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

Inna Nikolaevna Kolesnikova 1 · Vladimir Vladimirovich Kuznetsov 2 · Alexander Sergeevich Goloveshkin 3 · Nikolai Andreevich Chegodaev 1 · Nina Nikolaevna Makhova 2 · Igor Fedorovich Shishkov 1

Received: 28 April 2021 / Accepted: 18 June 2021 / Published online: 29 June 2021
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

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 CDCl3 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 C2 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 P21/c with molecular structure resembling the structure obtained by the means of QC calculations for the lowest energy form. However, the relative arrangement of the methyl groups of the solid BiDiMDAH molecule is similar to that of the one of the transition states. The data of NMR spectroscopy has revealed that only one conformer is present in CDCl3 solution in agreement with the data of QC and XRD studies. The gaseous standard enthalpy of formation of BiDiMDAH has been estimated to be 106.1±1.2 kcal/mol by means of G4 theory.

Keywords 6,6′-Dimethyl-1,1′,5,5′-tetraaza-6,6′-bi(bicyclo[3.1.0]hexane) · Diaziridines · Molecular structure · Quantum-chemical calculations · Natural Bond Orbitals · Enthalpy of formation · Anomeric effect · X-ray diffraction · Nuclear Overhauser effect

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 monocyclic and bicyclic heterocyclic structures [24–30]. These heterocycles possess high enthalpies of formation and though they
contain hydrazine fragment, they are of low toxic compounds. Since the most part of alkyl-substituted diaziridines have liquid form, they are considered 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 (Fig. 1). It was shown that the bicyclic fragment of these compounds exists exclusively as a boat conformation of \(\text{C}_2\) symmetry at 20 °C and the Natural Bond Orbital (NBO) analysis showed that the most important stabilization factor in the boat conformation is the \(\eta(\text{N}) \rightarrow \sigma^* (\text{C} - \text{C})\) 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 \([1,2\text{-bis-(3,3-dimethylaziridin-1-yl)ethane}],\) containing two diaziridine cycles in one molecule, by the GED method together with vibrational spectroscopy and quantum chemical calculations [12]. 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.

### QC calculations

Gaussian 09 program software [33] was used for to perform QC calculations. HF [34] B3LYP [35, 36] and MP2 [37] QC methods along with 6-31G(d,p) [38], 6-311++G(d,p) [39, 40], and cc-pVTZ [41] 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 \(\text{opt} = \text{verytight}\) and \(\text{int}=\text{ultrafine}\). Optimized Cartesian coordinates of BiDiMDAH at B3LYP/6-31G(d,p), B3LYP/cc-pVTZ, and 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 [42] at HF/6-311++G(d,p) level of theory in order to avoid computational artifacts [43, 44]. The topological analysis of electronic density was performed using QTAIM method [45] with the AIM2000 code [46, 47]. To predict the BiDiMDAH enthalpy of formation, the Gaussian-4 theory [48] was used as implemented into Gaussian 09 program software, yielding (BiDiMDAH, \(g\)) = 106.1±1.2 kcal mol\(^{-1}\).

### Experimental section

#### 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 spectrum, high-resolution mass spectrum (HRMS), mass spectrum under electron impulse (EI), NMR spectra, and XRD diffraction analysis. The IR spectrum was recorded on InfraLUM FT-801 and Bruker “Alpha” spectrometer in the range 400–4000 cm\(^{-1}\) (resolution 2 cm\(^{-1}\)). HRMS was 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 spectrum 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.

**Synthesis of BiDiMDAH**

The solution of 2,3-butanedione (1.76 ml, 20 mmol) in 5 ml H2O was added dropwise to the solution of 1,3-diaminopropane (3.02 ml, 40 mmol) in 50 ml H2O 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°С 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°С, and the reaction mixture was saturated with NaCl and extracted with CHCl3 (50 ml × 3). The organic layer was dried over K2CO3, the solvent was evaporated, and the residue was recrystallized from acetone. Yield 0.41 g (11%), colorless solid, mp = 187–188 °C. The IR and mass spectra of BiDiMDAH are deposited in the ESI.

**NMR experiments**

A 25-mg portion of the sample was dissolved in 0.6 mL of CDCl3. The 1H and 13C 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 CDCl3. 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 13C NMR, respectively. The numerical values are given as follows: 1H NMR (600.13 MHz, CDCl3) δ, ppm. 1H/Hz: 1.09 (s, 6H, 2×CH3), 1.76–1.82 (m, 2H, 2×CH2), 2.07–2.13 (m, 2H, 2×CH2), 2.78–2.82 (dt, 4H, 4×N–CH2), 3.18–3.23 (dt, 4H, 4×N–CH2) (ESI, Fig. S1).

**XRD experiments**

Single crystals of C10H18N4 were grown from acetone. The structure was solved with Olex2 [49] and Olex2.solve [50] program software, applying Charge Flipping and refined with the XL [51] 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.

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

| Molecular formula | C10H18N4 |
|-------------------|----------|
| Molecular weight [g/mol] | 194.28 |
| Crystal system | Monoclinic |
| Space group | P21/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 [Å3] | 494.25(9) |
| Z | 2 |
| Electrons wavelength [Å] | 0.71073 |
| No. of formula units per unit cell, Z | 2 |
| Density (calculated) [g/cm3] | 1.305 |
| F(000) | 212 |
| Radiation type | Mo-Kα |
| 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 |
| Rint | 0.0197 |
| Rsigmax | 0.0155 |
| Final R indexes [I>2σ(I)] | R1 = 0.0355, wR2 = 0.0959 |
| Final R indexes [all data] | R1 = 0.0388, wR2 = 0.0991 |
| Largest diff. peak/hole / e Å-3 | 0.39/-0.23 |
| Goodness-of-fit on F2 | 1.052 |

Fig. 2  Molecular model of BiDiMDAH with atom numbering

13C NMR (150.90 MHz, CDCl3) δ, ppm.: 8.1 (2×CH3), 32.1 (2×CH2), 48.4 (4×N–CH2), 65.7 (2×C_ring) (ESI, Fig. S2).

A set of 2D spectra, namely, 1H-13C HSQC (heteronuclear spectroscopy quantum correlation), 1H-13C HMBC (heteronuclear multiple bond correlation), and 1H-1H gNOESY (nuclear Overhauser effect spectroscopy), were measured in the CDCl3 solution at 298 K (see Fig. S3, Fig. S4, Fig. S5 and Fig. S6 of the ESI for 1H-13C HSQC, 1H-13C HMBC, 1H-1H gNOESY and 1H-1H COSY spectra, respectively). The mixing time in NOESY was 0.7 s. All correlation NMR spectra were acquired with standard Bruker parameters.
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.

Results and discussion

According to the data of QC computations, a free molecule of BiDiMDAH exists as single conformation I of $C_2$ symmetry with trans orientation of the methyl groups on the C–C bridge connecting two diaziridine cycles (Fig. 3).

BiDiMDAH species with cis orientation of the methyl groups were found to be transition states (TS3 and TS4, see Fig. 3). The TS4 has a similar molecular structure to the TS3 but differs in the orientation of one of the methyl groups which is rotated around the NC–CH$_3$ bond by about 60° in comparison to TS3. The TS3 and TS4 are more than 15 kcal mol$^{-1}$ higher in energy than the main conformer I (see Table 2).

The instability of the TS3 and TS4 may be connected with unfavorable electrostatic interactions of nitrogen atoms (the corresponding NPA charges were calculated to be $\sim -0.4\, \text{e}$). In order to obtain a qualitative measure of overall atom-atom electrostatics, NBO Natural Columbic Energy (NCE) concept was applied, yielding $\Delta E^{(\text{es})} = \Delta E_{\text{NCE}}(\text{TS3}) - \Delta E_{\text{NCE}}(\text{I}) = 34.1\, \text{kcal mol}^{-1}$ and $\Delta E^{(\text{es})} = \Delta E_{\text{NCE}}(\text{TS4}) - \Delta E_{\text{NCE}}(\text{I}) = 34.1\, \text{kcal mol}^{-1}$ consistent with trans conformation (I) advantage over cis forms (TS3 and TS4).

Among BiDiMDAH species with trans orientation of the methyl groups, two low-lying transition states were found (TS1 and TS2, see Fig. 3). The structures of these transition states differ from those of conformer I in the orientation of the methyl groups (see Fig. 3). Thus, in the TS1, one of the methyl groups is rotated around the corresponding NC–CH$_3$ bond by about 60° in comparison with the lowest energy conformation (I) and in the TS2 the both methyl groups are rotated around the NC–CH$_3$ bond by

| Species | Symmetry | $\Delta G^0$ (HF/6-311++G(d,p)) | $\Delta G^0$ (B3LYP/6-31G(d,p)) |
|---------|----------|-------------------------------|---------------------------------|
| I       | $C_2$    | 0.0                           | 0.0                             |
| TS1     | $C_s$    | 0.9                           | 1.0                             |
| TS2     | $C_i$    | 1.6                           | 1.9                             |
| TS3     | $C_{2v}$ | 18.3                          | 16.6                            |
| TS4     | $C_i$    | 21.4                          | 18.6                            |

Fig. 3 The main conformer (I) and various transition states (TS1–TS4) of BiDiMDAH
about 60° in comparison with the lowest energy conformation (I). The rotational analysis around one of the NC–CH₃ bonds of conformer I is presented in Fig. 4. The instability of the TS1 and TS2 may be connected with repulsions of the hydrogen atoms of the methyl groups and the hydrogen atoms of the five-membered rings.

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 3.

The average values of BiDiMDAH bond lengths and bond angles obtained by QC calculations are similar to those for solid state (see Table 3); the computed values of torsion angles are in most cases particularly the same as 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–N5–C4 torsion angles are by about 8° and 11° bigger in the crystal than in a free molecule. The greatest differences between the QC and the XRD molecular structures are observed in the positions of the hydrogen atoms of both methyl groups (confer Fig S7 of the ESI). In the crystal phase, both served in the positions of the hydrogen atoms of both methyl groups.

In the crystal than in a free molecule. The greatest differences between the QC and the XRD molecular structures are observed. This fact may be caused by the two possible tendencies. The first tendency is connected with the n(N)→σ*(C–C) and the n(N)→σ*(C–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(N1)→σ*(C2–C3) has E(2)=3.6 kcal mol⁻¹ (Fig. 5) and the n(N1)→σ*(C2–H16) interaction has E(2)=4.3 kcal mol⁻¹) and the lone pair of the N5 atom interacts with the C3–C4 and the C4–H20 antibonding orbitals (n(N5)→σ*(C3–C4) has E(2)=3.6 kcal mol⁻¹ and the n(N5)→σ*(C4–H20) interaction has E(2)=4.3 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: 2.3 kcal mol⁻¹ for the C7–H21 and the C3–H17 bonds, 1.6 kcal mol⁻¹ for the C7–H21 and the C4–H19 bonds, and 1.2 kcal mol⁻¹ for the C7–H21 and the C2–H15 bonds, respectively.

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(N)→σ*(C–C) and the n(N)→σ*(C–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(N1)→σ*(C2–C3) has E(2)=3.6 kcal mol⁻¹ (Fig. 5) and the n(N1)→σ*(C2–H16) interaction has E(2)=4.3 kcal mol⁻¹) and the lone pair of the N5 atom interacts with the C3–C4 and the C4–H20 antibonding orbitals (n(N5)→σ*(C3–C4) has E(2)=3.6 kcal mol⁻¹ and the n(N5)→σ*(C4–H20) interaction has E(2)=4.3 kcal mol⁻¹).
and 2 lack the methyl group and subsequently the repulsion of the corresponding hydrogen atoms as in BiDiMDAH, leading to the flattening of the 5-membered ring, is missing. It is worth to notice that the N5-N1-C2-C3 torsion angle in BiDiMDAH and compound 3 is practically the same (the 5-membered ring moiety of compound 3 is also nearly flat). This is probably connected with the presence of the methyl groups in compound 3 and the corresponding H…H repulsions as supposed for BiDiMDAH molecule.

The analysis of the 1H and 13C 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 13C 1D NMR spectra, respectively).

The data of 1H–13C HSQC and 1H–1H 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 1H–13C HSQC and 1H–13C HMBC spectra are presented in Table 5. These spectra show how far away each proton was found from a particular carbon atom, respectively, through one or 2–3 bonds.

![Fig. 5 Surface view of overlapping n(N1)→σ*(C2–C3) orbitals of BiDiMDAH](image)

| Table 3 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) |
| ∠C4-N5-C6 | 116.0 | 116.2 | 114.2 | 115.0(1) |
| ∠C2-N1-C6 | 115.6 | 115.7 | 113.4 | 114.9(1) |
| ∠C2-N1-C3 | 123.0 | 122.6 | 122.6 | 122.3(1) |
| ∠C1-N1-C6 | 113.4 | 113.8 | 113.2 | 112.1(1) |
| ∠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) |
| C3-C4-N5-C6 | 61.2 | 61.9 | 61.1 | 54.0(1) |
| N5-C6-N1-C2 | 97.1 | 97.1 | 97.7 | 96.4(1) |
| N5-C6-C13-C14 | 43.5 | 46.6 | 46.1 | 34.3(1) |
| N1-C6-C13-N12 | 122.5 | 125.4 | 124.0 | 111.9(1) |
| 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 2D NMR spectrum $^{1}$H-$^{1}$H$g$NOESY shows the spatial arrangement of protons relative to each other (Table 6, Fig. S5 of the ESI). Protons H15, H17, and H19 have cross-peaks with proton H21 (Fig. 6).

The detected cross-peaks of proton H17 with proton H21 (nuclear Overheuser 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 Overheuser effect. This fact supports that 6-membered rings of BiDiMDAH do not adopt a chair conformation, but rather a flattened boat form is preferred.

**Conclusions**

In summary, a new bicyclic diaziridine derivative 6,6'-dimethyl-1,1',5,5'-tetraaza-6,6'-bir(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. It has been shown that one of the low-energy transition states of a free molecule has such relative arrangement of methyl groups which is...
observed in the crystalline BiDiMDAH. 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.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11224-021-01806-x.

Author contribution 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.

Funding This project was made with financial support of the Russian Foundation for Basic Research (Grant number 20-03-00747 A). X-ray diffraction data were performed with the financial support from the Ministry of Science and Higher Education of the Russian Federation using the equipment of Center for molecular composition studies of A. N. Nesmeyanov Institute of Organoelement Compounds.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Kuznetsov VV, Makhova NN, Dekaprilevich MO (1999) 6,6'-Bis(1,5-diazabicyclo[3.1.0]hexane). Russ Chem Bull 48(3):617–619
2. Petukhova VY, Kuznetsov VV, Shevtsov AV, Strelenko YA, Makhova NN, Lyssenko KA, Antipin MY (2001) Synthesis and structures of 1,1'-dialkyl-3,3'-bidiaziridines. Russ Chem Bull 50(3):440–444
3. Kuznetsov VV, Kutepov SA, Makhova NN, Lyssenko KA, Dmitriev DE (2003) 1,5-Diazabicyclo[3.1.0]hexanes and 1,6-diazabicyclo[4.1.0]heptanes: a new method for the synthesis, quantum-chemical calculations, and X-ray diffraction study. Russ Chem Bull 52(3):665–673. https://doi.org/10.1023/a:1023962914.51979.5c
4. Atavin EG, Golubinskii AV, Popik MV, Kuznetsov VV, Makhova NN, Vilkov LV (2003) Electron diffraction study of the molecular structure of 6,6'-Bis(1,5-diazabicyclo[3.1.0]hexane). J Struct Chem 44(5):779–783. https://doi.org/10.1023/B:JORY.0000029814.51979.5c
5. Atavin EG, Golubinsky AV, Popik MV, Kuznetsov VV, Makhova NN, Anikeeva AV, Vilkov LV (2003) Gas-phase electron diffraction and quantum-chemical studies of the molecular structure of N,N-dimethylaziridine. Zh Strukt Khim 44(5):784–789
6. Petukhova VV, Makhova NN, Ananikov VP, Strelenko YA, Fedyanin IV (2004) 1,2-Bis(methylamino)ethane-1,2-diol dihydrochloride as a new precursor of 1,2,1′,2′-tetramethyl-3,3′-bisdiaziridine. Russ Chem Bull 53(3):612–617
7. Vishnevskiy VV, Vogt N, Vogt J, Rykov AN, Kuznetsov VV, Makhova NN, Vilkov LV (2008) Molecular structure of 1,5-diazabicyclo[3.1.0]hexane as determined by gas electron diffraction and quantum-chemical calculations. J Phys Chem A 112(23):5243–5250
8. Vishnevskiy VV, Schwabedissen J, Rykov AN, Kuznetsov VV, Makhova NN (2015) Conformational and bonding properties of 3,3-dimethyl- and 6,6-dimethyl-1,5-diazabicyclo[3.1.0]hexane: a case study employing the Monte Carlo method in gas electron diffraction. J Phys Chem A 119(44):10871–10881
9. Kuznetsov VV, Marochkin II, Goloveskikh AS, Makhova NN, Shishkov IF (2017) Comparable study of the structure of 1,2-bis(2-acetamidoethyl) diaziridine and 3,3-diyldiazidiaziridine with structures of related compounds by X-ray diffraction analysis and quantum chemical calculations. Struct Chem 28(4):1211–1221
10. Altova EP, Kuznetsov VV, Marochkin II, Rykov AN, Makhova NN, Shishkov IF (2018) 3-Cyclopropyl-1,2-dimethyl diaziridine: synthesis and study of molecular structure by gas electron diffraction method. Struct Chem 29(3):815–822
11. Marochkin II, Kuznetsov VV, Rykov AN, Makhova NN, Shishkov IF (2019) Molecular structure study of 1,2,3-trimethyl diaziridine by means of gas electron diffraction method. Struct Chem 30(2):457–464
12. Khaikin LS, Kochikov IV, Rykov AN, Grikina OE, Ageev GG, Shishkov IF, Kuznetsov VV, Makhova NN (2019) Equilibrium structures of the tetraine diastereomers and their ratio: joint analysis of gas phase electron diffraction, quantum chemistry, and spectroscopic data. Phys Chem Chem Phys 21(10):5598–5613
13. Marochkin II, Kuznetsov VV, Li Z, Rykov AN, Makhova NN, Shishkov IF (2020) Molecular structure study of 1,2,4-trimethyl diaziridine studied by gas electron diffraction supported by quantum chemistry calculations. J Mol Struct 1225:129066. https://doi.org/10.1016/j.molstruc.2020.129066
14. Paget CJ, Davis CS (1964) Synthesis and in vitro activity of some aryl diaziridines as potential monoamine oxidase inhibitors. J Med Chem 7(5):626–628
15. Kostyanovskii RG, Shustov GV, Nabiev OL (1986) Synthesis and psychotropic activity of functionally substituted diaziridines and bisdiaziridines. Pharm Chem J 20(6):385–388
16. Baichurina AZ, Semina II, Garaev RS (1996) Effects of amphazide (a hydrazide of phosphorylated carboxylic acids) and tetramezine (a carbonyl compound) on central dopaminergic structures. Bull Exp Mol Sci 12(5):584–586
17. Makhova NN, Petukhova VV, Shevtsov AV, Novakovskiy VV, Kuznetsov VV (2013) Agents for treating neurodegenerative disorders, US Pat., WO 2013/111117 A2.
18. Makhova NN, Petukhova VV, Shevtsov AV, Novakovskiy VV, Kuznetsov VV (2013) Agents for treating neurodegenerative disorders, US Pat., WO 2013/111118 A2.
19. Makhova NN, Petukhova VV, Shevtsov AV, Novakovskiy VV, Kuznetsov VV (2013) Agents for treating neurodegenerative disorders, US Pat., WO 2013/121334 A2.
20. Kuznetsov VV, Shevtsov AV, Pleschev MI, Strelenko YA, Makhova NN (2016) Diastereoselective synthesis of 1,3-di- and 1,3,3-trisubstituted diaziridines coupled with neurotransmitter amino acids. Mendeleev Commun 26(5):391–394
21. Mannscherck A, Radeglia R, Gründernan M, Ohme R (1967) Protonenresonanz-Untersuchungenzur Inversion am dreibindigen Stickstoffatom. I Der Diaziridin-Ring als Asymmetriezentrum. Chem Ber 100(6):1778–1785
22. Shustov GV, Kadorkina GK, Varlamov SV, Kachanov AV, Kostyanovskiy RG, Rauk AJ (1992) The nonplanar amide group in N-acylaziridines: conformational behavior and chiroptical properties. J Am Chem Soc 114(5):1616–1623
23. Kamuf M, Trapp O (2011) Stereodynamics of tetrazine. Chirality 23(2):113–117
24. Makhova NN, Shevtsov AV, Petukhova VV (2011) Transformations of diaziridines and their fused analogues induced by electrophilic reagents. Russ Chem Rev 80(11):1085
25. Petukhova VV, Pleschev MI, Fershtat LL, Kuznetsov VV, Khakimov DV, Lavina TS, Petukhova VV, Shishkov IF (2013) Metathesis of azomethine imines in the reaction of 6-aril-1,5-diazabicyclo[3.1.0]hexanes with carbonyl compounds. Mendeleev Commun 23(1):34–36
26. Pleschev MI, DasGupta NV, Kuznetsov VV, Fedyanin IV, Kachala VV, Makhova NN (2015) CAN-mediated new, regioselective one-pot access to bicyclic cationic structures with 2,3-dihydro-1H-pyrazolo[1,2-ajpyrazol-4-ium core. Tetrahedron 71(47):9012–9021
27. Chagarovskiy AO, Vasin VS, Kuznetsov VV, Ivanova OA, Rybakov VB, Shumskyy AN, Makhova NN, Trushkov IV (2018) (3 +3)-annulation of donor–acceptor cyclopropanes with diaziridines. Angew Chem Int Ed 57(32):10338–10342
28. Chagarovskiy AO, Kuznetsov VV, Ivanova OA, Goloveskikh AS, Levina II, Makhova NN, Trushkov IV (2019) Synthesis of 1-substituted pyrazolines by reaction of donor-acceptor cyclopropanes with 1,5-diazabicyclo[3.1.0]hexanes. Eur J Org Chem 2019(32):5475–5485
29. Sundaresan R, Jesin I, Arivalagan S, Nandia GC (2021) Recent advances in the preparations and synthetic applications of oxaziridines and diaziridines advanced synthesis & catalysis. DOE. https://doi.org/10.1002/ads.202001372.
30. Zhang X, Shen L, Luo Y, Jiang R, Sun H, Liu J, Fang T, Fan H, Liu Z (2017) Synthesis and ignition properties research of 1,5-diazabicyclo[3.1.0]hexane type compounds as potential green hypergolic propellants. Ind Eng Chem Res 56(11):2883–2888
31. Kuznetsov VV, Kachala VV, Makhova NN (2018) Synthesis of hybrid structures comprising diaziridine and cyclopropane rings in one molecule. Mendeleev Commun 28(5):497–500
32. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Lippert CD, Malmqvist AB, Bloino J, Zheng G, Sonnenberg TL, Marder K, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa I, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JJA, Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Keith T, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam J, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas O, Ochterski JW, Ortiz JV, Cioslowski J, Fox DJ (2010) Gaussian 09 (Revision B01), Wallingford CT
33. Roothaan CCJ (1951) New developments in molecular orbital theory. Rev Mod Phys 23(2):69
34. Becke AD (1988) Density-functional exchange-energy approximation with correct asymptotic behavior. Phys Rev A 38(6):3098
35. Lee C, Yang W, Parr RG (1988) Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys Rev B 37(2):785
36. Muller C, Plessert MS (1934) Note on an Approximation treatment for many-electron systems. Phys Rev 46(7):618
38. Petersson GA, Bennett A, Tensfeldt TG, Al-Laham MA, Shirley WA, Mantzaris J (1988) A complete basis set model chemistry. I. The total energies of closed-shell atoms and hydrides of the first-row elements. J Chem Phys 89(4):2193
39. McLean AD, Chandler GS (1980) Contracted Gaussian basis sets for molecular calculations. I. Second row atoms, Z=11–18. J Chem Phys 72(10):5639–5648
40. Clark T, Chandrasekhar J, Spitznagel GW, Schleyer PR (1983) Efficient diffuse function-augmented basis sets for anion calculations. III. The 3-21+G basis set for first-row elements. Li–F. J Comput Chem 4(3):294–301
41. Dunning TH (1989) Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. J Chem Phys 90(2):1007–1023
42. Glendening ED, Landis CR, Weinhold F (2019) NBO 7.0: New vistas in localized and delocalized chemical bonding theory. J Comput Chem 40:2234–2241
43. Weinhold F, Landis CR (2012) Discovering chemistry with natural bond orbitals. Upper Saddle River, NJ
44. NBO 7.0 Program Manual. Madison, Wisconsin. https://nbo6.chem.wisc.edu/nboman.pdf. Accessed 22 April 2021
45. Bader RFW (1994) Atoms in molecules: a quantum theory. Oxford Univ. Press, NY
46. Biegler-König F, Schönbohm J, Bayles D (2001) AIM2000. J Comput Chem 22(5):545–559
47. Biegler-König F, Schönbohm J (2002) Update of the AIM2000-Program for atoms in molecules. J Comput Chem 23(15):1489–1494
48. Curtiss LA, Redfern PC, Raghavachari K (2007) Gaussian-4 theory using reduced order perturbation theory. J Chem Phys 127:124105
49. Dolomanov OV, Bourhis LJ, Gildea RJ, Howard JAK, Puschmann H (2009) OLEX2: a complete structure solution, refinement and analysis program. J Appl Crystallogr 42(2):339–341
50. Bourhis LJ, Dolomanov OV, Gildea RJ, Howard JAK, Puschmann H (2015) The anatomy of a comprehensive constrained, restrained refinement program for the modern computing environment – Olex2 dissected. Acta Cryst A 71(1):59–75
51. Sheldrick GM (2008) A short history of SHELX. Acta Cryst A 64(1):112–122
52. Pauling L (1948) The nature of the chemical bond2nd edn. Ithaca, NY
53. Weinhold F (2012) Natural bond critical point analysis: quantitative relationships between NBO-based and QTAIM-based topological descriptors of chemical bonding. J Comput Chem 33(30):2440–2449

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.