*Chemistry of Heterocyclic Compounds, Vol. 43, No. 12, 2007*

# COMPUTER MODELLING OF THE CONFORMATIONAL EQUILIBRIUM OF 2- AND 2,5,5-SUBSTITUTED 1,3,2-DIOXABORINANES

**V. V. Kuznetsov, O. Yu. Valiakhmetova, and S. A. Bochkor**

*Empirical, semiempirical, and nonempirical quantum-chemical methods were used to study the conformational equilibrium of 2,5,5-substituted 1,3,2-dioxaborinanes. The sofa invertomers were found to correspond to the local and global minima on the potential energy surface. The position of the equilibrium between these forms is a function of the substituents at $C_{(5)}$ of the heterocycle.*

**Keywords:** 1,3,2-dioxaborinanes, cyclic borates, conformers, conformational equilibrium, potential energy surface, empirical, semiempirical, and nonempirical quantum-chemical calculations.

Interest in cyclic borates, namely, 1,3-dioxa-2-boracycloalkanes, is linked to the increasing importance of these compounds in the fine organic synthesis – production of enantiomeric alcohols and polyenes. These borates have a series of useful practical properties – they are biologically active compounds, corrosion inhibitors, components of polymers fuel and lubrications products. These compounds have interesting structural features involving electronic and steric intramolecular interactions [1-14]. These interactions are largely attributed to the presence of an electron-deficient boron atom and electron-donor oxygen atoms in a single molecule [4, 10, 11, 13].

It is know that molecules of 2-alkyl- or 2-alkoxy-5,5-dimethyl-1,3,2-dioxaborinanes exist at room temperature with a relatively low barrier to ring inversion, which is rapid on the NMR time scale [1, 4, 15-18]. Early the determinant effect of the substituents at $C_{(5)}$ atom in the ring on the conformational equilibrium of the molecules of 2,5,5-substituted 1,3,2-dioxaborinanes has been shown by $^1$H NMR spectroscopy [1, 4, 18].

The potential energy surfaces (PES) of molecules unsubstituted 1,3,2-dioxaborinane (**1**) as well as 2- and 2,5,5-substituted analogs **2-28** were calculated with the aim of further understanding the effect of structural factors on this equilibrium using empirical (MM+), semiempirical (AM1), and nonempirical methods [RHF/STO-3G, 3-21G, 6-31G, 6-31G(d), 6-31G(d,p)] using the Hyperchem computer program package [19].

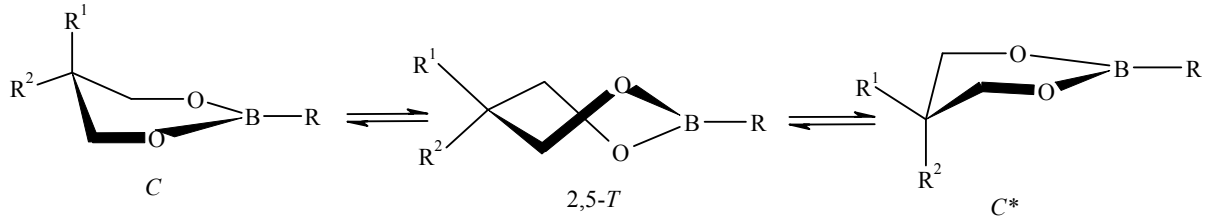
The PES of ester **1** and 2-substituted 1,3,2-dioxaborinanes **2** and **3** molecules have a single minimum corresponding to the *sofa* conformer (*C* and energy-degenerate form $C^*$) and also a single maximum corresponding to the 2,5-*twist* form (2,5-*T*). The values of $\Delta E^{\neq}$ of this process found in an MM+ calculation are independent of the nature and conformational bulk of the substituent at the boron atom (H, OMe, *i*-Pr, Table 1). Similar results were obtained in our previous work for 2-phenyl-1,3,2-dioxaborinane [20]. The experimental determination using low-temperature $^1$H NMR spectroscopy of the value of $\Delta G^{\neq}$ for ester **3** gave only the upper limit (<9.0 kcal/mole) due to the relatively low coalescence temperature [4].

---

Ufa State Petroleum Technological University, Ufa 450062, Russia; e-mail: kuzmaggy@mail.ru.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1860-1865, December, 2007. Original article submitted February 14, 2007.

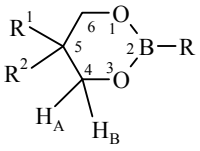
0009-3122/07/4312-1577 

All the 2,5,5-substituted borates studied **4-28** may be divided into three groups relative to their conformational behavior clearly reflected by the $^1$H NMR signal of the ring methylene protons [4, 18]. Group I compounds have identical substituents at $C_{(5)}$ (esters **4-17**). The singlet nature of the signal of the ring methylene protons in the $^1$H NMR spectra at room temperature with half-width ($\Delta\nu$) not exceeding 0.01-0.03 ppm in most cases indicates ring inversion rapid on the NMR time scale. Decreasing the temperature leads to broadening of this signal but an experimental activation free energy could be determined only for esters **4, 5** [15] and **10** [1, 18] due to a low coalescence temperature.




The values of $\Delta E^{\neq}$ for the inversion, proceeding, as in previous cases, through an intermidiate 2,5-*T* state found by the MM+ method are similar to the experimental $\Delta G^{\neq}$ values known for individual compounds. These values increase with increasing mass of the substituents and decrease for alkoxy, phenoxy, and allyl analogs (esters **8** and **9**, **11** and **12**, **8** and **15**).

Group II includes esters **18-23** with different substituents at $C_{(5)}$. The nature of the signal of the ring methylene group protons at room temperature indicates inversion between two energy-nondegenerate *sofa* forms. In this case, $\Delta\nu$ = 0.09-0.12 ppm (293K) and, as in the case of Group I compounds, increases significantly upon lowering the temperature of the sample.




**1–28**

| Compound | R | $R^1$ | $R^2$ | Compound | R | $R^1$ | $R^2$ |
|---|---|---|---|---|---|---|---|
| **1** | H | H | H | **15** | *i*-Pr | O-*i*-Pr | O-*i*-Pr |
| **2** | OMe | H | H | **16** | $C_2H_5$ | COOMe | COOMe |
| **3** | *i*-Pr | H | H | **17** | *i*-$C_4H_9$ | COOMe | COOMe |
| **4** | OMe | Me | Me | **18** | *i*-Pr | $CO_2Et$ | COMe |
| **5** | Et | Me | Me | **19** | *i*-Pr | $C_3H_5$ | $PhCH_2$ |
| **6** | *i*-Pr | Me | Me | **20** | *i*-Pr | Me | OMe |
| **7** | OH | Me | Me | **21** | *i*-Pr | Me | *i*-Pr |
| **8** | *i*-Pr | $C_2H_5$ | $C_2H_5$ | **22** | *i*-Pr | Me | $C_3H_5$ |
| **9** | *i*-Pr | $C_3H_5$ | $C_3H_5$ | **23** | *i*-Pr | *i*-Pr | $C_3H_5$ |
| **10** | *i*-Pr | $PhCH_2$ | $PhCH_2$ | **24** | *i*-Pr | Me | $CH_2OMe$ |
| **11** | *i*-Pr | Ph | Ph | **25** | *i*-Pr | Me | $C_6H_5$ |
| **12** | *i*-Pr | OPh | OPh | **26** | *i*-Pr | Me | PhO |
| **13** | *i*-Pr | COOMe | COOMe | **27** | *i*-Pr | Et | $CH_2OMe$ |
| **14** | *i*-Pr | $CO_2Et$ | $CO_2Et$ | **28** | *i*-Pr | $NO_2$ | Br |

TABLE 1. Characteristics of the Conformational Equilibrium of Esters **1-28**

| Com-pound | Method | Scanning procedure* | $\Delta E^{\neq}$*[2], kcal/mol | $\Delta E$, kcal/mol | Conformer with min $E$*[3] | Δν, ppm (T, K) |
|---|---|---|---|---|---|---|
| **1** | MM+ | 2-3-4-5 | 7.3 | 0 | — | — |
| | | 3-4-5-6 | 6.9 | | | |
| | AM1 | EV, RM | 3.4 | | | |
| | STO-3G | RM | 6.7 | | | |
| | 3-21G | RM | 8.1 | | | |
| | 6-31G | RM | 7.8 | | | |
| | 6-31G(d) | RM | 7.7 | | | |
| | 6-31G(d,p) | RM | 7.6 | | | |
| **2** | MM+ | 2-3-4-5 | 7.3 | 0 | — | — |
| | | 3-4-5-6 | 6.9 | | | |
| | AM1 | EV, RM | 2.8 | | | |
| **3** | MM+ | 3-4-5-6 | 6.9 (<9.0) | 0 | — | 0.01 (293) |
| **4** | MM+ | 3-4-5-6 | 7.7 (7.0) | 0 | — | — |
| **5** | MM+ | 3-4-5-6 | 7.7 (8.0) | 0 | — | 0.01 (293) |
| | STO-3G | RM | 7.4 | | | |
| | 3-21G | RM | 9.1 | | | |
| | 6-31G | RM | 8.3 | | | |
| **6** | MM+ | 3-4-5-6 | 7.8 | 0 | — | 0.01 (293) |
| **7** | MM+ | 3-4-5-6 | 7.7 | 0 | — | 0.02 (293) |
| **8** | MM+ | 3-4-5-6 | 9.1 | 0 | — | 0.03 (293) |
| **9** | MM+ | 3-4-5-6 | 7.7 | 0 | — | 0.07 (293) |
| **10** | MM+ | 2-3-4-5 | 9.8 (9.7) | 0 | — | 0.02 (293) |
| | | 3-4-5-6 | 9.5 | | | 0.14 (173) |
| **11** | MM+ | 3-4-5-6 | 9.3 | 0 | — | 0.01 (293) |
| **12** | MM+ | 3-4-5-6 | 8.8 | 0 | — | 0.01 (293) |
| **13** | MM+ | 3-4-5-6 | 9.5 | 0 | — | 0.03 (293), 0.14 (173) |
| **14** | MM+ | 3-4-5-6 | 10.0 | 0 | | 0.01 (293) |
| **15** | MM+ | 3-4-5-6 | 8.2 | 0 | | 0.01 (293) |
| **16** | MM+ | 3-4-5-6 | 8.3 | 0 | | 0.02 (293) |
| **17** | MM+ | 3-4-5-6 | 9.8 | 0 | | 0.02 (293) |
| **18** | MM+ | 3-4-5-6 | 10.4 | 0.5 | COMe (e) | 0.11 (293) |
| **19** | MM+ | 3-4-5-6 | 8.8 | 0.2 | $C_3H_5$ (e) | 0.09 (293) |
| **20** | MM+ | 3-4-5-6 | 8.8 | 1.4 | Me (e) | 0.09 (293) |
| **21** | MM+ | 3-4-5-6 | 8.7 | 0.1 | *i*-Pr (e) | 0.12 (293) |
| **22** | MM+ | 3-4-5-6 | 7.7 | 0.3 | $C_3H_5$ (e) | 0.09 (293) |
| **23** | MM+ | 3-4-5-6 | 9.7 | 0.4 | $C_3H_5$ (e) | 0.10 (293), 0.13 (203) |
| **24** | MM+ | 3-4-5-6 | 7.9 | 0.1 | Me (e) | 0.20 (293) |
| **25** | MM+ | 3-4-5-6 | 9.0 | 1.4 | Me (e) | 0.21 (293) |
| **26** | MM+ | 3-4-5-6 | 9.0 | 1.9 | Me (e) | 0.25 (293) |
| **27** | MM+ | 3-4-5-6 | 7.9 | 0.3 | Et (e) | 0.20 (293) |
| **28** | MM+ | 3-4-5-6 | 9.0 | 2.2 | $NO_2$ (e) | 0.22 (193) |
| | AM1 | EV, RM | 4.5 | 2.0 | Br (e) | 0.47 (293) |
| | STO-3G | RM | 6.3 | 0.8 | Br (e) | 0.48 (213) |

* EV – eigenvalue method, RM – reaction map method.

*[2] The experimental $\Delta G^{\neq}$ values, kcal/mol, for **3, 4,** and **10** (according to our previous data [18]) and for **5** (according to Carton [15]) are given in parentheses.

*[3] The orientation of one of the substituents in the most stable conformer.

The $\Delta E$ values for the two conformers corresponding to the energy minima on the PES fall in the range from 0.1 to 1.4 kcal/mole. We should note that the conformer with an axial methoxy group corresponds to the global minimum in an MM+ calculation for 5-methoxy-5-methyl analog **20**. This finding is in good accord with the $^1$H NMR spectral data for cyclic borates containing either alkoxy or aryloxy substituents at $C_{(5)}$ [1, 21, 22].

Our calculations showed that an axial ethoxycarbonyl group is more favorable than an axial acetyl group (ester **18**). In all cases, the equatorial orientation of the allyl substituent corresponds to the more stable conformer (esters **19, 22,** and **23**). The calculated activation barriers for these compounds increase with increasing mass of the substituents. It is readily seen that the magnitude of the shift of the conformational equilibrium is mainly a function of the conformational bulk and electronic properties of substituents $R^1$ and $R^2$.

In the case of Group III compounds, namely, esters **24-28,** these differences become sufficient for a predominant shift of the equilibrium toward one of the forms: the signals of the ring methylene protons appear as for an ordinary AB system [18]. The value $\Delta\nu$ = 0.20-0.47 ppm and is only slightly dependent on temperature. A relative preference for conformers with axial orientation of electron-withdrawing substituents, in particular, alkoxy (**20, 24, 27**), phenoxy (**26**), phenyl (**25**), carbonyl (**18**), and nitro groups (AM1, STO-3G, **28**), is characteristic for this equilibrium as in the case of Group II compounds [23].

On the other hand, the allyl substituent in esters **19, 22,** and **23** has predominantly equatorial orientation. The $\Delta E^{\neq}$ values in this case are close to the calculated values for the other 2,5,5-substituted 1,3,2-dioxaborinanes.

The results obtained suggest that the PES of substituted cyclic borates, in contrast to identically substituted but conformationally more rigid 1,3-dioxanes [24-26], contain only one maximum and have lower activation barriers.

## EXPERIMENTAL

The inversion pathways and interconversion pathways were established by a scanning procedure of individual torsion angles (3-4-5-6 corresponds to the minimum $\Delta E^{\neq}$ or 2-3-4-5, MM+) as well as the transition state mode (AM1, *ab initio*) [4, 16, 17, 20] in the framework of the HyperChem computer program package [19]. The applicability of the calculation methods for analyzing the structural and energy characteristics of cyclic borates was discussed in detail in our previous work [27, 28]. The $^1$H NMR spectral parameters of the 2,5,5-substituted 1,3,2-dioxaborinanes are given in our previous work [18]. The compounds studied were described in our earlier work [29].

## REFERENCES


1. A. I. Gren and V. V. Kuznetsov, *The Chemistry of Cyclic Borates* [in Russian], Naukova Dumka, Kiev (1988), 160 pp.
2. D. S. Matteson and D. Majumdar, *Organometallics*, **2**, 230 (1983).
3. P. G. M. Wuts and S. S. Bigelow, *Synth. Commun.*, **12**, 779 (1982).
4. V. V. Kuznetsov, Chem. Sci. Doctoral Dissertation, Ufa (2002).
5. D. S. Matteson, *Tetrahedron*, **45**, 1859 (1989).
6. D. S. Matteson, *Synthesis*, 973 (1986).
7. Y. Kobayashi, K. Watatani, and J. Tokoro, *Tetrahedron Lett.*, **39**, 7533 (1998).
8. R. J. Mears, H. De Silva, and A. Whiting, *Tetrahedron*, **53**, 17395 (1997).
9. W. Kliegel, *Pharmazie*, **27**, 1 (1972).
10. V. V. Kuznetsov, *Zh. Obshch. Khim.*, **70**, 71 (2000).

11. V. V. Kuznetsov, *Zh. Org. Khim.*, **36**, 307 (2000).
12. V. V. Kuznetsov, *Izv. Akad. Nauk, Ser. Khim.*, 1488 (2005).
13. V. V. Kuznetsov, *Zh. Obshch. Khim.*, **69**, 417 (1999).
14. V. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 643 (2006). [*Chem. Heterocycl. Comp.*, **39**, 559 (2006)].
15. D. Carton, A. Pontier, M. Ponet, J. Soulie, and P. Cadiot, *Tetrahedron Lett.*, **16**, 2333 (1975).
16. V. V. Kuznetsov and A. N. Novikov, *Khim. Geterotsikl. Soedin.*, 295 (2003). [*Chem. Heterocycl. Comp.*, **39**, 263 (2003)].
17. O. Yu. Valiakhmetova, S. A. Bochkor, and V. V. Kuznetsov, *Sovrem. Naukoemk. Tekhnol.*, No. 2, 72 (2006).
18. A. I. Gren, V. V. Kuznetsov, and K. S. Zakharov, *Khim. Geterotsikl. Soedin.*, 558 (1986). [*Chem. Heterocycl. Comp.*, **22**, 459 (1986)].
19. HyperChem 5.02, Trial version, www.hyper.com.
20. O. Yu. Valiakhmetova, S. A. Bochkor, and V. V. Kuznetsov, *Bashkir. Khim. Zh.*, **11**, 79 (2004).
21. F. Nakatsubo and T. Higuchi, *Holzforschung*, **29**, 193 (1975).
22. H. Matsubara, T. Tanaka, Y. Takai, M. Sawada, K. Seto, H. Imazaki, and S. Takahashi, *Bull. Chem. Soc. Jpn.*, **64**, 2103 (1991).
23. V. V. Kuznetsov and S. A. Bockor, *Khim. Geterotsikl. Soedin.*, 1065 (1999). [*Chem. Heterocycl. Comp.*, **35**, 935 (1999).
24. A. E. Kuramshina, A. A. Faizullin, S. A. Bochkor, and V. V. Kuznetsov, *Bashkir. Khim. Zh.*, **11**, 81 (2004).
25. E. G. Mazitova, A. E. Kuramshina, and V. V. Kuznetsov, *Zh. Org. Khim.*, **40**, 615 (2004).
26. A. E. Kuramshina, S. A. Bochkor, and V. V. Kuznetsov, *Fundament. Issledov.*, 87 (2006).
27. V. V. Kuznetsov, *Zh. Struktur. Khim.*, **42**, 591 (2001).
28. O. Yu. Valiakhmetova, S. A. Bochkor, and V. V. Kuznetsov, *Sovrem. Naukoemk. Tekhnol.*, No. 2, 71 (2006).
29. V. V. Kuznetsov, Physico-Chemical Institute, Academy of Sciences of the UkrSSR, Odessa (1983), Dep. VINITI, October 14, 1983, No. 5646-83.