

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

van der Peet, PL;Joyce, RD;Ott, H;Marcuccio, SM;White, JM;Williams, SJ

Title:

Synthesis and structure of clozapine N-oxide hemi(hydrochloride): an infinite hydrogen-bonded poly[n]catenane

Date:

2022-10-01

Citation:

van der Peet, P. L., Joyce, R. D., Ott, H., Marcuccio, S. M., White, J. M. & Williams, S. J. (2022). Synthesis and structure of clozapine N-oxide hemi(hydrochloride): an infinite hydrogen-bonded poly[n]catenane. *Acta Crystallographica Section E Crystallographic Communications*, 78 (10), pp.1056-1060. <https://doi.org/10.1107/S2056989022009306>.

Persistent Link:

<https://hdl.handle.net/11343/318027>

License:

[CC BY](#)



Synthesis and structure of clozapine *N*-oxide hemi(hydrochloride): an infinite hydrogen-bonded poly[*n*]catenane

Phillip L. van der Peet,^a Rohan D. Joyce,^b Holger Ott,^c Sebastian M. Marcuccio,^b Jonathan M. White^{a*} and Spencer J. Williams^a

Received 19 September 2022

Accepted 21 September 2022

Edited by W. T. A. Harrison, University of Aberdeen, Scotland

Keywords: hydrogen bonding; crystal structure; hydrogen-bonding catenation.

CCDC reference: 2208459

Supporting information: this article has supporting information at journals.iucr.org/e

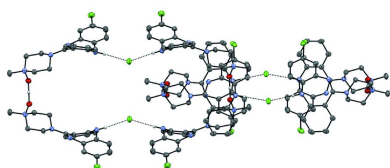
^aSchool of Chemistry and Bio21 Molecular Science and Biotechnology Institute, University of Melbourne, Parkville, 3010, Australia, ^bAdvanced Molecular Technologies, Unit 1, 7-11 Rocco Drive, Scoresby, Victoria, 3179, Australia, and ^cBruker AXS GmbH, Oestliche Rheinbrueckenstr. 49, 76187 Karlsruhe, Germany. *Correspondence e-mail: whitejm@unimelb.edu.au

The structure of the title compound, $2C_{18}H_{19}ClN_4O \cdot HCl$ or $(CNO)_2 \cdot HCl$ ($C_{36}H_{39}Cl_3N_8O_2$), at 100 K has tetragonal ($I4/m$) symmetry. The dihedral angle between the benzene rings of the fused ring system of the CNO molecule is $40.08(6)^\circ$ and the equivalent angle between the seven-membered ring and its pendant *N*-oxide ring is $31.14(7)^\circ$. The structure contains a very strong, symmetrical $O-H \cdots O$ hydrogen bond [$O \cdots O = 2.434(2) \text{ \AA}$] between two equivalent $R_3N^+ - O^-$ moieties, which share a proton lying on a crystallographic twofold rotation axis. These units then form a $(CNO)_4 \cdot (HCl)_2$ ring by way of two equivalent $N-H \cdots Cl$ hydrogen bonds (Cl^- site symmetry m). These rings are catenated into infinite chains propagating along the *c*-axis direction by way of shape complementarity and directional $C-H \cdots N$ and $C-H \cdots \pi$ interactions.

1. Chemical context

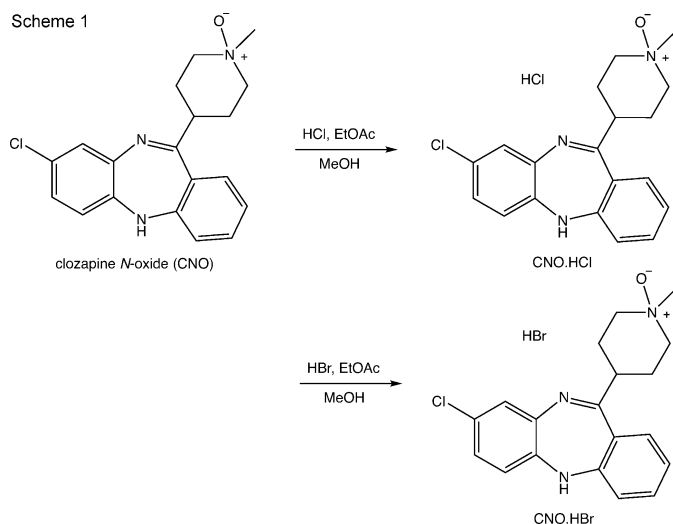
Coordination-driven self-assembly of supramolecular structures is a major focus area of materials science. However, hydrogen-bond-driven self-assembly has been less well studied, most likely as a consequence of the weakness of hydrogen bonding relative to coordinate bonding. Nevertheless, the directionality of hydrogen bonding can lend it to the controllable formation of supramolecular networks (González-Rodríguez & Schenning, 2011; Steiner, 2002; Prins *et al.*, 2001). The simplest infinite interlocking systems are the one-dimensional polycatenanes (poly[*n*]catenanes). Such systems have been described involving interpenetrating metallocycles of silver/bis(2-methylimidazolyl) (Jin *et al.*, 2006, 2008, 2018) and mercury/1,2-bis[(pyridin-4-ylthio)methyl]-benzene (Xue *et al.*, 2015). However, the lack of many examples beyond these suggests that the self-assembly of this interesting topological architecture is not easily achieved. Here, we report the serendipitous discovery of an infinite one-dimensional polycatenane architecture templated by a chloride anion that forms upon the attempted recrystallization of clozapine *N*-oxide ($C_{18}H_{19}ClN_4O$; hereafter CNO) monohydrochloride, an inactive metabolite of clozapine that is utilized as an actuator of engineered muscarinic acetylcholine receptors (Armbruster *et al.*, 2007; Urban & Roth, 2015; Dong *et al.*, 2010; Gomez *et al.*, 2017).

As part of efforts to develop a water-soluble salt form of CNO (van der Peet *et al.*, 2018) we synthesized CNO-HBr and CNO-HCl by formation of the salt in methanol (Scheme 1).

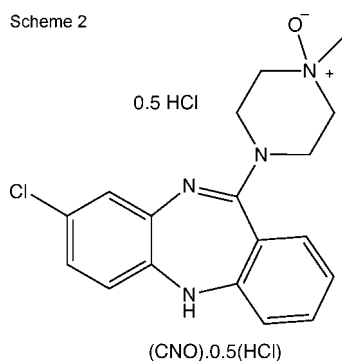


OPEN ACCESS

Published under a CC BY 4.0 licence



The latter compound has been reported previously (Allen *et al.*, 2019), but its preparation was not described. Elemental analysis of the precipitated CNO·HCl was consistent with the proposed structure in Scheme 1. Although crystals suitable for single crystal X-ray analysis were not obtained from the crude precipitate, powder X-ray diffraction of the precipitate suggested the material was substantially crystalline. To obtain structural verification and to locate the site of protonation, we attempted to grow single crystals of CNO·HCl for single crystal X-ray analysis. Slow evaporation of a solution of CNO·HCl from a variety of solvents, or by diffusion of diethyl ether into a variety of solvents consistently yielded small orange block-shaped crystals of the title hemihydrochloride, which were found to be no longer soluble in water or other solvents (Scheme 2).



2. Structural commentary

Single-crystal X-ray diffraction analysis of the orange crystals revealed that the CNO·HCl salt implied by the analysis for the initially formed salt (above) had lost half an equivalent of HCl upon crystallization and crystallized as a hemihydrochloride, (CNO)₂·HCl, in the tetragonal space group *I4/m* (Scheme 2 and Fig. 1). In this structure, two molecules of CNO, which are related by a crystallographic twofold axis, share a proton, which is located on the rotation axis and forms a strong,

Table 1
Selected torsion angles (°).

C8–N1–C1–C2	55.7 (2)	C7–N2–C9–C8	33.5 (2)
C9–N2–C7–C2	3.2 (2)	C1–N1–C8–C9	–54.0 (2)
N1–C1–C2–C7	0.9 (2)	N2–C9–C8–N1	–4.9 (2)
N2–C7–C2–C1	–35.2 (2)		

essentially linear and apparently symmetric O–H···O/O···H–O hydrogen bond between the two molecules *via* the *N*-oxide moieties [O1···O1ⁱ = 2.434 (2) Å; symmetry code (i) $-x, 1 - y, z$]. Within the structure, the chloride counter-ion (Cl2) is located on a crystallographic mirror plane and accepts equivalent N–H···Cl hydrogen bonds [N1···Cl2 = 3.3259 (14) Å] to two mirror-related (CNO)₂H⁺ moieties resulting in the formation of a cyclic structure templated by the Cl[–] counter-ions (Fig. 2). The diazepine ring core in (CNO)₂·HCl adopts a boat conformation (Table 1) in which the N1(H) group is at the bow and the C7=N2 imine group is the stern. A consequence of the boat conformation is the mean planes of the two fused benzene rings lie at an angle

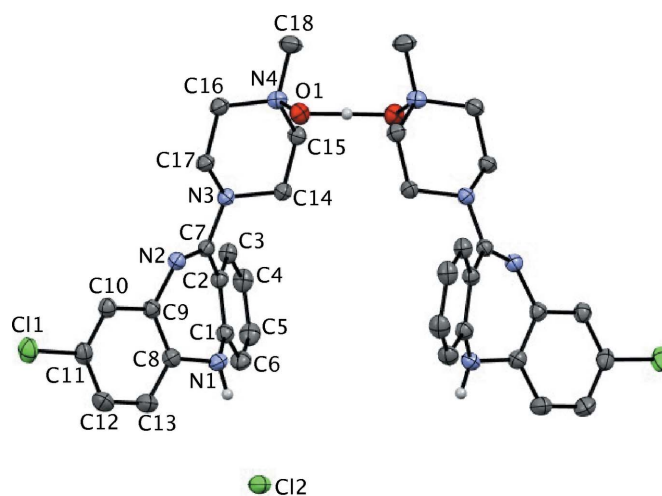


Figure 1
The molecular structure of (CNO)₂·HCl showing 50% displacement ellipsoids with C-bound H atoms omitted for clarity. The unlabelled atoms are generated by the symmetry operation $-x, 1 - y, z$.

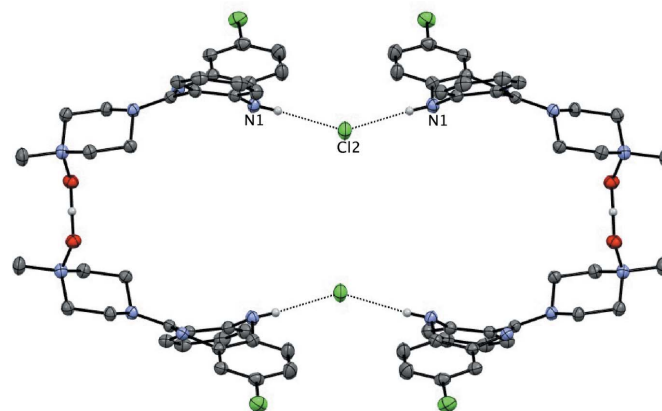


Figure 2
The cyclic tetramer (CNO)₄·(HCl)₂ templated by N–H···Cl hydrogen-bonding interactions.

Table 2
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>
O1—H1A...O1 ⁱ	1.22 (1)	1.22 (1)	2.434 (2)	179 (4)
N1—H1...Cl2	0.86 (2)	2.46 (2)	3.3259 (14)	176 (2)
C15—H15A...O1 ⁱ	0.97	2.64	3.2598 (19)	122
C15—H15A...N1 ⁱⁱ	0.97	2.51	3.416 (2)	156
C15—H15B...Cl1 ⁱⁱⁱ	0.97	2.91	3.8431 (17)	162

Symmetry codes: (i) $-x, -y + 1, z$; (ii) $-y + \frac{1}{2}, x + \frac{1}{2}, -z + \frac{1}{2}$; (iii) $-x + \frac{1}{2}, -y + \frac{1}{2}, -z + \frac{1}{2}$.

40.08 (6)° to one another; this represents a less puckered ring to that observed in the (CNO)·MeOH solvate in which the aromatic rings are at an angle of 56.2° (van der Peet *et al.*, 2018) demonstrating the flexibility of this ring system. The equivalent angle between the seven-membered diazepine ring and its pendant *N*-oxide ring is 31.14 (7)°

3. Supramolecular features

The tetrameric cyclic structures are catenated and form infinite chains extending along the *z*-direction (Figs. 3 and 4) in which adjacent links in the chain are related by a 4₂ screw axis. The catenated rings form both as a result of general complementarity in the shapes of the internal cavities of the interacting (CNO)₂ dimers related by the symmetry operation ($\frac{1}{2} - y, \frac{1}{2} + x, \frac{1}{2} - z$), and further stabilized by four equivalent non-classical hydrogen-bonding interactions involving the polarized C—H bond adjacent to the *N*-oxide moiety; (C15—H15A...N1, Table 2) in addition to four equivalent C—H... π interactions [H15A...C8 = 2.706 (2) Å] (Fig. 5). Solvent voids, which account for approximately 17% of the unit-cell volume,

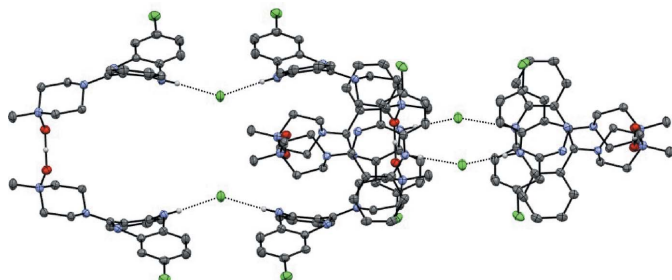


Figure 3
Partial structure of (CNO)₂·HCl catenated chain showing two members of the poly[*n*]catenane; adjacent links in the chain are related by a 4₂ screw axis.

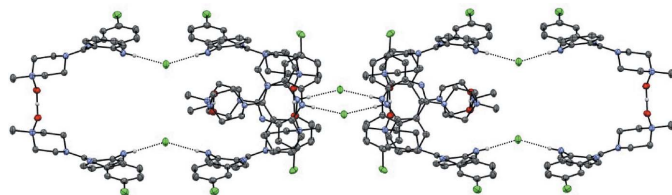


Figure 4
Partial structure of (CNO)₂·HCl catenated chain showing three members of the poly[*n*]catenane; adjacent links in the chain are related by a 4₂ screw axis.

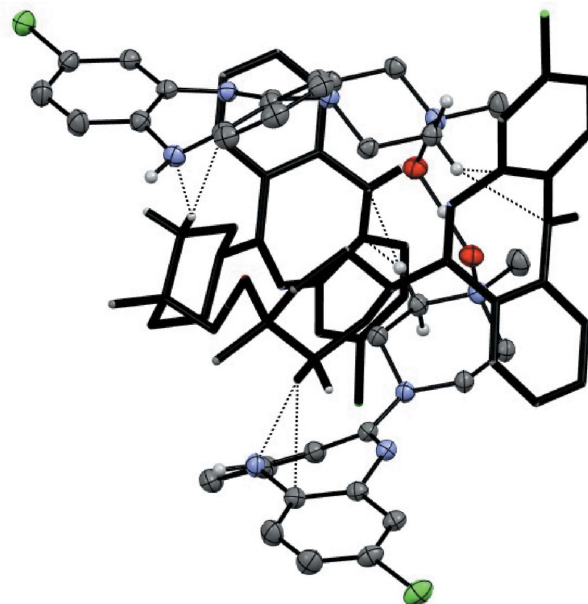


Figure 5
C—H...N and C—H... π interactions at the interface of neighbouring tetrameric (CNO)₄·(HCl) rings in the poly[*n*]catenane.

lie between the catenated chains: the disordered solvent was accounted for using the Squeeze procedure in *PLATON* (Spek, 2015). To establish the relationship between the original material and that obtained after crystallization, powder X-ray diffraction data were obtained for the orange crystals and compared to that for the original material (Fig. 6). The two powder diffraction patterns are substantially different, which is consistent with the combustion analysis of the original material that analysed as (CNO)·HCl, whereas the crystallized material is (CNO)₂·HCl. Application of the same approach to CNO·HBr did not lead to an equivalent polymeric material.

4. Database survey

The formation of strong hydrogen bonds is predicted to occur when the p*K*_a value for the donor acid matches that for the

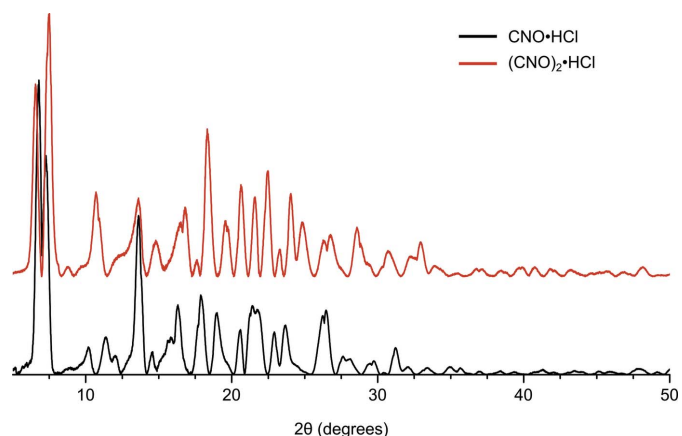


Figure 6
Overlay of powder patterns of the initial precipitate of (CNO)·HCl and the recrystallized material (CNO)₂·HCl.

acceptor's conjugate acid form (Gilli *et al.*, 2009). In this structure, a strong hydrogen bond between a protonated tertiary amine *N*-oxide and its conjugate base is predicted. A search of the Cambridge Structural Database (2022.2.0, September 2022; Groom *et al.*, 2016) for structures containing the $R_3N-OH \cdots O-NR_3$ moiety with constraints on the *R* factor to 5% or less and only organic structures surveyed gave eight good-quality structures (CSD refcodes: RAJDAL (Bettencourt *et al.*, 2021), AJESEQ (Wlaźlak *et al.*, 2018), AREREW (Moore *et al.*, 2016), BAYDEK (Jaskólski *et al.*, 1982), EPSPOX (Małuszyńska & Okaya, 1977), FUBMAS (Moore *et al.*, 2015), NUCDUK (Krzywda *et al.*, 1996) and OBECUV (Bohmer *et al.*, 2011); these structures are characterized by O \cdots O distances ranging from 2.426–2.445 Å, which is comparable to the O \cdots O distance of 2.434 (2) Å in this structure, thus all can be classified as strong O–H \cdots O hydrogen bonds as predicted.

5. Synthesis and crystallization

Preparation of clozapine *N*-oxide hydrochloride (CNO·HCl)

A 250 ml round-bottom flask was charged with clozapine *N*-oxide (5.00 g, 0.015 mol) and methanol (50 ml) and stirred under N₂. Initially, the solid dissolved but then precipitated as a presumed CNO-methanolate adduct. A solution of HCl in ethyl acetate (2.8 M, 6 ml, 0.017 mol, 1.1 eq) was added slowly to the suspension. After 10 min the solid dissolved, and then precipitated as a faint yellow solid. The suspension was stirred for 1 h, then the solid was collected by filtration, and washed with ethyl acetate to afford CNO·HCl as a yellow solid (2.2 g, 39%). Degradation point: 473–478 K (corrected); ¹H NMR (400 MHz, CD₃OD) δ 3.35–3.45 (*m*, 6 H), 3.65–3.80 (*m*, 4 H), 3.95 (*br s*, 2 H), 6.83 (*d*, *J* 8.4 Hz, 1 H), 6.87 (*d*, *J* 2.4, 8.4 Hz, 1 H), 6.97 (*dd*, *J* = 2.4 Hz, 1H), 7.01 (*dd*, *J* 1.0, 8.0 Hz, 1H), 7.06 (*dt*, *J* 1.1, 7.6 Hz, 1H), 7.33 (*dd*, *J* 1.4, 7.8 Hz, 1H), 7.37 (*dt*, *J* 1.5, 6.4 Hz, 1H); ¹³C NMR (100 MHz, CD₃OD) δ 43.1, 58.9, 65.3, 121.5, 121.6, 123.6, 124.3, 125.1, 127.4, 129.6, 131.2, 133.9, 142.5, 143.1, 155.5, 164.0. Elemental analysis: calculated for C₁₈H₂₀Cl₂N₄O: C 57.0, H 5.3, N 14.8. Found: C 56.8, H 5.6, N 14.8.

Preparation of clozapine *N*-oxide hemihydrochloride (CNO)₂·HCl

The above material (CNO·HCl) was recrystallized by diffusion of diethyl ether into a methanol solution giving (CNO)₂·HCl as small orange blocks.

Preparation of clozapine *N*-oxide hydrobromide

A 25 ml round-bottom flask was charged with clozapine *N*-oxide (1.00 g, 2.92 mmol, 1 eq.) and methanol (5 ml) and stirred under N₂. Initially, the solid dissolved but then precipitated as a presumed CNO-methanolate adduct. The solution was cooled in an ice–water bath and 48% HBr in water (0.35 ml, 3.07 mmol, 1.05 eq) was added slowly to the suspension. The mixture stirred for 1 h at rt, without formation of a precipitate. The solvent was evaporated and the residue suspended in EtOAc (10 ml). The resulting solid was collected by filtration and washed with EtOAc to afford CNO·HBr as a yellow solid (1.1 g, 89%). Degradation point: 483–493 K

Table 3
Experimental details.

Crystal data	
Chemical formula	2C ₁₈ H ₁₉ ClN ₄ O·HCl
<i>M_r</i>	722.10
Crystal system, space group	Tetragonal, <i>I4/m</i>
Temperature (K)	100
<i>a</i> , <i>c</i> (Å)	17.305 (2), 26.040 (5)
<i>V</i> (Å ³)	7798 (3)
<i>Z</i>	8
Radiation type	Synchrotron, λ = 0.710757 Å
μ (mm ⁻¹)	0.28
Crystal size (mm)	0.06 × 0.05 × 0.04
Data collection	
Diffractometer	ADSC Quantum 210r
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	66433, 5901, 5096
<i>R</i> _{int}	0.049
(sin θ/λ) _{max} (Å ⁻¹)	0.741
Refinement	
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.049, 0.138, 1.03
No. of reflections	5901
No. of parameters	231
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
Δρ _{max} , Δρ _{min} (e Å ⁻³)	0.81, −0.49

Computer programs: AS QEGUI, XDS (Kabsch, 1993), SHELXT (Sheldrick, 2015a), SHELXL2016/6 (Sheldrick, 2015b), Mercury (Macrae *et al.*, 2020) and WinGX (Farrugia, 2012).

(corrected); ¹H NMR (400 MHz, CD₃OD) δ 3.68 (*s*, 3 H), 3.87 (*br d*, *J* 11.6 Hz, 2 H), 3.9–4.2 (*m*, 6 H), 7.01 (*d*, *J* 8.6 Hz, 1 H), 7.13–7.23 (*m*, 3 H), 7.27 (*br s*, 1 H), 7.53–7.60 (*m*, 2 H); ¹³C NMR (100 MHz, CD₃OD) δ 44.7, 57.8, 57.9, 64.6, 64.7, 122.6, 124.9, 125.0, 126.7, 126.8, 128.4, 130.0, 133.1, 136.5, 145.9, 156.4.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. Regions of the unit cell occupied by disordered solvent (1409 Å³; ≈ 18.1% of the unit-cell volume) were processed with the Squeeze algorithm in PLATON (Spek, 2015); the stated composition, density, *etc.* do not take account of the solvent.

Acknowledgements

The Australian Synchrotron Collaborative Access Program is thanked for beamtime on MX1.

Funding information

Funding for this research was provided by: Australian Research Council (award No. DP160100597; award No. DP180101957); Australian Synchrotron (grant No. 13618b).

References

- Allen, D. C., Carlson, T. L., Xiong, Y., Jin, J., Grant, K. A. & Cuzon Carlson, V. C. (2019). *J. Pharmacol. Exp. Ther.* **368**, 199–207.
Armbruster, B. N., Li, X., Pausch, M. H., Herlitze, S. & Roth, B. L. (2007). *Proc. Natl Acad. Sci. USA*, **104**, 5163–5168.

- Bettencourt, C. J., Chow, S., Moore, P. W., Read, C. D. G., Jiao, Y., Bakker, J. P., Zhao, S., Bernhardt, P. V. & Williams, C. M. (2021). *Aust. J. Chem.* **74**, 652–659.
- Bohmer, V., Brusko, V. & Bolte, M. (2011). Private Communication (refcode OBECUV). CCDC, Cambridge, England. <https://doi.org/10.5517/ccx8ltk>
- Dong, S., Allen, J. A., Farrell, M. & Roth, B. L. (2010). *Mol. BioSyst.* **6**, 1376–1380.
- Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
- Gilli, P., Preto, V., Bertolasi, V. & Gilli, G. (2009). *Acc. Chem. Res.* **42**, 33–44.
- Gomez, J. L., Bonaventura, J., Lesniak, W., Mathews, W. B., Syya-Shah, P., Rodriguez, L. A., Ellis, R. J., Richie, C. T., Harvey, B. K., Dannals, R. F., Pomper, M. G., Bonci, A. & Michaelides, M. (2017). *Science*, **357**, 503–507.
- González-Rodríguez, D. & Schenning, A. P. H. J. (2011). *Chem. Mater.* **23**, 310–325.
- Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* **B72**, 171–179.
- Jaskólski, M., Olovsson, I., Tellgren, R. & Mickiewicz-Wichłacz, D. (1982). *Acta Cryst.* **B38**, 291–294.
- Jin, C. M., Lu, H., Wu, L. Y. & Huang, J. (2006). *Chem. Commun.* pp. 5039–5041.
- Jin, C.-M., Wu, L.-Y., Lu, H. & Xu, Y. (2008). *Cryst. Growth Des.* **8**, 215–218.
- Jin, T., Zhou, J., Pan, Y., Huang, Y. & Jin, C. (2018). *J. Mol. Struct.* **1160**, 222–226.
- Kabsch, W. (1993). *J. Appl. Cryst.* **26**, 795–800.
- Krzywda, S., Jaskólski, M., Gdaniec, M., Dega-Szafran, Z., Grundwald-Wyspiańska, M., Szafran, M., Dauter, Z. & Davies, G. (1996). *J. Mol. Struct.* **375**, 197–206.
- Macrae, C. F., Sovago, I., Cottrell, S. J., Galek, P. T. A., McCabe, P., Pidcock, E., Platings, M., Shields, G. P., Stevens, J. S., Towler, M. & Wood, P. A. (2020). *J. Appl. Cryst.* **53**, 226–235.
- Małuszyńska, H. & Okaya, Y. (1977). *Acta Cryst.* **B33**, 3049–3054.
- Moore, P. W., Jiao, Y., Mirzayans, P. M., Sheng, L. N. Q., Hooker, J. P. & Williams, C. M. (2016). *Eur. J. Org. Chem.* pp. 3401–3407.
- Moore, P. W., Mirzayans, P. M. & Williams, C. M. (2015). *Chem. Eur. J.* **21**, 3567–3571.
- Peet, P. L. van der, Gunawan, C., Abdul-Ridha, A., Ma, S., Scott, D. J., Gundlach, A. L., Bathgate, R. A. D., White, J. M. & Williams, S. J. (2018). *MethodsX*, **5**, 257–267.
- Prins, L. J., Reinhoudt, D. N. & Timmerman, P. (2001). *Angew. Chem. Int. Ed.* **40**, 2382–2426.
- Sheldrick, G. M. (2015a). *Acta Cryst.* **A71**, 3–8.
- Sheldrick, G. M. (2015b). *Acta Cryst.* **C71**, 3–8.
- Spek, A. L. (2015). *Acta Cryst.* **C71**, 9–18.
- Steiner, T. (2002). *Angew. Chem. Int. Ed.* **41**, 48–76.
- Urban, D. J. & Roth, B. L. (2015). *Annu. Rev. Pharmacol. Toxicol.* **55**, 399–417.
- Wlazlak, E., Kalinowska-Thuscik, J., Nitek, W., Klejna, S., Mech, K., Macyk, W. & Szaciłowski, K. (2018). *ChemElectroChem*, **5**, 3486–3497.
- Xue, H., Jiang, F., Chen, Q., Yuan, D., Pang, J., Lv, G., Wan, X., Liang, L. & Hong, M. (2015). *Chem. Commun.* **51**, 13706–13709.

supporting information

Acta Cryst. (2022). E78, 1056-1060 [https://doi.org/10.1107/S2056989022009306]

Synthesis and structure of clozapine *N*-oxide hemi(hydrochloride): an infinite hydrogen-bonded poly[*n*]catenane

Phillip L. van der Peet, Rohan D. Joyce, Holger Ott, Sebastian M. Marcuccio, Jonathan M. White and Spencer J. Williams

Computing details

Data collection: AS QEGUI; cell refinement: *XDS* (Kabsch, 1993); data reduction: *XDS* (Kabsch, 1993); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2016/6* (Sheldrick, 2015b); molecular graphics: *Mercury* (Macrae *et al.*, 2020); software used to prepare material for publication: *WinGX* (Farrugia, 2012).

8-Chloro-11-(4-methyl-1-piperazinyl)-5*H*-dibenzo[*b,e*][1,4]diazepine *N*-oxide hemi(hydrochloride)

Crystal data

2C₁₈H₁₉ClN₄O·HCl

M_r = 722.10

Tetragonal, *I4/m*

a = 17.305 (2) Å

c = 26.040 (5) Å

V = 7798 (3) Å³

Z = 8

F(000) = 3024

D_x = 1.230 Mg m⁻³

Synchrotron radiation, λ = 0.710757 Å

Cell parameters from 5908 reflections

θ = 1.4–31.8°

μ = 0.28 mm⁻¹

T = 100 K

Block, yellow

0.06 × 0.05 × 0.04 mm

Data collection

ADSC Quantum 210r
diffractometer

Radiation source: MX1 Beamline Australian
Synchrotron

Silicon Double Crystal monochromator

ω Scan scans

66433 measured reflections

5901 independent reflections

5096 reflections with *I* > 2σ(*I*)

*R*_{int} = 0.049

θ_{max} = 31.8°, θ_{min} = 1.4°

h = -25→25

k = -25→25

l = -36→36

Refinement

Refinement on *F*²

Least-squares matrix: full

R[*F*² > 2σ(*F*²)] = 0.049

wR(*F*²) = 0.138

S = 1.03

5901 reflections

231 parameters

0 restraints

Hydrogen site location: mixed

H atoms treated by a mixture of independent
and constrained refinement

w = 1/[σ²(*F_o*²) + (0.0661*P*)² + 11.4576*P*]

where *P* = (*F_o*² + 2*F_c*²)/3

(Δ/σ)_{max} = 0.001

Δρ_{max} = 0.81 e Å⁻³

Δρ_{min} = -0.49 e Å⁻³

Extinction correction: SHELXL2016/6
(Sheldrick 2015b),

*F_c** = *kF_c*[1 + 0.001*xF_c*²λ³/sin(2θ)]^{-1/4}

Extinction coefficient: 0.0069 (5)

Special details

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C11	0.13932 (3)	0.04426 (2)	0.37292 (2)	0.03680 (13)
C12	0.16534 (4)	0.44691 (3)	0.500000	0.03563 (15)
O1	0.02559 (6)	0.43450 (7)	0.13599 (5)	0.0285 (2)
N3	0.17304 (7)	0.39022 (7)	0.21729 (5)	0.0225 (2)
N2	0.15846 (7)	0.30145 (7)	0.28157 (5)	0.0228 (2)
N1	0.18161 (8)	0.38441 (8)	0.37970 (5)	0.0261 (3)
N4	0.10378 (8)	0.43810 (8)	0.12165 (5)	0.0248 (3)
C1	0.23713 (9)	0.42470 (8)	0.35074 (6)	0.0242 (3)
C7	0.18814 (8)	0.36630 (8)	0.26780 (5)	0.0216 (3)
C2	0.24220 (8)	0.41696 (8)	0.29712 (6)	0.0228 (3)
C10	0.15645 (9)	0.18517 (9)	0.32919 (6)	0.0252 (3)
H10	0.150809	0.159189	0.298148	0.030*
C14	0.14157 (9)	0.46872 (8)	0.21112 (6)	0.0239 (3)
H14A	0.170572	0.504443	0.232387	0.029*
H14B	0.088144	0.469610	0.222369	0.029*
C9	0.16811 (8)	0.26540 (8)	0.32932 (6)	0.0228 (3)
C16	0.13708 (9)	0.35868 (9)	0.12884 (6)	0.0254 (3)
H16A	0.190585	0.358444	0.117741	0.030*
H16B	0.108830	0.322118	0.107741	0.030*
C15	0.14617 (9)	0.49399 (8)	0.15559 (6)	0.0245 (3)
H15A	0.123725	0.545067	0.152003	0.029*
H15B	0.199875	0.496810	0.145089	0.029*
C3	0.29823 (9)	0.46033 (9)	0.27067 (6)	0.0256 (3)
H3	0.302804	0.454729	0.235282	0.031*
C11	0.15328 (9)	0.14442 (9)	0.37477 (6)	0.0291 (3)
C5	0.33991 (10)	0.52005 (10)	0.34901 (7)	0.0317 (3)
H5	0.371497	0.554918	0.366272	0.038*
C8	0.17647 (9)	0.30343 (9)	0.37683 (6)	0.0253 (3)
C17	0.13260 (9)	0.33393 (8)	0.18470 (5)	0.0237 (3)
H17A	0.078931	0.330314	0.195175	0.028*
H17B	0.156037	0.283374	0.188721	0.028*
C6	0.28604 (9)	0.47695 (10)	0.37606 (6)	0.0291 (3)
H6	0.282259	0.482756	0.411475	0.035*
C4	0.34685 (9)	0.51128 (9)	0.29616 (7)	0.0294 (3)
H4	0.383731	0.539293	0.278039	0.035*
C13	0.17144 (12)	0.26047 (10)	0.42216 (6)	0.0352 (4)
H13	0.176053	0.285737	0.453531	0.042*
C12	0.15973 (11)	0.18114 (10)	0.42162 (7)	0.0361 (4)
H12	0.156323	0.153376	0.452117	0.043*

C18	0.10927 (11)	0.46237 (11)	0.06669 (6)	0.0345 (4)
H18A	0.079973	0.427372	0.045739	0.052*
H18B	0.162386	0.461630	0.056060	0.052*
H18C	0.088990	0.513702	0.062973	0.052*
H1	0.1789 (13)	0.3988 (13)	0.4114 (9)	0.037 (6)*
H1A	0.000000	0.500000	0.1357 (17)	0.077 (14)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C11	0.0421 (2)	0.02417 (19)	0.0442 (2)	0.00136 (15)	0.01026 (17)	0.00663 (15)
C12	0.0513 (4)	0.0331 (3)	0.0224 (2)	0.0004 (2)	0.000	0.000
O1	0.0225 (5)	0.0313 (6)	0.0318 (6)	-0.0003 (4)	-0.0012 (4)	0.0007 (4)
N3	0.0265 (6)	0.0200 (5)	0.0210 (5)	-0.0002 (4)	-0.0015 (4)	-0.0017 (4)
N2	0.0234 (6)	0.0225 (5)	0.0224 (5)	0.0017 (4)	0.0001 (4)	-0.0013 (4)
N1	0.0321 (7)	0.0252 (6)	0.0211 (6)	0.0006 (5)	0.0007 (5)	-0.0034 (4)
N4	0.0263 (6)	0.0271 (6)	0.0210 (6)	-0.0012 (5)	0.0007 (4)	-0.0003 (4)
C1	0.0234 (6)	0.0237 (6)	0.0256 (7)	0.0024 (5)	-0.0024 (5)	-0.0013 (5)
C7	0.0216 (6)	0.0219 (6)	0.0214 (6)	0.0025 (5)	0.0000 (5)	-0.0024 (5)
C2	0.0219 (6)	0.0214 (6)	0.0249 (6)	0.0018 (5)	-0.0018 (5)	-0.0015 (5)
C10	0.0234 (6)	0.0241 (7)	0.0282 (7)	0.0020 (5)	0.0025 (5)	0.0007 (5)
C14	0.0272 (7)	0.0211 (6)	0.0233 (6)	0.0015 (5)	-0.0014 (5)	-0.0014 (5)
C9	0.0203 (6)	0.0236 (6)	0.0246 (6)	0.0021 (5)	0.0006 (5)	0.0006 (5)
C16	0.0286 (7)	0.0256 (7)	0.0220 (6)	-0.0001 (6)	0.0009 (5)	-0.0028 (5)
C15	0.0264 (7)	0.0228 (6)	0.0241 (6)	-0.0020 (5)	-0.0011 (5)	0.0003 (5)
C3	0.0239 (6)	0.0236 (6)	0.0293 (7)	0.0010 (5)	0.0000 (5)	-0.0010 (5)
C11	0.0286 (7)	0.0238 (7)	0.0349 (8)	0.0030 (6)	0.0051 (6)	0.0046 (6)
C5	0.0275 (7)	0.0284 (7)	0.0392 (9)	-0.0019 (6)	-0.0071 (6)	-0.0053 (6)
C8	0.0258 (7)	0.0257 (7)	0.0245 (7)	0.0022 (5)	-0.0009 (5)	0.0001 (5)
C17	0.0275 (7)	0.0230 (6)	0.0205 (6)	-0.0010 (5)	-0.0005 (5)	-0.0027 (5)
C6	0.0294 (7)	0.0304 (7)	0.0274 (7)	0.0016 (6)	-0.0056 (6)	-0.0055 (6)
C4	0.0233 (7)	0.0262 (7)	0.0387 (8)	-0.0019 (5)	-0.0006 (6)	-0.0014 (6)
C13	0.0494 (10)	0.0340 (8)	0.0224 (7)	0.0029 (7)	-0.0001 (7)	0.0013 (6)
C12	0.0477 (10)	0.0327 (8)	0.0279 (8)	0.0034 (7)	0.0032 (7)	0.0070 (6)
C18	0.0464 (9)	0.0368 (8)	0.0203 (7)	-0.0016 (7)	0.0000 (6)	0.0033 (6)

Geometric parameters (Å, °)

C11—C11	1.7506 (17)	C9—C8	1.409 (2)
O1—N4	1.4051 (17)	C16—C17	1.518 (2)
O1—H1A	1.2169 (12)	C16—H16A	0.9700
N3—C7	1.4035 (18)	C16—H16B	0.9700
N3—C17	1.4692 (18)	C15—H15A	0.9700
N3—C14	1.4723 (18)	C15—H15B	0.9700
N2—C7	1.2852 (19)	C3—C4	1.388 (2)
N2—C9	1.4012 (19)	C3—H3	0.9300
N1—C1	1.406 (2)	C11—C12	1.380 (2)
N1—C8	1.406 (2)	C5—C6	1.386 (2)

N1—H1	0.86 (2)	C5—C4	1.390 (2)
N4—C18	1.494 (2)	C5—H5	0.9300
N4—C15	1.5016 (19)	C8—C13	1.398 (2)
N4—C16	1.502 (2)	C17—H17A	0.9700
C1—C6	1.403 (2)	C17—H17B	0.9700
C1—C2	1.405 (2)	C6—H6	0.9300
C7—C2	1.492 (2)	C4—H4	0.9300
C2—C3	1.406 (2)	C13—C12	1.388 (3)
C10—C11	1.382 (2)	C13—H13	0.9300
C10—C9	1.403 (2)	C12—H12	0.9300
C10—H10	0.9300	C18—H18A	0.9600
C14—C15	1.513 (2)	C18—H18B	0.9600
C14—H14A	0.9700	C18—H18C	0.9600
C14—H14B	0.9700		
N4—O1—H1A	107.9 (6)	N4—C15—H15A	109.5
C7—N3—C17	115.75 (12)	C14—C15—H15A	109.5
C7—N3—C14	116.31 (11)	N4—C15—H15B	109.5
C17—N3—C14	111.87 (11)	C14—C15—H15B	109.5
C7—N2—C9	126.07 (13)	H15A—C15—H15B	108.1
C1—N1—C8	120.58 (13)	C4—C3—C2	121.53 (15)
C1—N1—H1	114.0 (15)	C4—C3—H3	119.2
C8—N1—H1	109.5 (15)	C2—C3—H3	119.2
O1—N4—C18	109.17 (12)	C12—C11—C10	121.41 (15)
O1—N4—C15	110.03 (11)	C12—C11—C11	119.43 (13)
C18—N4—C15	110.59 (12)	C10—C11—C11	119.16 (13)
O1—N4—C16	107.20 (11)	C6—C5—C4	120.17 (15)
C18—N4—C16	110.61 (12)	C6—C5—H5	119.9
C15—N4—C16	109.18 (12)	C4—C5—H5	119.9
C6—C1—C2	119.37 (14)	C13—C8—N1	119.28 (14)
C6—C1—N1	118.67 (14)	C13—C8—C9	119.13 (15)
C2—C1—N1	121.88 (13)	N1—C8—C9	121.24 (13)
N2—C7—N3	116.40 (13)	N3—C17—C16	110.00 (12)
N2—C7—C2	128.37 (13)	N3—C17—H17A	109.7
N3—C7—C2	115.03 (12)	C16—C17—H17A	109.7
C1—C2—C3	118.60 (14)	N3—C17—H17B	109.7
C1—C2—C7	121.68 (13)	C16—C17—H17B	109.7
C3—C2—C7	119.68 (13)	H17A—C17—H17B	108.2
C11—C10—C9	120.58 (14)	C5—C6—C1	120.92 (15)
C11—C10—H10	119.7	C5—C6—H6	119.5
C9—C10—H10	119.7	C1—C6—H6	119.5
N3—C14—C15	110.58 (12)	C3—C4—C5	119.38 (15)
N3—C14—H14A	109.5	C3—C4—H4	120.3
C15—C14—H14A	109.5	C5—C4—H4	120.3
N3—C14—H14B	109.5	C12—C13—C8	121.79 (16)
C15—C14—H14B	109.5	C12—C13—H13	119.1
H14A—C14—H14B	108.1	C8—C13—H13	119.1
N2—C9—C10	114.92 (13)	C11—C12—C13	118.44 (15)

N2—C9—C8	125.70 (13)	C11—C12—H12	120.8
C10—C9—C8	118.63 (13)	C13—C12—H12	120.8
N4—C16—C17	110.97 (12)	N4—C18—H18A	109.5
N4—C16—H16A	109.4	N4—C18—H18B	109.5
C17—C16—H16A	109.4	H18A—C18—H18B	109.5
N4—C16—H16B	109.4	N4—C18—H18C	109.5
C17—C16—H16B	109.4	H18A—C18—H18C	109.5
H16A—C16—H16B	108.0	H18B—C18—H18C	109.5
N4—C15—C14	110.53 (12)		
C8—N1—C1—C6	-127.64 (15)	C18—N4—C15—C14	-179.16 (13)
C8—N1—C1—C2	55.7 (2)	C16—N4—C15—C14	-57.23 (15)
C9—N2—C7—N3	177.72 (13)	N3—C14—C15—N4	57.38 (16)
C9—N2—C7—C2	3.2 (2)	C1—C2—C3—C4	-1.4 (2)
C17—N3—C7—N2	-6.69 (19)	C7—C2—C3—C4	176.48 (14)
C14—N3—C7—N2	127.72 (14)	C9—C10—C11—C12	1.4 (2)
C17—N3—C7—C2	168.54 (12)	C9—C10—C11—C11	-179.55 (11)
C14—N3—C7—C2	-57.05 (17)	C1—N1—C8—C13	132.81 (16)
C6—C1—C2—C3	2.0 (2)	C1—N1—C8—C9	-54.0 (2)
N1—C1—C2—C3	178.72 (13)	N2—C9—C8—C13	168.37 (15)
C6—C1—C2—C7	-175.82 (13)	C10—C9—C8—C13	-1.2 (2)
N1—C1—C2—C7	0.9 (2)	N2—C9—C8—N1	-4.9 (2)
N2—C7—C2—C1	-35.2 (2)	C10—C9—C8—N1	-174.45 (14)
N3—C7—C2—C1	150.21 (14)	C7—N3—C17—C16	-166.50 (12)
N2—C7—C2—C3	146.92 (15)	C14—N3—C17—C16	57.13 (16)
N3—C7—C2—C3	-27.63 (19)	N4—C16—C17—N3	-57.28 (16)
C7—N3—C14—C15	166.35 (12)	C4—C5—C6—C1	-0.8 (2)
C17—N3—C14—C15	-57.55 (16)	C2—C1—C6—C5	-1.0 (2)
C7—N2—C9—C10	-156.61 (14)	N1—C1—C6—C5	-177.76 (15)
C7—N2—C9—C8	33.5 (2)	C2—C3—C4—C5	-0.3 (2)
C11—C10—C9—N2	-170.69 (14)	C6—C5—C4—C3	1.4 (2)
C11—C10—C9—C8	0.0 (2)	N1—C8—C13—C12	174.49 (17)
O1—N4—C16—C17	-61.75 (15)	C9—C8—C13—C12	1.1 (3)
C18—N4—C16—C17	179.32 (13)	C10—C11—C12—C13	-1.5 (3)
C15—N4—C16—C17	57.41 (16)	C11—C11—C12—C13	179.46 (14)
O1—N4—C15—C14	60.16 (15)	C8—C13—C12—C11	0.2 (3)

Hydrogen-bond geometry (\AA , $^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1A \cdots O1 ⁱ	1.22 (1)	1.22 (1)	2.434 (2)	179 (4)
N1—H1 \cdots C12	0.86 (2)	2.46 (2)	3.3259 (14)	176 (2)
C15—H15A \cdots O1 ⁱ	0.97	2.64	3.2598 (19)	122
C15—H15A \cdots N1 ⁱⁱ	0.97	2.51	3.416 (2)	156
C15—H15B \cdots C11 ⁱⁱⁱ	0.97	2.91	3.8431 (17)	162

Symmetry codes: (i) $-x, -y+1, z$; (ii) $-y+1/2, x+1/2, -z+1/2$; (iii) $-x+1/2, -y+1/2, -z+1/2$.