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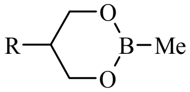
# CONFORMATIONAL COMPOSITION OF 2,5-DISUBSTITUTED 1,3,2-DIOXABORINANES

**V. V. Kuznetsov, A. N. Novikov, I. S. Rublev, and P. Yu. Markolenko**

*We have used $^1$H NMR spectra and also MM+ and AM1 calculation methods to show that the conformational equilibrium of 2,5-disubstituted 1,3,2-dioxaborinane molecules, including two sofa forms, is shifted toward the equatorial conformer. We have established the values of $\Delta G^0$ for a number of substituents on the $C_{(5)}$ ring atom.*

**Keywords:** 1,3,2-dioxaborinane, conformer, conformational equilibrium, *sofa*, conformational free energy.

We know that six-membered cyclic esters of boric acids, owing to their structural features, have mesomorphic properties (they form smectic and nematic phases over a broad temperature range [1-3]) and are convenient model compounds for studying the effect of heteroatoms on the change in conformational characteristics of hetero analogs of cyclohexane [4]. Earlier [4-8] it was shown that 2,5-disubstituted 1,3,2-dioxaborinane molecules exist in the *sofa* conformation with predominantly equatorial alkyl, allyl, or phenyl groups on the $C_{(5)}$ ring atom. This work is devoted to further study of the conformational composition of individual cyclic boric esters in this series **1-10**, and also estimation of the conformational free energy of substituents on the $C_{(5)}$ atom using $^1$H NMR spectra and calculations by the MM+ method and also the AM1 method (in the restricted Hartree–Fock approximation), using the HyperChem software [9].



**1–10**

**1** R = Et, **2** R = *i*-Pr, **3** R = $CH_2{=}CH{-}CH_2$, **4** R = Bu, **5** R = *i*-Bu, **6** R = *t*-Bu,
**7** R = $C_5H_{11}$, **8** R = $C_6H_{11}$, **9** R = Ph, **10** R = $PhCH_2$

2-Methyl-substituted esters were selected as the model compounds for analysis of the conformational properties of 2-isopropyl- and 2-isobutyl derivatives [4-7], since the nature of the substituent on the boron atom does not have a substantial effect on the conformational equilibrium parameters of the molecules of the substances under discussion [10].

The calculations for the optimal geometry and the energy of the molecules of the studied compounds suggest that on the potential energy surface, there are only two minima, corresponding to the *sofa* conformers $C_e$ and $C_a$, the first of which is the major conformer (Table 1).

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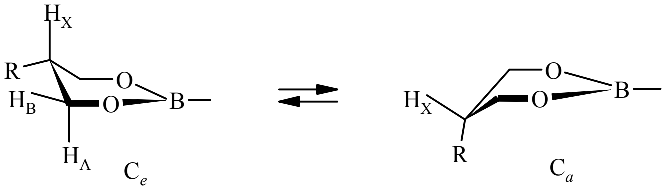
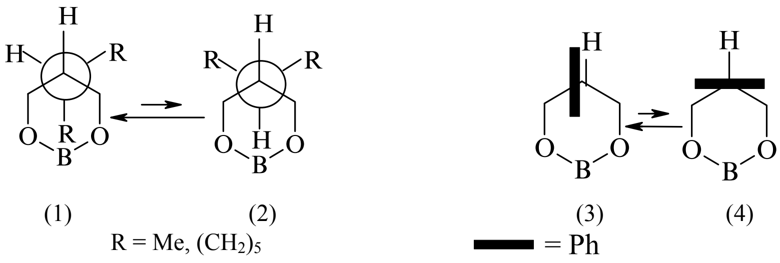
A. V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Odessa 65080; e-mail: physchem@paco.odessa.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 426-432, March, 2003. Original article submitted April 24, 2000.



The calculated energy differences between these forms ($\Delta E$) to a certain extent depend on the nature and conformational volume of the substituent on the $C_{(5)}$ atom. The conformational properties of the equilibrium form $C_e$, described using the Zefirov–Palyulin–Dashevskaya puckering parameters ($S$ is the degree of puckering, $\Theta$ and $\Psi$ are the polar angles characterizing the type of conformation [11]), are close to those for the canonical *sofa* conformation. The most stable conformation of the secondary alkyl group on $C_{(5)}$ for the form $C_e$ (esters **2, 8**) presumes an asymmetric *gauche* orientation of the β carbon bond (1), which within both calculation methods is 0.3-0.5 kcal/mol more stable than the symmetric orientation (2). For the phenyl group of ester **9**, the "bisector" orientation of the phenyl ring (3) is more stable than the "orthogonal" form (4).

In the case of ester **10**, the corresponding value of $\Delta E$ is 0.7 kcal/mol (MM+) in favor of the "bisector" orientation. For the form $C_a$, the most stable conformation of the R group presumes an "exterior" orientation (relative to the heterocyclic ring) of the β-carbon atom.



R = Me, $(CH_2)_5$

$\Delta E$ = 2.8 kcal/mol (MM+)
$\Delta E$ = 1.4 kcal/mol (AM1)

TABLE 1. Energy Differences ($\Delta E$) of Conformers $C_e$ and $C_a$ and Puckering Parameters of the $C_e$ Form for Molecules of Cyclic Boric Esters **1-10**

| Compound | $\Delta E$, kcal/mol |  | Puckering parameters of $C_e$* |  |  |
|---|---|---|---|---|---|
|  | MM+ | AM1 | $S$ | $\Theta$ | $\Psi$ |
| **1** | 0.9 | 1.3 | 0.76 | 38.3 | 2.1 |
| **2** | 0.9 | 1.6 | 0.75 | 36.0 | 0.1 |
| **3** | 0.8 | 1.2 | 0.76 | 40.1 | 0.6 |
| **4** | 0.8 | 1.3 | 0.76 | 38.3 | 2.3 |
| **5** | 0.9 | 1.3 | 0.77 | 39.3 | 0.9 |
| **6** | 1.9 | 2.9 | 0.78 | 36.3 | 1.1 |
| **7** | 0.9 | 1.4 | 0.76 | 38.7 | 2.4 |
| **8** | 1.1 | 2.2 | 0.78 | 36.4 | 0.1 |
| **9** | 1.2 | 2.2 | 0.77 | 36.3 | 0.1 |
| **10** | 0.7 | 0.8 | 0.77 | 36.6 | 1.4 |

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* Obtained from optimal geometry data (endocyclic torsion angles) by the MM+ method. For the ideal *sofa*, $\Theta = 45°$, $\Psi = 0°$ [11].

TABLE 2. Calculated Torsion Angles Between Protons, Spin-Spin Coupling Constants, and Conformational Equilibrium Parameters (N, $\Delta G^0$*) for Molecules of Esters **1-10** at 293 K

| Compound | Calculation method | Conformation | $\varphi_{AX}$, deg. | $\varphi_{BX}$, deg. | Equation for spin-spin coupling constant | Calc. spin-spin coupling constant, *J*, Hz | | Exp. spin-spin coupling constant, *J*, Hz | | N | $\Delta G^0$, kcal/mol | $\Delta G^0$, kcal/mol, avg. | $\Delta G^0$, kcal/mol, 1,3-dioxanes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $^3J_{AX}$ | $^3J_{BX}$ | $^3J_{AX}$ | $^3J_{BX}$ | | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| **1** | MM+ | $C_e$ | 179.4 | 56.4 | A | 11.5 | 4.7 | 10.3 | 4.2 | 0.838 | 0.96 | 1.0 | 0.67-0.81 |
| | | $C_a$ | 57.0 | 65.2 | | 2.3 | 3.4 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.894 | 1.24 | | |
| | | $C_a$ | | | | 3.9 | 3.0 | | | | | | |
| | AM1 | $C_e$ | 173.4 | 51.1 | A | 11.7 | 5.5 | | | 0.763 | 0.68 | | |
| | | $C_a$ | 46.4 | 75.6 | | 3.7 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.824 | 0.90 | | |
| | | $C_a$ | | | | 5.4 | 2.1 | | | | | | |
| **2** | MM+ | $C_e$ | 176.5 | 59.9 | A | 11.6 | 4.1 | 10.0 | 4.5 | 0.854 | 1.03 | 1.2 | 0.98-1.10 |
| | | $C_a$ | 58.7 | 62.9 | | 3.7 | 3.8 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 3.6 | | | 0.950 | 1.71 | | |
| | | $C_a$ | | | | 3.7 | 3.2 | | | | | | |
| | AM1 | $C_e$ | 176.5 | 53.9 | A | 11.6 | 5.0 | | | 0.807 | 0.83 | | |
| | | $C_a$ | 48.8 | 73.0 | | 3.3 | 2.4 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.3 | | | 0.871 | 1.11 | | |
| | | $C_a$ | | | | 4.8 | 2.3 | | | | | | |
| **3** | MM+ | $C_e$ | 179.8 | 56.8 | A | 11.5 | 4.6 | 8.7 | 3.9 | 0.663 | 0.39 | 0.3 | — |
| | | $C_a$ | 56.3 | 66.0 | | 2.4 | 3.3 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.671 | 0.41 | | |
| | | $C_a$ | | | | 4.0 | 2.9 | | | | | | |
| | AM1 | $C_e$ | 173.6 | 51.4 | A | 11.7 | 5.4 | | | 0.598 | 0.23 | | |
| | | $C_a$ | 45.7 | 76.1 | | 3.8 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.595 | 0.22 | | |
| | | $C_a$ | | | | 5.5 | 2.1 | | | | | | |

TABLE 2 (continued)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **4** | MM+ | $C_e$ | 179.4 | 56.4 | A | 11.5 | 4.7 | 10.2 | 4.3 | 0.838 | 0.96 | 1.0 | 0.91 |
| | | $C_a$ | 57.1 | 65.1 | | 2.3 | 3.4 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.894 | 1.24 | | |
| | | $C_a$ | | | | 3.9 | 3.0 | | | | | | |
| | AM1 | $C_e$ | 173.4 | 51.2 | A | 11.7 | 5.5 | | | 0.763 | 0.68 | | |
| | | $C_a$ | 46.3 | 75.6 | | 3.7 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.824 | 0.90 | | |
| | | $C_a$ | | | | 5.4 | 2.1 | | | | | | |
| **5** | MM+ | $C_e$ | 179.3 | 56.8 | A | 11.5 | 4.6 | 10.8 | 4.3 | 0.905 | 1.31 | 1.4 | — |
| | | $C_a$ | 56.5 | 65.6 | | 2.3 | 3.3 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.965 | 1.93 | | |
| | | $C_a$ | | | | 4.0 | 2.9 | | | | | | |
| | AM1 | $C_e$ | 173.9 | 51.5 | A | 11.7 | 5.4 | | | 0.984 | 1.24 | | |
| | | $C_a$ | 46.3 | 75.7 | | 5.4 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.894 | 1.24 | | |
| | | $C_a$ | | | | 5.4 | 2.1 | | | | | | |
| **6** | MM+ | $C_e$ | 176.5 | 59.4 | A | 11.6 | 4.2 | 11.0 | 4.1 | 0.931 | 1.51 | 1.3 | 1.36-1.97 |
| | | $C_a$ | 52.0 | 69.2 | | 2.9 | 2.8 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 3.6 | | | 1.030 | — | | |
| | | $C_a$ | | | | 4.6 | 2.6 | | | | | | |
| | AM1 | $C_e$ | 176.6 | 53.7 | A | 11.6 | 5.1 | | | 0.848 | 1.00 | | |
| | | $C_a$ | 41.3 | 80.0 | | 4.5 | 1.7 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.4 | | | 0.922 | 1.44 | | |
| | | $C_a$ | | | | 6.1 | 1.9 | | | | | | |
| **7** | MM+ | $C_e$ | 179.4 | 56.4 | A | 11.5 | 4.7 | 10.3 | 4.0 | 0.821 | 0.89 | 0.9 | — |
| | | $C_a$ | 57.2 | 65.0 | | 2.2 | 3.4 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.871 | 1.11 | | |
| | | $C_a$ | | | | 3.9 | 3.0 | | | | | | |
| | AM1 | $C_e$ | 173.5 | 51.2 | A | 11.7 | 5.5 | | | 0.746 | 0.63 | | |
| | | $C_a$ | 46.3 | 75.6 | | 3.7 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.800 | 0.81 | | |
| | | $C_a$ | | | | 5.4 | 2.1 | | | | | | |

TABLE 2 (continued)

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **8** | MM+ | $C_e$ | 177.2 | 57.5 | A | 11.6 | 4.5 | 10.5 | 4.2 | 0.864 | 1.08 | 1.1 | — |
| | | $C_a$ | 59.1 | 62.4 | | 2.0 | 3.8 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 3.9 | | | 0.928 | 1.49 | | |
| | | $C_a$ | | | | 3.7 | 3.3 | | | | | | |
| | AM1 | $C_e$ | 174.7 | 52.1 | A | 11.7 | 5.3 | | | 0.795 | 0.79 | | |
| | | $C_a$ | 48.6 | 73.2 | | 3.4 | 2.4 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.6 | | | 0.860 | 1.06 | | |
| | | $C_a$ | | | | 5.1 | 2.2 | | | | | | |
| **9** | MM+ | $C_e$ | 178.1 | 58.6 | A | 11.1 | 4.0 | 10.1 | 4.9 | 0.990 | 2.67 | 2.0 | 1.03 |
| | | $C_a$ | 55.3 | 66.8 | | 2.1 | 3.0 | | | | | | |
| | | $C_e$ | | | B | 10.8 | 3.5 | | | 1.091 | — | | |
| | | $C_a$ | | | | 3.9 | 2.7 | | | | | | |
| | AM1 | $C_e$ | 174.9 | 52.5 | A | 11.2 | 4.8 | | | 0.904 | 1.30 | | |
| | | $C_a$ | 41.5 | 80.7 | | 3.9 | 1.7 | | | | | | |
| | | $C_e$ | | | B | 10.7 | 4.3 | | | 1.000 | — | | |
| | | $C_a$ | | | | 5.8 | 1.7 | | | | | | |
| **10** | MM+ | $C_e$ | 179.6 | 56.8 | A | 11.5 | 4.6 | 10.8 | 4.5 | 0.924 | 1.45 | 1.6 | — |
| | | $C_a$ | 56.6 | 65.8 | | 2.3 | 3.3 | | | | | | |
| | | $C_e$ | | | B | 11.4 | 4.0 | | | 0.988 | 2.57 | | |
| | | $C_a$ | | | | 4.0 | 2.9 | | | | | | |
| | AM1 | $C_e$ | 173.5 | 51.2 | A | 11.7 | 5.5 | | | 0.835 | 0.94 | | |
| | | $C_a$ | 46.7 | 76.0 | | 3.6 | 2.1 | | | | | | |
| | | $C_e$ | | | B | 11.3 | 4.7 | | | 0.918 | 1.41 | | |
| | | $C_a$ | | | | 5.4 | 2.1 | | | | | | |

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* $\Delta G^0$ = -RT ln N / 1 – N.

The unknown values of the conformational free energy for the substituent R ($\Delta G^0$) can be estimated based on the experimental ([4, 6-8] and the data in this paper) and the calculated (standard) values of the spin–spin coupling constants $^3J_{AX}$ and $^3J_{BX}$. The latter are obtained based on the torsion angles φ between the corresponding protons (optimal geometry data for the forms $C_e$ and $C_a$ with the most stable conformation of the substituent R) from equations in [12] (A) and [13] (B), utilizing the values from [14-16] for the electronegativity of the atoms and groups substituting the ethane moiety under consideration. Estimation of the changes in the values of $\varphi_{AX}$ and $\varphi_{BX}$ and also the spin–spin coupling constants $^3J_{AX}$ and $^3J_{BX}$ for free rotation of the substituent R about the $C_{(5)}$–$C_\alpha$ bond for the examples of esters **1**, **4**, and **9** showed that the maximum deviation of the average value of φ from the corresponding optimal conformation of R ($\Delta\varphi$) within MM+ and AM1 does not exceed 2.7°; the corresponding value of $\Delta J$ for both computational equations used is no more than 0.3 Hz. For a quantitative estimate of the state of the conformational equilibrium, we used the familiar approach comparing the weighted mean (experimental) and standard spin–spin coupling constants [17].

$$^3J_{AX} + {}^3J_{BX} = N\,(J_{aa} + J_{ae}) + (1 - N)\,(J_{ea} + J_{ee})$$

$$\underset{N}{C_e} \rightleftarrows \underset{1\text{-}N}{C_a}$$

The results obtained (Table 2) are compared with known values of $\Delta G^0$ for R of the closest non-boron analogs: 1,3-dioxanes [18-21]. It is not difficult to see that in most cases, the value of $\Delta G^0$ for the boric esters is higher than in the cyclic acetal and ketal molecules; this is due to the characteristic differences in the orientation of the lone electron pairs of the ring oxygen atoms [4, 10]. At the same time, $\Delta G^0$ for *t*-Bu (ester **6**) practically coincides with the lower limit for the values in 1,3-dioxanes. For the boric esters themselves, we observe practically an unchanged value of $\Delta G^0$ for the unbranched alkyl groups (0.9-1.0 kcal/mol), close to the MM+ data (Table 1), and we see an increase in the values of $\Delta G^0$ for *i*-Pr, *t*-Bu, *i*-Bu, Ph, and Bn. At the moment, it is complicated to unambiguously explain both the rather high values of $\Delta G^0$ for the last three substituents and the low value of the conformational free energy for the allyl group (ester **3**). We can only note that the conformational equilibrium of the molecules of compounds **1-10** rules out any appreciable presence of alternative flexible forms that are not taken into account within the binary model under consideration: according to the calculations in [10], all conformations other than the *sofa* (*half-chair*, 1,4- and 2,5-*twist*) are realized only if the torsion angles are fixed in the heteroatomic portion of the ring, and therefore correspond to points on the ascending section of the curve for the two-dimensional cross section of the potential energy surface and are not local minima.

## EXPERIMENTAL

In order to refine the individual experimental spin–spin coupling constants, we obtained the $^1$H NMR spectra of the previously described [22] 5-allyl-2-isopropyl- and 5-phenyl-1,3,2-dioxaborinanes, to which the model esters **3** and **9** correspond. The spectra were measured on a Bruker AM-250 for 10% solutions of the studied compounds in $CDCl_3$ relative to TMS (internal standard).

## REFERENCES

1. V. S. Bezborodov, *Zh. Org. Khim.*, **25**, 2168 (1989).
2. V. S. Bezborodov, M. F. Grebenkin, and V. I. Lapanik, *Zh. Org. Khim.*, **27**, 385 (1991).
3. H. Matsubara, K. Seto, T. Tahara, and Sh. Takahashi, *Bull. Chem. Soc. Jpn.*, **62**, 3896 (1989).

4. A. I. Gren' and V. V. Kuznetsov, *The Chemistry of Cyclic Boric Acid Esters* [in Russian], Naukova Dumka, Kiev (1988).
5. V. V. Kuznetsov, A. I. Gren', A. V. Bogatskii, S. P. Egorova, and V. I. Sidorov, *Khim. Geterotsikl. Soedin.*, 26 (1978).
6. V. V. Kuznetsov, K. S. Zakharov, I. V. Petrovskii, and A. I. Gren', *Khim. Geterotsikl. Soedin.*, 1107 (1990).
7. V. V. Kuznetsov, A. R. Kalyuskii, A. I. Gren', *Zh. Org. Khim.*, **31**, 439 (1995).
8. V. V. Kuznetsov, E. A. Alekseeva, and A. I. Gren', *Zh. Obshch. Khim.*, **67**, 423 (1997).
9. HyperChem 5.02. Trial version. http://www.hyper.com.
10. V. V. Kuznetsov, *Zh. Obshch. Khim.*, **69**, 417 (1999).
11. N. S. Zefirov, V. A. Palulin, and E. E. Dashevskaya, *J. Phys. Org. Chem.*, **3**, 143 (1990).
12. C. A. G. Haasnoot, F. A. A. M. de Leeuw, and C. Altona, *Tetrahedron*, **36**, 2783 (1980).
13. P. L. Durette and D. Horton, *Org. Magn. Reson.*, **3**, 417 (1971).
14. M. L. Huggins, *J. Am. Chem. Soc.*, **75**, 4123 (1953).
15. S. S. Batsanov, *Usp. Khim.*, **51**, 1201 (1982).
16. F. A. Carey and R. J. Sandberg, *Advanced Organic Chemistry* [Russian translation], Khimiya, Moscow (1981), **1**, p. 21.
17. N. S. Zefirov, V. S. Blagoveshchenskii, I. V. Kazimirchik, and O. P. Yakovleva, *Zh. Org. Khim.*, **7**, 594 (1971).
18. M. Anteunis, D. Tvernier, and T. Borremans, *Heterocycles*, **4**, 293 (1976).
19. W. J. Orville-Thomas, ed., *Internal Rotation in Molecules* [Russian translation], Mir, Moscow (1977), p. 355.
20. A. I. Gren', in: *Topics in Stereochemistry, Interinstitute Scientific Collection* [in Russian], Kiev University, Kiev (1973), **3**, p. 60.
21. D. L. Rakhmankulov, D. M. Syrkin, R. A. Karakhanov, E. A. Kantor, S. S. Zlotskii, and U. B. Imashev, *Physicochemical Properties of 1,3-Dioxanes* [in Russian], Khimiya, Moscow (1980), p. 194.
22. V. V. Kuznetsov, Physico-Chemical Institute, Academy of Sciences of the Ukrainian SSR, Odessa (1983). Deposited in VINITI 14 October 1983, No. 5646-83; *Ref. Zh. Khim.*, No. 5, Zh 343 (1984).