Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(1*S**,5*R**)-9-Phenyl-9-azabicyclo[3.3.1]-nonan-3-one

Zhen-ju Jiang,[a] Qi He,[a] Zhen Li[b] and Zhou-yu Wang[a]*

[a]Department of Pharmaceutics Engineering, Xihua University, Chengdu 610039, People's Republic of China, and [b]Research Institute of Natural Gas Economy, Petrochina Oil and Gas Field Company, Chengdu 610051, People's Republic of China
Correspondence e-mail: zhouyuwang77@gmail.com

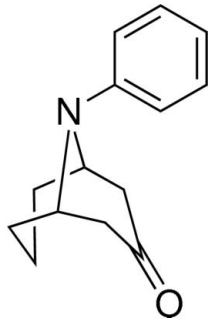
Received 1 March 2012; accepted 4 May 2012

Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.003 Å; R factor = 0.043; wR factor = 0.092; data-to-parameter ratio = 15.3.

In the title compound, $C_{14}H_{17}NO$, the piperidinone and piperidine rings both adopt a chair conformation. The chiral crystals were obtained from a racemic reaction product *via* spontaneous resolution.

Related literature

For the synthesis, see: Zhang (2003). For applications of the compound, see: Vernekar *et al.* (2010); Lazny *et al.* (2011). For puckering analysis, see: Cremer & Pople (1975).



Experimental

Crystal data

$C_{14}H_{17}NO$
M_r = 215.29
Orthorhombic, $P2_12_12_1$
a = 9.4028 (3) Å
b = 10.2524 (5) Å
c = 12.0473 (6) Å
V = 1161.38 (9) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 293 K
0.40 × 0.40 × 0.35 mm

Data collection

Agilent Xcalibur Eos diffractometer
Absorption correction: multi-scan (*ABSPACK* in *CrysAlis PRO*; Agilent, 2011)
T_{min} = 0.918, T_{max} = 1.000
3285 measured reflections
2218 independent reflections
1722 reflections with $I > 2\sigma(I)$
R_{int} = 0.015

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.092
S = 1.02
2218 reflections
145 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.12 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-3}

Data collection: *CrysAlis PRO* (Agilent, 2011); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2*.

This work was supported by the Open Fund of the Key Laboratory of Sichuan Province (grant No. Szjj2011-005) and the Research Fund of the Key Laboratory of TCM Biotechnology (Xihua University).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: FY2049).

References

Agilent (2011). *CrysAlis PRO*. Agilent Technologies UK Ltd, Yarnton, Oxfordshire, England.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
Lazny, R., Wolosewicz, K., Zielinska, P., Lipkowska, Z. U. & Kalicki, P. (2011). *Tetrahedron*, **67**, 9433–9439.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Vernekar, S. K. V., Hallaq, H. Y., Clarkson, G., Thompson, A. J., Silvestri, L., Lummis, S. C. R. & Lochner, M. (2010). *J. Med. Chem.* **53**, 2324–2328.
Zhang, Y. (2003). CN Patent 1451660A.

supplementary materials

Acta Cryst. (2012). E**68**, o1691 [doi:10.1107/S1600536812020065]

(1*S**,5*R**)-9-Phenyl-9-azabicyclo[3.3.1]nonan-3-one

Zhen-ju Jiang, Qi He, Zhen Li and Zhou-yu Wang

Comment

The compound 1*S**,5*R**-9-phenyl-9-aza-bicyclo[3.3.1]nonan-3-one is an important intermediate for synthesizing granisetron derivatives. The bicyclic skeleton of 9-azabicyclo[3.3.1]nonane is a key substructure of a variety of bioactive compounds (Vernekar *et al.*, 2010; Lazny *et al.*, 2011). The racemic title compound was synthesized by the Mannich reaction and spontaneous resolution occurred on recrystallization from a mixture of ethyl acetate and petroleum ether.

In the title structure the N1/C1—C5 piperidinone ring adopts a chair conformation with puckering parameters (Cremer & Pople, 1975): Q = 0.5159 (3) Å, θ = 158.26 (3)° and φ = 173.0692 (12)°. The N1/C1/C8—C5 piperidine ring has a chair conformation, too [Q = 0.5727 (3) Å, θ = 7.74 (12)° and φ = 23.8669 (13)°]. The relative configuration of C1 and C5 is S*, *R** respectively.

Experimental

To a stirred solution of glutaraldehyde (1.32 ml, 5 mmol) and aniline (0.55 ml,6 mmol) in water (10 ml), 3-oxopentane-dioic acid (0.88 g,6 mmol) was added. The mixture was stirred overnight at room temperature. Then the pH was adjusted to 5 with aq. HCl and the mixture was refluxed for another one hour. Then sodium hydroxide was added to increase the pH to 9. The mixture was extracted with ethyl-acetate. The combined extract was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*. The residue was purified through column chromatography on silica gel (eluent: hexane/EtOAc = 4/1) to give 9-phenyl-9-aza-bicyclo[3.3.1]nonan-3-one. Then the racemic mixture was crystallized from a solution in a 1:10 (*v*/*v*) mixture of ethyl acetate and petroleum ether to produce the title compound.

Refinement

All H atoms were positioned geometrically and treated using a riding model, fixing the bond lengths at 0.97 Å for aliphatic CH, 0.98 Å for CH_2 and 0.93 Å for aromatic CH groups, respectively. The displacement parameters of the H atoms were constrained with $U_{iso}(H) = 1.2U_{eq}(C)$. In the absence of significant anomalous scattering effects, the absolute configuration is not determined.

Computing details

Data collection: *CrysAlis PRO* (Agilent, 2011); cell refinement: *CrysAlis PRO* (Agilent, 2011); data reduction: *CrysAlis PRO* (Agilent, 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: OLEX2 (Dolomanov *et al.*, 2009); software used to prepare material for publication: OLEX2 (Dolomanov *et al.*, 2009).

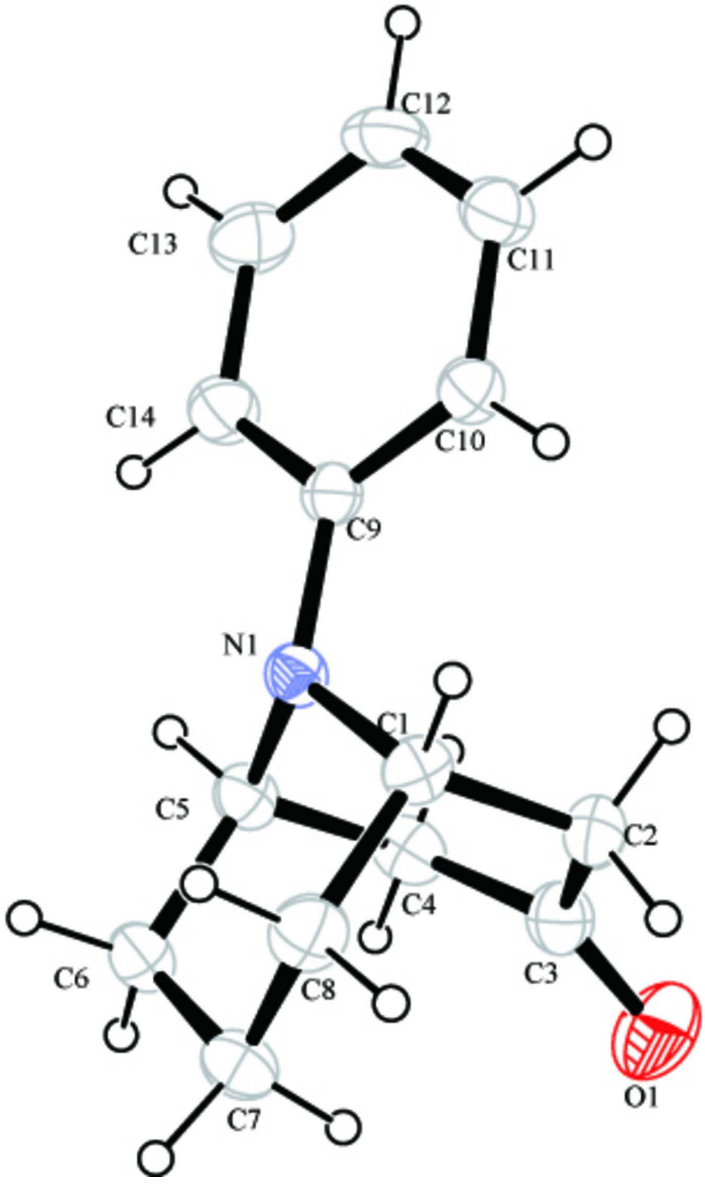


Figure 1

The molecular structure of the title compound.

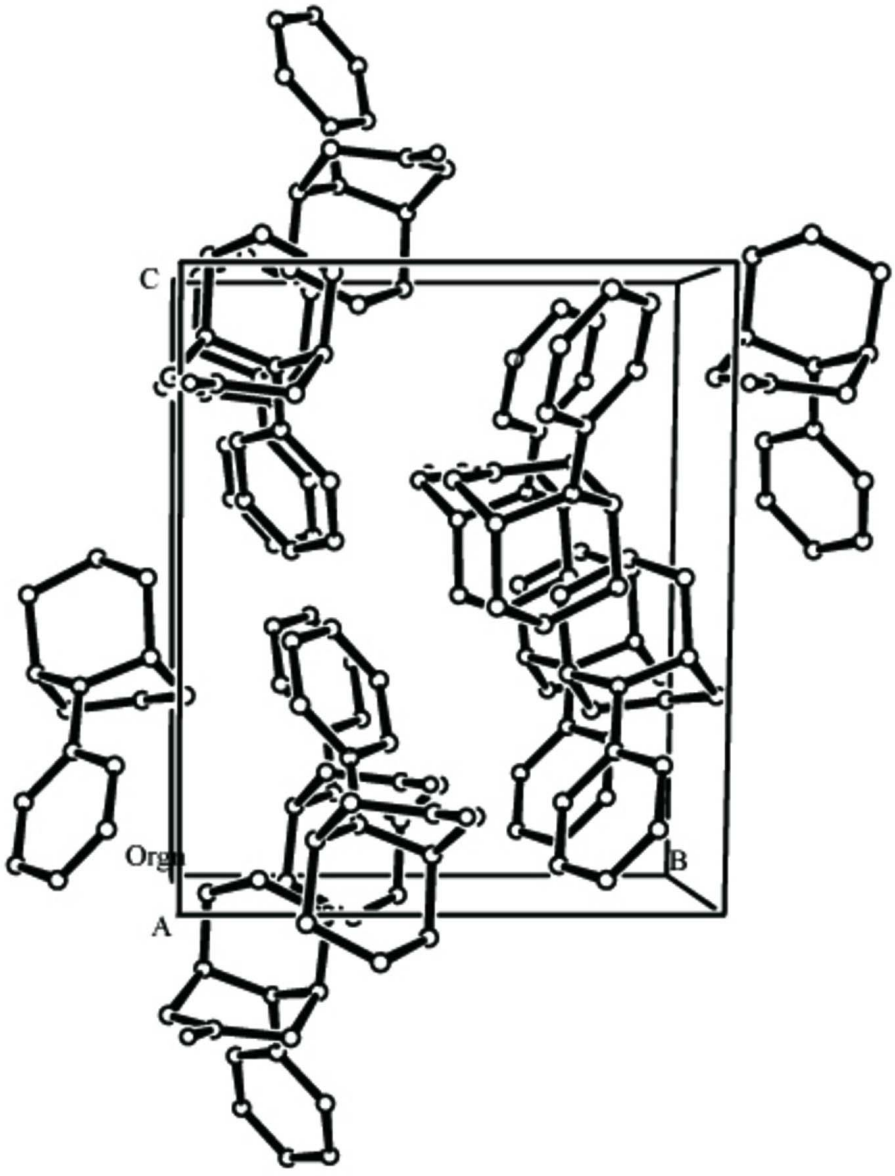


Figure 2

A packing diagram for the title compound.

(1*S,5*R**)-9-Phenyl-9-azabicyclo[3.3.1]nonan-3-one**

Crystal data

$C_{14}H_{17}NO$
$M_r = 215.29$
Orthorhombic, $P2_12_12_1$
$a = 9.4028$ (3) Å
$b = 10.2524$ (5) Å
$c = 12.0473$ (6) Å
$V = 1161.38$ (9) Å^3
$Z = 4$
$F(000) = 464$
$D_x = 1.231$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.7107$ Å
Cell parameters from 1237 reflections
$\theta = 2.9$–$29.0°$
$\mu = 0.08$ mm^{-1}
$T = 293$ K
Block, colourless
0.40 × 0.40 × 0.35 mm

Data collection

Agilent Xcalibur Eos diffractometer
Radiation source: Enhance (Mo) X-ray Source
Graphite monochromator
Detector resolution: 16.0874 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (ABSPACK in *CrysAlis PRO*; Agilent, 2011)
T_{min} = 0.918, T_{max} = 1.000
3285 measured reflections
2218 independent reflections
1722 reflections with $I > 2\sigma(I)$
R_{int} = 0.015
θ_{max} = 26.4°, θ_{min} = 2.9°
h = −11→7
k = −9→12
l = −8→15

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.092
S = 1.02
2218 reflections
145 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0394P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.12 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
O1	−0.58709 (17)	−0.01586 (16)	−0.68342 (15)	0.0838 (6)
N1	−0.19284 (14)	−0.18245 (14)	−0.65084 (12)	0.0368 (4)
C1	−0.31907 (18)	−0.26416 (18)	−0.63463 (16)	0.0409 (5)
H1	−0.2985	−0.3506	−0.6653	0.049*
C2	−0.4480 (2)	−0.20832 (19)	−0.69713 (16)	0.0472 (5)
H2A	−0.4367	−0.2265	−0.7757	0.057*
H2B	−0.5329	−0.2532	−0.6721	0.057*
C3	−0.4692 (2)	−0.0642 (2)	−0.68231 (16)	0.0510 (6)
C4	−0.3376 (2)	0.01633 (18)	−0.67070 (17)	0.0489 (5)
H4A	−0.3618	0.0971	−0.6332	0.059*
H4B	−0.3032	0.0386	−0.7442	0.059*
C5	−0.2173 (2)	−0.05077 (18)	−0.60634 (17)	0.0412 (5)
H5	−0.1302	0.0001	−0.6174	0.049*
C6	−0.2468 (2)	−0.0573 (2)	−0.48223 (17)	0.0494 (5)
H6A	−0.1612	−0.0854	−0.4442	0.059*
H6B	−0.2703	0.0293	−0.4556	0.059*

C7	−0.3672 (2)	−0.1497 (2)	−0.45334 (16)	0.0522 (6)
H7A	−0.3705	−0.1626	−0.3736	0.063*
H7B	−0.4571	−0.1122	−0.4766	0.063*
C8	−0.3452 (2)	−0.2797 (2)	−0.51068 (17)	0.0510 (5)
H8A	−0.4286	−0.3338	−0.4994	0.061*
H8B	−0.2646	−0.3239	−0.4774	0.061*
C9	−0.11420 (18)	−0.19480 (18)	−0.75009 (15)	0.0363 (4)
C10	−0.1472 (2)	−0.28634 (19)	−0.83142 (16)	0.0435 (5)
H10	−0.2261	−0.3400	−0.8221	0.052*
C11	−0.0647 (2)	−0.2989 (2)	−0.92593 (16)	0.0537 (6)
H11	−0.0896	−0.3602	−0.9794	0.064*
C12	0.0534 (2)	−0.2223 (2)	−0.94206 (16)	0.0597 (6)
H12	0.1084	−0.2308	−1.0058	0.072*
C13	0.0880 (2)	−0.1329 (2)	−0.8617 (2)	0.0605 (6)
H13	0.1680	−0.0807	−0.8712	0.073*
C14	0.0069 (2)	−0.1187 (2)	−0.76732 (18)	0.0497 (5)
H14	0.0333	−0.0574	−0.7142	0.060*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0585 (9)	0.0818 (13)	0.1110 (16)	0.0252 (10)	−0.0147 (10)	0.0074 (12)
N1	0.0385 (8)	0.0357 (8)	0.0362 (9)	−0.0040 (7)	0.0001 (7)	−0.0009 (7)
C1	0.0411 (10)	0.0361 (10)	0.0455 (12)	−0.0027 (9)	0.0024 (9)	0.0022 (9)
C2	0.0401 (10)	0.0537 (12)	0.0478 (13)	−0.0053 (10)	−0.0056 (9)	−0.0027 (11)
C3	0.0514 (12)	0.0589 (13)	0.0428 (13)	0.0091 (12)	−0.0071 (10)	0.0064 (11)
C4	0.0646 (13)	0.0389 (10)	0.0431 (12)	0.0059 (11)	0.0016 (11)	0.0032 (9)
C5	0.0461 (11)	0.0371 (10)	0.0405 (11)	−0.0071 (9)	0.0010 (9)	−0.0024 (9)
C6	0.0536 (11)	0.0577 (13)	0.0370 (12)	0.0021 (11)	−0.0035 (10)	−0.0052 (11)
C7	0.0590 (13)	0.0634 (13)	0.0343 (11)	−0.0013 (11)	0.0053 (10)	0.0057 (10)
C8	0.0501 (12)	0.0536 (12)	0.0494 (12)	−0.0058 (11)	0.0045 (10)	0.0128 (11)
C9	0.0371 (9)	0.0379 (10)	0.0340 (10)	0.0052 (9)	−0.0020 (8)	0.0040 (9)
C10	0.0425 (10)	0.0446 (11)	0.0434 (11)	0.0035 (10)	−0.0026 (9)	−0.0023 (10)
C11	0.0581 (13)	0.0581 (14)	0.0450 (13)	0.0129 (12)	−0.0016 (11)	−0.0081 (11)
C12	0.0618 (14)	0.0737 (16)	0.0436 (13)	0.0145 (13)	0.0173 (12)	0.0027 (12)
C13	0.0533 (13)	0.0651 (15)	0.0630 (16)	−0.0072 (12)	0.0156 (12)	0.0051 (13)
C14	0.0495 (11)	0.0528 (13)	0.0467 (13)	−0.0078 (11)	0.0043 (10)	−0.0023 (10)

Geometric parameters (Å, º)

O1—C3	1.215 (2)	C6—C7	1.517 (3)
N1—C1	1.466 (2)	C7—H7A	0.9700
N1—C5	1.471 (2)	C7—H7B	0.9700
N1—C9	1.412 (2)	C7—C8	1.516 (3)
C1—H1	0.9800	C8—H8A	0.9700
C1—C2	1.537 (3)	C8—H8B	0.9700
C1—C8	1.522 (3)	C9—C10	1.392 (3)
C2—H2A	0.9700	C9—C14	1.396 (3)
C2—H2B	0.9700	C10—H10	0.9300
C2—C3	1.501 (3)	C10—C11	1.384 (3)

C3—C4	1.494 (3)	C11—H11	0.9300
C4—H4A	0.9700	C11—C12	1.374 (3)
C4—H4B	0.9700	C12—H12	0.9300
C4—C5	1.534 (3)	C12—C13	1.373 (3)
C5—H5	0.9800	C13—H13	0.9300
C5—C6	1.522 (3)	C13—C14	1.376 (3)
C6—H6A	0.9700	C14—H14	0.9300
C6—H6B	0.9700		

C1—N1—C5	110.46 (14)	C7—C6—C5	112.88 (17)
C9—N1—C1	119.07 (15)	C7—C6—H6A	109.0
C9—N1—C5	118.22 (14)	C7—C6—H6B	109.0
N1—C1—H1	107.9	C6—C7—H7A	109.6
N1—C1—C2	111.11 (15)	C6—C7—H7B	109.6
N1—C1—C8	108.76 (15)	H7A—C7—H7B	108.2
C2—C1—H1	107.9	C8—C7—C6	110.08 (16)
C8—C1—H1	107.9	C8—C7—H7A	109.6
C8—C1—C2	113.10 (16)	C8—C7—H7B	109.6
C1—C2—H2A	108.7	C1—C8—H8A	109.2
C1—C2—H2B	108.7	C1—C8—H8B	109.2
H2A—C2—H2B	107.6	C7—C8—C1	112.14 (16)
C3—C2—C1	114.39 (17)	C7—C8—H8A	109.2
C3—C2—H2A	108.7	C7—C8—H8B	109.2
C3—C2—H2B	108.7	H8A—C8—H8B	107.9
O1—C3—C2	121.5 (2)	C10—C9—N1	122.68 (16)
O1—C3—C4	122.1 (2)	C10—C9—C14	117.02 (18)
C4—C3—C2	116.42 (18)	C14—C9—N1	120.20 (17)
C3—C4—H4A	108.7	C9—C10—H10	119.4
C3—C4—H4B	108.7	C11—C10—C9	121.13 (19)
C3—C4—C5	114.20 (16)	C11—C10—H10	119.4
H4A—C4—H4B	107.6	C10—C11—H11	119.5
C5—C4—H4A	108.7	C12—C11—C10	121.1 (2)
C5—C4—H4B	108.7	C12—C11—H11	119.5
N1—C5—C4	110.04 (15)	C11—C12—H12	120.9
N1—C5—H5	108.0	C13—C12—C11	118.28 (19)
N1—C5—C6	110.25 (16)	C13—C12—H12	120.9
C4—C5—H5	108.0	C12—C13—H13	119.3
C6—C5—C4	112.44 (16)	C12—C13—C14	121.5 (2)
C6—C5—H5	108.0	C14—C13—H13	119.3
C5—C6—H6A	109.0	C9—C14—H14	119.5
C5—C6—H6B	109.0	C13—C14—C9	121.0 (2)
H6A—C6—H6B	107.8	C13—C14—H14	119.5

O1—C3—C4—C5	146.4 (2)	C5—N1—C1—C2	61.85 (19)
N1—C1—C2—C3	−46.2 (2)	C5—N1—C1—C8	−63.28 (19)
N1—C1—C8—C7	58.9 (2)	C5—N1—C9—C10	−142.12 (17)
N1—C5—C6—C7	−54.0 (2)	C5—N1—C9—C14	41.6 (2)
N1—C9—C10—C11	−177.64 (17)	C5—C6—C7—C8	49.0 (2)
N1—C9—C14—C13	177.52 (18)	C6—C7—C8—C1	−51.6 (2)

C1—N1—C5—C4	−63.47 (19)	C8—C1—C2—C3	76.4 (2)
C1—N1—C5—C6	61.12 (19)	C9—N1—C1—C2	−79.9 (2)
C1—N1—C9—C10	−3.3 (2)	C9—N1—C1—C8	155.02 (16)
C1—N1—C9—C14	−179.62 (16)	C9—N1—C5—C4	78.60 (18)
C1—C2—C3—O1	−148.4 (2)	C9—N1—C5—C6	−156.81 (15)
C1—C2—C3—C4	34.0 (2)	C9—C10—C11—C12	0.7 (3)
C2—C1—C8—C7	−65.0 (2)	C10—C9—C14—C13	1.0 (3)
C2—C3—C4—C5	−35.9 (2)	C10—C11—C12—C13	0.2 (3)
C3—C4—C5—N1	49.8 (2)	C11—C12—C13—C14	−0.4 (3)
C3—C4—C5—C6	−73.5 (2)	C12—C13—C14—C9	−0.2 (3)
C4—C5—C6—C7	69.2 (2)	C14—C9—C10—C11	−1.2 (3)