

Short Note

Homopiperazine (Hexahydro-1,4-diazepine)

R. Alan Aitken , Dheirya K. Sonecha and Alexandra M. Z. Slawin 

EaStCHEM School of Chemistry, University of St Andrews, North Haugh, St Andrews, Fife, KY16 9ST, UK; dks1@st-and.ac.uk (D.K.S.); amzs@st-and.ac.uk (A.M.Z.S.)

* Correspondence: raa@st-and.ac.uk; Tel.: +44-1334-463865

Abstract: The X-ray structure of the title compound has been determined for the first time. Data on its ^1H – ^{13}C -NMR coupling constants and ^{15}N -NMR spectrum are also given.

Keywords: homopiperazine; X-ray structure; C–C bond length; ^{15}N -NMR

1. Introduction

The fundamental heterocyclic compound hexahydro-1,4-diazepine or “homopiperazine” **1** was first reported in 1899 [1,2] and a convenient industrial preparation was described in 1961 [3]. At present, it is commercially available from several major suppliers and it has recently found various applications, including as a component of liquids for CO_2 capture [4] and as a component of various organic and organic/inorganic supramolecular ionic salts and transition metal complexes. In these latter applications, the materials are often characterised by X-ray diffraction and so there are a large number of X-ray structures involving a homopiperazinium dication in salts or mixed salts with, for example, carboxylic acids [5–7], potassium perchlorate [8], ammonium perchlorate [9], manganese sulfate oxalate [10], cobalt sulfate [11], zinc phosphate [12], arsenic oxide [13], tellurium phosphate [14], cadmium phosphate [15], cadmium chlorides [16,17], lead bromide [18], bismuth iodide [19], uranium fluoride [20] and uranium sulfate [21]. There are also a significant number of structures in which homopiperazine acts as a bidentate ligand on nickel [22,23], copper [24] and platinum [25–28]. However, in all of these, the structure is significantly distorted either by protonation or metal complexation, and it appears that the X-ray structure of homopiperazine on its own has not so far been determined, quite possibly because its low melting point of $42\text{ }^\circ\text{C}$ [2] makes it difficult to obtain suitable crystals. We have now determined its structure and present here the result as well as several key NMR parameters.

2. Results

Crystals suitable for diffraction were obtained from the inner surface of a commercial bottle (Sigma Aldrich) which had been stored for >5 years, allowing slow sublimation. The resulting structure (Figure 1) shows how three adjacent molecules are aligned with the NH atoms of the central ring, viewed from above, hydrogen-bonding to the nitrogen lone pairs of the molecules on either side, which are viewed side-on. The bond lengths and angles in the symmetrical molecule are unremarkable, with the exception of the carbon–carbon bond of the $\text{N-CH}_2\text{-CH}_2\text{-N}$ moiety, which is rather long at $1.603(10)\text{ \AA}$. This may be compared with a mean value of $1.524\text{ \AA}$ for $sp^3\text{ CH}_2\text{-CH}_2$ in general [29] and is in stark contrast to the values of $1.5204(15)$ and $1.5190(15)\text{ \AA}$ observed in piperazine hydrate [30], the value of $1.513(2)\text{ \AA}$ in the monoprotonated homopiperazinium perchlorate [31] and $1.521(4)\text{ \AA}$ in an N,N' -dibenzylated homopiperazine [32]. The reason for the long bond in this case is unclear, although other examples of such long $\text{NCH}_2\text{-CH}_2\text{N}$ bonds have been located [33].



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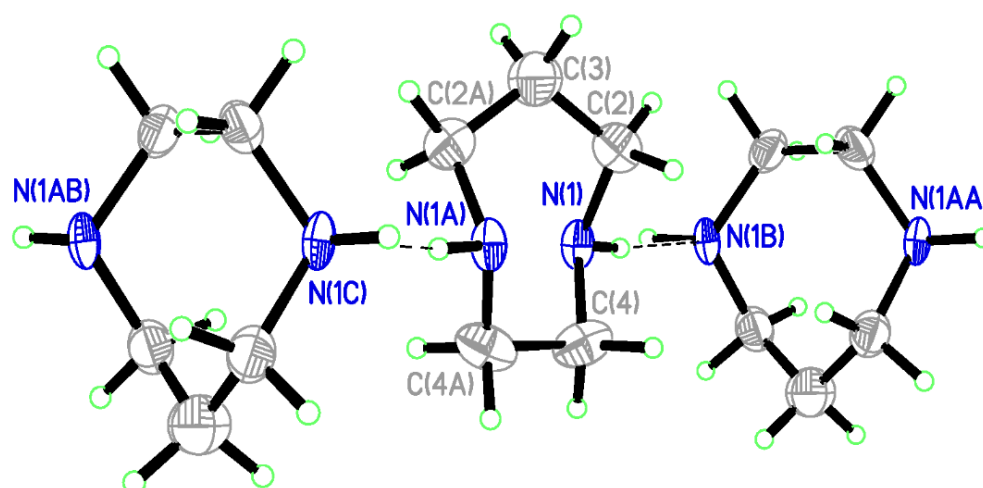


Figure 1. Molecular structure of **1** with anisotropic displacement ellipsoids drawn at 50% probability level and showing numbering system used. Bond lengths and angles: N(1)–C(2) 1.455(5), C(2)–C(3) 1.481(5), N(1)–C(4) 1.470(5), C(4)–C(4A) 1.603(10), N(1)–H(1) 0.977(7) Å; C(2)–N(1)–C(4) 112.0(3), N(1)–C(4)–C(4A) 111.0(3), N(1)–C(2)–C(3) 114.9(4), C(2)–C(3)–C(2A) 114.8(6)°. Symmetry operator to generate the whole molecule is $-X + 1, -Y, Z$.

The conformation of **1** is shown in Figure 2 and the N–C–C–N torsion angle of 58.2(4)° confirms that the left-hand end of the molecule has an almost ideal chair-type conformation, which is only slightly distorted by the insertion of the extra atom at the right-hand end. The two nitrogen lone pairs are aligned in opposite directions, which facilitates the formation of a hydrogen-bonded network due to interaction with the NH of adjacent molecules, as shown in Figure 1. The hydrogen-bonding parameters (Table 1) are well within the normal ranges. It should be noted that the present structure is quite different from previously reported structures of both metal complexes and protonated salts of **1** since, in the former case, coordination of the nitrogen lone pairs to the metal dominates, whereas, in the latter, protonation removes any opportunity for hydrogen bonding.

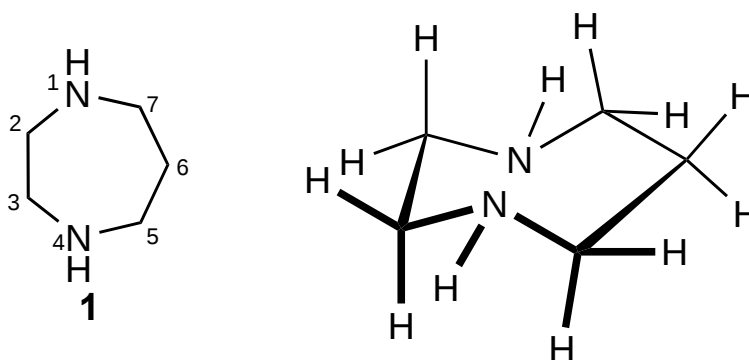


Figure 2. Structures of **1** showing IUPAC numbering and observed conformation.

Table 1. Hydrogen bonding parameters for **1** (Å, °).

D–H ... A	D–H	H ... A	D ... A	D–H ... A
N(1)–H(1) ... N(1B)	0.977(7)	2.21(3)	3.189(4)	175(4)

The symmetry operator to generate N(1B) is $Y + 1, -X + 1, -Z + 1$.

The ^1H and ^{13}C NMR spectra for **1** are documented in D_2O in a recent publication [4] along with HSQC and HMBC spectra, allowing complete and unambiguous assignment.

Our data in CDCl_3 were in good agreement with these values but, by recording the non- ^1H -decoupled ^{13}C spectrum, all three values of $^1J_{\text{C-H}}$ were readily determined as $^1J_{\text{C(2)-H(2)}}$ 132.6 Hz, $^1J_{\text{C(5)-H(5)}}$ 132.7 Hz, $^1J_{\text{C(6)-H(6)}}$ 124.3 Hz, and, in addition, $^2J_{\text{C(6)-H(5/7)}}$ could be measured as 2.6 Hz. The remaining $^2J_{\text{C-H}}$ values as well as longer-range couplings were not readily determined due to the complexity of the signals. The larger values of $^1J_{\text{C-H}}$ for CH_2N are in agreement with literature reports with values of 136.1 Hz for C-3 of a tetrahydroisoquinoline [34] and 132.0–139.0 Hz for C-4/5 of imidazolidines [35], while the value for C(6)–H(6) is in good agreement with 124.6 Hz for cyclohexane [36].

Finally, the ^{15}N NMR signal observed at -344.6 ppm with respect to MeNO_2 is in good agreement with those for similar cyclic secondary amines such as piperidine (-342.3) and pyrrolidine (-342.6) [37].

In summary, we obtained the X-ray crystal structure of homopiperazine for the first time and found the molecule to exist in a pseudo-chair conformation, with each NH acting both as a hydrogen-bonding donor and acceptor, leading to a complex network structure overall. The values of the three one-bond CH coupling constants and the ^{15}N chemical shift have been determined from its NMR spectra.

3. Experimental

The structure was determined on a Rigaku XtaLAB P200 diffractometer using graphite monochromated Mo $\text{K}\alpha$ radiation $\lambda = 0.71075$ Å.

Crystal data for $\text{C}_5\text{H}_{12}\text{N}_2$, $M = 100.16$ g mol $^{-1}$, colourless prism, crystal dimensions $0.10 \times 0.10 \times 0.10$ mm 3 , tetragonal, space group I-42d (No. 122), $a = b = 7.208(2)$, $c = 23.094(7)$ Å, $\alpha = \beta = \gamma = 90.00^\circ$, $V = 1199.9(6)$ Å 3 , $Z = 8$, $D_{\text{calc}} = 1.109$ g cm $^{-3}$, $T = 93$ K, $R_1 = 0.0637$, $R_w = 0.1633$ for 536 reflections with $I > 2\sigma(I)$, and 37 variables, $R_{\text{int}} = 0.0374$, goodness of fit on $F^2 = 1.137$. Data have been deposited at the Cambridge Crystallographic Data Centre as CCDC 2049324. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk/getstructures> (accessed on 30 March 2021). The structure was solved by direct methods and refined by full-matrix least-squares against F^2 (SHELXL Version 2018/3 [38]).

NMR spectra were recorded using a Bruker (Bruker, Billerica, MA, USA) AV instrument at 75.458 MHz (^{13}C) and a Bruker AVIII-HD instrument at 50.69 MHz (^{15}N) in CDCl_3 with chemical shifts given with respect to Me_4Si (^{13}C) and MeNO_2 (^{15}N) and coupling constants in Hz.

δ_{C} (non-decoupled) 33.3 (t of quintets, 1J 124.3, 2J 2.6, C-6), 47.8 (t of m, 1J 132.7, C-5,7), 51.5 (t of m, 1J 132.6, C-2,3); δ_{N} -344.6 .

Supplementary Materials: The following are available online, Figure S1: Undecoupled ^{13}C -NMR spectrum of **1**; Figure S2: Undecoupled ^{13}C -NMR spectrum of **1**—expansion of C-6 signal; Figure S3: ^{15}N -NMR spectrum of **1**.

Author Contributions: A.M.Z.S. collected the X-ray data; D.K.S. obtained a preliminary solution of the structure, which was then optimised by A.M.Z.S.; R.A.A. designed the experiments, ran the NMR spectra, analysed the data, and wrote the paper. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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