Chemistry of Heterocyclic Compounds, Vol. 34, No. 3, 1998

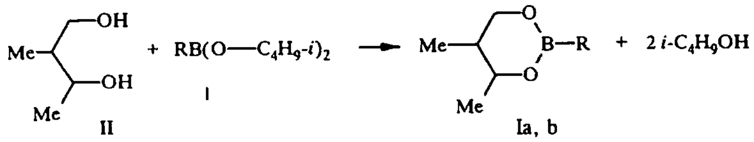
STEREOCHEMISTRY OF THE FORMATION OF 2-ALKYL-4,5-DIMETHYL-1,3,2-DIOXABORINANES

V. V. Kuznetsov and L. V. Spirikhin

It is demonstrated with the help of ^1H and ^{13}C NMR spectroscopy and GLC that the formation of the stereoisomers of 2-alkyl-4,5-dimethyl-1,3,2-dioxaborinanes from 2-methyl-1,3-butanediol and acyclic boric acid esters occurs stereospecifically. This conclusion was confirmed by calculations of the optimal geometries and relative energies of the molecules of the cis- *and* trans-*isomers of model 4,5-dimethyl-1,3,2-dioxaborinanes and the proposed intermediate with a tetravalent boron atom using the method of molecular mechanics.*

Information on the steric results of any reaction, particularly the formation of heterocyclic compounds with chiral centers, may provide the key to understanding the intimate details of its mechanism and the spatial relationships in any proposed intermediate and the transition state [1]. We have shown [2] that 2-isobutyl-4-methyl-5-benzyl- and 2-isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinanes are formed stereospecifically: the ratios of the *cis-trans* isomers correspond to the ratios of the *erthyro-threo* forms of the initial 1,3-diols. However, in previous studies [1, 3, 4] of the stereochemistry of the formation of 2,4,5-trialkyl-1,3,2-dioxaborinanes no correspondence was observed between the stereochemical composition of the 2-alkyl-1,3-butanediols and the boron heterocycles synthesized from them: the amount of the *trans* form in the mixture of stereoisomers of the products was larger than expected. In order to determine the limit of the observed stereoselectivity we have now investigated the stereochemistry of the formation of 2-alkyl-4,5-dimethyl-1,3,2-dioxaborinanes (I).

The compounds were prepared by the reaction of diisobutyl esters of isobutyl- and isopropylboronic acids with 2-methyl-1,3-butanediol (II):



Ia R = $i\text{-}C_3H_7$, Ib R = $i\text{-}C_4H_9$

(the *erythro-threo* ratio in diol II was 50:50 and 70:30 respectively) [5]. The stereoisomeric composition of the cyclic esters I was monitored by GLC and the configurational ratio for compounds Ib was determined by ^1H and ^{13}C NMR spectroscopy using information on the stereochemistry of the pure stereoisomers of ester Ia [6]. The ratios of the isomers of compounds Ia and Ib obtained from diol II with a 50:50 ratio of isomers were also 50:50 within the limits of accuracy of the GLC method (±3%), and similarly the boric esters from diol II with an *erythro-threo* ratio of 70:30 had an isomeric ratio of 70:30. The ^1H and ^{13}C NMR spectroscopic parameters of the mixtures of the stereoisomers of compound Ib are given in Tables 1 and 2.

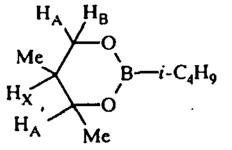
The nature of the proton signals of the AA'B portion of the spectrum of the minor isomer and the values of the $^3J_{AX}$ and $^3J_{BX}$ coupling constants show that the methyl group at $C_{(5)}$ has an equatorial orientation. The chemical shift of the 4-CH_3 group in the spectrum of *trans*-Ia was analogous [6], which indicates unambiguously the equatorial orientation of this substituent and the *trans*-configuration of the minor isomer which exists in the sofa configuration [1, 6]. The molecules of the major isomer

---

A. V. Bogatskii Physicochemical Institute, National Academy of Sciences of Ukraine, Odessa 270080, Ukraine. Institute of Organic Chemistry, Ufa Science Center, Russian Academy of Science, Ufa 450054, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 400-404, March, 1998. Original article submitted May 19, 1997.

0009-3122/98/3403-0367$20.00 ©1998 Plenum Publishing Corporation

TABLE 1. ^{1}H NMR Spectra of 2-Isobutyl-4,5-dimethyl-1,3,2-dioxaborinane Ib (mixture of stereoisomers)

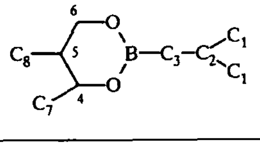


Configuration	Chemical shift, ppm						Coupling constant, Hz			Ratio of *cis-trans* isomers*		
	H_A	H_B	$H_{A'}$	H_X	4-CH_3	5-CH_3	$^2J_{AB}$	$^3J_{AX}$	$^3J_{BX}$	4-CH_3	H_X	H_A
cis-	3,71	3,88	4,12	2,05	1,17	0,91	11,2	7,5	4,2	65 : 35	66 : 34	67 : 33
trans -	3,52	3,85	3,67	1,65	1,25	0,86	10,8	10,8	4,6			

---

*From the integrated intensities of the protons.

TABLE 2. ^{12}C NMR Spectrum of 2-Isobutyl-4,5-dimethyl-1,3,2-dioxaborinanes Ib (mixture of stereoisomers)



Configuration	Chemical shift, ppm						
	$C_{(1)}$	$C_{(2)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$
cis -	25,26	29,93	65,36	34,38	69,88	17,77	11,21
trans -	24,80	32,16	66,94	37,88	73,24	21,15	13,35

belong to the *cis*-series; the values of the $^3J_{AX}$ and $^3J_{BX}$ coupling constants show that the 5-CH_3 groups has a pseudoaxial orientation. The predominant conformation of the *cis*-isomer is distorted toward one of the twisted forms [6]. The ratio of *cis-trans* isomers determined from the integrated intensities of the protons is close to that observed from GLC chromatography (Table 1).

Conclusions about the configurations of the molecules of ester Ib were confirmed by ^{13}C spectroscopy (Table 2). Comparison with the ^{13}C signals of the pure stereoisomers of compound Ia [6] show that the *cis* and *trans* isomers differ in the configuration at $C_{(5)}$ of the ring. The high field shifts of the carbon substituents at $C_{(7)}$ and $C_{(8)}$ in the *cis* isomer relative to the *trans* isomer confirm that the molecules of the major conformer are distorted towards one of the twisted forms with a pseudoequatorial substituent at $C_{(4)}$ and a pseudoaxial substituent at $C_{(5)}$.

Thus, in spite of the previous conclusions [3, 4] the formation of molecules of 2-alkyl-4,5-dimethyl-1,3,2-dioxaborinanes occurred stereospecifically: only *cis*-I is formed from the *erythro*-isomer of diol II, and only *trans*-I from *threo*-II. This means that the reactions of *erythro*- and *threo*-diol-II with acyclic boronic esters occur by the same mechanism with the rupture and formation of two B-O bonds [1, 7, 8]:

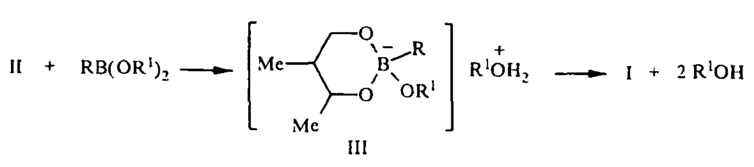
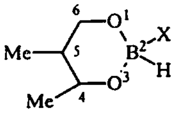


TABLE 3. Optimal Geometric Parameters for Molecules of the Stereoisomers of the Cyclic Esters Ic and the Intermediates IIIc



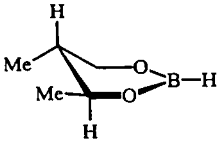
Compound	X	Bond lengths, Å				Bond angles, deg		
		1—2	2—3	3—4	1—6	1—2—3	2—3—4	6—1—2
trans-Ic	—	1,353	1,354	1,409	1,405	121,0	122,8	122,0
cis-Ic	—	1,355	1,355	1,408	1,406	120,9	122,2	122,1
trans-IIIc	OH	1,544	1,544	1,410	1,406	110,4	110,2	109,2
trans-IIIc	OH	1,545	1,546	1,409	1,406	110,9	109,8	109,3

Compound	X	Torsion angles, τ, deg						τ_{mean}
		1—2—3—4	2—3—4—5	3—4—5—6	4—5—6—1	5—6—1—2	6—1—2—3	
trans-Ic	—	4,0	-29,0	52,8	-54,2	31,2	-5,2	29,4
cis-Ic	—	6,2	-31,5	54,3	-54,5	31,6	-6,3	30,7
trans-IIIc	OH	58,6	-58,1	58,6	-59,6	58,9	-58,6	58,7
trans-IIIc	OH	57,1	-58,4	60,7	-61,3	59,3	-57,4	59,0

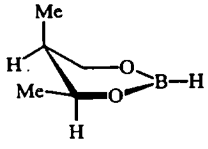
TABLE 4. Relative Energies of Stereoisomers of Compounds Ic and IIIc

Compound	*E*, kcal/mol	ΔE, kcal/mol
trans-Ic	7,34	0,0
cis-Ic	8,37	1,03
trans-IIIc	7,62	0,0
cis-IIIc	7,81	0,19

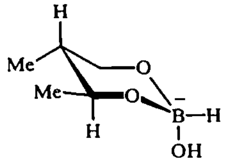
It seemed interesting to estimate the stability of the individual stereoisomers of the proposed intermediates III and the esters I. We used the MM 2 method with standard parametrization [9] to calculate the optimal geometry and energy of the molecules of *cis*- and *trans*-I and III for the case with R = R^1 = H (Ic, IIIc) (the nature of the acyclic boronate esters has little effect on the stereoisomeric composition of 2,4,5-trialkyl-1,3,2-dioxoborinanes [4]).



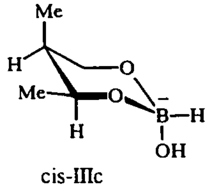
trans-Ic



cis-Ic



trans-IIIc



cis-IIIc

Results of calculations of the optimal geometry and energy (Tables 3 and 4) indicate that the B—O and C—O bond lengths in the *cis*- and *trans*-forms of ester Ic scarcely differ from experimental values for 1,3,2-dioxaborinanes, while the bond angles in the heteroatom fragment are close to 120°, which is characteristic of six-membered cyclic boronate esters [1, 10, 11]. Analysis of the torsion angles τ indicated that both stereoisomers have the sofa conformation with the boron, oxygen, $C_{(4)}$, and

$C_{(6)}$ almost coplanar. Comparison of the values of τ_{mean} show that configurational differences have virtually no effect on the compression of the ring.

The *cis*- and *trans*-isomers of the intermediate IIIc are characterized by a noticeable increase in the length of the B–O bond, which corresponds to experimental data for tetravalent boron compounds [1]. Intracyclic bond angles are close to tetrahedral and the values of τ show that both isomers have the chair conformation (Table 3).

The difference in energy between the *cis*- and *trans*-forms of ester Ic is 1.03 kcal/mol whereas for the stereoisomers of IIIc it is decreased to 0.19 kcal/mol in favor of the *trans*-form (Table 4). This shows that there is no significant difference in the mechanism for the formation of *cis*- and *trans*-4,5-dimethyl-1,3,2-dioxoborinanes and that the previous suggestion of alternative schemes for the conversion of the *erythro*-diol II into the *cis*- and *trans*-isomers of the boronic esters is untenable [4]. Data on configurational isomerization [12, 13] and ^1H NMR spectra [14] indicate that the experimental values of ΔE for the *cis*- and *trans*-forms of esters I are considerably greater than the calculated values and for compound Ia it is not less than 2 kcal/mol in favor of the *trans*-isomer. This difference is explained by the distortion of the real molecules of *cis*-I towards one of the twist conformers because of strong nonbonded interactions between the axial alkyl group at $C_{(5)}$ and the heteroatom fragment in the sofa conformation [6] and the failure to take these interactions into account completely in strong field MM 2 calculations. However, these data show that the noticeable differences in energy between the *cis*- and *trans*-forms of 4,5-dimethyl-1,3,2-dioxaborinanes do not lead to the predominant formation of the more stable *trans*-isomer. The stereospecificity of the reaction is explained by the small differences in stability of the *cis*- and *trans*-forms of the intermediate III.

EXPERIMENTAL

The ^1H NMR spectra of 10% $CDCl_3$ solutions of compound Ib with TMS as internal standard were recorded with a Bruker AM-300 spectrometer at 300 MHz. The ^{13}C NMR spectra of a 20% solution of Ib in $CDCl_3$ with natural content of ^{13}C were recorded at 75.4 MHz on the same machine using Fourier transformation conditions. Study of compounds Ia and Ib has been reported elsewhere [15] and the synthesis of diol II has been previously published [5]. Conditions for GLC analysis were analogous to those in [4].

REFERENCES

1. A. I. Gren' and V. V. Kuznetsov, Chemistry of Cyclic Esters of Boronic Acids. Naukova Dumka, Kiev (1988).
2. V. V. Kuznetsov, E. A. Alekseeva, and A. I. Gren', Khim. Geterotsikl. Soedin., No. 9, 1291 (1995).
3. V. V. Kuznetsov and A. I. Gren', Zh. Org. Khim., **19**, 1987 (1983).
4. V. V. Kuznetsov and A. I. Gren', Zh. Obshch. Khim., **56**, 613 (1986).
5. V. V. Kuznetsov and A. I. Gren', Zh. Obshch. Khim., **65**, 850 (1995).
6. V. V. Kuznetsov and A. I. Gren', Zh. Obshch. Khim., **54**, 2263 (1984).
7. L. Babcock and R. Pitzer, Inorg. Chem., **19**, 56 (1980).
8. L. Babcock and R. Pitzer, Inorg. Chem., **16**, 1677 (1980).
9. N. L. Allinger, J. Am. Chem. Soc., **99**, 8127 (1977).
10. Sh. Kuribayashi, Bull. Chem. Soc. Jpn., **46**, 1045 (1973).
11. W. Kliegel, L. Preu, S. J. Rettig, and J. Trotter, Can. J. Chem., **64**, 1855 (1986).
12. V. V. Kuznetsov and A. I. Gren', Khim. Geterotsikl. Soedin., No. 7, 993 (1983).
13. V. V. Kuznetsov and A. I. Gren', Ukr. Khim. Zh., **51**, 535 (1985).
14. V. V. Kuznetsov, K. S. Zakharov, I. V. Petrovskii, and A. I. Gren', Khim. Geterotsikl. Soedin., No. 8, 1107 (1990).
15. V. V. Kuznetsov, Odessa, 1983; Dep. in VINITI, 10.14.83, No. 5646-83.