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14b-Chloro-4a-methoxy-3,3-dimethyl-2,3,4a,14b-tetrahydro-1*H*-benzo[*a*]-pyrano[2,3-*c*]phenazine: a new active structural type against *Mycobacterium tuberculosis*

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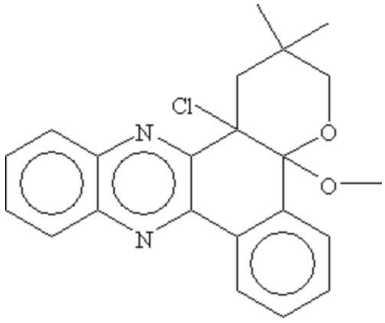
Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.003 Å; R factor = 0.047; wR factor = 0.121; data-to-parameter ratio = 17.5.

The title compound, $C_{22}H_{21}ClN_2O_2$, obtained from the reaction of the phenazine of β-lapachone with trichloroisocyanuric acid, showed a minimum inhibitory concentration of 6.25 ng ml^{-1} in tuberculostatic assays against *Mycobacterium tuberculosis* and established a new structural type with potential interest in medicinal chemistry. The dihydropyran ring adopts a pure chair conformation, while the ring fused to it has a half-chair conformation. The two substituents, OMe and Cl, are in axial positions, due to anomeric effects towards the methoxy derivative.

Related literature

For general background, see: Agrawal *et al.* (2007); Andrade-de Neto *et al.* (2004); Bahnmüller *et al.* (1988); Emoto *et al.* (2000); Franzblau *et al.* (1998); Geiger *et al.* (1988); Rewcastle *et al.* (1987); Van Rensburg *et al.* (2000); Wang *et al.* (2000); Janin (2007); Laursen *et al.* (2002); Mackgatho *et al.* (2000). For related literature, see: Allen *et al.* (1987); Cremer & Pople (1975).



Experimental

Crystal data

$C_{22}H_{21}ClN_2O_2$
M_r = 380.86
Monoclinic, $P2_1/n$
a = 15.5498 (6) Å
b = 6.9700 (1) Å
c = 17.4872 (7) Å
β = 92.488 (2)°
V = 1893.51 (11) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.22 mm^{-1}
T = 293 (2) K
0.23 × 0.21 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: none
13253 measured reflections
4312 independent reflections
3296 reflections with $I > 2\sigma(I)$
R_{int} = 0.032

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.121
S = 1.03
4312 reflections
246 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *SCALEPACK* and *DENZO* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: DN2211).

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supplementary materials

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14b-Chloro-4a-methoxy-3,3-dimethyl-2,3,4a,14b-tetrahydro-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine: a new active structural type against *Mycobacterium tuberculosis*

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Comment

The search for new antiviral and antibacterial compounds has accelerated in recent years due to the prevalence of antibiotic resistance. Thus, in the development of antibiotics as well as anticancer drugs, attention has been drawn towards a series of new targets, one of these being regulation of cell growth at the DNA/RNA level. A large group of antibiotics affect protein synthesis or nucleic acid metabolism, for example, *via* interference with DNA replication, DNA transcription, aminoacyl-tRNA formation or RNA translation. Intercalation, that is formation of a non-covalent complex of the drug with the duplex DNA, will result in inhibition of DNA replication and/or transcription, presumably due to deformation of double helix. Many intercalating drugs contain planar aromatic ring systems with cationic moieties. In the 80t h, a group of potential antibiotics containing the planar tricyclic heteroaromatic phenazine was isolated (Geiger *et al.*, 1988) and since then, a number of phenazine carboxylic acids have been synthesized showing significant antimicrobial activity towards a broad range of bacteria (Bahnmüller *et al.*, 1988; Laursen *et al.*, 2002).

In general, natural and synthetic phenazines have attracted considerable attention because of their interesting biological activities. Benzo[*a*]phenazine derivatives have been considered efficient DNA intercalating ligands, with antitumor activity in leukaemia and solid tumors(Rewcastle *et al.*, 1987). They also show broad-spectrum antibiotic activity (Emoto *et al.*, 2000), antimalarial (Mackgatho *et al.*, 2000; Andrade-Neto *et al.*, 2004), anti-hepatitis C viral replication (Wang *et al.*, 2000).

More specifically, tetramethylpiperidine (TMP)-substituted phenazines were assayed against *Mycobacterium tuberculosis* H37Rv (ATCC 27294) and some of them were significantly more active than clofazimine, including multidrug-resistant clinical strains of this microbial pathogen (Van Rensburg *et al.*, 2000).

Tuberculosis is one of the most devastating bacterial disease having high rates of morbidity and mortality. *M. tuberculosis* invades the host immune system and persists in pulmonary granulomas (Agrawal *et al.*, 2007). As resistant strains of *M. tuberculosis* have slowly emerged, treatment failure is too often a fact. This infectious disease is the focus of renewed scientific interest (Janin, 2007).

Due to these facts, the alpha-chlorine-acetal obtained from the reaction of the phenazine of β-lapachone with trichlorine-isocianuric acid (ATIC), named 14*b*-chloro-4a-methoxy-3,3-dimethyl-2,3,4a,14*b*-tetrahydro-1*H*-benzo[*a*]pyrano[2,3-*c*]phenazine, was assayed against *Mycobacterium tuberculosis* and showed Minimum Inhibitory Concentration (MIC) of 6.25 ng/ml in tests obtained for the evaluation of the tuberculostatic potencial, and established a new structural type with potential in future studies in medicinal chemistry. As the knowledge of its topology may assist in the understanding of its pharmacological behaviour, the crystal structure determination was undertaken in order to establish the perfect three-dimensional configuration of the molecule.

The bond lengths and angles in molecular structure of (I) are in accordance with values found in literature (Allen *et al.*, 1987). The region of the molecule that contains the conjugated benzene ring attached to the phenazinic ring is planar, with the biggest distance to the plan of least squares, for the C14*a* [0.016 (1) Å]. The benzene ring plane (C4b—C8a) is

inclined at an angle of 19.36 (5)° to this planar region of the conjugated rings. The piridinic ring presents a conformation of pure chair with puckering amplitude (Q) = 0.500 (2) Å, Θ = 13.9 (2)° and φ = 220.6 (9) ° (Cremer & Pople, 1975) while the ring formed by the atoms C4a—C4b—C8a—C8b—C14*a* and C14*b* has a conformation of half chair according to the puckering parameters: Q= 0.493 (2) Å, θ = 65.3 (2)° and φ= 335.6 (2)°. The two substituents, –Cl and –OMe are located in axial positions in the ring junction (Fig. 1). This special arrangement could be explained by anomeric effect toward the methoxy derivative.

In terms of biological activity, the lack of planarity would preclude its DNA intercalating activity, ruling out such type of DNA interaction. Alternative mechanisms of action should be searched to explain its significant tuberculostatic activity. Work on this line are in progress.

Experimental

To solution of 1 9300 mg (0.95 mmol) in 10 ml of methanol was a dded 660 mg (2,85 mmol) of triccloro-isocyanuric acid. After 30 min 1was fully reacted and the solvent was evaporated under vacum furnisshing directly 346 mg of 2 (yielding 96%). The antimicobacterial activity was determined by Microplate Alamar Blue Assay (MABA) (Franzblau *et al.*, 1998). Crystals for X-ray diffraction studies were grown by slow evaporation from chloroform solution at room temperature.

Refinement

All H atoms were fixed geometrically and treated as riding with C—H = 0.93Å (aromatic), 0.97Å (methylene) and 0. 96Å (methyl) with U_{iso}(H) = xU_{eq}(C) where x=1.2 for C(aromatic) or C(methylene) and x=1.5 for methyl group. One of the methyl group is statistically disordered over two positions.

Figures

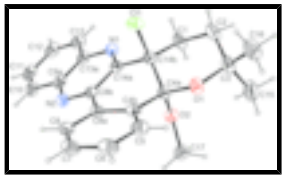


Fig. 1. Molecular view of the title compound with the atom-numbering scheme. Ellipsoids are drawn at the 50% probability level. H atoms are represented as small spheres of arbitrary radii. Only one component of the disordered methyl is shown for clarity.

14*b*-Chloro-4a-methoxy-3,3-dimethyl-2,3,4a,14*b*-tetrahydro-1*H*- benzo[*a*]pyrano[2,3-*c*]phenazine

Crystal data

$C_{22}H_{21}ClN_2O_2$	F_{000} = 800
M_r = 380.86	D_x = 1.336 Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation λ = 0.71073 Å
Hall symbol: -P 2yn	Cell parameters from 6803 reflections
a = 15.5498 (6) Å	θ = 1.0–27.5º
b = 6.97000 (10) Å	μ = 0.22 mm^{-1}
c = 17.4872 (7) Å	T = 293 (2) K
β = 92.488 (2)º	Prism, colourless

V = 1893.51 (11) Å^3
Z = 4

0.23 × 0.21 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
Radiation source: Enraf Nonius FR590
Monochromator: graphite
Detector resolution: 9 pixels mm^{-1}
CCD rotation images, thick slices scans
Absorption correction: none
13253 measured reflections
4312 independent reflections

3296 reflections with $I > 2\sigma(I)$
R_{int} = 0.032
θ_{max} = 27.5º
θ_{min} = 3.2º
h = −20→20
k = −7→9
l = −17→22

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.121
S = 1.03
4312 reflections
246 parameters
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
$w = 1/[\sigma^2(F_o^2) + (0.0494P)^2 + 0.7263P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}
Extinction correction: none

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 $F^2 > 2\text{sigma}(F^2)$ 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}	Occ. (<1)
Cl1	0.60842 (3)	0.47479 (7)	0.27257 (3)	0.04980 (16)	
O1	0.55673 (8)	0.79150 (19)	0.38387 (7)	0.0453 (3)	
O2	0.51499 (8)	0.99877 (17)	0.28314 (7)	0.0413 (3)	
N1	0.60735 (9)	0.7679 (2)	0.11522 (8)	0.0403 (3)	

N2	0.42903 (9)	0.7027 (2)	0.08825 (8)	0.0403 (3)	
C1	0.67792 (11)	0.8320 (3)	0.26508 (10)	0.0481 (5)	
H1A	0.6710	0.9670	0.2528	0.058*	
H1B	0.7202	0.7786	0.2319	0.058*	
C2	0.70950 (13)	0.8104 (4)	0.34836 (11)	0.0567 (5)	
H2A	0.7600	0.8905	0.3572	0.068*	
H2B	0.7270	0.6783	0.3570	0.068*	
C3	0.64303 (13)	0.8637 (3)	0.40649 (11)	0.0538 (5)	
C4A	0.52704 (11)	0.8046 (2)	0.30762 (9)	0.0352 (4)	
C4B	0.44283 (11)	0.6946 (2)	0.29803 (10)	0.0373 (4)	
C5	0.39476 (12)	0.6402 (3)	0.35961 (11)	0.0480 (5)	
H5	0.4148	0.6668	0.4094	0.058*	
C6	0.31697 (13)	0.5462 (3)	0.34683 (13)	0.0543 (5)	
H6	0.2851	0.5091	0.3881	0.065*	
C7	0.28660 (12)	0.5072 (3)	0.27344 (13)	0.0525 (5)	
H7	0.2341	0.4449	0.2654	0.063*	
C8	0.33343 (11)	0.5600 (3)	0.21171 (12)	0.0450 (4)	
H8	0.3126	0.5329	0.1622	0.054*	
C8A	0.41219 (10)	0.6541 (2)	0.22335 (10)	0.0362 (4)	
C8B	0.46512 (10)	0.7012 (2)	0.15768 (9)	0.0344 (4)	
C9A	0.48209 (12)	0.7370 (2)	0.02923 (10)	0.0400 (4)	
C10	0.44713 (14)	0.7424 (3)	−0.04654 (11)	0.0515 (5)	
H10	0.3886	0.7211	−0.0561	0.062*	
C11	0.49913 (16)	0.7787 (3)	−0.10583 (11)	0.0570 (6)	
H11	0.4756	0.7832	−0.1556	0.068*	
C12	0.58722 (16)	0.8092 (3)	−0.09234 (11)	0.0559 (5)	
H12	0.6219	0.8333	−0.1333	0.067*	
C13	0.62300 (14)	0.8040 (3)	−0.01983 (10)	0.0506 (5)	
H13	0.6818	0.8235	−0.0116	0.061*	
C13A	0.57077 (12)	0.7688 (2)	0.04271 (10)	0.0398 (4)	
C14A	0.55539 (10)	0.7363 (2)	0.17077 (9)	0.0345 (4)	
C14B	0.59274 (11)	0.7292 (2)	0.25169 (9)	0.0366 (4)	
C15	0.63936 (19)	1.0779 (4)	0.42060 (16)	0.0821 (8)	
H15A	0.6305	1.1436	0.3727	0.123*	
H15B	0.6925	1.1196	0.4451	0.123*	
H15C	0.5927	1.1062	0.4530	0.123*	
C16	0.66321 (17)	0.7573 (5)	0.48143 (12)	0.0785 (8)	
H16A	0.6202	0.7871	0.5173	0.118*	
H16B	0.7187	0.7963	0.5021	0.118*	
H16C	0.6635	0.6216	0.4720	0.118*	
C17	0.44922 (14)	1.1035 (3)	0.31927 (13)	0.0556 (5)	
H17A	0.4464	1.2314	0.2989	0.083*	0.50
H17B	0.4622	1.1089	0.3734	0.083*	0.50
H17C	0.3949	1.0407	0.3098	0.083*	0.50
H17D	0.4226	1.0226	0.3558	0.083*	0.50
H17E	0.4068	1.1450	0.2814	0.083*	0.50
H17F	0.4741	1.2133	0.3449	0.083*	0.50

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0478 (3)	0.0496 (3)	0.0521 (3)	0.0132 (2)	0.0039 (2)	0.0091 (2)
O1	0.0465 (7)	0.0591 (8)	0.0304 (6)	−0.0038 (6)	0.0019 (5)	0.0041 (5)
O2	0.0453 (7)	0.0380 (6)	0.0408 (7)	0.0001 (5)	0.0036 (5)	0.0028 (5)
N1	0.0410 (8)	0.0471 (8)	0.0329 (8)	0.0013 (6)	0.0042 (6)	0.0019 (6)
N2	0.0436 (8)	0.0361 (8)	0.0407 (8)	0.0001 (6)	−0.0060 (6)	−0.0006 (6)
C1	0.0346 (9)	0.0712 (13)	0.0383 (10)	−0.0102 (9)	0.0009 (7)	0.0062 (9)
C2	0.0413 (10)	0.0857 (16)	0.0423 (11)	−0.0103 (10)	−0.0070 (8)	0.0079 (10)
C3	0.0515 (12)	0.0735 (14)	0.0356 (10)	−0.0087 (10)	−0.0075 (8)	0.0029 (9)
C4A	0.0377 (9)	0.0393 (9)	0.0287 (8)	−0.0008 (7)	0.0018 (7)	0.0029 (7)
C4B	0.0350 (9)	0.0347 (9)	0.0428 (10)	0.0040 (7)	0.0065 (7)	0.0057 (7)
C5	0.0466 (11)	0.0525 (11)	0.0458 (11)	0.0030 (8)	0.0114 (8)	0.0073 (8)
C6	0.0438 (11)	0.0547 (12)	0.0660 (14)	0.0018 (9)	0.0195 (10)	0.0173 (10)
C7	0.0356 (10)	0.0438 (11)	0.0785 (15)	−0.0030 (8)	0.0068 (10)	0.0103 (10)
C8	0.0354 (9)	0.0399 (10)	0.0596 (12)	0.0008 (7)	0.0016 (8)	0.0008 (8)
C8A	0.0333 (8)	0.0308 (8)	0.0445 (10)	0.0030 (6)	0.0030 (7)	0.0029 (7)
C8B	0.0357 (9)	0.0302 (8)	0.0371 (9)	0.0017 (6)	0.0000 (7)	0.0005 (6)
C9A	0.0520 (11)	0.0315 (8)	0.0363 (9)	0.0041 (7)	−0.0016 (8)	0.0004 (7)
C10	0.0660 (13)	0.0453 (11)	0.0418 (11)	0.0033 (9)	−0.0109 (10)	−0.0020 (8)
C11	0.0934 (17)	0.0447 (11)	0.0322 (10)	0.0072 (11)	−0.0049 (10)	−0.0014 (8)
C12	0.0841 (16)	0.0476 (11)	0.0368 (11)	0.0066 (10)	0.0123 (10)	0.0029 (8)
C13	0.0615 (12)	0.0523 (11)	0.0387 (10)	0.0038 (9)	0.0107 (9)	0.0034 (8)
C13A	0.0508 (10)	0.0366 (9)	0.0322 (9)	0.0044 (8)	0.0039 (8)	0.0007 (7)
C14A	0.0349 (8)	0.0363 (9)	0.0323 (8)	0.0014 (7)	0.0027 (7)	0.0010 (6)
C14B	0.0340 (9)	0.0420 (9)	0.0337 (9)	−0.0002 (7)	0.0019 (7)	0.0059 (7)
C15	0.0859 (19)	0.0804 (18)	0.0777 (18)	−0.0164 (15)	−0.0243 (15)	−0.0165 (14)
C16	0.0726 (16)	0.121 (2)	0.0405 (12)	0.0030 (15)	−0.0079 (11)	0.0141 (13)
C17	0.0578 (12)	0.0448 (11)	0.0644 (13)	0.0068 (9)	0.0058 (10)	−0.0062 (9)

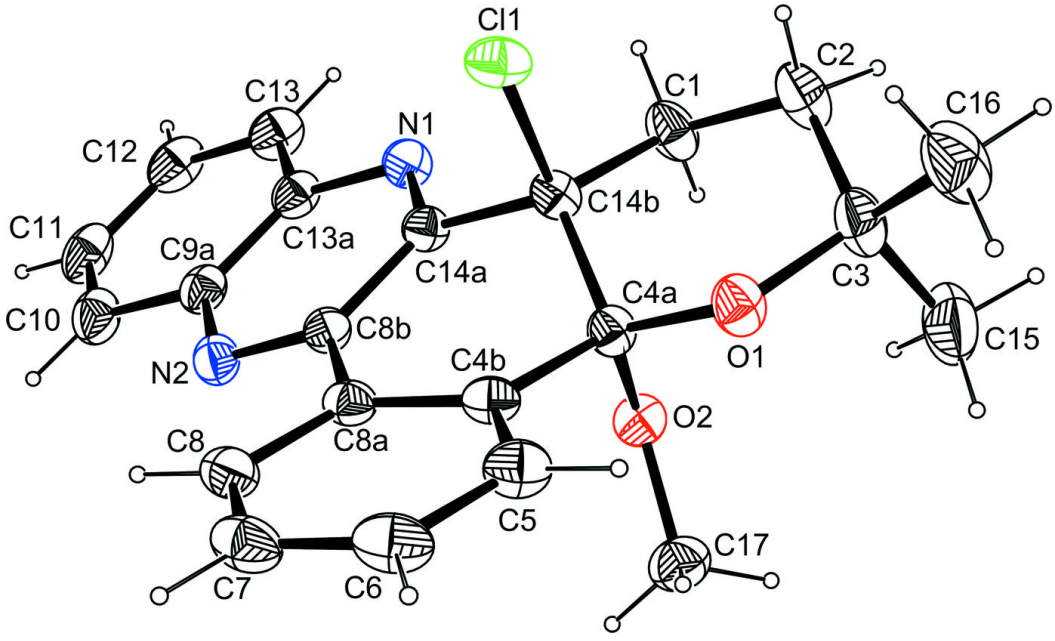
Geometric parameters (Å, °)

Cl1—C14B	1.8247 (18)	C8—C8A	1.396 (2)
O1—C4A	1.3950 (19)	C8—H8	0.9300
O1—C3	1.471 (2)	C8A—C8B	1.479 (2)
O2—C17	1.426 (2)	C8B—C14A	1.433 (2)
O2—C4A	1.429 (2)	C9A—C13A	1.406 (3)
N1—C14A	1.309 (2)	C9A—C10	1.411 (3)
N1—C13A	1.367 (2)	C10—C11	1.366 (3)
N2—C8B	1.315 (2)	C10—H10	0.9300
N2—C9A	1.370 (2)	C11—C12	1.396 (3)
C1—C14B	1.515 (2)	C11—H11	0.9300
C1—C2	1.524 (3)	C12—C13	1.363 (3)
C1—H1A	0.9700	C12—H12	0.9300
C1—H1B	0.9700	C13—C13A	1.412 (2)
C2—C3	1.527 (3)	C13—H13	0.9300
C2—H2A	0.9700	C14A—C14B	1.507 (2)

C2—H2B	0.9700	C15—H15A	0.9600
C3—C15	1.514 (3)	C15—H15B	0.9600
C3—C16	1.527 (3)	C15—H15C	0.9600
C4A—C4B	1.521 (2)	C16—H16A	0.9600
C4A—C14B	1.537 (2)	C16—H16B	0.9600
C4B—C5	1.390 (2)	C16—H16C	0.9600
C4B—C8A	1.399 (2)	C17—H17A	0.9600
C5—C6	1.385 (3)	C17—H17B	0.9600
C5—H5	0.9300	C17—H17C	0.9600
C6—C7	1.375 (3)	C17—H17D	0.9600
C6—H6	0.9300	C17—H17E	0.9600
C7—C8	1.378 (3)	C17—H17F	0.9600
C7—H7	0.9300		
C4A—O1—C3	119.65 (13)	C10—C11—C12	120.58 (19)
C17—O2—C4A	116.04 (14)	C10—C11—H11	119.7
C14A—N1—C13A	116.34 (15)	C12—C11—H11	119.7
C8B—N2—C9A	116.75 (15)	C13—C12—C11	120.7 (2)
C14B—C1—C2	110.13 (15)	C13—C12—H12	119.6
C14B—C1—H1A	109.6	C11—C12—H12	119.6
C2—C1—H1A	109.6	C12—C13—C13A	120.0 (2)
C14B—C1—H1B	109.6	C12—C13—H13	120.0
C2—C1—H1B	109.6	C13A—C13—H13	120.0
H1A—C1—H1B	108.1	N1—C13A—C9A	121.35 (16)
C1—C2—C3	114.38 (17)	N1—C13A—C13	119.28 (17)
C1—C2—H2A	108.7	C9A—C13A—C13	119.36 (17)
C3—C2—H2A	108.7	N1—C14A—C8B	122.82 (15)
C1—C2—H2B	108.7	N1—C14A—C14B	118.51 (15)
C3—C2—H2B	108.7	C8B—C14A—C14B	118.63 (14)
H2A—C2—H2B	107.6	C14A—C14B—C1	115.37 (14)
O1—C3—C15	109.91 (18)	C14A—C14B—C4A	110.29 (14)
O1—C3—C16	102.45 (17)	C1—C14B—C4A	109.91 (15)
C15—C3—C16	110.3 (2)	C14A—C14B—Cl1	105.21 (11)
O1—C3—C2	111.94 (16)	C1—C14B—Cl1	108.68 (13)
C15—C3—C2	112.3 (2)	C4A—C14B—Cl1	106.96 (11)
C16—C3—C2	109.48 (19)	C3—C15—H15A	109.5
O1—C4A—O2	112.47 (13)	C3—C15—H15B	109.5
O1—C4A—C4B	108.66 (13)	H15A—C15—H15B	109.5
O2—C4A—C4B	110.09 (13)	C3—C15—H15C	109.5
O1—C4A—C14B	112.59 (14)	H15A—C15—H15C	109.5
O2—C4A—C14B	102.43 (13)	H15B—C15—H15C	109.5
C4B—C4A—C14B	110.50 (14)	C3—C16—H16A	109.5
C5—C4B—C8A	119.68 (17)	C3—C16—H16B	109.5
C5—C4B—C4A	122.80 (16)	H16A—C16—H16B	109.5
C8A—C4B—C4A	117.48 (14)	C3—C16—H16C	109.5
C6—C5—C4B	119.95 (19)	H16A—C16—H16C	109.5
C6—C5—H5	120.0	H16B—C16—H16C	109.5
C4B—C5—H5	120.0	O2—C17—H17A	109.5
C7—C6—C5	120.40 (18)	O2—C17—H17B	109.5
C7—C6—H6	119.8	H17A—C17—H17B	109.5

C5—C6—H6	119.8	O2—C17—H17C	109.5
C6—C7—C8	120.45 (18)	H17A—C17—H17C	109.5
C6—C7—H7	119.8	H17B—C17—H17C	109.5
C8—C7—H7	119.8	O2—C17—H17D	109.5
C7—C8—C8A	120.06 (19)	H17A—C17—H17D	141.1
C7—C8—H8	120.0	H17B—C17—H17D	56.3
C8A—C8—H8	120.0	H17C—C17—H17D	56.3
C8—C8A—C4B	119.46 (16)	O2—C17—H17E	109.5
C8—C8A—C8B	120.35 (16)	H17A—C17—H17E	56.3
C4B—C8A—C8B	120.10 (15)	H17B—C17—H17E	141.1
N2—C8B—C14A	121.44 (15)	H17C—C17—H17E	56.3
N2—C8B—C8A	119.29 (15)	H17D—C17—H17E	109.5
C14A—C8B—C8A	119.22 (15)	O2—C17—H17F	109.5
N2—C9A—C13A	121.28 (16)	H17A—C17—H17F	56.3
N2—C9A—C10	119.48 (17)	H17B—C17—H17F	56.3
C13A—C9A—C10	119.24 (17)	H17C—C17—H17F	141.1
C11—C10—C9A	120.1 (2)	H17D—C17—H17F	109.5
C11—C10—H10	120.0	H17E—C17—H17F	109.5
C9A—C10—H10	120.0		

Fig. 1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