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Crystal structure of 4,4′-bis[3-(piperidin-1-yl)prop-1-yn-1-yl]-1,1′-biphenyl

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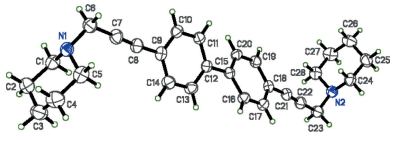
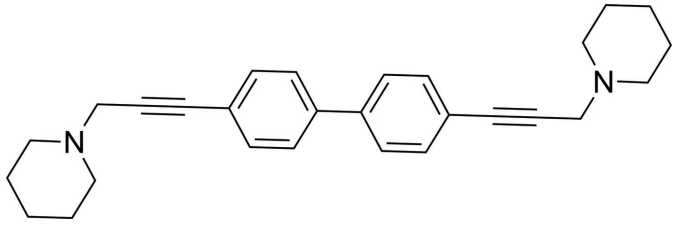
The title compound, $C_{28}H_{32}N_2$, (I), is one of a second generation of compounds designed and synthesized based on a very potent and selective $\alpha9\alpha10$ nicotinic acetylcholine receptor antagonist ZZ161C {1,1′-[[1,1′-biphenyl]-4,4′-diylbis-(prop-2-yne-3,1-diyl)]bis(3,4-dimethylpyridin-1-ium) bromide}, which has shown analgesic effects in a chemotherapy-induced neuropathy animal model. Compound (I) was synthesized by the reaction of 4,4′-bis(3-bromoprop-1-yn-1-yl)-1,1′-biphenyl with piperidine at room temperature in acetonitrile. The single-crystal used for X-ray analysis was obtained by dissolving (I) in a mixture of dichloromethane and methanol, followed by slow evaporation of the solvent. In the crystal of (I), the biphenyl moiety has a twisted conformation, with a dihedral angle of 25.93 (4)° between the benzene rings. Both piperidine head groups in (I) are in the chair conformation and are oriented so that the N-atom lone pairs of each piperidine group point away from the central biphenyl moiety.

1. Chemical context

The $\alpha9\alpha10$ nicotinic acetylcholine receptor is a novel therapeutic target with potential significance for pain management. Previous studies have shown that antagonism of the $\alpha9\alpha10$ nAChR by the non-peptide small molecule, ZZ161C {10-[(1,1′-biphenyl)-4,4′-diyl *bis*(prop-2-yne-3,1-diyl)]*bis*(3,4-dimethylpyridin-1-ium) bromide} produced analgesia in the vincristine-induced neuropathic pain model in rats (Zheng *et al.*, 2011; Wala *et al.*, 2012). In order to improve the drug-like and pharmacokinetic properties of ZZ161C, the title compound (I) was designed and synthesized. Compound (I) is a biphenyl system with ethynyl appendages at the 4 and 4′ positions, as in ZZ161C, but the terminal aza-aromatic rings have been replaced by piperidine moieties. Single-crystal X-ray analysis of compound (I) was used to determine the structural conformation of the compound.





2. Structural commentary

The title compound (I) is shown in Fig. 1. X-ray crystallographic study was conducted in order to determine the geometry of the biphenyl system as well as to obtain detailed information about the conformation of the terminal piperidine groups. In compound (I), the biphenyl rings (C9-C14) and (C15-C20) are non-coplanar, with a dihedral angle of 25.93 (4)° between them. The torsion angles of the ethynyl groups between the planes of the phenyl rings and the piperidine ring N atoms are 167.49 (9) and 34.01 (12)° (defined by atoms N1/C6/C9/C10, N2/C23/C18/C19, respectively). The lone pair on each N atom is oriented away from the biphenyl core of the molecule.

3. Supramolecular features

Aside from weak van der Waals interactions, there are no noteworthy intermolecular contacts in (I). The molecules pack into layers in the *ab* plane bounded top and bottom by piperidine groups, which in turn stack along *c*.

4. Database survey

A search of the November 2014 release of the Cambridge Structure Database (Groom *et al.*, 2016), with updates through May 2015, using the program *Mogul* (Bruno *et al.*, 2004) for 4,4′-substituted biphenyl fragments was conducted. The search was restricted to purely organic, solvent-free structures with R <5% and Cl as the heaviest element. There were over 1000 hits, which produced a bimodal distribution of biphenyl torsion angles with a tight peak at 0° and a broader peak centred at 30°. Therefore the biphenyl torsion angle in (I) is not unusual.

5. Synthesis and crystallization

Synthetic procedure: The intermediate 4,4′-bis(3-bromoprop-1-yn-1-yl)-1,1′-biphenyl (Wan *et al.*, 2015) was obtained utilizing a previously reported procedure; compound (I) was synthesized by reacting piperidine with this intermediate.

To a suspension of 4,4′-*bis*(3-bromoprop-1-yn-1-yl)-1,1′-biphenyl (100.0 mg, 0.26 mmol) in acetonitrile (7 mL), piperidine (66.4 mg, 0.78 mmol) was added at room temperature and the mixture was stirred continuously for 2 h, resulting in the formation of compound (I). Acetonitrile was removed under vacuum and the mixture was partitioned between water (50 mL) and dichloromethane (50 mL). The dichloromethane layer was collected and dried over anhydrous sodium sulfate. Sodium sulfate was removed by filtration, and the filtrate containing crude (I) was concentrated and purified by column chromatography (dichloromethane/methanol) to afford pure compound (I) in 80% yield.

Crystallization: Light-yellow crystals of compound (I) suitable for X-ray analysis were grown in a mixture of dichloromethane and methanol (2:1) by slow evaporation of the solvent at room temperature over a period of 24 h.

^{1}H-NMR (400 Mz, $CDCl_3$): δ 7.51 (*q*, 8H), 3.53 (*s*, 4H), 2.62 (*s*, 8H), 1.65–1.71 (*m*, 8H), 1.47 (*s*, 4H) ppm.

^{1}C-NMR (100 Mz, $CDCl_3$): δ 140.07, 132.35, 126.91, 122.54, 85.25, 53.56, 48.62, 25.93, 23.93 ppm.

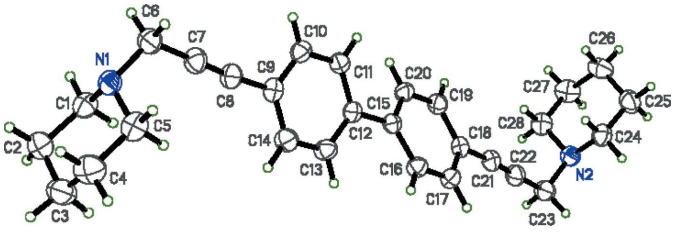


Figure 1
The molecular structure of (I), with ellipsoids drawn at the 50% probability level.

Table 1
Experimental details.

Crystal data	
Chemical formula	$C_{28}H_{32}N_2$
M_r	396.55
Crystal system, space group	Monoclinic, *C*2/*c*
Temperature (K)	210
a, *b*, *c* (Å)	40.2728 (8), 6.9679 (1), 16.0119 (3)
β (°)	92.588 (1)
V (Å^3)	4488.63 (14)
Z	8
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.51
Crystal size (mm)	0.25 × 0.24 × 0.05
Data collection	
Diffractometer	Bruker X8 Proteum diffractometer
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.822, 0.942
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	28464, 4089, 3656
R_{int}	0.040
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.603
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.038, 0.120, 1.08
No. of reflections	4089
No. of parameters	272
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.15, −0.14

Computer programs: *APEX2* and *SAINT* (Bruker, 2006), *SHELXS* (Sheldrick, 2008), *SHELXL2014* (Sheldrick, 2015), *SHELXTL* and *XP* in *SHELXTL* (Sheldrick, 2008) and *CIFFIX* (Parkin, 2013).

6. Refinement details

Crystal data, data collection and structure refinement details are summarized in Table 1. H atoms were found in difference-Fourier maps, but subsequently included in the refinement using riding models, with constrained distances set to 0.94 Å (Csp^2—H) and 0.98 Å (R_2—CH_2). U_{iso}(H) values were set to 1.2U_{eq} of the attached carbon atom.

Acknowledgements

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Computing details

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2006); data reduction: *SAINT* (Bruker, 2006); program(s) used to solve structure: *SHELXS* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008) and *CIFFIX* (Parkin, 2013).

4,4′-Bis[3-(piperidin-1-yl)prop-1-yn-1-yl]-1,1′-biphenyl

Crystal data

$C_{28}H_{32}N_2$
M_r = 396.55
Monoclinic, *C*2/*c*
a = 40.2728 (8) Å
b = 6.9679 (1) Å
c = 16.0119 (3) Å
β = 92.588 (1)°
V = 4488.63 (14) Å^3
Z = 8
F(000) = 1712
D_x = 1.174 Mg m^{-3}
Cu *Kα* radiation, *λ* = 1.54178 Å
Cell parameters from 9828 reflections
θ = 2.2–68.5°
μ = 0.51 mm^{-1}
T = 210 K
Plate, light yellow
0.25 × 0.24 × 0.05 mm

Data collection

Bruker X8 Proteum diffractometer
Radiation source: fine-focus rotating anode
Detector resolution: 5.6 pixels mm^{-1}
φ and *ω* scans
Absorption correction: multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min} = 0.822, T_{max} = 0.942
28464 measured reflections
4089 independent reflections
3656 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 68.5°, θ_{min} = 2.2°
h = −48→48
k = −8→7
l = −12→19

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.120
S = 1.08
4089 reflections
272 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: difference Fourier map
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0642P)^2 + 1.3326P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL2014* (Sheldrick, 2015), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.00034 (8)

Special details

Experimental. The crystal was mounted using polyisobutene oil on the tip of a fine glass fibre, which was fastened in a copper mounting pin with electrical solder. It was placed directly into the cold gas stream of a liquid-nitrogen based cryostat (Hope, 1994; Parkin & Hope, 1998).
At 90K the diffraction pattern showed some diffuse scatter and the Bragg diffraction spots were fuzzy. Visual inspection of crystal integrity and diffraction quality vs temperature established a safe temperature for data collection of -63° C.

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.

Refinement. Refinement progress was checked using *Platon* (Spek, 2009) and by an *R*-tensor (Parkin, 2000). The final model was further checked with the IUCr utility *checkCIF*.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.09256 (2)	0.51979 (13)	0.25747 (5)	0.0358 (2)
N2	0.40754 (2)	0.51181 (13)	0.99141 (5)	0.0375 (2)
C1	0.08446 (3)	0.34286 (16)	0.30095 (7)	0.0408 (3)
H1A	0.0960	0.3411	0.3561	0.049*
H1B	0.0921	0.2325	0.2692	0.049*
C2	0.04725 (3)	0.32626 (19)	0.31130 (8)	0.0510 (3)
H2A	0.0358	0.3157	0.2562	0.061*
H2B	0.0426	0.2097	0.3429	0.061*
C3	0.03424 (3)	0.4991 (2)	0.35658 (8)	0.0531 (3)
H3A	0.0432	0.4996	0.4145	0.064*
H3B	0.0100	0.4920	0.3576	0.064*
C4	0.04421 (3)	0.6818 (2)	0.31330 (8)	0.0524 (3)
H4A	0.0375	0.7929	0.3461	0.063*
H4B	0.0327	0.6893	0.2581	0.063*
C5	0.08159 (3)	0.68738 (16)	0.30341 (7)	0.0429 (3)
H5A	0.0874	0.8043	0.2734	0.051*
H5B	0.0930	0.6906	0.3587	0.051*
C6	0.12794 (3)	0.52990 (17)	0.24185 (7)	0.0408 (3)
H6A	0.1319	0.6458	0.2091	0.049*
H6B	0.1337	0.4192	0.2077	0.049*
C7	0.15040 (3)	0.53310 (16)	0.31739 (7)	0.0390 (3)
C8	0.16846 (3)	0.53582 (15)	0.37892 (7)	0.0363 (3)
C9	0.19232 (3)	0.53774 (13)	0.44832 (6)	0.0326 (2)
C10	0.22585 (3)	0.50840 (14)	0.43383 (6)	0.0335 (2)
H10A	0.2324	0.4867	0.3790	0.040*
C11	0.24966 (2)	0.51066 (14)	0.49867 (6)	0.0313 (2)
H11A	0.2721	0.4898	0.4873	0.038*
C12	0.24091 (2)	0.54353 (13)	0.58071 (6)	0.0284 (2)
C13	0.20725 (2)	0.57162 (15)	0.59484 (6)	0.0355 (2)
H13A	0.2007	0.5932	0.6497	0.043*
C14	0.18335 (3)	0.56848 (16)	0.53020 (6)	0.0378 (3)
H14A	0.1609	0.5872	0.5416	0.045*
C15	0.26622 (2)	0.54789 (13)	0.65079 (6)	0.0281 (2)

C16	0.26055 (2)	0.64996 (14)	0.72383 (6)	0.0326 (2)
H16A	0.2409	0.7220	0.7272	0.039*
C17	0.28313 (2)	0.64730 (14)	0.79115 (6)	0.0331 (2)
H17A	0.2786	0.7173	0.8395	0.040*
C18	0.31256 (2)	0.54258 (14)	0.78869 (6)	0.0316 (2)
C19	0.31910 (2)	0.44566 (15)	0.71481 (6)	0.0337 (2)
H19A	0.3391	0.3779	0.7108	0.040*
C20	0.29630 (2)	0.44858 (14)	0.64742 (6)	0.0312 (2)
H20A	0.3012	0.3823	0.5983	0.037*
C21	0.33448 (2)	0.53494 (15)	0.86180 (6)	0.0352 (2)
C22	0.35066 (3)	0.53208 (16)	0.92647 (7)	0.0390 (3)
C23	0.37192 (3)	0.52602 (18)	1.00433 (7)	0.0424 (3)
H23A	0.3679	0.6422	1.0368	0.051*
H23B	0.3653	0.4158	1.0377	0.051*
C24	0.41943 (3)	0.68044 (16)	0.94747 (7)	0.0413 (3)
H24A	0.4138	0.7965	0.9784	0.050*
H24B	0.4083	0.6878	0.8919	0.050*
C25	0.45676 (3)	0.67152 (19)	0.93867 (7)	0.0498 (3)
H25A	0.4640	0.7830	0.9069	0.060*
H25B	0.4680	0.6759	0.9942	0.060*
C26	0.46631 (3)	0.48932 (19)	0.89439 (8)	0.0519 (3)
H26A	0.4906	0.4800	0.8937	0.062*
H26B	0.4575	0.4927	0.8364	0.062*
C27	0.45268 (3)	0.3159 (2)	0.93827 (8)	0.0528 (3)
H27A	0.4638	0.3029	0.9937	0.063*
H27B	0.4572	0.2000	0.9061	0.063*
C28	0.41548 (3)	0.33533 (17)	0.94746 (7)	0.0434 (3)
H28A	0.4042	0.3357	0.8920	0.052*
H28B	0.4074	0.2248	0.9784	0.052*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0341 (5)	0.0429 (5)	0.0297 (4)	−0.0006 (4)	−0.0047 (3)	0.0028 (3)
N2	0.0329 (5)	0.0501 (6)	0.0288 (4)	−0.0020 (4)	−0.0046 (3)	0.0012 (4)
C1	0.0456 (6)	0.0379 (6)	0.0388 (6)	−0.0012 (5)	0.0003 (4)	−0.0013 (4)
C2	0.0479 (7)	0.0545 (7)	0.0509 (7)	−0.0114 (6)	0.0054 (5)	−0.0028 (6)
C3	0.0438 (7)	0.0675 (8)	0.0488 (7)	0.0022 (6)	0.0096 (5)	0.0003 (6)
C4	0.0492 (7)	0.0564 (8)	0.0514 (7)	0.0146 (6)	0.0012 (5)	0.0027 (6)
C5	0.0485 (6)	0.0378 (6)	0.0418 (6)	0.0030 (5)	−0.0050 (5)	0.0029 (5)
C6	0.0363 (6)	0.0528 (7)	0.0326 (5)	−0.0018 (5)	−0.0045 (4)	0.0057 (5)
C7	0.0356 (6)	0.0426 (6)	0.0382 (6)	−0.0008 (4)	−0.0042 (5)	0.0025 (4)
C8	0.0361 (6)	0.0345 (6)	0.0379 (6)	0.0006 (4)	−0.0034 (4)	0.0011 (4)
C9	0.0348 (5)	0.0269 (5)	0.0356 (5)	−0.0001 (4)	−0.0053 (4)	0.0016 (4)
C10	0.0388 (5)	0.0324 (5)	0.0293 (5)	−0.0012 (4)	0.0001 (4)	−0.0003 (4)
C11	0.0299 (5)	0.0302 (5)	0.0338 (5)	−0.0006 (4)	0.0016 (4)	−0.0001 (4)
C12	0.0312 (5)	0.0221 (5)	0.0315 (5)	0.0001 (3)	−0.0002 (4)	0.0012 (4)
C13	0.0335 (5)	0.0411 (6)	0.0319 (5)	0.0060 (4)	0.0009 (4)	−0.0022 (4)

C14	0.0304 (5)	0.0434 (6)	0.0393 (6)	0.0064 (4)	−0.0013 (4)	−0.0007 (5)
C15	0.0293 (5)	0.0249 (5)	0.0300 (5)	−0.0009 (4)	0.0008 (4)	0.0020 (4)
C16	0.0319 (5)	0.0316 (5)	0.0343 (5)	0.0047 (4)	0.0014 (4)	−0.0016 (4)
C17	0.0351 (5)	0.0330 (5)	0.0310 (5)	−0.0002 (4)	0.0005 (4)	−0.0033 (4)
C18	0.0298 (5)	0.0300 (5)	0.0346 (5)	−0.0044 (4)	−0.0020 (4)	0.0020 (4)
C19	0.0276 (5)	0.0342 (5)	0.0391 (5)	0.0032 (4)	−0.0006 (4)	−0.0011 (4)
C20	0.0304 (5)	0.0309 (5)	0.0323 (5)	0.0014 (4)	0.0017 (4)	−0.0033 (4)
C21	0.0312 (5)	0.0365 (6)	0.0375 (6)	−0.0030 (4)	−0.0015 (4)	0.0005 (4)
C22	0.0330 (5)	0.0461 (6)	0.0374 (6)	−0.0026 (4)	−0.0026 (4)	−0.0007 (4)
C23	0.0344 (6)	0.0607 (7)	0.0317 (5)	−0.0029 (5)	−0.0031 (4)	−0.0023 (5)
C24	0.0420 (6)	0.0419 (6)	0.0394 (6)	−0.0032 (5)	−0.0036 (4)	−0.0013 (5)
C25	0.0415 (6)	0.0599 (8)	0.0479 (7)	−0.0104 (5)	−0.0007 (5)	0.0020 (5)
C26	0.0401 (7)	0.0682 (8)	0.0480 (7)	0.0049 (6)	0.0079 (5)	0.0065 (6)
C27	0.0494 (7)	0.0566 (8)	0.0523 (7)	0.0125 (6)	0.0025 (5)	0.0084 (6)
C28	0.0464 (6)	0.0425 (6)	0.0408 (6)	0.0004 (5)	−0.0026 (5)	0.0045 (5)

Geometric parameters (Å, º)

N1—C5	1.4592 (14)	C13—C14	1.3814 (14)
N1—C6	1.4595 (14)	C13—H13A	0.9400
N1—C1	1.4599 (14)	C14—H14A	0.9400
N2—C28	1.4596 (15)	C15—C16	1.3964 (13)
N2—C24	1.4614 (14)	C15—C20	1.3985 (13)
N2—C23	1.4616 (14)	C16—C17	1.3787 (13)
C1—C2	1.5194 (16)	C16—H16A	0.9400
C1—H1A	0.9800	C17—C18	1.3938 (14)
C1—H1B	0.9800	C17—H17A	0.9400
C2—C3	1.5113 (18)	C18—C19	1.3974 (14)
C2—H2A	0.9800	C18—C21	1.4352 (13)
C2—H2B	0.9800	C19—C20	1.3849 (13)
C3—C4	1.5126 (19)	C19—H19A	0.9400
C3—H3A	0.9800	C20—H20A	0.9400
C3—H3B	0.9800	C21—C22	1.1984 (15)
C4—C5	1.5210 (16)	C22—C23	1.4807 (14)
C4—H4A	0.9800	C23—H23A	0.9800
C4—H4B	0.9800	C23—H23B	0.9800
C5—H5A	0.9800	C24—C25	1.5176 (15)
C5—H5B	0.9800	C24—H24A	0.9800
C6—C7	1.4776 (14)	C24—H24B	0.9800
C6—H6A	0.9800	C25—C26	1.5123 (18)
C6—H6B	0.9800	C25—H25A	0.9800
C7—C8	1.1980 (15)	C25—H25B	0.9800
C8—C9	1.4360 (13)	C26—C27	1.5133 (18)
C9—C14	1.3921 (15)	C26—H26A	0.9800
C9—C10	1.3956 (14)	C26—H26B	0.9800
C10—C11	1.3810 (14)	C27—C28	1.5177 (16)
C10—H10A	0.9400	C27—H27A	0.9800
C11—C12	1.3944 (14)	C27—H27B	0.9800

C11—H11A	0.9400	C28—H28A	0.9800
C12—C13	1.3979 (13)	C28—H28B	0.9800
C12—C15	1.4817 (13)		

C5—N1—C6	111.59 (9)	C13—C14—C9	120.42 (9)
C5—N1—C1	110.87 (8)	C13—C14—H14A	119.8
C6—N1—C1	111.31 (8)	C9—C14—H14A	119.8
C28—N2—C24	111.19 (8)	C16—C15—C20	117.33 (9)
C28—N2—C23	111.30 (9)	C16—C15—C12	120.78 (8)
C24—N2—C23	111.03 (9)	C20—C15—C12	121.89 (8)
N1—C1—C2	111.04 (9)	C17—C16—C15	121.39 (9)
N1—C1—H1A	109.4	C17—C16—H16A	119.3
C2—C1—H1A	109.4	C15—C16—H16A	119.3
N1—C1—H1B	109.4	C16—C17—C18	121.11 (9)
C2—C1—H1B	109.4	C16—C17—H17A	119.4
H1A—C1—H1B	108.0	C18—C17—H17A	119.4
C3—C2—C1	110.89 (10)	C17—C18—C19	118.03 (9)
C3—C2—H2A	109.5	C17—C18—C21	119.27 (9)
C1—C2—H2A	109.5	C19—C18—C21	122.69 (9)
C3—C2—H2B	109.5	C20—C19—C18	120.59 (9)
C1—C2—H2B	109.5	C20—C19—H19A	119.7
H2A—C2—H2B	108.0	C18—C19—H19A	119.7
C2—C3—C4	110.24 (10)	C19—C20—C15	121.48 (9)
C2—C3—H3A	109.6	C19—C20—H20A	119.3
C4—C3—H3A	109.6	C15—C20—H20A	119.3
C2—C3—H3B	109.6	C22—C21—C18	174.81 (11)
C4—C3—H3B	109.6	C21—C22—C23	177.50 (11)
H3A—C3—H3B	108.1	N2—C23—C22	114.63 (9)
C3—C4—C5	110.71 (10)	N2—C23—H23A	108.6
C3—C4—H4A	109.5	C22—C23—H23A	108.6
C5—C4—H4A	109.5	N2—C23—H23B	108.6
C3—C4—H4B	109.5	C22—C23—H23B	108.6
C5—C4—H4B	109.5	H23A—C23—H23B	107.6
H4A—C4—H4B	108.1	N2—C24—C25	111.07 (9)
N1—C5—C4	110.83 (9)	N2—C24—H24A	109.4
N1—C5—H5A	109.5	C25—C24—H24A	109.4
C4—C5—H5A	109.5	N2—C24—H24B	109.4
N1—C5—H5B	109.5	C25—C24—H24B	109.4
C4—C5—H5B	109.5	H24A—C24—H24B	108.0
H5A—C5—H5B	108.1	C26—C25—C24	110.61 (10)
N1—C6—C7	115.27 (9)	C26—C25—H25A	109.5
N1—C6—H6A	108.5	C24—C25—H25A	109.5
C7—C6—H6A	108.5	C26—C25—H25B	109.5
N1—C6—H6B	108.5	C24—C25—H25B	109.5
C7—C6—H6B	108.5	H25A—C25—H25B	108.1
H6A—C6—H6B	107.5	C25—C26—C27	110.31 (10)
C8—C7—C6	179.62 (12)	C25—C26—H26A	109.6
C7—C8—C9	175.36 (11)	C27—C26—H26A	109.6

C14—C9—C10	118.25 (9)	C25—C26—H26B	109.6
C14—C9—C8	122.49 (9)	C27—C26—H26B	109.6
C10—C9—C8	119.26 (9)	H26A—C26—H26B	108.1
C11—C10—C9	121.15 (9)	C26—C27—C28	110.76 (10)
C11—C10—H10A	119.4	C26—C27—H27A	109.5
C9—C10—H10A	119.4	C28—C27—H27A	109.5
C10—C11—C12	120.92 (9)	C26—C27—H27B	109.5
C10—C11—H11A	119.5	C28—C27—H27B	109.5
C12—C11—H11A	119.5	H27A—C27—H27B	108.1
C11—C12—C13	117.61 (9)	N2—C28—C27	111.13 (9)
C11—C12—C15	121.50 (8)	N2—C28—H28A	109.4
C13—C12—C15	120.90 (8)	C27—C28—H28A	109.4
C14—C13—C12	121.63 (9)	N2—C28—H28B	109.4
C14—C13—H13A	119.2	C27—C28—H28B	109.4
C12—C13—H13A	119.2	H28A—C28—H28B	108.0

C5—N1—C1—C2	59.37 (11)	C11—C12—C15—C20	−26.18 (13)
C6—N1—C1—C2	−175.79 (9)	C13—C12—C15—C20	153.55 (10)
N1—C1—C2—C3	−56.43 (13)	C20—C15—C16—C17	−2.33 (14)
C1—C2—C3—C4	53.55 (14)	C12—C15—C16—C17	176.66 (8)
C2—C3—C4—C5	−53.83 (14)	C15—C16—C17—C18	0.11 (15)
C6—N1—C5—C4	175.67 (9)	C16—C17—C18—C19	2.24 (14)
C1—N1—C5—C4	−59.65 (11)	C16—C17—C18—C21	−176.50 (9)
C3—C4—C5—N1	57.03 (13)	C17—C18—C19—C20	−2.32 (14)
C5—N1—C6—C7	62.09 (12)	C21—C18—C19—C20	176.37 (9)
C1—N1—C6—C7	−62.35 (12)	C18—C19—C20—C15	0.08 (15)
C14—C9—C10—C11	−0.34 (14)	C16—C15—C20—C19	2.24 (14)
C8—C9—C10—C11	179.46 (9)	C12—C15—C20—C19	−176.74 (8)
C9—C10—C11—C12	−0.38 (14)	C28—N2—C23—C22	−61.65 (12)
C10—C11—C12—C13	0.76 (14)	C24—N2—C23—C22	62.79 (12)
C10—C11—C12—C15	−179.51 (8)	C28—N2—C24—C25	−58.93 (11)
C11—C12—C13—C14	−0.43 (15)	C23—N2—C24—C25	176.57 (9)
C15—C12—C13—C14	179.83 (9)	N2—C24—C25—C26	56.67 (12)
C12—C13—C14—C9	−0.29 (16)	C24—C25—C26—C27	−54.12 (13)
C10—C9—C14—C13	0.67 (15)	C25—C26—C27—C28	53.94 (14)
C8—C9—C14—C13	−179.13 (9)	C24—N2—C28—C27	58.70 (11)
C11—C12—C15—C16	154.88 (10)	C23—N2—C28—C27	−176.96 (9)
C13—C12—C15—C16	−25.40 (13)	C26—C27—C28—N2	−56.26 (13)