

# Cyclolinopeptide A methanol solvate

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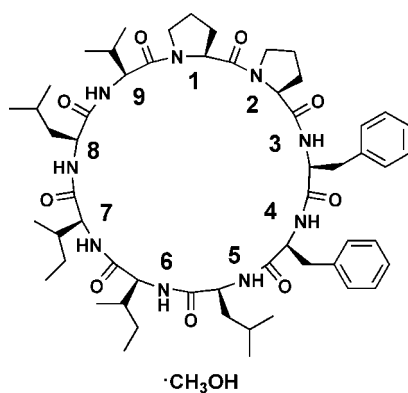
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Key indicators: single-crystal X-ray study;  $T = 173$  K; mean  $\sigma(\text{C}-\text{C}) = 0.007$  Å;  $R$  factor = 0.055;  $wR$  factor = 0.110; data-to-parameter ratio = 8.2.

Crystals of the title compound,  $\text{C}_{57}\text{H}_{85}\text{N}_9\text{O}_9 \cdot \text{CH}_4\text{O}$ , the methanol solvate of a nine peptide polypeptide, *cyclo*-(Pro-Pro-Phe-Phe-Leu-Ile-Ile-Leu-Val), were obtained after separation of the cyclic peptide from flax oil. The cyclolinopeptide A (CLP-A) molecules are linked in chains along the  $a$  axis by  $\text{N}-\text{H} \cdots \text{O}$  hydrogen bonds. Each methanol O atom is hydrogen bonded to one O atom and two  $\text{N}-\text{H}$  groups in the same CLP-A molecule. There are a total of eight hydrogen bonds in each CLP-A-MeOH unit.

## Related literature

For the isolation of CLP-A, see: Kaufmann & Tobschirbel (1959). For its synthesis and absolute configuration, see: Prox & Weygand (1966). For the crystal structure of the 2-propanol solvate, see: Di Blasio *et al.* (1989). For NMR studies and the crystal structure of a solvate of unstated composition of CLP-A, see: Matsumoto *et al.* (2002). For the cytoprotective ability of CLP-A, see: Kessler *et al.* (1986).



## Experimental

### Crystal data

$\text{C}_{57}\text{H}_{85}\text{N}_9\text{O}_9 \cdot \text{CH}_4\text{O}$   
 $M_r = 1072.38$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 9.8650$  (4) Å  
 $b = 22.6135$  (5) Å  
 $c = 26.5723$  (10) Å

$V = 5927.8$  (4) Å<sup>3</sup>  
 $Z = 4$   
 Mo  $K\alpha$  radiation  
 $\mu = 0.08$  mm<sup>-1</sup>  
 $T = 173$  K  
 $0.20 \times 0.05 \times 0.05$  mm

### Data collection

Nonius KappaCCD diffractometer  
 Absorption correction: none  
 10352 measured reflections

5817 independent reflections  
 3987 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.070$

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.055$   
 $wR(F^2) = 0.110$   
 $S = 1.04$   
 5817 reflections

707 parameters  
 H-atom parameters constrained  
 $\Delta\rho_{\text{max}} = 0.18$  e Å<sup>-3</sup>  
 $\Delta\rho_{\text{min}} = -0.18$  e Å<sup>-3</sup>

**Table 1**

Hydrogen-bond geometry (Å, °).

| $D-\text{H} \cdots A$                    | $D-\text{H}$ | $\text{H} \cdots A$ | $D \cdots A$ | $D-\text{H} \cdots A$ |
|--|--------------|---------------------|--------------|-----------------------|
| $\text{N3}-\text{H3} \cdots \text{O10}$  | 0.88         | 2.09                | 2.912 (5)    | 154                   |
| $\text{N4}-\text{H4} \cdots \text{O10}$  | 0.88         | 2.28                | 3.139 (5)    | 166                   |
| $\text{N4}-\text{H4} \cdots \text{O9}$   | 0.88         | 2.51                | 3.103 (5)    | 125                   |
| $\text{N5}-\text{H5} \cdots \text{O3}$   | 0.88         | 2.18                | 2.935 (5)    | 143                   |
| $\text{N6}-\text{H6} \cdots \text{O8}^i$ | 0.88         | 2.49                | 3.208 (5)    | 139                   |
| $\text{N7}-\text{H7} \cdots \text{O4}$   | 0.88         | 2.50                | 3.266 (5)    | 145                   |
| $\text{N8}-\text{H8} \cdots \text{O5}$   | 0.88         | 2.11                | 2.971 (5)    | 165                   |
| $\text{N9}-\text{H9} \cdots \text{O4}$   | 0.88         | 2.13                | 2.975 (5)    | 161                   |
| $\text{O10}-\text{H10} \cdots \text{O9}$ | 0.84         | 1.91                | 2.698 (4)    | 156                   |

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

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXTL* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: PV2179).

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## supporting information

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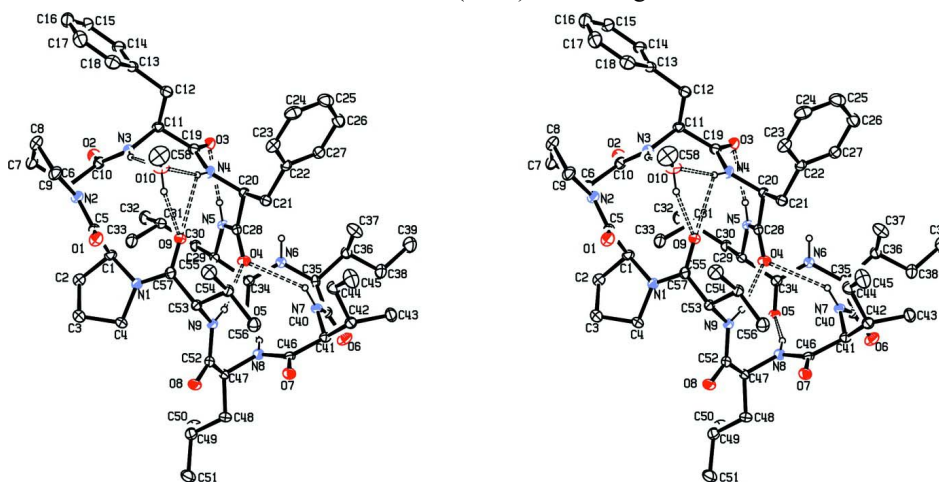
### S1. Experimental

The title compound was extracted from flax oil by successive elution of a mixture of 700 ml of flax oil and 700 ml of 5% ethyl acetate in hexane. Fractions containing several cyclicpeptides were collected and dried by rotary evaporation. Further separation was achieved by using HPLC and acetonitrile/water solvent gradient. Each cyclicpeptide fraction was collected and identified by NMR and MS. CLP-A was crystallized by dissolving it in minimum amount of methanol and then adding a few drops of water to the solution. After two days of slow evaporation of the methanol at room temperature, suitable crystals were harvested for crystallographic studies.

### S2. Refinement

H atoms bonded to N atoms were located in a difference map and then positioned geometrically with  $U_{\text{iso}}$  constrained to be 1.2 times  $U_{\text{eq}}(\text{N})$ , and the bond length constrained to 0.88 Å. Other H atoms were positioned geometrically and refined using a riding model (including free rotation for methyl groups with C—H = 0.95–0.99 Å and with  $U_{\text{iso}}(\text{H}) = 1.2(1.5$  for methyl groups) times  $U_{\text{eq}}(\text{C})$ ).

The chirality of the amino acids can not be determined from the anomalous dispersion, but the relative chirality is clearly all the same. The structure has no atom with  $Z > 8$ . With Mo radiation and low resolution data, it is impossible to determine the absolute chirality from these data. Based on the synthesis of the molecule by Prox & Weygand (1966), we have assumed that all amino acids are S. All Friedel mates (4536) were merged in the refinement.



**Figure 1**

The stereo molecular structure of the title compound, with atom labels and 20% probability displacement ellipsoids for non-H atoms. Only H atoms on N or O atoms are included. The methanol molecule (C58—O10) has the C atom pointing toward the viewer.

## Cyclolinopeptide A methanol solvate

## Crystal data

$C_{57}H_{85}N_9O_9 \cdot CH_4O$   
 $M_r = 1072.38$   
 Orthorhombic,  $P2_12_12_1$   
 Hall symbol: P 2ac 2ab  
 $a = 9.8650$  (4) Å  
 $b = 22.6135$  (5) Å  
 $c = 26.5723$  (10) Å  
 $V = 5927.8$  (4) Å<sup>3</sup>  
 $Z = 4$

$F(000) = 2320$   
 $D_x = 1.202$  Mg m<sup>-3</sup>  
 Mo  $K\alpha$  radiation,  $\lambda = 0.71073$  Å  
 Cell parameters from 5719 reflections  
 $\theta = 1.0$ – $25.0^\circ$   
 $\mu = 0.08$  mm<sup>-1</sup>  
 $T = 173$  K  
 Rod, colourless  
 $0.20 \times 0.05 \times 0.05$  mm

## Data collection

Nonius KappaCCD  
 diffractometer  
 Radiation source: fine-focus sealed tube  
 Horizontally mounted graphite crystal  
 monochromator  
 Detector resolution: 9 pixels mm<sup>-1</sup>  
 $\varphi$  scans and  $\omega$  scans with  $\kappa$  offsets  
 10352 measured reflections

5817 independent reflections  
 3987 reflections with  $I > 2\sigma(I)$   
 $R_{int} = 0.070$   
 $\theta_{max} = 25.0^\circ$ ,  $\theta_{min} = 2.5^\circ$   
 $h = -11 \rightarrow 11$   
 $k = -26 \rightarrow 26$   
 $l = -31 \rightarrow 31$

## Refinement

Refinement on  $F^2$   
 Least-squares matrix: full  
 $R[F^2 > 2\sigma(F^2)] = 0.055$   
 $wR(F^2) = 0.110$   
 $S = 1.04$   
 5817 reflections  
 707 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  
 $w = 1/[\sigma^2(F_o^2) + (0.0289P)^2 + 2.503P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} < 0.001$   
 $\Delta\rho_{max} = 0.18$  e Å<sup>-3</sup>  
 $\Delta\rho_{min} = -0.18$  e Å<sup>-3</sup>  
 Extinction correction: *SHELXTL* (Sheldrick,  
 2008),  $F_c^* = kFc[1 + 0.001x \cdot Fc^2 \lambda^3 / \sin(2\theta)]^{-1/4}$   
 Extinction coefficient: 0.0040 (3)  
 Absolute structure: syn

## 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<sup>2</sup>)

|    | <i>x</i>   | <i>y</i>     | <i>z</i>     | $U_{iso}^*/U_{eq}$ |
|----|------------|--------------|--------------|--------------------|
| O1 | 0.6490 (4) | 0.14168 (15) | 0.41141 (12) | 0.0430 (9)         |
| O2 | 1.1761 (4) | 0.24064 (13) | 0.42479 (13) | 0.0478 (9)         |
| O3 | 1.3224 (3) | 0.14204 (15) | 0.30740 (11) | 0.0416 (8)         |
| O4 | 0.9549 (3) | 0.15024 (13) | 0.20281 (11) | 0.0347 (8)         |

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|     |            |              |              |             |
|-----|------------|--------------|--------------|-------------|
| O5  | 1.0026 (3) | 0.27819 (12) | 0.13135 (10) | 0.0339 (8)  |
| O6  | 1.0140 (4) | 0.20528 (15) | 0.00902 (12) | 0.0473 (9)  |
| O7  | 0.6008 (3) | 0.14060 (13) | 0.09504 (11) | 0.0378 (8)  |
| O8  | 0.4485 (3) | 0.20492 (14) | 0.19539 (12) | 0.0396 (8)  |
| O9  | 0.8048 (3) | 0.11313 (13) | 0.31070 (11) | 0.0366 (8)  |
| N1  | 0.6840 (4) | 0.19658 (15) | 0.32071 (13) | 0.0315 (9)  |
| N2  | 0.8407 (4) | 0.17833 (15) | 0.44576 (13) | 0.0326 (9)  |
| N3  | 1.0975 (4) | 0.14799 (15) | 0.40928 (13) | 0.0301 (9)  |
| H3  | 1.0270     | 0.1242       | 0.4105       | 0.036*      |
| N4  | 1.1175 (4) | 0.09880 (15) | 0.30765 (13) | 0.0311 (9)  |
| H4  | 1.0487     | 0.0865       | 0.3260       | 0.037*      |
| N5  | 1.1410 (4) | 0.19582 (14) | 0.23273 (12) | 0.0293 (9)  |
| H5  | 1.2181     | 0.1928       | 0.2492       | 0.035*      |
| N6  | 1.1765 (4) | 0.21291 (14) | 0.12955 (12) | 0.0306 (9)  |
| H6  | 1.2336     | 0.1916       | 0.1474       | 0.037*      |
| N7  | 0.9621 (4) | 0.15497 (15) | 0.08001 (13) | 0.0297 (9)  |
| H7  | 0.9907     | 0.1431       | 0.1097       | 0.036*      |
| N8  | 0.7432 (4) | 0.21286 (14) | 0.11963 (13) | 0.0300 (9)  |
| H8  | 0.8267     | 0.2266       | 0.1198       | 0.036*      |
| N9  | 0.6568 (4) | 0.16721 (15) | 0.21162 (13) | 0.0303 (9)  |
| H9  | 0.7424     | 0.1668       | 0.2022       | 0.036*      |
| C1  | 0.7682 (5) | 0.21527 (17) | 0.36348 (15) | 0.0317 (11) |
| H1  | 0.8661     | 0.2166       | 0.3538       | 0.038*      |
| C2  | 0.7145 (5) | 0.27780 (19) | 0.37430 (18) | 0.0396 (12) |
| H2A | 0.7217     | 0.2873       | 0.4106       | 0.047*      |
| H2B | 0.7653     | 0.3078       | 0.3548       | 0.047*      |
| C3  | 0.5667 (5) | 0.2754 (2)   | 0.35773 (18) | 0.0413 (13) |
| H3A | 0.5092     | 0.2566       | 0.3838       | 0.050*      |
| H3B | 0.5313     | 0.3154       | 0.3504       | 0.050*      |
| C4  | 0.5729 (5) | 0.23786 (19) | 0.31047 (17) | 0.0349 (12) |
| H4A | 0.4865     | 0.2165       | 0.3050       | 0.042*      |
| H4B | 0.5926     | 0.2624       | 0.2805       | 0.042*      |
| C5  | 0.7468 (5) | 0.17461 (19) | 0.40867 (17) | 0.0329 (11) |
| C6  | 0.9504 (5) | 0.22168 (18) | 0.45025 (16) | 0.0318 (11) |
| H6A | 0.9202     | 0.2601       | 0.4354       | 0.038*      |
| C7  | 0.9657 (6) | 0.2288 (2)   | 0.50758 (17) | 0.0472 (14) |
| H7A | 1.0596     | 0.2399       | 0.5167       | 0.057*      |
| H7B | 0.9025     | 0.2591       | 0.5208       | 0.057*      |
| C8  | 0.9302 (6) | 0.1678 (2)   | 0.52744 (18) | 0.0493 (15) |
| H8A | 1.0090     | 0.1408       | 0.5250       | 0.059*      |
| H8B | 0.9005     | 0.1699       | 0.5630       | 0.059*      |
| C9  | 0.8159 (6) | 0.1470 (2)   | 0.49388 (16) | 0.0444 (13) |
| H9A | 0.8190     | 0.1036       | 0.4892       | 0.053*      |
| H9B | 0.7267     | 0.1580       | 0.5082       | 0.053*      |
| C10 | 1.0851 (5) | 0.20366 (19) | 0.42662 (16) | 0.0322 (11) |
| C11 | 1.2247 (5) | 0.12615 (18) | 0.38849 (15) | 0.0297 (11) |
| H11 | 1.2966     | 0.1552       | 0.3982       | 0.036*      |
| C12 | 1.2646 (5) | 0.06659 (18) | 0.41182 (16) | 0.0349 (12) |

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|      |            |               |              |             |
|------|------------|---------------|--------------|-------------|
| H12A | 1.1928     | 0.0372        | 0.4047       | 0.042*      |
| H12B | 1.3496     | 0.0525        | 0.3960       | 0.042*      |
| C13  | 1.2848 (5) | 0.07110 (18)  | 0.46802 (16) | 0.0333 (11) |
| C14  | 1.3965 (6) | 0.1017 (2)    | 0.48615 (18) | 0.0409 (13) |
| H14  | 1.4596     | 0.1186        | 0.4633       | 0.049*      |
| C15  | 1.4166 (6) | 0.1079 (2)    | 0.53792 (19) | 0.0485 (14) |
| H15  | 1.4920     | 0.1298        | 0.5500       | 0.058*      |
| C16  | 1.3284 (7) | 0.0826 (2)    | 0.5714 (2)   | 0.0557 (17) |
| H16  | 1.3433     | 0.0862        | 0.6065       | 0.067*      |
| C17  | 1.2180 (7) | 0.0521 (2)    | 0.5536 (2)   | 0.0598 (17) |
| H17  | 1.1556     | 0.0349        | 0.5765       | 0.072*      |
| C18  | 1.1972 (6) | 0.0460 (2)    | 0.5022 (2)   | 0.0485 (14) |
| H18  | 1.1212     | 0.0243        | 0.4904       | 0.058*      |
| C19  | 1.2238 (5) | 0.12317 (19)  | 0.33097 (16) | 0.0314 (11) |
| C20  | 1.1107 (5) | 0.09171 (17)  | 0.25296 (15) | 0.0269 (10) |
| H20  | 1.2049     | 0.0842        | 0.2406       | 0.032*      |
| C21  | 1.0242 (5) | 0.03878 (16)  | 0.23827 (17) | 0.0329 (11) |
| H21A | 0.9398     | 0.0392        | 0.2584       | 0.039*      |
| H21B | 0.9986     | 0.0424        | 0.2024       | 0.039*      |
| C22  | 1.0956 (5) | -0.01974 (17) | 0.24623 (16) | 0.0298 (11) |
| C40  | 1.0429 (5) | 0.18986 (18)  | 0.05201 (17) | 0.0326 (11) |
| C23  | 1.0602 (6) | -0.0571 (2)   | 0.28522 (18) | 0.0439 (13) |
| H23  | 0.9903     | -0.0462       | 0.3080       | 0.053*      |
| C24  | 1.1268 (6) | -0.1108 (2)   | 0.2911 (2)   | 0.0524 (15) |
| H24  | 1.1013     | -0.1366       | 0.3177       | 0.063*      |
| C25  | 1.2290 (6) | -0.1269 (2)   | 0.2589 (2)   | 0.0529 (15) |
| H25  | 1.2744     | -0.1636       | 0.2633       | 0.064*      |
| C26  | 1.2657 (6) | -0.0897 (2)   | 0.2200 (2)   | 0.0483 (14) |
| H26  | 1.3366     | -0.1006       | 0.1976       | 0.058*      |
| C27  | 1.1989 (5) | -0.03658 (19) | 0.21373 (17) | 0.0380 (12) |
| H27  | 1.2239     | -0.0112       | 0.1868       | 0.046*      |
| C28  | 1.0596 (5) | 0.14826 (19)  | 0.22772 (15) | 0.0284 (11) |
| C29  | 1.1011 (5) | 0.25230 (17)  | 0.21081 (15) | 0.0279 (11) |
| H29  | 1.0096     | 0.2627        | 0.2244       | 0.033*      |
| C30  | 1.1993 (5) | 0.30132 (18)  | 0.22619 (15) | 0.0323 (11) |
| H30A | 1.1669     | 0.3389        | 0.2113       | 0.039*      |
| H30B | 1.2888     | 0.2925        | 0.2111       | 0.039*      |
| C31  | 1.2193 (5) | 0.31099 (18)  | 0.28272 (16) | 0.0348 (12) |
| H31  | 1.2666     | 0.2755        | 0.2968       | 0.042*      |
| C32  | 1.3105 (6) | 0.3640 (2)    | 0.28986 (19) | 0.0497 (14) |
| H32A | 1.3969     | 0.3572        | 0.2726       | 0.075*      |
| H32B | 1.3271     | 0.3701        | 0.3259       | 0.075*      |
| H32C | 1.2667     | 0.3992        | 0.2757       | 0.075*      |
| C33  | 1.0869 (6) | 0.3191 (2)    | 0.31117 (18) | 0.0483 (14) |
| H33A | 1.1061     | 0.3247        | 0.3470       | 0.072*      |
| H33B | 1.0302     | 0.2838        | 0.3068       | 0.072*      |
| H33C | 1.0391     | 0.3538        | 0.2981       | 0.072*      |
| C34  | 1.0895 (5) | 0.24901 (18)  | 0.15363 (16) | 0.0279 (11) |

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|      |            |              |              |             |
|------|------------|--------------|--------------|-------------|
| C35  | 1.1790 (5) | 0.20796 (19) | 0.07441 (15) | 0.0327 (11) |
| H35  | 1.2018     | 0.2479       | 0.0607       | 0.039*      |
| C36  | 1.2942 (5) | 0.16549 (19) | 0.05862 (17) | 0.0380 (12) |
| H36  | 1.3796     | 0.1816       | 0.0736       | 0.046*      |
| C37  | 1.2770 (6) | 0.1035 (2)   | 0.0797 (2)   | 0.0570 (16) |
| H37A | 1.2546     | 0.1058       | 0.1155       | 0.085*      |
| H37B | 1.3617     | 0.0813       | 0.0754       | 0.085*      |
| H37C | 1.2038     | 0.0832       | 0.0617       | 0.085*      |
| C38  | 1.3130 (6) | 0.1670 (2)   | 0.00099 (18) | 0.0566 (16) |
| H38A | 1.2324     | 0.1490       | -0.0150      | 0.068*      |
| H38B | 1.3176     | 0.2088       | -0.0101      | 0.068*      |
| C39  | 1.4375 (6) | 0.1354 (3)   | -0.0172 (2)  | 0.0685 (18) |
| H39A | 1.5183     | 0.1544       | -0.0031      | 0.103*      |
| H39B | 1.4413     | 0.1372       | -0.0540      | 0.103*      |
| H39C | 1.4341     | 0.0940       | -0.0064      | 0.103*      |
| C41  | 0.8284 (5) | 0.13627 (18) | 0.06258 (16) | 0.0302 (11) |
| H41  | 0.8180     | 0.1522       | 0.0277       | 0.036*      |
| C42  | 0.8155 (5) | 0.06915 (17) | 0.05847 (16) | 0.0334 (11) |
| H42  | 0.7187     | 0.0600       | 0.0504       | 0.040*      |
| C43  | 0.9024 (6) | 0.04506 (19) | 0.01514 (17) | 0.0432 (13) |
| H43A | 0.8737     | 0.0634       | -0.0165      | 0.065*      |
| H43B | 0.8909     | 0.0021       | 0.0129       | 0.065*      |
| H43C | 0.9979     | 0.0543       | 0.0214       | 0.065*      |
| C44  | 0.8494 (6) | 0.03857 (19) | 0.10812 (17) | 0.0430 (13) |
| H44A | 0.8101     | 0.0619       | 0.1361       | 0.052*      |
| H44B | 0.9490     | 0.0383       | 0.1125       | 0.052*      |
| C45  | 0.7974 (7) | -0.0249 (2)  | 0.1119 (2)   | 0.0662 (19) |
| H45A | 0.6985     | -0.0251      | 0.1083       | 0.099*      |
| H45B | 0.8222     | -0.0414      | 0.1447       | 0.099*      |
| H45C | 0.8381     | -0.0488      | 0.0851       | 0.099*      |
| C46  | 0.7138 (5) | 0.16320 (19) | 0.09380 (16) | 0.0293 (11) |
| C47  | 0.6373 (5) | 0.24396 (18) | 0.14739 (16) | 0.0296 (11) |
| H47  | 0.6852     | 0.2751       | 0.1674       | 0.036*      |
| C48  | 0.5339 (5) | 0.27708 (18) | 0.11482 (17) | 0.0349 (12) |
| H48A | 0.5687     | 0.2789       | 0.0799       | 0.042*      |
| H48B | 0.4485     | 0.2541       | 0.1142       | 0.042*      |
| C49  | 0.5025 (5) | 0.33970 (18) | 0.13241 (17) | 0.0381 (12) |
| H49  | 0.4957     | 0.3395       | 0.1700       | 0.046*      |
| C50  | 0.6146 (6) | 0.3831 (2)   | 0.1172 (2)   | 0.0574 (16) |
| H50A | 0.6124     | 0.3891       | 0.0807       | 0.086*      |
| H50B | 0.7030     | 0.3670       | 0.1270       | 0.086*      |
| H50C | 0.6001     | 0.4210       | 0.1342       | 0.086*      |
| C51  | 0.3655 (6) | 0.3595 (2)   | 0.1108 (2)   | 0.0532 (15) |
| H51A | 0.3689     | 0.3581       | 0.0740       | 0.080*      |
| H51B | 0.3462     | 0.4001       | 0.1217       | 0.080*      |
| H51C | 0.2939     | 0.3331       | 0.1230       | 0.080*      |
| C52  | 0.5702 (5) | 0.20273 (19) | 0.18643 (16) | 0.0318 (11) |
| C53  | 0.6163 (5) | 0.12948 (18) | 0.25350 (15) | 0.0299 (11) |

|      |            |              |              |             |
|------|------------|--------------|--------------|-------------|
| H53  | 0.5214     | 0.1403       | 0.2630       | 0.036*      |
| C54  | 0.6182 (5) | 0.06326 (19) | 0.24054 (16) | 0.0352 (12) |
| H54  | 0.7131     | 0.0513       | 0.2321       | 0.042*      |
| C55  | 0.5690 (6) | 0.0265 (2)   | 0.28561 (19) | 0.0494 (14) |
| H55A | 0.4757     | 0.0377       | 0.2940       | 0.074*      |
| H55B | 0.6278     | 0.0339       | 0.3146       | 0.074*      |
| H55C | 0.5720     | -0.0156      | 0.2770       | 0.074*      |
| C56  | 0.5271 (5) | 0.05127 (19) | 0.19503 (17) | 0.0418 (13) |
| H56A | 0.5341     | 0.0095       | 0.1855       | 0.063*      |
| H56B | 0.5560     | 0.0761       | 0.1668       | 0.063*      |
| H56C | 0.4329     | 0.0605       | 0.2037       | 0.063*      |
| C57  | 0.7083 (5) | 0.14515 (19) | 0.29755 (15) | 0.0316 (11) |
| O10  | 0.9112 (4) | 0.05125 (13) | 0.38798 (13) | 0.0459 (9)  |
| H10  | 0.8568     | 0.0675       | 0.3680       | 0.069*      |
| C58  | 0.8484 (7) | 0.0016 (2)   | 0.4104 (2)   | 0.077 (2)   |
| H58A | 0.9140     | -0.0190      | 0.4318       | 0.115*      |
| H58B | 0.8163     | -0.0253      | 0.3840       | 0.115*      |
| H58C | 0.7714     | 0.0147       | 0.4309       | 0.115*      |

*Atomic displacement parameters (Å<sup>2</sup>)*

|    | $U^{11}$  | $U^{22}$    | $U^{33}$    | $U^{12}$     | $U^{13}$     | $U^{23}$     |
|----|-----------|-------------|-------------|--------------|--------------|--------------|
| O1 | 0.036 (2) | 0.056 (2)   | 0.0375 (19) | -0.0097 (19) | 0.0011 (17)  | 0.0004 (17)  |
| O2 | 0.039 (2) | 0.0397 (18) | 0.065 (2)   | -0.0085 (18) | 0.000 (2)    | -0.0096 (17) |
| O3 | 0.028 (2) | 0.065 (2)   | 0.0321 (18) | -0.0092 (18) | 0.0015 (17)  | -0.0004 (16) |
| O4 | 0.025 (2) | 0.0398 (17) | 0.0397 (18) | -0.0002 (15) | -0.0053 (16) | 0.0026 (15)  |
| O5 | 0.035 (2) | 0.0353 (16) | 0.0312 (17) | 0.0046 (16)  | -0.0063 (16) | 0.0005 (14)  |
| O6 | 0.036 (2) | 0.074 (2)   | 0.0314 (19) | -0.009 (2)   | -0.0023 (17) | 0.0084 (17)  |
| O7 | 0.027 (2) | 0.0432 (18) | 0.043 (2)   | 0.0017 (17)  | -0.0029 (17) | -0.0028 (16) |
| O8 | 0.024 (2) | 0.0544 (19) | 0.0400 (19) | 0.0091 (17)  | -0.0007 (16) | 0.0018 (16)  |
| O9 | 0.033 (2) | 0.0461 (18) | 0.0306 (18) | 0.0125 (17)  | -0.0018 (16) | 0.0001 (15)  |
| N1 | 0.027 (2) | 0.040 (2)   | 0.027 (2)   | 0.0016 (19)  | -0.0005 (18) | -0.0023 (17) |
| N2 | 0.027 (2) | 0.042 (2)   | 0.029 (2)   | -0.0045 (19) | -0.0007 (19) | 0.0025 (17)  |
| N3 | 0.027 (2) | 0.0294 (19) | 0.034 (2)   | -0.0047 (17) | -0.0002 (18) | -0.0032 (17) |
| N4 | 0.028 (2) | 0.039 (2)   | 0.027 (2)   | -0.0071 (18) | -0.0003 (19) | -0.0032 (17) |
| N5 | 0.027 (2) | 0.0325 (19) | 0.028 (2)   | 0.0026 (18)  | -0.0056 (18) | -0.0006 (16) |
| N6 | 0.031 (2) | 0.032 (2)   | 0.029 (2)   | 0.0040 (18)  | -0.0012 (18) | -0.0013 (16) |
| N7 | 0.028 (2) | 0.034 (2)   | 0.027 (2)   | 0.0058 (18)  | -0.0013 (18) | 0.0046 (16)  |
| N8 | 0.022 (2) | 0.036 (2)   | 0.032 (2)   | 0.0002 (18)  | -0.0001 (17) | -0.0021 (17) |
| N9 | 0.023 (2) | 0.043 (2)   | 0.025 (2)   | 0.0054 (18)  | 0.0006 (17)  | -0.0012 (17) |
| C1 | 0.024 (3) | 0.040 (2)   | 0.031 (2)   | 0.000 (2)    | -0.005 (2)   | 0.001 (2)    |
| C2 | 0.042 (3) | 0.043 (3)   | 0.035 (3)   | 0.004 (3)    | -0.004 (2)   | -0.002 (2)   |
| C3 | 0.038 (3) | 0.043 (3)   | 0.043 (3)   | 0.008 (2)    | 0.000 (3)    | -0.004 (2)   |
| C4 | 0.027 (3) | 0.040 (2)   | 0.037 (3)   | 0.010 (2)    | -0.001 (2)   | -0.003 (2)   |
| C5 | 0.028 (3) | 0.038 (3)   | 0.032 (3)   | 0.001 (2)    | -0.001 (2)   | -0.004 (2)   |
| C6 | 0.027 (3) | 0.032 (2)   | 0.036 (3)   | 0.000 (2)    | -0.004 (2)   | -0.004 (2)   |
| C7 | 0.049 (4) | 0.059 (3)   | 0.033 (3)   | 0.001 (3)    | -0.004 (3)   | -0.011 (2)   |
| C8 | 0.059 (4) | 0.059 (3)   | 0.030 (3)   | 0.005 (3)    | -0.007 (3)   | -0.005 (2)   |



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|     |           |           |           |            |            |              |
|-----|-----------|-----------|-----------|------------|------------|--------------|
| C9  | 0.054 (4) | 0.049 (3) | 0.029 (3) | 0.000 (3)  | 0.001 (3)  | 0.007 (2)    |
| C10 | 0.034 (3) | 0.033 (2) | 0.031 (2) | -0.006 (2) | -0.005 (2) | -0.005 (2)   |
| C11 | 0.022 (3) | 0.037 (2) | 0.030 (2) | 0.000 (2)  | -0.002 (2) | 0.003 (2)    |
| C12 | 0.032 (3) | 0.036 (2) | 0.037 (3) | 0.004 (2)  | 0.001 (2)  | 0.003 (2)    |
| C13 | 0.031 (3) | 0.037 (2) | 0.032 (3) | 0.006 (2)  | -0.002 (2) | 0.005 (2)    |
| C14 | 0.035 (3) | 0.051 (3) | 0.037 (3) | 0.007 (3)  | 0.001 (3)  | 0.007 (2)    |
| C15 | 0.055 (4) | 0.048 (3) | 0.043 (3) | 0.009 (3)  | -0.008 (3) | -0.002 (2)   |
| C16 | 0.088 (5) | 0.042 (3) | 0.037 (3) | 0.017 (3)  | 0.001 (3)  | 0.001 (3)    |
| C17 | 0.087 (5) | 0.047 (3) | 0.045 (3) | 0.010 (3)  | 0.023 (4)  | 0.016 (3)    |
| C18 | 0.046 (4) | 0.042 (3) | 0.057 (4) | -0.001 (3) | 0.003 (3)  | 0.009 (3)    |
| C19 | 0.028 (3) | 0.035 (2) | 0.031 (3) | 0.003 (2)  | 0.000 (2)  | 0.003 (2)    |
| C20 | 0.020 (3) | 0.034 (2) | 0.027 (2) | 0.000 (2)  | 0.001 (2)  | -0.0012 (19) |
| C21 | 0.031 (3) | 0.032 (2) | 0.035 (3) | 0.004 (2)  | -0.004 (2) | -0.003 (2)   |
| C22 | 0.032 (3) | 0.028 (2) | 0.029 (2) | -0.002 (2) | -0.008 (2) | -0.004 (2)   |
| C40 | 0.030 (3) | 0.036 (2) | 0.032 (3) | 0.001 (2)  | 0.000 (2)  | 0.001 (2)    |
| C23 | 0.048 (4) | 0.048 (3) | 0.036 (3) | -0.007 (3) | -0.005 (3) | 0.002 (2)    |
| C24 | 0.059 (4) | 0.043 (3) | 0.054 (4) | -0.009 (3) | -0.015 (3) | 0.015 (3)    |
| C25 | 0.056 (4) | 0.035 (3) | 0.068 (4) | 0.005 (3)  | -0.015 (3) | 0.000 (3)    |
| C26 | 0.049 (4) | 0.042 (3) | 0.054 (3) | 0.008 (3)  | -0.002 (3) | -0.011 (3)   |
| C27 | 0.043 (3) | 0.037 (2) | 0.034 (3) | 0.003 (2)  | -0.004 (3) | -0.001 (2)   |
| C28 | 0.027 (3) | 0.034 (2) | 0.025 (2) | 0.006 (2)  | 0.000 (2)  | -0.0059 (19) |
| C29 | 0.027 (3) | 0.026 (2) | 0.030 (2) | 0.005 (2)  | -0.002 (2) | -0.0034 (19) |
| C30 | 0.034 (3) | 0.033 (2) | 0.030 (2) | 0.001 (2)  | 0.002 (2)  | -0.002 (2)   |
| C31 | 0.035 (3) | 0.035 (2) | 0.035 (3) | 0.007 (2)  | -0.006 (2) | -0.001 (2)   |
| C32 | 0.046 (4) | 0.049 (3) | 0.054 (3) | 0.000 (3)  | -0.009 (3) | -0.018 (3)   |
| C33 | 0.047 (4) | 0.062 (3) | 0.035 (3) | 0.003 (3)  | 0.003 (3)  | -0.008 (2)   |
| C34 | 0.024 (3) | 0.029 (2) | 0.031 (2) | -0.005 (2) | -0.004 (2) | -0.003 (2)   |
| C35 | 0.034 (3) | 0.037 (2) | 0.027 (2) | 0.001 (2)  | 0.011 (2)  | -0.005 (2)   |
| C36 | 0.031 (3) | 0.045 (3) | 0.038 (3) | 0.002 (2)  | -0.003 (2) | -0.010 (2)   |
| C37 | 0.044 (4) | 0.045 (3) | 0.082 (4) | 0.010 (3)  | 0.004 (3)  | -0.002 (3)   |
| C38 | 0.052 (4) | 0.078 (4) | 0.040 (3) | 0.015 (3)  | 0.000 (3)  | -0.017 (3)   |
| C39 | 0.058 (4) | 0.098 (4) | 0.050 (4) | 0.013 (4)  | 0.006 (3)  | -0.014 (3)   |
| C41 | 0.024 (3) | 0.036 (2) | 0.031 (2) | 0.002 (2)  | -0.004 (2) | -0.001 (2)   |
| C42 | 0.031 (3) | 0.034 (2) | 0.035 (3) | -0.001 (2) | -0.003 (2) | -0.003 (2)   |
| C43 | 0.049 (4) | 0.038 (3) | 0.042 (3) | 0.007 (3)  | 0.005 (3)  | -0.006 (2)   |
| C44 | 0.048 (4) | 0.039 (3) | 0.042 (3) | 0.005 (3)  | 0.003 (3)  | 0.006 (2)    |
| C45 | 0.082 (5) | 0.047 (3) | 0.070 (4) | 0.001 (3)  | 0.025 (4)  | 0.005 (3)    |
| C46 | 0.024 (3) | 0.038 (3) | 0.027 (2) | 0.003 (2)  | -0.005 (2) | 0.002 (2)    |
| C47 | 0.025 (3) | 0.031 (2) | 0.033 (2) | 0.008 (2)  | -0.001 (2) | -0.004 (2)   |
| C48 | 0.032 (3) | 0.036 (2) | 0.036 (3) | 0.009 (2)  | -0.006 (2) | 0.003 (2)    |
| C49 | 0.044 (3) | 0.037 (2) | 0.033 (3) | 0.004 (2)  | -0.001 (3) | 0.002 (2)    |
| C50 | 0.065 (4) | 0.049 (3) | 0.059 (4) | -0.009 (3) | -0.006 (3) | 0.010 (3)    |
| C51 | 0.053 (4) | 0.052 (3) | 0.054 (3) | 0.022 (3)  | 0.002 (3)  | 0.008 (3)    |
| C52 | 0.031 (3) | 0.037 (2) | 0.027 (2) | 0.007 (2)  | -0.003 (2) | -0.008 (2)   |
| C53 | 0.025 (3) | 0.041 (2) | 0.024 (2) | 0.004 (2)  | -0.001 (2) | -0.003 (2)   |
| C54 | 0.028 (3) | 0.045 (3) | 0.032 (3) | 0.003 (2)  | -0.001 (2) | -0.005 (2)   |
| C55 | 0.056 (4) | 0.041 (3) | 0.051 (3) | -0.005 (3) | 0.000 (3)  | 0.006 (2)    |
| C56 | 0.041 (3) | 0.042 (3) | 0.043 (3) | -0.005 (3) | 0.000 (3)  | -0.005 (2)   |

|     |           |             |           |              |              |             |
|-----|-----------|-------------|-----------|--------------|--------------|-------------|
| C57 | 0.027 (3) | 0.043 (3)   | 0.025 (2) | 0.001 (2)    | 0.008 (2)    | 0.002 (2)   |
| O10 | 0.040 (2) | 0.0381 (18) | 0.060 (2) | -0.0069 (17) | -0.0121 (19) | 0.0105 (16) |
| C58 | 0.085 (5) | 0.062 (4)   | 0.083 (5) | -0.034 (4)   | -0.002 (4)   | 0.017 (3)   |

*Geometric parameters (Å, °)*

|        |           |          |           |
|--------|-----------|----------|-----------|
| O1—C5  | 1.221 (5) | C23—H23  | 0.9500    |
| O2—C10 | 1.228 (5) | C24—C25  | 1.372 (8) |
| O3—C19 | 1.233 (5) | C24—H24  | 0.9500    |
| O4—C28 | 1.227 (5) | C25—C26  | 1.381 (7) |
| O5—C34 | 1.233 (5) | C25—H25  | 0.9500    |
| O6—C40 | 1.228 (5) | C26—C27  | 1.380 (6) |
| O7—C46 | 1.227 (5) | C26—H26  | 0.9500    |
| O8—C52 | 1.225 (6) | C27—H27  | 0.9500    |
| O9—C57 | 1.246 (5) | C29—C34  | 1.526 (6) |
| N1—C57 | 1.337 (5) | C29—C30  | 1.528 (6) |
| N1—C4  | 1.465 (5) | C29—H29  | 1.0000    |
| N1—C1  | 1.470 (5) | C30—C31  | 1.531 (6) |
| N2—C5  | 1.355 (6) | C30—H30A | 0.9900    |
| N2—C6  | 1.465 (5) | C30—H30B | 0.9900    |
| N2—C9  | 1.482 (5) | C31—C32  | 1.512 (6) |
| N3—C10 | 1.346 (5) | C31—C33  | 1.520 (7) |
| N3—C11 | 1.457 (6) | C31—H31  | 1.0000    |
| N3—H3  | 0.8800    | C32—H32A | 0.9800    |
| N4—C19 | 1.337 (6) | C32—H32B | 0.9800    |
| N4—C20 | 1.464 (5) | C32—H32C | 0.9800    |
| N4—H4  | 0.8800    | C33—H33A | 0.9800    |
| N5—C28 | 1.349 (5) | C33—H33B | 0.9800    |
| N5—C29 | 1.458 (5) | C33—H33C | 0.9800    |
| N5—H5  | 0.8800    | C35—C36  | 1.546 (6) |
| N6—C34 | 1.346 (5) | C35—H35  | 1.0000    |
| N6—C35 | 1.470 (5) | C36—C37  | 1.520 (6) |
| N6—H6  | 0.8800    | C36—C38  | 1.543 (6) |
| N7—C40 | 1.346 (6) | C36—H36  | 1.0000    |
| N7—C41 | 1.460 (6) | C37—H37A | 0.9800    |
| N7—H7  | 0.8800    | C37—H37B | 0.9800    |
| N8—C46 | 1.348 (5) | C37—H37C | 0.9800    |
| N8—C47 | 1.459 (5) | C38—C39  | 1.502 (8) |
| N8—H8  | 0.8800    | C38—H38A | 0.9900    |
| N9—C52 | 1.350 (6) | C38—H38B | 0.9900    |
| N9—C53 | 1.458 (5) | C39—H39A | 0.9800    |
| N9—H9  | 0.8800    | C39—H39B | 0.9800    |
| C1—C5  | 1.527 (6) | C39—H39C | 0.9800    |
| C1—C2  | 1.537 (6) | C41—C42  | 1.527 (6) |
| C1—H1  | 1.0000    | C41—C46  | 1.529 (6) |
| C2—C3  | 1.524 (7) | C41—H41  | 1.0000    |
| C2—H2A | 0.9900    | C42—C44  | 1.526 (6) |
| C2—H2B | 0.9900    | C42—C43  | 1.535 (6) |

|           |           |              |           |
|-----------|-----------|--------------|-----------|
| C3—C4     | 1.517 (6) | C42—H42      | 1.0000    |
| C3—H3A    | 0.9900    | C43—H43A     | 0.9800    |
| C3—H3B    | 0.9900    | C43—H43B     | 0.9800    |
| C4—H4A    | 0.9900    | C43—H43C     | 0.9800    |
| C4—H4B    | 0.9900    | C44—C45      | 1.527 (6) |
| C6—C10    | 1.525 (6) | C44—H44A     | 0.9900    |
| C6—C7     | 1.539 (6) | C44—H44B     | 0.9900    |
| C6—H6A    | 1.0000    | C45—H45A     | 0.9800    |
| C7—C8     | 1.519 (6) | C45—H45B     | 0.9800    |
| C7—H7A    | 0.9900    | C45—H45C     | 0.9800    |
| C7—H7B    | 0.9900    | C47—C48      | 1.533 (6) |
| C8—C9     | 1.513 (7) | C47—C52      | 1.544 (6) |
| C8—H8A    | 0.9900    | C47—H47      | 1.0000    |
| C8—H8B    | 0.9900    | C48—C49      | 1.523 (6) |
| C9—H9A    | 0.9900    | C48—H48A     | 0.9900    |
| C9—H9B    | 0.9900    | C48—H48B     | 0.9900    |
| C11—C19   | 1.530 (6) | C49—C50      | 1.533 (7) |
| C11—C12   | 1.534 (6) | C49—C51      | 1.535 (7) |
| C11—H11   | 1.0000    | C49—H49      | 1.0000    |
| C12—C13   | 1.510 (6) | C50—H50A     | 0.9800    |
| C12—H12A  | 0.9900    | C50—H50B     | 0.9800    |
| C12—H12B  | 0.9900    | C50—H50C     | 0.9800    |
| C13—C18   | 1.376 (7) | C51—H51A     | 0.9800    |
| C13—C14   | 1.388 (7) | C51—H51B     | 0.9800    |
| C14—C15   | 1.397 (7) | C51—H51C     | 0.9800    |
| C14—H14   | 0.9500    | C53—C57      | 1.523 (6) |
| C15—C16   | 1.369 (8) | C53—C54      | 1.537 (6) |
| C15—H15   | 0.9500    | C53—H53      | 1.0000    |
| C16—C17   | 1.374 (8) | C54—C56      | 1.531 (6) |
| C16—H16   | 0.9500    | C54—C55      | 1.537 (6) |
| C17—C18   | 1.386 (7) | C54—H54      | 1.0000    |
| C17—H17   | 0.9500    | C55—H55A     | 0.9800    |
| C18—H18   | 0.9500    | C55—H55B     | 0.9800    |
| C20—C21   | 1.521 (6) | C55—H55C     | 0.9800    |
| C20—C28   | 1.530 (6) | C56—H56A     | 0.9800    |
| C20—H20   | 1.0000    | C56—H56B     | 0.9800    |
| C21—C22   | 1.514 (6) | C56—H56C     | 0.9800    |
| C21—H21A  | 0.9900    | O10—C58      | 1.414 (6) |
| C21—H21B  | 0.9900    | O10—H10      | 0.8400    |
| C22—C23   | 1.383 (6) | C58—H58A     | 0.9800    |
| C22—C27   | 1.388 (6) | C58—H58B     | 0.9800    |
| C40—C35   | 1.525 (7) | C58—H58C     | 0.9800    |
| C23—C24   | 1.389 (7) |              |           |
| C57—N1—C4 | 127.1 (4) | C29—C30—H30A | 108.1     |
| C57—N1—C1 | 120.3 (4) | C31—C30—H30A | 108.1     |
| C4—N1—C1  | 112.5 (3) | C29—C30—H30B | 108.1     |
| C5—N2—C6  | 127.3 (4) | C31—C30—H30B | 108.1     |

|            |           |               |           |
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| C5—N2—C9   | 119.0 (4) | H30A—C30—H30B | 107.3     |
| C6—N2—C9   | 111.8 (4) | C32—C31—C33   | 110.7 (4) |
| C10—N3—C11 | 121.7 (4) | C32—C31—C30   | 108.3 (4) |
| C10—N3—H3  | 119.2     | C33—C31—C30   | 113.2 (4) |
| C11—N3—H3  | 119.2     | C32—C31—H31   | 108.2     |
| C19—N4—C20 | 122.7 (4) | C33—C31—H31   | 108.2     |
| C19—N4—H4  | 118.6     | C30—C31—H31   | 108.2     |
| C20—N4—H4  | 118.6     | C31—C32—H32A  | 109.5     |
| C28—N5—C29 | 119.9 (4) | C31—C32—H32B  | 109.5     |
| C28—N5—H5  | 120.1     | H32A—C32—H32B | 109.5     |
| C29—N5—H5  | 120.1     | C31—C32—H32C  | 109.5     |
| C34—N6—C35 | 122.1 (4) | H32A—C32—H32C | 109.5     |
| C34—N6—H6  | 119.0     | H32B—C32—H32C | 109.5     |
| C35—N6—H6  | 119.0     | C31—C33—H33A  | 109.5     |
| C40—N7—C41 | 121.9 (4) | C31—C33—H33B  | 109.5     |
| C40—N7—H7  | 119.0     | H33A—C33—H33B | 109.5     |
| C41—N7—H7  | 119.0     | C31—C33—H33C  | 109.5     |
| C46—N8—C47 | 120.3 (4) | H33A—C33—H33C | 109.5     |
| C46—N8—H8  | 119.8     | H33B—C33—H33C | 109.5     |
| C47—N8—H8  | 119.8     | O5—C34—N6     | 122.6 (4) |
| C52—N9—C53 | 123.5 (4) | O5—C34—C29    | 120.3 (4) |
| C52—N9—H9  | 118.2     | N6—C34—C29    | 117.1 (4) |
| C53—N9—H9  | 118.2     | N6—C35—C40    | 113.2 (4) |
| N1—C1—C5   | 110.9 (4) | N6—C35—C36    | 109.3 (4) |
| N1—C1—C2   | 102.4 (3) | C40—C35—C36   | 112.0 (3) |
| C5—C1—C2   | 111.0 (4) | N6—C35—H35    | 107.3     |
| N1—C1—H1   | 110.8     | C40—C35—H35   | 107.3     |
| C5—C1—H1   | 110.8     | C36—C35—H35   | 107.3     |
| C2—C1—H1   | 110.8     | C37—C36—C38   | 113.5 (4) |
| C3—C2—C1   | 104.1 (4) | C37—C36—C35   | 113.1 (4) |
| C3—C2—H2A  | 110.9     | C38—C36—C35   | 110.1 (4) |
| C1—C2—H2A  | 110.9     | C37—C36—H36   | 106.5     |
| C3—C2—H2B  | 110.9     | C38—C36—H36   | 106.5     |
| C1—C2—H2B  | 110.9     | C35—C36—H36   | 106.5     |
| H2A—C2—H2B | 109.0     | C36—C37—H37A  | 109.5     |
| C4—C3—C2   | 102.8 (4) | C36—C37—H37B  | 109.5     |
| C4—C3—H3A  | 111.2     | H37A—C37—H37B | 109.5     |
| C2—C3—H3A  | 111.2     | C36—C37—H37C  | 109.5     |
| C4—C3—H3B  | 111.2     | H37A—C37—H37C | 109.5     |
| C2—C3—H3B  | 111.2     | H37B—C37—H37C | 109.5     |
| H3A—C3—H3B | 109.1     | C39—C38—C36   | 114.0 (5) |
| N1—C4—C3   | 103.5 (4) | C39—C38—H38A  | 108.7     |
| N1—C4—H4A  | 111.1     | C36—C38—H38A  | 108.7     |
| C3—C4—H4A  | 111.1     | C39—C38—H38B  | 108.7     |
| N1—C4—H4B  | 111.1     | C36—C38—H38B  | 108.7     |
| C3—C4—H4B  | 111.1     | H38A—C38—H38B | 107.6     |
| H4A—C4—H4B | 109.0     | C38—C39—H39A  | 109.5     |
| O1—C5—N2   | 122.3 (4) | C38—C39—H39B  | 109.5     |

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| O1—C5—C1      | 121.6 (4) | H39A—C39—H39B | 109.5     |
| N2—C5—C1      | 116.1 (4) | C38—C39—H39C  | 109.5     |
| N2—C6—C10     | 115.6 (3) | H39A—C39—H39C | 109.5     |
| N2—C6—C7      | 102.9 (4) | H39B—C39—H39C | 109.5     |
| C10—C6—C7     | 110.5 (4) | N7—C41—C42    | 112.7 (4) |
| N2—C6—H6A     | 109.2     | N7—C41—C46    | 112.4 (3) |
| C10—C6—H6A    | 109.2     | C42—C41—C46   | 111.9 (4) |
| C7—C6—H6A     | 109.2     | N7—C41—H41    | 106.4     |
| C8—C7—C6      | 103.1 (4) | C42—C41—H41   | 106.4     |
| C8—C7—H7A     | 111.2     | C46—C41—H41   | 106.4     |
| C6—C7—H7A     | 111.2     | C44—C42—C41   | 111.7 (3) |
| C8—C7—H7B     | 111.2     | C44—C42—C43   | 111.4 (4) |
| C6—C7—H7B     | 111.2     | C41—C42—C43   | 111.1 (4) |
| H7A—C7—H7B    | 109.1     | C44—C42—H42   | 107.4     |
| C9—C8—C7      | 104.4 (4) | C41—C42—H42   | 107.4     |
| C9—C8—H8A     | 110.9     | C43—C42—H42   | 107.4     |
| C7—C8—H8A     | 110.9     | C42—C43—H43A  | 109.5     |
| C9—C8—H8B     | 110.9     | C42—C43—H43B  | 109.5     |
| C7—C8—H8B     | 110.9     | H43A—C43—H43B | 109.5     |
| H8A—C8—H8B    | 108.9     | C42—C43—H43C  | 109.5     |
| N2—C9—C8      | 103.7 (4) | H43A—C43—H43C | 109.5     |
| N2—C9—H9A     | 111.0     | H43B—C43—H43C | 109.5     |
| C8—C9—H9A     | 111.0     | C42—C44—C45   | 114.1 (4) |
| N2—C9—H9B     | 111.0     | C42—C44—H44A  | 108.7     |
| C8—C9—H9B     | 111.0     | C45—C44—H44A  | 108.7     |
| H9A—C9—H9B    | 109.0     | C42—C44—H44B  | 108.7     |
| O2—C10—N3     | 123.9 (4) | C45—C44—H44B  | 108.7     |
| O2—C10—C6     | 118.1 (4) | H44A—C44—H44B | 107.6     |
| N3—C10—C6     | 118.0 (4) | C44—C45—H45A  | 109.5     |
| N3—C11—C19    | 112.9 (4) | C44—C45—H45B  | 109.5     |
| N3—C11—C12    | 111.4 (4) | H45A—C45—H45B | 109.5     |
| C19—C11—C12   | 111.5 (4) | C44—C45—H45C  | 109.5     |
| N3—C11—H11    | 106.9     | H45A—C45—H45C | 109.5     |
| C19—C11—H11   | 106.9     | H45B—C45—H45C | 109.5     |
| C12—C11—H11   | 106.9     | O7—C46—N8     | 121.9 (4) |
| C13—C12—C11   | 112.0 (3) | O7—C46—C41    | 121.4 (4) |
| C13—C12—H12A  | 109.2     | N8—C46—C41    | 116.7 (4) |
| C11—C12—H12A  | 109.2     | N8—C47—C48    | 115.2 (4) |
| C13—C12—H12B  | 109.2     | N8—C47—C52    | 110.8 (3) |
| C11—C12—H12B  | 109.2     | C48—C47—C52   | 112.9 (4) |
| H12A—C12—H12B | 107.9     | N8—C47—H47    | 105.7     |
| C18—C13—C14   | 118.3 (4) | C48—C47—H47   | 105.7     |
| C18—C13—C12   | 122.9 (5) | C52—C47—H47   | 105.7     |
| C14—C13—C12   | 118.8 (4) | C49—C48—C47   | 114.6 (4) |
| C13—C14—C15   | 120.3 (5) | C49—C48—H48A  | 108.6     |
| C13—C14—H14   | 119.9     | C47—C48—H48A  | 108.6     |
| C15—C14—H14   | 119.9     | C49—C48—H48B  | 108.6     |
| C16—C15—C14   | 120.5 (6) | C47—C48—H48B  | 108.6     |

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| C16—C15—H15   | 119.7     | H48A—C48—H48B | 107.6     |
| C14—C15—H15   | 119.7     | C48—C49—C50   | 111.6 (4) |
| C15—C16—C17   | 119.4 (5) | C48—C49—C51   | 109.6 (4) |
| C15—C16—H16   | 120.3     | C50—C49—C51   | 110.5 (4) |
| C17—C16—H16   | 120.3     | C48—C49—H49   | 108.4     |
| C16—C17—C18   | 120.4 (6) | C50—C49—H49   | 108.4     |
| C16—C17—H17   | 119.8     | C51—C49—H49   | 108.4     |
| C18—C17—H17   | 119.8     | C49—C50—H50A  | 109.5     |
| C13—C18—C17   | 121.1 (6) | C49—C50—H50B  | 109.5     |
| C13—C18—H18   | 119.4     | H50A—C50—H50B | 109.5     |
| C17—C18—H18   | 119.4     | C49—C50—H50C  | 109.5     |
| O3—C19—N4     | 121.7 (4) | H50A—C50—H50C | 109.5     |
| O3—C19—C11    | 119.2 (4) | H50B—C50—H50C | 109.5     |
| N4—C19—C11    | 119.0 (4) | C49—C51—H51A  | 109.5     |
| N4—C20—C21    | 111.5 (4) | C49—C51—H51B  | 109.5     |
| N4—C20—C28    | 111.0 (3) | H51A—C51—H51B | 109.5     |
| C21—C20—C28   | 111.1 (4) | C49—C51—H51C  | 109.5     |
| N4—C20—H20    | 107.7     | H51A—C51—H51C | 109.5     |
| C21—C20—H20   | 107.7     | H51B—C51—H51C | 109.5     |
| C28—C20—H20   | 107.7     | O8—C52—N9     | 123.2 (5) |
| C22—C21—C20   | 113.0 (4) | O8—C52—C47    | 121.8 (4) |
| C22—C21—H21A  | 109.0     | N9—C52—C47    | 114.9 (4) |
| C20—C21—H21A  | 109.0     | N9—C53—C57    | 106.7 (3) |
| C22—C21—H21B  | 109.0     | N9—C53—C54    | 113.3 (3) |
| C20—C21—H21B  | 109.0     | C57—C53—C54   | 113.0 (4) |
| H21A—C21—H21B | 107.8     | N9—C53—H53    | 107.9     |
| C23—C22—C27   | 118.9 (4) | C57—C53—H53   | 107.9     |
| C23—C22—C21   | 121.4 (4) | C54—C53—H53   | 107.9     |
| C27—C22—C21   | 119.6 (4) | C56—C54—C53   | 110.0 (4) |
| O6—C40—N7     | 122.9 (5) | C56—C54—C55   | 109.5 (4) |
| O6—C40—C35    | 119.4 (4) | C53—C54—C55   | 110.4 (4) |
| N7—C40—C35    | 117.6 (4) | C56—C54—H54   | 108.9     |
| C22—C23—C24   | 119.9 (5) | C53—C54—H54   | 108.9     |
| C22—C23—H23   | 120.0     | C55—C54—H54   | 108.9     |
| C24—C23—H23   | 120.0     | C54—C55—H55A  | 109.5     |
| C25—C24—C23   | 120.6 (5) | C54—C55—H55B  | 109.5     |
| C25—C24—H24   | 119.7     | H55A—C55—H55B | 109.5     |
| C23—C24—H24   | 119.7     | C54—C55—H55C  | 109.5     |
| C24—C25—C26   | 119.9 (5) | H55A—C55—H55C | 109.5     |
| C24—C25—H25   | 120.1     | H55B—C55—H55C | 109.5     |
| C26—C25—H25   | 120.1     | C54—C56—H56A  | 109.5     |
| C27—C26—C25   | 119.7 (5) | C54—C56—H56B  | 109.5     |
| C27—C26—H26   | 120.2     | H56A—C56—H56B | 109.5     |
| C25—C26—H26   | 120.2     | C54—C56—H56C  | 109.5     |
| C26—C27—C22   | 121.0 (5) | H56A—C56—H56C | 109.5     |
| C26—C27—H27   | 119.5     | H56B—C56—H56C | 109.5     |
| C22—C27—H27   | 119.5     | O9—C57—N1     | 120.9 (4) |
| O4—C28—N5     | 121.7 (4) | O9—C57—C53    | 122.4 (4) |

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| O4—C28—C20      | 123.0 (4)  | N1—C57—C53      | 116.7 (4)  |
| N5—C28—C20      | 115.3 (4)  | C58—O10—H10     | 109.5      |
| N5—C29—C34      | 112.1 (3)  | O10—C58—H58A    | 109.5      |
| N5—C29—C30      | 110.9 (4)  | O10—C58—H58B    | 109.5      |
| C34—C29—C30     | 110.4 (3)  | H58A—C58—H58B   | 109.5      |
| N5—C29—H29      | 107.7      | O10—C58—H58C    | 109.5      |
| C34—C29—H29     | 107.7      | H58A—C58—H58C   | 109.5      |
| C30—C29—H29     | 107.7      | H58B—C58—H58C   | 109.5      |
| C29—C30—C31     | 116.6 (4)  |                 |            |
|                 |            |                 |            |
| C57—N1—C1—C5    | -66.9 (5)  | C29—N5—C28—O4   | 3.8 (6)    |
| C4—N1—C1—C5     | 109.6 (4)  | C29—N5—C28—C20  | -179.0 (3) |
| C57—N1—C1—C2    | 174.6 (4)  | N4—C20—C28—O4   | -118.6 (4) |
| C4—N1—C1—C2     | -8.9 (5)   | C21—C20—C28—O4  | 6.1 (6)    |
| N1—C1—C2—C3     | 29.3 (4)   | N4—C20—C28—N5   | 64.3 (5)   |
| C5—C1—C2—C3     | -89.1 (5)  | C21—C20—C28—N5  | -171.0 (4) |
| C1—C2—C3—C4     | -38.9 (5)  | C28—N5—C29—C34  | -62.7 (5)  |
| C57—N1—C4—C3    | 161.1 (4)  | C28—N5—C29—C30  | 173.4 (4)  |
| C1—N1—C4—C3     | -15.1 (5)  | N5—C29—C30—C31  | -56.4 (5)  |
| C2—C3—C4—N1     | 32.7 (5)   | C34—C29—C30—C31 | 178.7 (4)  |
| C6—N2—C5—O1     | -170.5 (4) | C29—C30—C31—C32 | -175.6 (4) |
| C9—N2—C5—O1     | -7.6 (7)   | C29—C30—C31—C33 | -52.4 (5)  |
| C6—N2—C5—C1     | 8.1 (6)    | C35—N6—C34—O5   | 3.3 (7)    |
| C9—N2—C5—C1     | 170.9 (4)  | C35—N6—C34—C29  | -177.3 (4) |
| N1—C1—C5—O1     | -16.6 (6)  | N5—C29—C34—O5   | 145.4 (4)  |
| C2—C1—C5—O1     | 96.5 (5)   | C30—C29—C34—O5  | -90.4 (5)  |
| N1—C1—C5—N2     | 164.8 (4)  | N5—C29—C34—N6   | -33.9 (6)  |
| C2—C1—C5—N2     | -82.1 (5)  | C30—C29—C34—N6  | 90.3 (4)   |
| C5—N2—C6—C10    | -91.5 (5)  | C34—N6—C35—C40  | -57.2 (5)  |
| C9—N2—C6—C10    | 104.6 (4)  | C34—N6—C35—C36  | 177.2 (4)  |
| C5—N2—C6—C7     | 148.0 (4)  | O6—C40—C35—N6   | 152.2 (4)  |
| C9—N2—C6—C7     | -15.9 (5)  | N7—C40—C35—N6   | -30.8 (5)  |
| N2—C6—C7—C8     | 32.5 (5)   | O6—C40—C35—C36  | -83.6 (5)  |
| C10—C6—C7—C8    | -91.4 (5)  | N7—C40—C35—C36  | 93.3 (5)   |
| C6—C7—C8—C9     | -37.8 (5)  | N6—C35—C36—C37  | 60.5 (5)   |
| C5—N2—C9—C8     | -172.7 (4) | C40—C35—C36—C37 | -65.8 (5)  |
| C6—N2—C9—C8     | -7.3 (5)   | N6—C35—C36—C38  | -171.4 (4) |
| C7—C8—C9—N2     | 28.0 (5)   | C40—C35—C36—C38 | 62.3 (5)   |
| C11—N3—C10—O2   | 2.7 (7)    | C37—C36—C38—C39 | -62.0 (7)  |
| C11—N3—C10—C6   | -176.8 (4) | C35—C36—C38—C39 | 170.1 (5)  |
| N2—C6—C10—O2    | 172.7 (4)  | C40—N7—C41—C42  | 119.7 (4)  |
| C7—C6—C10—O2    | -71.0 (5)  | C40—N7—C41—C46  | -112.7 (4) |
| N2—C6—C10—N3    | -7.7 (6)   | N7—C41—C42—C44  | 55.7 (5)   |
| C7—C6—C10—N3    | 108.6 (4)  | C46—C41—C42—C44 | -72.1 (5)  |
| C10—N3—C11—C19  | -103.2 (5) | N7—C41—C42—C43  | -69.5 (5)  |
| C10—N3—C11—C12  | 130.5 (4)  | C46—C41—C42—C43 | 162.8 (4)  |
| N3—C11—C12—C13  | -60.8 (5)  | C41—C42—C44—C45 | 161.9 (4)  |
| C19—C11—C12—C13 | 172.1 (4)  | C43—C42—C44—C45 | -73.2 (6)  |

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| C11—C12—C13—C18 | 109.8 (5)  | C47—N8—C46—O7   | -4.4 (6)   |
| C11—C12—C13—C14 | -70.3 (6)  | C47—N8—C46—C41  | 175.4 (4)  |
| C18—C13—C14—C15 | -1.6 (7)   | N7—C41—C46—O7   | -158.5 (4) |
| C12—C13—C14—C15 | 178.5 (4)  | C42—C41—C46—O7  | -30.6 (6)  |
| C13—C14—C15—C16 | 1.7 (7)    | N7—C41—C46—N8   | 21.7 (5)   |
| C14—C15—C16—C17 | -1.3 (8)   | C42—C41—C46—N8  | 149.6 (4)  |
| C15—C16—C17—C18 | 1.0 (8)    | C46—N8—C47—C48  | -72.2 (5)  |
| C14—C13—C18—C17 | 1.3 (7)    | C46—N8—C47—C52  | 57.5 (5)   |
| C12—C13—C18—C17 | -178.9 (5) | N8—C47—C48—C49  | -134.0 (4) |
| C16—C17—C18—C13 | -1.0 (8)   | C52—C47—C48—C49 | 97.3 (5)   |
| C20—N4—C19—O3   | 1.1 (7)    | C47—C48—C49—C50 | 78.3 (5)   |
| C20—N4—C19—C11  | -177.2 (4) | C47—C48—C49—C51 | -159.0 (4) |
| N3—C11—C19—O3   | 134.6 (4)  | C53—N9—C52—O8   | -2.6 (7)   |
| C12—C11—C19—O3  | -99.1 (5)  | C53—N9—C52—C47  | 173.5 (3)  |
| N3—C11—C19—N4   | -47.0 (5)  | N8—C47—C52—O8   | -142.7 (4) |
| C12—C11—C19—N4  | 79.3 (5)   | C48—C47—C52—O8  | -11.7 (6)  |
| C19—N4—C20—C21  | 151.1 (4)  | N8—C47—C52—N9   | 41.1 (5)   |
| C19—N4—C20—C28  | -84.4 (5)  | C48—C47—C52—N9  | 172.1 (4)  |
| N4—C20—C21—C22  | -76.0 (5)  | C52—N9—C53—C57  | -125.3 (4) |
| C28—C20—C21—C22 | 159.6 (4)  | C52—N9—C53—C54  | 109.7 (5)  |
| C20—C21—C22—C23 | 106.8 (5)  | N9—C53—C54—C56  | -56.7 (5)  |
| C20—C21—C22—C27 | -73.3 (5)  | C57—C53—C54—C56 | -178.2 (4) |
| C41—N7—C40—O6   | -4.6 (6)   | N9—C53—C54—C55  | -177.7 (4) |
| C41—N7—C40—C35  | 178.5 (3)  | C57—C53—C54—C55 | 60.8 (5)   |
| C27—C22—C23—C24 | -0.6 (7)   | C4—N1—C57—O9    | -178.1 (4) |
| C21—C22—C23—C24 | 179.3 (4)  | C1—N1—C57—O9    | -2.2 (6)   |
| C22—C23—C24—C25 | 0.8 (8)    | C4—N1—C57—C53   | 4.3 (6)    |
| C23—C24—C25—C26 | -0.4 (8)   | C1—N1—C57—C53   | -179.8 (4) |
| C24—C25—C26—C27 | -0.2 (8)   | N9—C53—C57—O9   | -103.7 (5) |
| C25—C26—C27—C22 | 0.4 (8)    | C54—C53—C57—O9  | 21.5 (6)   |
| C23—C22—C27—C26 | -0.1 (7)   | N9—C53—C57—N1   | 73.9 (5)   |
| C21—C22—C27—C26 | -179.9 (4) | C54—C53—C57—N1  | -160.9 (4) |

## Hydrogen-bond geometry (Å, °)

| <i>D</i> —H... <i>A</i> | <i>D</i> —H | H... <i>A</i> | <i>D</i> ... <i>A</i> | <i>D</i> —H... <i>A</i> |
|-------------------------|-------------|---------------|-----------------------|-------------------------|
| N3—H3...O10             | 0.88        | 2.09          | 2.912 (5)             | 154                     |
| N4—H4...O10             | 0.88        | 2.28          | 3.139 (5)             | 166                     |
| N4—H4...O9              | 0.88        | 2.51          | 3.103 (5)             | 125                     |
| N5—H5...O3              | 0.88        | 2.18          | 2.935 (5)             | 143                     |
| N6—H6...O8 <sup>i</sup> | 0.88        | 2.49          | 3.208 (5)             | 139                     |
| N7—H7...O4              | 0.88        | 2.50          | 3.266 (5)             | 145                     |
| N8—H8...O5              | 0.88        | 2.11          | 2.971 (5)             | 165                     |
| N9—H9...O4              | 0.88        | 2.13          | 2.975 (5)             | 161                     |
| O10—H10...O9            | 0.84        | 1.91          | 2.698 (4)             | 156                     |

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