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Conformational Transformations and Autooxidation of 5-Bromo-2-(2-methylpropyl)-5-nitro-1,3,2-dioxaborinane

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Abstract—Conformational study of 5-bromo-2-(2-methylpropyl)-5-nitro-1,3,2-dioxaborinane at the DFT PBE/3ξ level of theory revealed the only *sofa–sofa* interconversion pathway through a transition state corresponding to 2,5-*twist* conformer. The barrier to internal rotation of the axial nitro group is several times higher than that for the equatorial nitro group. According to the ^{1}H, ^{13}C, and ^{11}B NMR, IR, and X-ray diffraction data, the main autooxidation products of 5-bromo-2-(2-methylpropyl)-5-nitro-1,3,2-dioxaborinane are 2-bromo-2-nitropropane-1,3-diol and boric acid.

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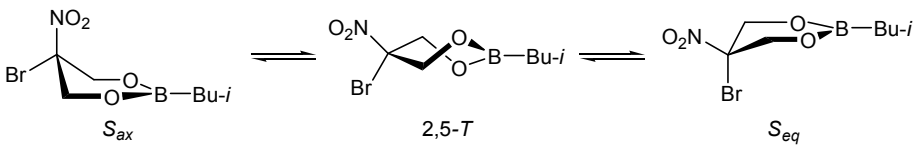
Interest in six-membered cyclic boric and boronic acid esters, 1,3,2-dioxaborinanes, is determined by importance of these compounds for fine organic synthesis, combination of their practically useful properties (biologically active compounds, corrosion inhibitors, and components of polymeric materials, fuels, and lubricants), and specific structural features (electronic and steric intramolecular interactions) [1–3]. 2,5,5-Trisubstituted 1,3,2-dioxaborinanes with different substituents on C^5 characteristically give rise to conformational equilibrium between *sofa* invertomers, which is shifted (partially or completely) toward one invertomer [4]. Of particular interest is the structure of cyclic boronic esters with polar substituents on C^5, e.g., with a nitro group. According to the X-ray diffraction data, 5-methyl-5-nitro-2-phenyl-1,3,2-dioxaborinane molecule has a *sofa* conformation with the axial nitro group [5]. On the other hand, ^{1}H NMR study has shown that 5-bromo-2-(2-methylpropyl)-5-nitro-1,3,2-dioxaborinane (**1**) in solution is conformationally homogeneous. This follows from the signals of methylene protons on C^4 and C^6, which appear as a typical *AB* quartet with $\Delta\delta = 0.47$ ppm [4]. In this work we studied conformational transformations of cyclic ester **1** in terms of the density functional theory (DFT) using PBE/3ξ approximation (PRIRODA [6]), as well as chemical transformations of **1** on prolonged storage.

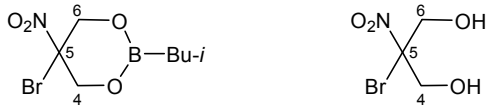
The results of computer simulation of conformational transformations of **1** were consistent with the experimental data. They indicated almost complete shift of conformational equilibrium toward conformer S_{ax} with the axial nitro group. A local minimum (structure S_{eq}) and transition state (TS) having 2,5-*twist* conformation (2,5-*T*) were also localized on the potential energy surface (Scheme 1). The data in Table 1 show

Scheme 1.



S_{ax} 2,5-*T* S_{eq}

Table 1. Calculated energy parameters of minima and transition states on the PES of ester **1** and minima on the PES of diol **3**



1 **3**

Conformer	$-E_0$,[a] hartree	ΔE_0° ($\Delta E_0^{\neq}$), kcal/mol	ΔH_{298}° ($\Delta H_{298}^{\neq}$), kcal/mol	ΔG_{298}° ($\Delta G_{298}^{\neq}$), kcal/mol	ΔS_{298}° ($\Delta S_{298}^{\neq}$), cal mol^{-1} K^{-1}
1, S_{ax}	3228.185057	0	0	0	0
1, S_{eq}	3228.182939	1.3	1.3	1.3	0.02
1, 2,5-*T*	3228.174630	(6.5)	(6.1)	(7.2)	(–3.9)
1, NO_2 (*ax*) (TS)	3228.180674	(2.8)	(2.2)	(4.0)	(–6.0)
1, NO_2 (*eq*) (TS)[b]	3228.181432	(0.9)	(0.4)	(1.9)	(–5.1)
1, NO_2 (*eq*) (BS)[b]	3228.181947	0.6	0.7	0.1	1.8
3a	3046.885254	0	0	0	0
3b[c]	3046.883239	1.8	2.0	1.5	2.2
3c[c]	3046.875849	5.9	6.3	5.1	4.1

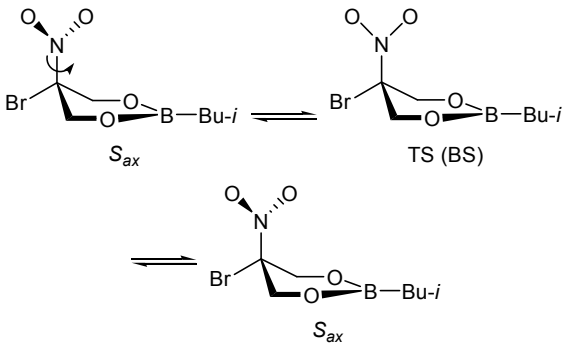
[a] With correction for zero-point energy.
[b] Relative to S_{eq}.
[c] Relative to **3a**.

that the $\Delta H^{\neq}$ and $\Delta G^{\neq}$ values for the ring interconversion approach those found experimentally for most structurally related compounds [7].

The preferentially axial orientation of the 5-nitro group in 1,3,2-dioxaborinanes is accounted for by stabilizing dipole–dipole and orbital interactions with the heteroatom part of the ring [1, 3]. This should affect the barrier to internal rotation of that substituent. Computer simulation revealed transition states for internal rotation of the axial and equatorial nitro groups; the corresponding $\Delta H^{\neq}$ and $\Delta G^{\neq}$ values are given in Table 1. The global minimum for conformer S_{ax} corresponds to orthogonal arrangement of the nitro group, and the transition state has bisector structure (*BS*) (Scheme 2; Fig. 1).

The global energy minimum for S_{eq} is also achieved with orthogonal orientation of the nitro group. The PES also contained a local minimum corresponding to bisector conformer; the energy difference with the global minimum does not exceed 0.7 kcal/mol (Scheme 3; Table 1, Fig. 2).

Scheme 2.



The energy-degenerate transition states correspond to the *gauche* conformation of the nitro group (α = 33.9°). It is seen that the activation parameters for internal rotation of the axial nitro group are considerably higher (2.1 to 5 times) than those for the equato-

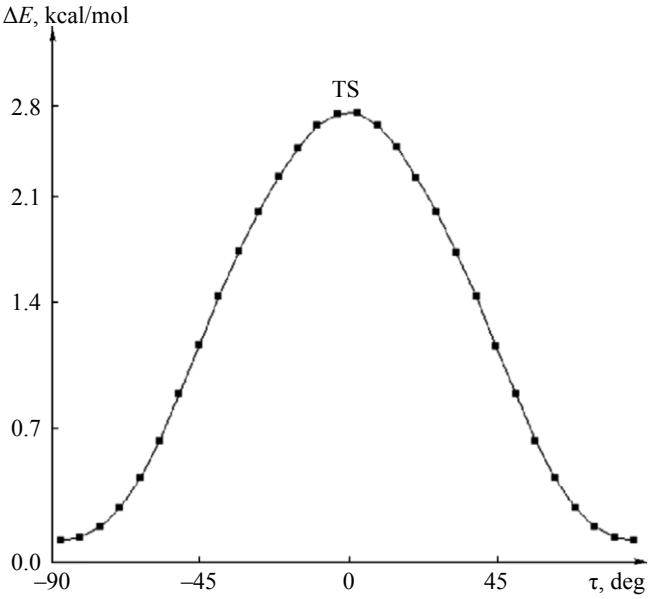
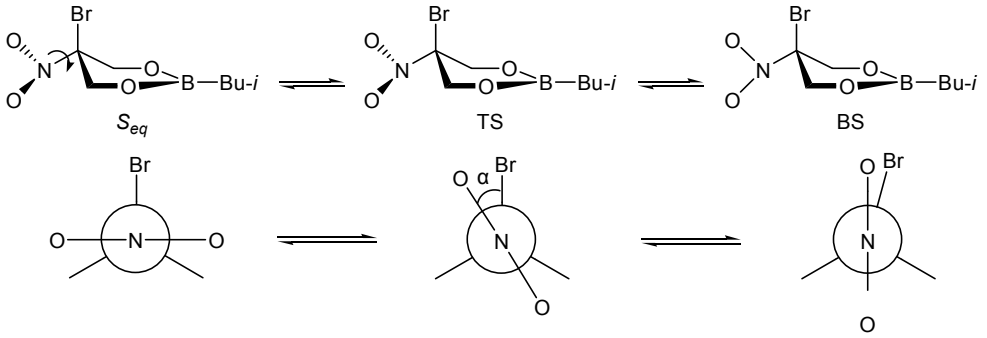
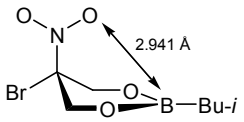


Fig. 1. Energy profile for the rotation of the axial nitro group in conformer S_{ax} of ester **1** about the C–N bond at 0 K.

Scheme 3.



rial nitro group (Table 1). This suggests appreciable, most probably dipole–dipole interaction between the axial substituent and heteroatom moiety of the ring. The boron atom and oxygen atom of the nitro group in the transition state approach each other most closely.



Analogous character of internal rotation of the nitro group was observed for 5,5-dinitro-1,3-dioxane molecule [8]. On the other hand, internal rotation of the axial nitro group in 2-methyl-5-nitro-1,3,2-dioxaborinane is accompanied by conformational rearrangement of the ring, which additionally increases the activation barrier of this process [9].

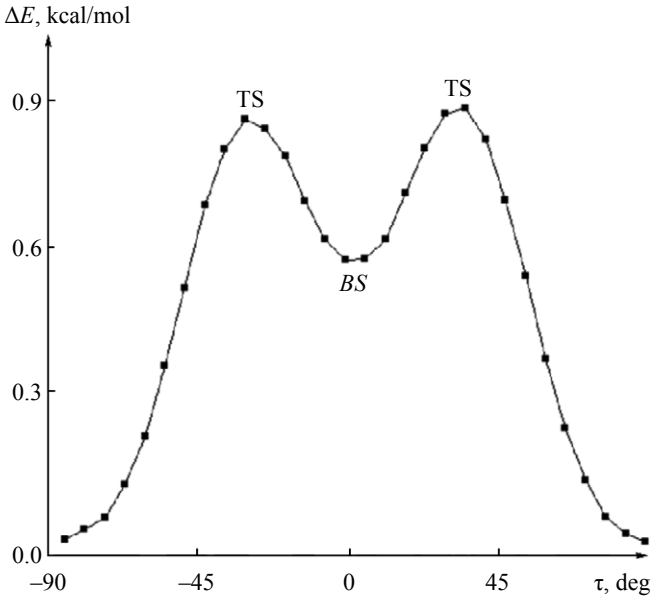
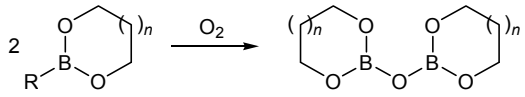


Fig. 2. Energy profile for the rotation of the equatorial nitro group in conformer S_{eq} of ester **1** about the C–N bond at 0 K.

It is known that cyclic boronic acid esters are prone to autooxidation; after prolonged storage (for several years) even in a closed vessel containing air, 2,2′-oxybis(1,3-dioxa-2-boracycloalkanes) are formed. This transformation was reported for the first time for a seven-membered cyclic boronic ester, 3-(2-methylpropyl)-1,5-dihydro-2,4,3-benzodioxaborepine [10]; later on, analogous reactions were described for five- and six-membered analogs [11, 12] (Scheme 4).

Scheme 4.



n = 0–2.

A probable autooxidation mechanism was proposed in [12]. A sample of **1** (which is a high-boiling liquid) was stored in a closed vessel for more than 12 years and was gradually converted to almost colorless crystalline solid. It may be presumed that the major product of autooxidation of **1** would be the corresponding 2,2′-oxybis(dioxaborinane) **5** (Scheme 5).

Scheme 5.

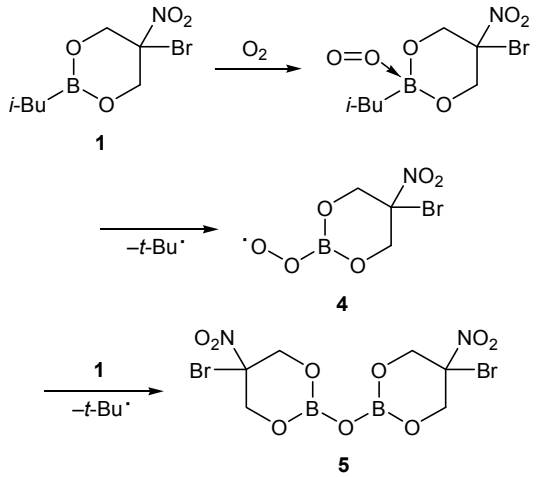


Table 2. ^{1}H and ^{13}C NMR spectra of 5-bromo-2-(2-methylpropyl)-5-nitro-1,3,2-dioxaborinane (**1**), crystalline product of its autooxidation (**2**), and 2-bromo-2-nitropropane-1,3-diol (**3**) in D_2O

Compound no.	^{1}H NMR spectrum, δ, ppm (*J*, Hz)		^{13}C NMR spectrum, δ_C, ppm		
	$(CH_2)_2$	*i*-Bu	C^4, C^6	C^5	*i*-Bu
1	4.19 q (–12.0)	0.63 d (CH_2, ^3J = 7.2), 0.82 d (Me, ^3J = 6.6), 1.73 m (CH)	61.58	97.07	21.01, 21.33
2	4.21 q (–13.0)	–	64.82	100.42	–
3	4.21 q (–13.0)	–	64.86	100.40	–

We analyzed both liquid sample of **1** after prolonged storage and colorless crystalline solid formed under the liquid. The IR spectrum of the liquid phase contained the expected $\nu_{as}(NO_2)$ band at 1561 cm^{-1}, as well as C=C, B–H, and O–H stretching bands at 1640, 2524, and 3434 cm^{-1}, respectively. In the ^{1}H NMR spectrum of this sample ($CDCl_3$) we observed methylene proton quartet at δ 4.21 ppm due to 4-H and 6-H protons of **1** [1, 4] and a low-intense multiplet signal at δ 5.1 ppm assignable to an olefinic proton.

Presumably, the transformation of cyclic ester **1** on storage involves radical addition of oxygen molecule to the boron atom in keeping with the known scheme for autooxidation of organoboron compounds [13], followed by elimination of *tert*-butyl radical (isomerization product of isobutyl radical) with formation of peroxide **4**. A series of secondary reactions leading to isobutylene, cyclic and acyclic boronic acid esters with B–H bond, and alkoxyl and hydroxyl radicals are also possible. By analogy with the known data for autooxidation of some 2-alkyl-1,3,2-dioxaborinanes [10–12], expected product **5** should reside in the crystalline phase.

The crystalline residue (**2**) began to melt at 122°C (cf. mp 131°C for pure diol **3**) [14]. On the basis of the ^{1}H and ^{13}C NMR data (Table 2), the product was identified as 2-bromo-2-nitropropane-1,3-diol (**3**). Compound **3** (Bronopol) is widely used in cosmetics as antibacterial agent [15–17]. Its structure was studied by X-ray analysis [18–20] and IR spectroscopy [21]. Conformational transformations of individual molecules and crystal structure as a whole were observed when a crystalline sample of **3** was heated to a temperature approaching phase transition. Fedorov et al. [20] synthesized two samples of **3** from different precursors, and each sample was studied by X-ray diffraction. In the present work, X-ray analysis of the crystalline product obtained from ester **1** after prolonged storage showed the presence of diol **3** with a structure corresponding to that of a sample of **3** described in [20] with antiperiplanar orientation of the C–C and C–O bonds (Fig. 3, **3a**); the tabulated bond lengths of **3** are available from the authors by e-mail. The crystallographic parameters are given in Experimental. The bond lengths were consistent with those reported in [18, 19] and found in other aliphatic nitro compounds [22, 23].

It is reasonable to expect that a structure stabilized by intramolecular hydrogen bond should predominate in the gas phase and in solution. The ^{1}H NMR spectrum of **3** in D_2O showed an *AB* quartet analogous to that observed in the spectrum of **1** (^2J = –13.0 Hz, Δδ = 0.13 ppm (Table 2). This means that the structure with pseudo-*chair* conformation of the $(CH_2OH)_2$ fragment should predominate in conformational equilibrium in solution at room temperature. Quantum-chemical study of the conformational behavior of **3** at the PBE/3ξ level of theory revealed three main conformers **3a**–**3c** on the potential energy surface (Scheme 6). In accordance with their relative energies (Table 1), the most favorable conformer is **3a** with pseudoaxial nitro group, which is stabilized by intramolecular hydrogen bond between the hydroxy groups (O···H 2.0 Å, Mulliken bond order 0.07).

Structure **3c** has the highest energy despite analogous intramolecular hydrogen bond. Assuming that the concentration of **3c** is negligible, the relative populations of **3a** and **3b** were estimated using the known equation $\Delta G° = -R\,T\ln(\mathbf{3a}/\mathbf{3b})$. The $\Delta G°$ value

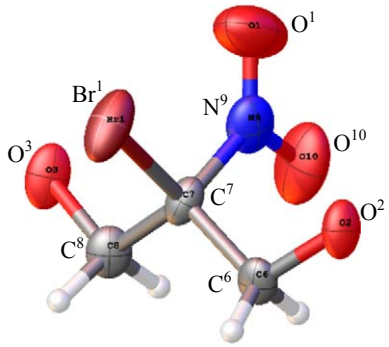
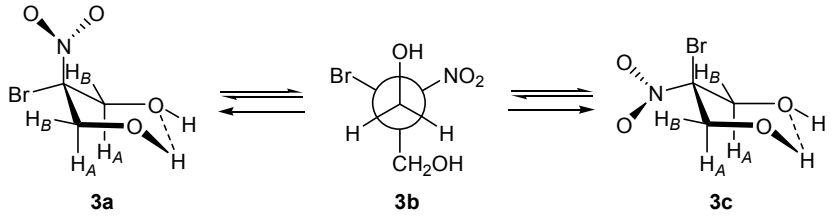


Fig. 3. Structure of the molecule of 2-bromo-2-nitropropane-1,3-diol (**3**) according to the X-ray diffraction data.

Scheme 6.

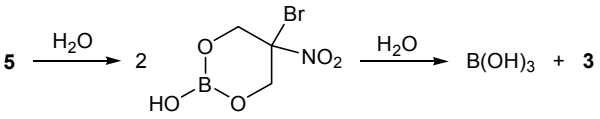


3a **3b** **3c**

1.5 kcal/mol for **3b** (Table 1) at 298 K corresponds to the **3a**/**3b** ratio ~93 : 7. Thus, the population of **3a** is fairly high. These results are consistent with the conformational analysis data for propane-1,3-diol which was also found to prefer pseudo-*chair* conformation with intramolecular hydrogen bond [24].

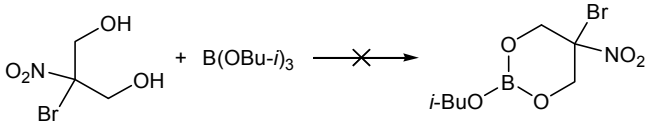
Additional information on the composition of crystalline residue **2** was inferred from the ^{11}B NMR spectra recorded in $CDCl_3$ and D_2O, which contained an intense signal at δ_B 19.5 ($CDCl_3$) or 18.4 ppm (D_2O) and a weak signal at δ_B 31.5 ($CDCl_3$) or 33.1 ppm (D_2O). The downfield signal is likely to belong to boric acid as the final boron-containing autooxidation product [25], and the upfield signal was assigned to traces of **1**. We failed to obtain single crystals of boric acid suitable for X-ray analysis. Thus, hydrolysis of unstable 2,2′-oxybis(dioxa-borinane) **5** gives initial 1,3-diol and boric acid (Scheme 7).

Scheme 7.



Obviously, hydrolytic instability is intrinsic to cyclic boric and boronic esters derived from diol **3**. In fact, our attempt to synthesize 5-bromo-2-(2-methylpropyloxy)-5-nitro-1,3,2-dioxaborinane by reaction of diol **3** with triisobutyl borate was unsuccessful, and the only liquid product was the initial boric ester (Scheme 8). Nevertheless, numerous examples of stable six-membered cyclic boric esters are known [1].

Scheme 8.



EXPERIMENTAL

Conformational behavior of ester **1** was simulated using PRIRODA software package [6] in the DFT PBE/3ξ approximation by optimizing geometric parameters of conformers S_{ax} and S_{eq} (preliminarily calculated at the AM1 level; HyperChem [26]); for this purpose, the torsion angles OCCC or OBOC were varied in the range from –50 to +50°; the conformation of the isobutyl group on the boron atom always corresponded to minimum on the potential energy surface to eliminate its effect on the ring conformation. The interconversion pathway and potential barriers were determined by the transition state search algorithm implemented in the software used. Internal rotation of the nitro group in molecule **1** was simulated by scanning the torsion angle ONCBr from 90 to –90°. Analogous calculations were performed for conformers of diol **3**. Stationary points on the potential energy surface were identified as minima by the absence of imaginary frequencies in the corresponding Hessian matrix, and as transition states, by the presence of one imaginary frequency.

The X-ray diffraction data for diol **3** were obtained on an XCalibur Eos automated four-circle diffractometer (Mo K_α radiation, λ 0.71073 Å, graphite monochromator, ω-scanning, $2\theta_{max} = 62°$) using CrysAlis^{Pro} version 1.171.36.20 (Oxford Diffraction Ltd.). The structure was solved by the direct method and was refined by full-matrix least-square method in anisotropic approximation for non-hydrogen atoms. Hydrogen atoms were localized by Fourier difference syntheses and were refined in isotropic approximation. All calculations were performed using SHELX97 [27]. Crystallographic data and experimental details: temperature 293(2) K; monoclinic crystal system, space group *Cc*; unit cell parameters: a = 8.000(2), b = 9.6403(14), c = 8.9416 (16) Å; β = 91.08(2)°; V = 689.5(2) Å^3; Z = 2; d_{calc} = 2.088 g/cm^3; μ = 5.923 mm^{-1}; $F(000)$ = 420.0; scan range $6.62 \le \theta \le 62.36$; reflection indices: $-11 \le h \le 6$, $-13 \le k \le 10$, $-12 \le l \le 6$; number of independent reflections 923 (R_{int} = 0.0274); goodness of fit 1.254; final divergence factors: R_1 = 0.0683 [reflections with $I_{hkl} > 2\sigma(I)$], wR_2 = 0.1671; R_1 = 0.0751 (all reflections), wR_2 = 0.1754; Δρ, min/max: 1.00/–1.10 $\bar{e}$Å^{-3}. The X-ray diffraction data for diol **3** were deposited to the Cambridge Crystallographic Data Centre (CCDC entry no. 1040940).

The ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400.13, 100.62, and 128.33 MHz, respectively, from solutions in $CDCl_3$ and D_2O with a concentration of 0.01 M. Diol **3** is poorly soluble in $CDCl_3$; therefore, the data obtained in D_2O were used for comparison. The chemical shifts were measured relative to tetramethylsilane (^{1}H, ^{13}C) or $BF_3 \cdot Et_2O$ (^{11}B) as internal standard. The IR spectrum (film) was recorded on a Bruker Vertex 70V spectrometer.

Ester **1** was described in [4]. A fresh sample of **1** was obtained by reaction of diisobutyl isobutylboronate with an equimolar amount of diol **3** in benzene. Yield 68%, bp 90–92°C (4 mm).

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REFERENCES

1. Gren', A.I. and Kuznetsov, V.V., *Khimiya tsiklicheskikh efirov bornykh kislot* (Chemistry of Cyclic Boronic Acid Esters), Kiev: Naukova Dumka, 1988.
2. Kuznetsov, V.V., *Panorama sovremennoi khimii Rossii. Uspekhi organicheskogo kataliza i khimii geterotsiklov* (Prospect of Modern Chemistry in Russia. Advances in Organic Catalysis and Chemistry of Heterocycles), Rakhmankulov, D.L., Ed., Moscow: Khimiya, 2006, p. 336.
3. Kuznetsov, V.V., *Russ. J. Org. Chem*., 2014, vol. 50, p. 1227.
4. Kuznetsov, V.V., Valiakhmetova, O.Yu., and Bochkor, S.A., *Chem. Heterocycl. Compd*., 2007, vol. 43, p. 1577.
5. Kliegel, W., Preu, L., Rettig, S.J., and Trotter, J., *Can. J. Chem*., 1986, vol. 64, p. 1855.
6. Laikov, D.N. and Ustynyuk, Yu.A., *Russ. Chem. Bull., Int. Ed*., 2005, vol. 54, p. 820.
7. Carton, D., Pontier, A., Ponet, M., Soulie, J., and Cadiot, P., *Tetrahedron Lett*., 1975, vol. 16, p. 2333.
8. Khaibullina, G.S., Bochkor, S.A., and Kuznetsov, V.V., *Russ. J. Org. Chem*., 2014, vol. 50, p. 725.
9. Valiakhmetova, O.Yu., Bochkor, S.A., and Kuznetsov, V.V., *Russ. J. Gen. Chem*., 2010, vol. 80, p. 737.
10. Kuznetsov, V.V., Mazepa, A.V., and Spirikhin, L.V., *Chem. Heterocycl. Compd*., 1998, vol. 34, p. 1207.
11. Kuznetsov, V.V. and Mazepa, A.V., *Dopov. Nats. Akad. Nauk Ukr*., 1998, no. 11, p. 142.
12. Kuznetsov, V.V., Mazepa, A.V., and Spirikhin, L.V., *Russ. J. Gen. Chem*., 2000, vol. 70, p. 1576.
13. Mikhailov, B.M. and Bubnov, Yu.N., *Bororganicheskie soedineniya v organicheskom sinteze* (Organoboron Compounds in Organic Synthesis), Moscow: Nauka, 1977, p. 171.
14. Namba, K., Indzyka, C., and Joneno, M., *J. Chem. Soc. Jpn., Ind. Chem. Sect*., 1963, vol. 66, p. 1446.
15. Bryce, D.M., Crosnaw, B., Hall, J.E., Holland, V.R., and Lessel, B., *J. Soc. Cosmet. Chem*., 1978, vol. 29, p. 3.
16. Shepherd, J.A., Waigh, R.D., and Gilbert, P., *Antimicrob. Agents Chemother*., 1988, vol. 32, p. 1693.
17. Legin, G.Ya., *Pharm. Chem. J*., 1996, vol. 30, no. 4, p. 273.
18. Gowda, D.S. and Rudman, R., *J. Chem. Phys*., 1982, vol. 77, p. 4666.
19. Golovina, N.I., Raevskii, A.V., Fedorov, B.S., Gusakovskaya, L.G., Trofimova, R.F., and Atovmyan, L.O., *J. Solid State Chem*., 1998, vol. 137, p. 231.
20. Fedorov, B.S., Golovina, N.I., Arakcheeva, V.V., Trofimova, R.F., and Atovmyan, L.O., *Russ. Chem. Bull*., 1996, vol. 45, p. 1157.
21. Golovina, N.I., Chukanov, N.V., Raevskii, A.V., and Atovmyan, L.O., *J. Struct. Chem*., 2000, vol. 41, p. 238.
22. Nordenson, S., Skramstad, J., and Fløtra, E., *Acta Chem. Scand., Ser. B*, 1984, vol. 38, p. 461.
23. Trotter, J., *Tetrahedron*, 1960, vol. 8, p. 13.
24. Shagidullin, Rif.R., Chernova, A.V., Plyamovatyi, A.Kh., and Shagidullin, R.R., *Russ. Chem. Bull*., 1991, vol. 40, p. 1993.
25. Nöth, H. and Wrackmeyer, B., *NMR: Basic Princ. Prog*., 1978, vol. 14, p. 1.
26. *HyperChem 8.0*. http://www.hyper.com
27. Sheldrick, G.M., *Acta Crystallogr., Sect. A*, 2008, vol. 64, p. 112.