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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, C28H32N2, (I), is one of a second generation of compounds designed and synthesized based on a very potent and selective α9α10 nicotinic acetylcholine receptor antagonist ZZ161C {10-[[1,1′-biphenyl]-4,4′-diyl]bis(prop-2-yn-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 α9α10 nicotinic acetylcholine receptor is a novel therapeutic target with potential significance for pain management. Previous studies have shown that antagonism of the α9α10 nAChR by the non-peptide small molecule, ZZ161C [10-[[1,1′-biphenyl]-4,4′-diyl]bis(prop-2-yn-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system with ethynyl appendages at the 4 and 4′ positions, as in ZZ161C, but the terminal aza-aromatic rings have been replaced by piperidine moieties.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 (100.0 mg, 0.26 mmol) in acetonitrile (7 mL), piperidine groups, which in turn stack along a.

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 (Csp2—H) and 0.98 Å (R2—CH3). Uiso(H) values were set to 1.2Ueq of the attached carbon atom.

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

| Table 1 | Experimental details. |
|----------|-----------------------|
| Crystal data | Chemical formula C28H32N2 |
|             | Mw 396.55             |
| System, space group | Monoclinic, C2/c |
| Temperature (K) | 210 |
| a, b, c (Å) | 40.2728 (8), 6.9679 (1), 16.0119 (3) |
| β (°) | 92.588 (1) |
| V (Å3) | 4488.63 (14) |
| Z | 8 |
| Radiation type | Cu Ka |
| μ (mm−1) | 0.51 |
| Crystal size (mm) | 0.25 × 0.24 × 0.05 |
| Data collection | Diffraclometer Bruker X8 Proteum diffractometer |
| Absorption correction | Multi-scan (SADABS; Krause et al., 2015) |
| Tmin, Tmax | 0.822, 0.942 |
| No. of measured, independent and observed [I > 2σ(I)] reflections | 28464, 4089, 3656 |
| Rint | 0.040 |
| (sinθ/λ)max (Å−1) | 0.603 |
| R[F2 > 2σ(F2)], wR(F2), S | 0.038, 0.120, 1.08 |
| No. of reflections | 4089 |
| No. of parameters | 272 |
| H-atom treatment | H-atom parameters constrained |
| Δρmax, Δρmin (e Å−3) | 0.15, −0.14 |

Computer programs: APEX2 and SAINT (Bruker, 2006), SHELX (Sheldrick, 2008), SHELXL2014 (Sheldrick, 2015), SHELXTL and XP in SHELXTL (Sheldrick, 2008) and CIFIX (Parkin, 2013).
Acknowledgements

This investigation was supported by the Arkansas Research Alliance (ARA).

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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}  
Mr = 396.55

Monoclinic, C2/c

a = 40.2728 (8) Å
b = 6.9679 (1) Å
c = 16.0119 (3) Å
β = 92.588 (1)°

V = 4488.63 (14) Å³
Z = 8

F(000) = 1712

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

Refinement

Refinement on F²

Least-squares matrix: full
R[F² > 2σ(F²)] = 0.038
wR(F²) = 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/[σ²(F²) + (0.0642P)² + 1.3326P]

where P = (F² + 2F_C²)/3

(Δ/σ)_{max} = 0.001
Δρ_{max} = 0.15 e Å⁻³
Δρ_{min} = −0.14 e Å⁻³

Extinction correction: SHELXL2014 (Sheldrick, 2015), Fc°=kFc[1+0.001xFc²λ²/sin(2θ)]⁴/₃
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)**

| Atom | x     | y     | z     | Uiso*/Ueq |
|------|-------|-------|-------|-----------|
| N1   | 0.0926 (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) |
### 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) |
|    | x   | y   | z   | U11 | U22 | U33 | U12 | U13 | U23 |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 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, ″)**

|    |    |    |    |    |    |    |    |    |    |
|----|----|----|----|----|----|----|----|----|----|
| 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  C28—H28B 0.9800
C12—C13 1.3979 (13)  C12—C15 1.4817 (13)  C5—N1—C6 111.59 (9)
C5—N1—C1 110.87 (8)   C13—C14—C9 120.42 (9)  C13—C14—H14A 119.8
C6—N1—C1 111.31 (8)   C9—C14—H14A 119.8  C5—N1—C1 110.87 (8)
C28—N2—C24 111.19 (8)  C16—C15—C12 121.89 (8)  C16—C15—C20 117.33 (9)
C28—N2—C23 111.03 (9)  C20—C15—C12 121.89 (8)  C15—N2—C24 111.19 (8)
N1—C1—C2 110.4 (9)   C28—N2—C23 111.03 (9)  C28—N2—C24 111.19 (8)
N1—C1—H1A 109.4  C1—C2—C1 110.89 (10)  C16—C17—C18 121.11 (9)
C2—C1—H1A 109.4  C2—C3—C4 110.24 (10)  C16—C17—H17A 119.4
C2—C1—H1B 109.4  C2—C3—H3A 109.6  C17—C18—C19 118.03 (9)
H1A—C1—H1B 108.0  C3—C2—C1 110.89 (10)  C17—C18—C21 122.69 (9)
C3—C2—H2A 109.5  C1—C2—C3 109.5  C19—C18—C21 120.59 (9)
C1—C2—H2A 109.5  C3—C2—H2B 109.5  C19—C18—C23 119.7
H2A—C2—H2B 108.0  C1—C2—H2B 109.5  C20—C19—C18 120.59 (9)
C3—C2—H2B 109.5  C1—C2—H2B 109.5  C20—C19—H19A 119.7
C3—C3—C4 110.71 (10)  C2—C3—C4 110.71 (10)  H2A—C2—H2B 108.0
C3—C3—H3A 109.6  C4—C3—C5 111.07 (9)  C2—C3—H3A 110.89 (10)
C4—C3—H3A 109.6  C5—C4—C3 109.5  C2—C3—H3A 110.89 (10)
C5—C4—H4A 109.5  C4—C5—C6 111.04 (9)  C3—C4—H4B 109.5
C5—C4—H4B 109.5  C5—C4—H4A 109.5  C3—C4—H4B 109.5
C6—C5—C4 110.83 (9)   C4—C5—C6 110.83 (9)  C5—C4—H4B 109.5
C6—C5—H5A 109.5  C7—C6—C5 115.27 (9)  C2—C3—H3B 109.6
C6—C5—H5A 109.5  C7—C6—H6A 108.5  C2—C3—H3B 109.6
N1—C5—C6 109.5  C7—C6—H6A 108.5  C4—C5—H5B 109.5
C7—C6—H6B 108.5  C5—C6—C7 111.27 (9)  C4—C5—H5B 109.5
C7—C6—H6B 108.5  C6—C7—C8 179.62 (12)  H5A—C5—H5B 108.1
C7—C6—H6B 108.5  C7—C6—H6B 108.5  C26—C25—C24 110.61 (10)
H6A—C6—H6B 107.5  C6—C7—C8 175.36 (11)  C25—C26—C27 110.31 (10)
C8—C7—C6 179.62 (12)  C7—C6—H6B 108.5  C25—C26—H26A 109.6
C7—C8—C9 175.36 (11)  C8—C7—C6 179.62 (12)  C26—C25—H25A 109.5
C8—C7—C9 175.36 (11)  C8—C7—C6 179.62 (12)  C26—C25—H25A 109.5
C7—C8—C9 175.36 (11)  C7—C8—C9 175.36 (11)
| Bond                  | Angle (degrees) | Bond                  | Angle (degrees) |
|----------------------|-----------------|----------------------|-----------------|
| 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)      | C28—C27—C28         | 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)     |