6,6'-Dimethyl-1,1',5,5'-tetraaza-6,6'-bi(bicyclo[3.1.0]hexane): synthesis and investigation of molecular structure by quantum-chemical calculations, NMR spectroscopy and X-ray diffraction analysis

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Abstract

A new diaziridine derivative with two bicyclic diaziridine-containing moieties in one molecule, 6,6'-dimethyl-1,1',5,5'-tetraaza-6,6'-bi(bicyclo[3.1.0]hexane) (BiDiMDAH), has been synthesized for the first time. Its molecular structure has been investigated in the gas phase by means of quantum-chemical (QC) calculations, in CDCl_3 solution by 1D and 2D NMR spectroscopy and in the solid state by the X-ray diffraction (XRD) technique. It was found by QC calculations that BiDiMDAH molecule in a free state presents a single conformer of C_2 symmetry with *trans* orientation of the methyl groups about two carbons connecting diaziridine cycles. The 5-membered rings in BiDiMDAH molecule has been found to be essentially planar. In order to explain conformational preferences of BiDiMDAH Natural Bond Orbitals (NBO) and Atoms in Molecules (AIM) analyses have been performed. According to the XRD data BiDiMDAH crystallizes in space group $P2_1/c$ with molecular structure similar to that obtained by the means of QC calculations. The data of NMR spectroscopy has revealed that only one conformer is present in CDCl_3 solution in agreement with the data of QC and XRD studies. The gaseous standard enthalpy of formation of BiDiMDAH has been estimated to be 443.8 ± 5.0 kJ/mol by means of G4 theory.

1. Introduction

The study of conformational properties and molecular structure of diaziridines (1,2-diazacyclopropanes) comes in a field of our scientific interests for many years [1–13]. The attention to diaziridines is provided by a high theoretical and practical significance of this class of compounds. The diaziridine derivatives are capable of direct action on the central nervous system, possessing various types of neurotropic activity [14–20]. Diaziridines appeared to be suitable objects for studying of the stereochemistry of the nitrogen atom due to the high stability of the two stereogenic pyramidal nitrogens [21–23]. Strained diaziridine ring is inclined to ring-expansion reactions resulting in various five-to-eight-membered mono- and bicyclic heterocyclic structures [24–30]. These heterocycles possess high enthalpies of formation and though they contain hydrazine fragment are of low toxic compounds. Since the most part of alkyl-substituted diaziridines have liquid form, they are considered as potential components of liquid rocket propellants (LRP) instead of toxic hydrazine derivatives [31, 32].

Earlier we studied the molecular structures and peculiarity of conformational behavior of bicyclic diaziridine derivatives – 1,5-diazabicyclo[3.1.0]hexane **1** (DABH) by the gas electron diffraction (GED) method [7] and 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane) **2** – by the X-ray diffraction (XRD) [1] and the gas electron diffraction (GED) [4] methods. It was shown that the bicyclic fragment of these compounds exists exclusively as a boat conformation of C_s symmetry at 20°C and the Natural Bond Orbital (NBO) analysis showed that the most important stabilization factor in the boat conformation is the $n(\text{N}) \rightarrow \sigma^*(\text{C}-\text{C})$ anomeric effect. We also investigated the molecular structure of 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexane **3** by the GED and the XRD methods [3]. The introduction of two methyl substituents to the carbon atom of diaziridine cycle of compound **3** makes the pyrazolidine moiety of this

substance almost planar. The obtained results demonstrate great influence of substituents on the conformation of the DABH system.

The direction of action on the central nervous system of diaziridine derivatives also depends on the type of substituents in the diaziridine ring [16]. In particular, it was found that the neurotropic activity of diaziridine derivatives increases when the second diaziridine ring is introduced [15]. Recently we have studied the molecular structure of tetramezine [1,2-bis-(3,3-dimethyldiaziridin-1-yl)ethane], containing two diaziridine cycles in one molecule, by the GED method together with vibrational spectroscopy and quantum chemical calculations [33]. Herein the results of theoretical and experimental investigations of molecular structure of 6,6'-dimethyl-1,1',5,5'-tetraaza-6,6'-bi(bicyclo[3.1.0]hexane) (BiDiMDAH) (**4**), containing two DABH cycles in one molecule, by the means of QC calculations, NMR spectroscopy and XRD analysis are presented.

2. Cq Calculations

Gaussian 09 program software [34] was used for to perform QC calculations. HF [35] B3LYP [36, 37] and MP2 [38] QC methods along with 6-31G(d,p) [39], 6-311++G(d,p) [40, 41] and cc-pVTZ [42] basis sets were used as implemented into Gaussian 09. Geometry optimizations and subsequent frequency calculations were performed at B3LYP/6-31G(d,p), B3LYP/cc-pVTZ, and MP2/cc-pVTZ levels of theory, applying options *opt=verytight* and *int=ultrafine*. Optimized Cartesian coordinates of BiDiMDAH at B3LYP/6-31G(d,p), B3LYP/cc-pVTZ MP2/cc-pVTZ levels of theory are deposited in the ESI as Tables S1, S2, and S3, respectively. The atomic numbering is shown in Fig. 2.

The NBO analysis of BiDiMDAH was performed with NBO 7.0 program [43] at HF/6-311++G(d,p) level of theory in order to avoid computational artifacts [44, 45]. The topological analysis of electronic density was performed using QTAIM method [46] with the AIM2000 code [47, 48]. To predict the BiDiMDAH enthalpy of formation the Gaussian-4 theory [49] was used as implemented into Gaussian 09 program software.

3. Experimental Section

3.1 General remarks

BiDiMDAH was synthesized for the first time in the N. D. Zelinsky Institute of Organic Chemistry. All starting materials were purchased from ACROS catalog and were used as purchased. The structure of BiDiMDAH was elucidated with the help of IR spectra, high resolution mass spectra (HRMS), mass spectra under electron impulse (EI), NMR spectra, and XRD diffraction analysis. The IR spectra were recorded on InfraLUM FT-801 and Bruker "Alpha" spectrometer in the range 400–4000 cm^{-1} (resolution 2 cm^{-1}). HRMS were recorded on a Bruker micro TOF-QTM spectrometer with electrospray ionization (ESI). All measurements were performed in a positive (+ MS) ion mode (interface capillary voltage: 4500 V) with scan range m/z : 50–3000. External calibration of the mass spectrometer was performed with

Electrospray Calibrant Solution (Fluka). A direct syringe injection was used for all analyzed solutions in MeCN (flow rate: 3 $\mu\text{L min}^{-1}$). Mass spectra EI were recorded using a Finnigan MAT INCOS-50 instrument. All NMR spectra were recorded on Bruker AV-600 spectrometer equipped with a Z-gradient broadband observe probe at room temperature. The X-ray diffraction experiment for a single crystal of BiDiMDAH was carried out on a 'Bruker APEX-II CCD' diffractometer at 120 K during data collection.

3.2 Synthesis of BiDiMDAH

The solution of 2,3-butanedione (1.76 ml, 20 mmol) in 5 ml H_2O was added dropwise to the solution of 1,3-diaminopropane (3.02 ml, 40 mmol) in 50 ml H_2O at stirring and at the temperature of 0–10 °C. Then the aqueous solutions 15% HCl and 12% NaOCl were added dropwise to the reaction mixture to adjust pH = 11.0. The reaction mixture was stirred at 0–5° C and pH value not exceeding 11.5–12.0 (which was supported by addition of 20% aqueous solution NaOH when it was necessary) for 12 h. Then the temperature was raised to 20 °C, the reaction mixture was saturated with NaCl and extracted with CHCl_3 (50 ml $\times$ 3). The organic layer was dried over K_2CO_3 , the solvent was evaporated and the residue was recrystallized from acetone. Yield 0.41 g (11%), colorless solid, mp = 187–188°C. IR (KBr): ν = 2975, 2953, 2890, 1629, 1483, 1382, 1344, 1288, 1265, 1240, 1227, 1148, 1105, 1093, 1012, 974, 916, 858, 810, 754, 644, 548 cm^{-1} . HRMS (ESI): m/z for $\text{C}_{10}\text{H}_{18}\text{N}_4$ ($\text{M} + \text{H}$) $^+$: calculated 195.1604, found 195.1603; Mass-spectra (EI, 70 eV), m/z : 194 [M] $^+$, 193 [$\text{M} - \text{H}$] $^+$, 179 [$\text{M} - \text{Me}$] $^+$, 165 [$\text{M} - \text{Me} - \text{CH}_2$] $^+$, 164 [$\text{M} - 2 \text{ Me}$] $^+$, 150 [$\text{M} - 2 \text{ Me} - \text{CH}_2$] $^+$, 138 [$\text{M} - 2 \text{ Me} - 2 \text{ CH}_2 + 2 \text{ H}$] $^+$, 136 [$\text{M} - 2 \text{ Me} - 2 \text{ CH}_2$] $^+$, 123 [$\text{M} - 2 \text{ Me} - 3 \text{ CH}_2 + \text{H}$] $^+$, 122 [$\text{M} - 2 \text{ Me} - 3 \text{ CH}_2$] $^+$, 110 [$\text{M} - 2 \text{ Me} - 4 \text{ CH}_2 + 2 \text{ H}$] $^+$, 96 [$\text{M} - 2 \text{ Me} - 5 \text{ CH}_2 + 2 \text{ H}$] $^+$, 94 [$\text{M} - 2 \text{ Me} - 5 \text{ CH}_2$] $^+$, 82 [$\text{M} - 2 \text{ Me} - 6 \text{ CH}_2 + 2 \text{ H}$] $^+$, 80 [$\text{M} - 2 \text{ Me} - 6 \text{ CH}_2$] $^+$, 42 [$(-\text{CH}_2)_3$] $^+$, 28 [N_2] $^+$.

3.3 NMR experiments

To collect all kinds of NMR spectra a 25-mg portion of the sample was dissolved in 0.6 mL of CDCl_3 . The ^1H and ^{13}C chemical shifts (δ), for which values are reported in ppm, were calibrated against the residual protons (7.27 ppm) and carbon atoms (77.00 ppm) of the CDCl_3 . The coupling constants, J , are given in Hz. Multiplicities are indicated by s (singlet), d (doublet) and q (quartet). The 1D spectra of BiDiMDAH are presented in the ESI as Fig. S1 and Fig. S2, for ^1H and ^{13}C NMR, respectively. The numerical values are listed below. ^1H NMR (600.13 MHz, CDCl_3) δ , ppm. J/Hz : 1.09 (s, 6H, $2\times\text{CH}_3$), 1.76–1.82 (m, 2H, $2\times\text{CH}_a$), 2.07–2.13 (m, 2H, $2\times\text{CH}_b$), 2.78–2.82 (dt, 4H, $4\times\text{N}-\text{CH}_a$), 3.18–3.23 (dt, 4H, $4\times\text{N}-\text{CH}_b$) (ESI, Fig. S1). ^{13}C NMR (150.90 MHz, CDCl_3) δ , ppm.: 8.1 ($2\times\text{CH}_3$), 32.1 ($2\times\text{CH}_2$), 48.4 ($4\times\text{N}-\text{CH}_2$), 65.7 ($2\times\text{C}_{ring}$) (ESI, Fig. S2).

A set of 2D spectra, namely, $\{^1\text{H}-^{13}\text{C}\}$ HSQC (heteronuclear spectroscopy quantum correlation), $\{^1\text{H}-^{13}\text{C}\}$ HMBC (heteronuclear multiple bond correlation), and $\{^1\text{H}^1\text{H}\}$ gNOESY (nuclear Overhauser effect spectroscopy), were measured in the CDCl_3 solution at 298 K (see Fig. S3, Fig. S4, Fig. S5 and Fig. S6 of the ESI for $\{^1\text{H}-^{13}\text{C}\}$ HSQC, $\{^1\text{H}-^{13}\text{C}\}$ HMBC, $\{^1\text{H}^1\text{H}\}$ gNOESY and $\{^1\text{H}-^1\text{H}\}$ COSY spectra, respectively. The

mixing time in NOESY was 0.7 s. All correlation NMR spectra were acquired with standard Bruker parameters.

3.4 XRD experiments

Single crystals of $C_{10}H_{18}N_4$ were grown from acetone. The structure was solved with Olex2 [50] and Olex2.solve [51] program software, applying Charge Flipping and refined with the XL [52] refinement package using Least Squares minimization. The conditions of the X-ray diffraction experiment and the refined cell constants for BiDiMDABH are listed in Table 1. The structure parameters were deposited with the Cambridge Structural Database (CCDC 2080380). Fractional atomic coordinates and equivalent isotropic displacement parameters for BiDiMDAH molecule are deposited in the ESI as Table S4, anisotropic displacement parameters as Table S5, and hydrogen atom coordinates as Table S6, respectively. For XRD atom numbering see Fig. S7 of the ESI.

Table 1. Data collection statistics and conditions of the X-ray diffraction experiment.

Molecular formula	$C_{10}H_{18}N_4$
Molecular weight [g/mol]	194.28
Crystal system	Monoclinic
Space group	$P2_1/c$
Cell dimensions: a, b, c [Å]	5.5062(6), 9.4504(10), 9.5120(10)
α, β, γ [°]	90.00, 93.089(2), 90.00
Unit cell volume [Å ³]	494.25(9)
Z	2
Electrons wavelength [Å]	0.71073
No. of formula units per unit cell, Z	2
Density (calculated) [g/cm ³]	1.305
$F(000)$	212
Radiation type	Mo-K α
Absorption coefficient, μ [mm ⁻¹]	0.083
θ range [°]	6.08 – 61.0
Limiting indices: h, k, l	-7 – 7, -13 – 13, -13 – 13
No. of reflections measured	6396
No. of independent reflections	1509
Temperature [K]	120
R_{int}	0.0197
R_{sigma}	0.0155
Final R indexes [$I \geq 2\sigma(I)$]	$R_I = 0.0355$, $wR_2 = 0.0959$
Final R indexes [all data]	$R_I = 0.0388$, $wR_2 = 0.0991$
Largest diff. peak/hole / e Å ⁻³	0.39/-0.23
Goodness-of-fit on F^2	1.052

4. Results And Discussion

According to the data of QC computations a free molecule of BiDiMDAH molecule exists as single conformation of C_2 symmetry with *trans* orientation of the methyl groups (see Fig. 1). The conformation

with *cis* orientation of the methyl groups was found to be a transitional state. The instability of the TS may be connected with unfavorable electrostatic interactions of nitrogen atoms (the corresponding NPA charges were calculated to be $\sim -0.4 e$ for the TS conformation). In order to obtain a qualitative measure of overall atom-atom electrostatics NBO Natural Columbic Energy (NCE) concept was applied, yielding $\Delta E^{(es)} = \Delta E_{NCE}(cis) - \Delta E_{NCE}(trans) = 34.1 \text{ kcal/mol}$, consistent with *trans* conformer advantage over *cis*.

The computed geometrical parameters of a stable BiDiMDAH conformation at B3LYP/6-31G(d,p), B3LYP/cc-pVTZ and MP2/cc-pVTZ levels of theory and the experimental values obtained by the XRD diffraction for the solid state are given in Table 2.

Table 2
Structural parameters for BiDiMDAH obtained by means of QC calculations and the XRD method.

method/basis				
	B3LYP/6-31G(d,p)	B3LYP/cc-PVTZ	MP2/cc-PVTZ	XRD
Bond lengths, Å				
N1-C2	1.479	1.475	1.473	1.480(2)
C2-C3	1.549	1.545	1.539	1.536(2)
C3-C4	1.549	1.545	1.539	1.540(2)
C4-N5	1.478	1.473	1.472	1.481(2)
N5-C6	1.461	1.456	1.457	1.468(2)
N1-C6	1.461	1.457	1.458	1.465(2)
N1-N5	1.506	1.503	1.518	1.522(1)
C6-C7	1.515	1.511	1.503	1.517(2)
C6-C13	1.542	1.539	1.519	1.534(2)
Bond angles, °				
∠N1-C2-C3	109.0	109.0	109.4	109.4(1)
∠C2-C3-C4	104.6	104.7	104.8	103.8(1)
∠C3-C4-N5	109.0	108.9	109.4	109.3(1)
∠C4-N5-N1	108.7	108.7	108.3	107.6(1)
∠N5-N1-C2	108.6	108.6	108.2	107.8(1)
∠N5-C6-N1	62.0	62.1	62.8	62.5(1)
∠N1-N5-C6	59.0	58.9	58.6	58.6(1)
∠N5-N1-C6	59.0	58.9	58.6	58.8(1)
∠C4-N5-C6	116.0	116.2	114.2	115.0(1)
∠C2-N1-C6	115.6	115.7	113.4	114.9(1)
∠N1-C6-C7	123.0	122.6	122.6	122.3(1)
∠N5-C6-C7	123.5	123.3	123.4	122.0(1)
∠N1-C6-C13	113.4	113.8	113.2	112.1(1)
∠N5-C6-C13	111.8	111.6	111.4	112.1(1)

method/basis				
∠C7-C6-C13	113.6	113.8	114.0	115.4(1)
Torsion angles,°				
N1-C2-C3-C4	-3.3	-2.3	-1.7	-13.8(1)
C2-C3-C4-N5	3.7	2.6	2.3	13.8(1)
C3-C4-N5-N1	-2.6	-2.0	-2.0	-8.9(1)
C4-N5-N1-C2	0.4	0.5	0.9	0.1(1)
N5-N1-C2-C3	1.9	1.1	0.6	8.8(1)
C6-N1-C2-C3	-61.8	-62.6	-62.4	-54.4(1)
C3-C4-N5-C6	61.2	61.9	61.1	54.0(1)
C4-N5-C6-N1	-97.0	-97.0	-97.4	-96.2(1)
N5-C6-N1-C2	97.1	97.1	97.7	96.4(1)
C2-N1-C6-C7	-16.4	-16.5	-16.2	-15.8(2)
C4-N5-C6-C7	15.8	15.4	15.3	16.5(2)
C2-N1-C6-C13	-159.7	-160.1	-159.2	-159.3(1)
C4-N5-C6-C13	157.2	156.7	156.7	159.6(1)
C7-C6-C13-C14	-171.1	-168.3	-168.7	-180.0(1)
N1-C6-C13-C14	-24.3	-21.4	-22.3	-33.8(1)
N5-C6-C13-C14	43.5	46.6	46.1	34.3(1)
N1-C6-C13-N8	-169.7	-166.6	-167.5	-180.0(1)
N1-C6-C13-N12	122.5	125.4	124.0	111.9(1)
N5-C6-C13-N8	-101.9	-98.6	-99.0	-111.9(1)
N5-C6-C13-N12	-169.7	-166.6	-167.5	-180.0(1)
N5-N1-C6-C13	103.2	102.9	103.1	104.2(1)
N5-N1-C6-C7	-113.6	-113.5	-113.9	-112.2(1)
C6-N1-N5-C4	109.7	109.9	107.7	108.9(1)
C6-N5-N1-C2	-109.2	-109.4	-106.8	-108.8(1)
N1-N5-C6-C13	-105.8	-106.3	-106.0	-104.3(1)
N1-N5-C6-C7	112.8	112.4	112.7	112.7(1)

method/basis				
N1-C6-C7-H21	44.8	46.2	49.6	96.6(1)
N1-C6-C7-H22	-77.3	-75.6	-72.3	-23.4(1)
N1-C6-C7-H23	166.1	167.5	170.9	-143.4(1)

The average values of BiDiMDAH bond lengths and bond angles obtained by QC calculations are similar to those for solid state (see Table 2), the computed values of torsion angles are in most cases particularly the same that in the crystal. However, there is a noticeable difference within the 5-membered ring: the values of the N5-N1-C2-C3 and the C2-C3-C4-N5 torsion angles are by about 8° and 11° bigger in the crystal than in a free molecule. There is also a difference in the conformation of the hydrogen atoms of the both methyl groups (confer Fig S7 of the ESI). Thus, though the structure of BiDiMDAH in a free state resembles the one in the crystal, it has a different positions of methyl hydrogens and possess flatter skeletons of the both 5-membered rings, comparing with the solid state.

According to the results of QC computations and XRD analysis the essentially planar skeletons of the 5-ring moieties are observed. This fact may be caused by the two possible tendencies. The first tendency is connected with the $n(\text{N}) \rightarrow \sigma^*(\text{C}-\text{C})$ and the $n(\text{N}) \rightarrow \sigma^*(\text{C}-\text{H})$ anomeric effects, stabilizing the boat conformation of the 6-membered rings. Thus, the lone pair of the N1 atom interacts with the C2–C3 and the C2–H16 antibonding orbitals $n(\text{N1}) \rightarrow \sigma^*(\text{C2}-\text{C3})$ has $E(2)=3.6 \text{ kcal mol}^{-1}$ and the $n(\text{N1}) \rightarrow \sigma^*(\text{C2}-\text{H16})$ interaction has $E(2) = 4.3 \text{ kcal mol}^{-1}$ and the lone pair of the N5 atom interacts with the C3–C4 and the C4–H20 antibonding orbitals $n(\text{N5}) \rightarrow \sigma^*(\text{C3}-\text{C4})$ has $E(2) = 3.6 \text{ kcal mol}^{-1}$ and the $n(\text{N5}) \rightarrow \sigma^*(\text{C4}-\text{H20})$ interaction has $E(2) = 4.3 \text{ kcal mol}^{-1}$. The second tendency is the steric repulsion of the H21 atom of the methyl group and the H17, the H19 and the H15 atoms of the 5-membered ring. Thus, NBO STERIC analysis reveals the corresponding pairwise steric exchange energies: $2.26 \text{ kcal mol}^{-1}$ for the C7–H21 and the C3–H17 bonds, $1.58 \text{ kcal mol}^{-1}$ for the C7–H21 and the C4–H19 bonds, and $1.15 \text{ kcal mol}^{-1}$ for the C7–H21 and the C2–H15 bonds, respectively. The interatomic distance between H21 and H17 is equal to 2.06 Å according to B3LYP/G(d,p), 2.08 Å according to B3LYP/ cc-PVTZ, and 2.00 Å according to MP2/cc-PVTZ levels of theory. That is a little bit less than the sum of the two atomic Wan der Waals radii [53] or natural atomic Wan der Waals radii of the H atoms [44]. However, AIM computations didn't reveal a critical point between the corresponding H atoms as well as natural bond critical point analysis [54] applied as implemented into NBO 7.0 program. Therefore, it seems that the steric repulsion of the H atoms is the leading force, which causes the flattening of the 5-membered ring in order to achieve the minimal H...H distance which the sum of the Wan der Waals radii permit. The steric hindrance of BiDiMDAH molecule is also confirmed with its high value of standard enthalpy of formation in the gas phase calculated from commonly used atomization approach by the means of Gaussian-4 computations, which yielded $(\text{BiDiMDAH}, \text{g}) = 443.8 \pm 5.0 \text{ kJ/mol}$.

According to NBO analysis BiDiMDAH molecule also has relatively strong $\sigma(\text{C}-\text{N}) \rightarrow \sigma^*(\text{N}-\text{N})$ ($E(2) = 5.5 \text{ kcal mol}^{-1}$) and $\sigma(\text{N}-\text{N}) \rightarrow \sigma^*(\text{C}-\text{N})$ ($E(2) = 7.3 \text{ kcal mol}^{-1}$) interactions in the three-membered ring and some additional important types of conjugations. Thus, there is a strong interaction between N–N bonding orbital and the methyl antibonding C6–C7 orbital: $\sigma(\text{N}-\text{N}) \rightarrow \sigma^*(\text{C6}-\text{C7})$ with $E(2) = 6.1 \text{ kcal mol}^{-1}$. The lone pair of the N1 atom also interacts with antibonding orbital of the the C6–C7 bond (the $n(\text{N1}) \rightarrow \sigma^*(\text{C6}-\text{C7})$ interaction has $E(2) = 4.9 \text{ kcal mol}^{-1}$) as well as the lone pair of the N5 atom interacts with the antibonding orbital of the C6–C7 bonds (the $n(\text{N5}) \rightarrow \sigma^*(\text{C6}-\text{C7})$ interaction has $E(2) = 5.3 \text{ kcal mol}^{-1}$). Additionally, there are strong interactions between two C–H bonding orbitals of the methyl group and antibonding orbital C6–N5, namely $\sigma(\text{C7}-\text{H22}) \rightarrow \sigma^*(\text{C6}-\text{N5})$ with $E(2) = 7.0 \text{ kcal mol}^{-1}$ and $\sigma(\text{C7}-\text{H23}) \rightarrow \sigma^*(\text{C6}-\text{N5})$ with $E(2) = 7.2 \text{ kcal mol}^{-1}$.

The structure of BiDiMDAH was compared with the structures of similar compounds (see Table 3). The largest difference was found for the value of the torsional angle N5N1C2C3 in 1,5-diazabicyclo[3.1.0]hexane and 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane). This two molecules lack the methyl group and subsequently there are no repulsion of the corresponding hydrogen atoms, leading to the flattening of the 5-membered ring. It is worth to notice, that the value of the N5N1C2C3 torsion angle is practically the same in BiDiMDAH and 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexane, in which 5-membered ring moiety is also nearly flat, probably due to the H...H repulsions as supposed for BiDiMDAH molecule.

Table 3. The selected geometric parameters of BiDiMDAH **4**, 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexane **3**, 1,5-diazabicyclo[3.1.0]hexane **1** and 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane) **2** (distances are Angstroms, angles are in degrees).

Parameter	4 [this work], r_e	3 [8], r_e	1 [7], r_g	2 [1,4], r_g
r(N1-C2)	1.479/1.474/1.473	1.472(7)	1.479(4)	1.483(2)
r(N1-N5)	1.506/1.503/1.518	1.522(7)	1.518(13)	1.511(2)
r(N1-C6)	1.461/1.457/1.458	1.455(7)	1.453(2)	1.452(2)
r(C2-C3)	1.549/1.545/1.539	1.538(7)	1.535(5)	1.543(2)
r(C6-C13)	1.542/1.539/1.519	-	-	1.494(2)
r(C-H) _{av}	1.093/1.089/1.088	1.095(6)	1.122	1.102(12)
N1-C6-N5	62.0/62.1/62.8	63.1	63.0	62.9
N1-C6-C7	123.3/123.0/123.0	122.4(14)	-	-
C2-N1-C6	115.8/116.0/113.8	114.4	114.8(8)	111.1(1.6)
N1-C2-C3	109.0/109.0/109.4	109.3(18)	106.5(9)	107.6(1.1)
C2-C3-C4	104.6/104.7/104.8	105.1(20)	104.0(10)	102.75
C2-N1-N5	108.7/108.7/108.3	108.2(7)	107.7(4)	107.53
N5-N1-C2-C3	1.9/1.1/0.6	0.8	88.3	25.5

The analysis of the ^1H and ^{13}C 1D NMR spectra of BiDiMDAH showed that in solution the compound exists only in a single conformation (i.e., there are clear peaks of only one compound, Fig. S1 and S2, for ^1H and ^{13}C 1D NMR spectra, respectively).

The data of $\{^1\text{H}-^{13}\text{C}\}$ HSQC and $\{^1\text{H}-^1\text{H}\}$ gNOESY 2D spectra helped to enable all protons and carbon atoms to be assigned together with their inter relationships. The results of the heteronuclear correlation NMR $\{^1\text{H}-^{13}\text{C}\}$ HSQC and $\{^1\text{H}-^{13}\text{C}\}$ HMBC spectra are presented in Table 4. These spectra show how far away each proton was found from a particular carbon atom, respectively, through one or 2–3 bonds.

Table 4
Selected $\{^1\text{H}-^{13}\text{C}\}$ HSQC and $\{^1\text{H}-^{13}\text{C}\}$ HMBC data for BiDiMDAH. Atom numeration is given in Fig. 1.

Atom number	^{13}C NMR, chemical shift, ppm	$\{^1\text{H}-^{13}\text{C}\}$ HSQC interactions	$\{^1\text{H}-^{13}\text{C}\}$ HMBC interactions
C2	48.4	H15, H16	H17, H18
C3	32.1	H17, H18	H16, H20
C4	48.4	H19, H20	H17, H18
C6	65.7	-	H15, H16, H19, H20, H21, H22, H23
C7	8.1	H21, H22, H23	-

The 2D NMR spectrum $\{^1\text{H}-^1\text{H}\}$ gNOESY shows the spatial arrangement of protons relative to each other (Table 5, Fig S5 of the ESI). Protons H15, H17 and H19 have cross-peaks with proton H21.

Table 5

Partial data $\{^1\text{H}-^1\text{H}\}$ gNOESY for BiDiMDAH 4. Atom numeration is given in Fig. 1.

Atom number	^1H NMR chemical shift, ppm	Coupling constant J , Hz	$^1\text{H}^1\text{H}$ gNOESY Interactions
H15	2.78–2.82, dt	11.7 ($^2J_{\text{H15-H16}}$) 7.1 ($^3J_{\text{H15-H18}}$)	H16, H17, H21
H16	3.18–3.23, dt	11.7 ($^2J_{\text{H16-H15}}$) 8.7 ($^3J_{\text{H16-H17}}$)	H15, H17, H18
H17	1.76–1.82, m	-	H15, H16, H18, H19, H20, H21
H18	2.07–2.13, m	-	H16, H17, H20
H19	2.78–2.82, dt	11.7 ($^2J_{\text{H19-H20}}$) 7.1 ($^3J_{\text{H19-H18}}$)	H17, H20
H20	3.18–3.23, dt	11.7 ($^2J_{\text{H20-H19}}$) 8.7 ($^3J_{\text{H20-H17}}$)	H18, H19
H21, H22, H23	1.09, s	-	H21 – H15, H17, H19

The detected cross-peaks of proton H17 with proton H21 (Nuclear Overhauser effect) confirms of the endo-position of the methyl groups at the C ring atom in the diaziridine moiety.

Thus, the results of 1D and 2D NMR spectra reveal that in CDCl_3 solution BiDiMDAH molecule exists only in a single conformation and the distances between H21 proton of the methyl group and the protons H17 of the ring moiety are small enough to produce Nuclear Overhauser effect. This fact supports that 6-membered rings of BiDiMDAH do not adopt a chair conformation, but rather a boat form is amiable.

4. Conclusions

In summary, a new bicyclic diaziridine derivative – 6,6'-dimethyl1,1',5,5'-tetraaza6,6'-bi(bicyclo[3.1.0]hexane) (BiDiMDAH) was synthesized for the first time and its molecular structure was studied by QC calculations, NMR spectroscopy and XRD analysis. The molecular structures of BiDiMDAH obtained by the means of QC computations and the XRD analysis were found to be quite similar with *trans* orientation of the methyl groups and an essentially planar 5-ring moieties. Two competing effects were found to define the resulting molecular structure of BiDiMDAH: the hyperconjugation effect supporting a boat

conformation of the both 6-membered rings, and the effect of steric repulsion of the terminal hydrogen atoms of the methyl groups with the corresponding hydrogen atoms of 5-membered cycles, leading to a planarity of 5-membered ring moieties. The results obtained for the CDCl₃ solution by NMR method are in agreement with those obtained by means of QC computations.

Declarations

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Conflicts of interest. There are no conflicts to declare.

Availability of data and material.

Code availability.

Authors' contributions. Inna N. Kolesnikova: conceptualization, QC computations, writing of original draft. Vladimir V. Kuznetsov: synthesis, NMR spectroscopy investigations, editing of original draft. Alexander S. Goloveshkin: XRD analysis. Nikolai A. Chegodaev: QC computations. Nina N. Makhova: NMR spectroscopy investigations, editing of original draft, Igor F. Shishkov: supervision, editing of original draft.

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Figures

Figure 1

Structures: 1 – 1,5-diazabicyclo[3.1.0]hexane (DABH) GED [7]; 2 – 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane), XRD [1], GED [4]; 3 – 6,6- dimethyl-1,5-diazabicyclo[3.1.0]hexane, GED [8]; 4 – 6,6'-dimethyl-1,1',5,5'-tetraaza-6,6'-bi(bicyclo[3.1.0]hexane), XRD and QC calculations, this work.

Figure 2

Molecular model of BiDiMDAH with atom numbering.

Figure 3

Surface view of overlapping $n(\text{N1}) \rightarrow \sigma^*(\text{C2}-\text{C3})$ orbitals of BiDiMDAH.

Figure 4

Fragment of the $\{^1\text{H}-^1\text{H}\}_g\text{NOESY}$ spectrum for BiDiMDAH

Supplementary Files

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