	110.2
C13—C8—C7	118.08 (16)	C15—C14—H14A	110.2
C9—C8—C7	122.68 (17)	N1—C14—H14B	110.2
C10—C9—C8	119.88 (19)	C15—C14—H14B	110.2
C11—C10—C9	120.4 (2)	H14A—C14—H14B	108.5
C12—C11—C10	120.04 (19)	N3—C16—H16A	109.5
C11—C12—C13	120.1 (2)	N3—C16—H16B	109.5
C12—C13—C8	120.31 (19)	H16A—C16—H16B	109.5
N1—C14—C15	107.42 (14)	N3—C16—H16C	109.5
N2—C15—N3	121.51 (16)	H16A—C16—H16C	109.5
N2—C15—C14	122.57 (16)	H16B—C16—H16C	109.5
N3—C15—C14	115.91 (16)	C13—C17—H17A	109.0
C13—C17—C12	112.88 (15)	C12—C17—H17A	109.0
C7—N1—O1	124.88 (15)	C13—C17—H17B	109.0
C7—N1—C14	118.94 (14)	C12—C17—H17B	109.0
O1—N1—C14	116.05 (13)	H17A—C17—H17B	107.8
C15—N2—C5	118.83 (15)	C15—N3—H3A	117.0 (15)

C15—N3—C16	121.24 (16)	C16—N3—H3A	119.7 (15)
C2—C1—H1	119.9		

Hydrogen-bond geometry (Å, °)

<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>
N3—H3A \cdots O1 ⁱ	0.85 (2)	2.08 (2)	2.916 (2)	166 (2)

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