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REACTION OF STEREOISOMERS OF 5-ISOPROPYL-4-METHYL-1,3-DIOXANE WITH ESTERS OF MONOSUBSTITUTED BORIC ACID

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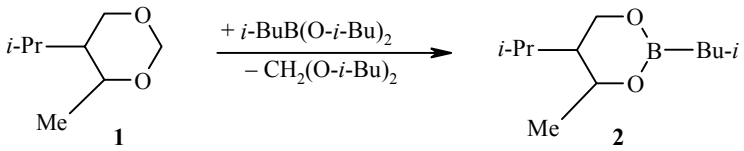
Gas-liquid chromatography was used to establish that the reactivity of the cis isomer in the reaction of 5-isopropyl-4-methyl-1,3-dioxane with the diisobutyl ester of isobutylboric acid leading to the corresponding 1,3,2-dioxaborinane is greater than for the trans isomer. An AM1 calculation for the energy of the intermediate ions in this reaction with model derivatives of boric acids: dioxyborane and the dimethyl ester of methylboric acid showed that one of the probable reasons for the observed behavior is the lower barrier for conversion of the intermediate bipolar structure of the cis derivative in the step involving formation of the endocyclic B–O bond.

Keywords: 1,3,2-dioxaborinanes, 1,3-dioxanes, trialkyl borates.

A study of the interconversion of six-membered 1,3- and 1,3,2-heterocycles permits us to evaluate the relative thermodynamic stability of these compounds and follow the stereochemistry in ring formation and opening [1]. 1,3-Dioxanes react with acyclic borate esters to give the corresponding 1,3,2-dioxaborinanes [2-6]. In the present work, we studied this reaction for 5-isopropyl-4-methyl-1,3-dioxane (**1**) (mixture of *cis* and *trans* isomers) with acyclic boric acid derivatives.

Gas-liquid chromatography showed that the products of the reaction of dioxane **1** with the diisobutyl ester of isobutylboric acid are 2-isobutyl-5-isopropyl-4-methyl-1,3,2-borinane (**2**) and diisobutylformal.



1 **2**

For a detailed analysis of the dynamics of the change in the stereoisomeric composition of **1** and **2** during the reaction, we studied the conversions of two samples of formal **1** with *cis/trans* isomer ratio equal to 60:40 (**1a**) and 39:61 (**1b**) [8]. Gas-liquid chromatography indicated that the conversion of formal **1** to cyclic ester **2** 24 h after onset of the reaction was relatively low (Table 1). The *cis/trans* isomer ratio of **1** and **2** unequivocally showed a greater rate for the conversion of *cis*-**1** in comparison to *trans*-**1**. The addition of catalytic amounts of $ZnCl_2$ or $BF_3 \cdot OEt_2$ increased the conversion of formal **1** but the reactivity of *cis*-**1** remained higher than for the *trans* form also under these conditions. A control experiment showed that configurational isomerization of dioxane **1** and borinane **2** by the action of catalyst does not occur.

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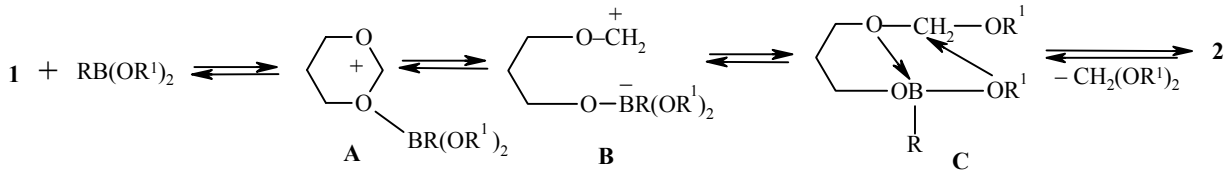
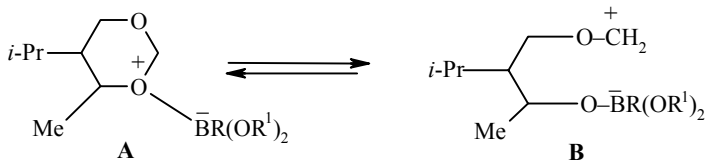
TABLE 1. Change in the Stereoisomeric Composition of Starting and Final Compounds in the Reaction of 5-Isopropyl-4-methyl-1,3-dioxane with Diisobutyl Ester of Isobutylboric Acid

Starting compound	Position on reaction coordinate	*cis*-**1** : *trans*-**1**	*cis*-**2** : *trans*-**2**	**1**:**2**
1a	Prior to reaction onset	60 : 40	—	100 : 0
	After 24 h without catalyst	45 : 55	67 : 33	85 : 15
	After 30 min heating with $ZnCl_2$	37 : 63	65 : 35	12 : 88
	After 30 min heating with BF_3 etherate	47 : 53	63 : 37	14 : 86
1b	Prior to reaction onset	39 : 61	—	100 : 0
	After 24 h without catalyst	11 : 89	47 : 53	71 : 29
	After 30 min heating with $ZnCl_2$	9 : 91	55 : 45	11 : 89
	After 30 min heating with BF_3 etherate	11 : 89	37 : 63	9 : 91

In order to elucidate the possible reasons for the observed behavior, we carried out an LCAO MO SCF calculation using the AM1 parameters [9, 10] on the mechanism of the reaction of dioxane **1** with model boric acid derivatives: dioxyborane and the dimethyl ester of methylboric acid. The probable pathway of this reaction involves coordination of the acetal oxygen at the boron atom to give complex **A**, which slowly isomerizes to give ion **B**, which converts to **C**, which loses a molecule of acyclic formal to give final ester **2**.



The calculation of the energy of the most stable forms of ions **A** and **B** with complete geometrical optimization showed that complex **A** with an equatorial boryl group at O^3 of the ring, which converts to corresponding ion **B**, corresponds to the optimal reaction pathway.



The stability of alternative ($B–O^1$) derivatives **A** and **B** is less than 2-3 kcal/mol. The conformer with approximated acetal and borate ester fragments corresponds to the main energy minimum of structure **B**.

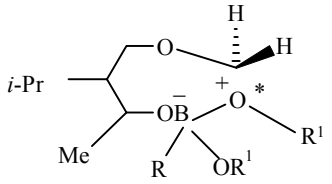


TABLE 2. Calculated Energies of Intermediate Ions **A** and **B** (kcal/mol) for the Reaction of 5-Isopropyl-4-methyl-1,3-dioxane with Model Boric Acid Derivatives

R	R^1	Configuration	$-E_A$	$-E_B$	$-\Delta E_{AB}$
		cis-	3021.7	3014.1	7.6
H	H	*trans*-	3020.4	3014.3	6.5
		cis-	3826.7	3818.7	8.0
Me	Me	*trans*-	3826.5	3823.3	3.2

The length of the B–O* bond (1.91-2.08 Å) is much greater than the value observed in compounds with sp^3-hybrid boron (1.44-1.59 Å [1]), while the distance between C^+ and O* is 1.42-1.44 Å, which is similar to the length of the C–O covalent bond in cyclic borate esters [1]. The carbocation site is pyramidal rather than planar in configuration. Table 2 clearly shows that with the observed greater reactivity of *cis*-**1**, the relative stability of ion **B** (ΔE_{AB}) for the reaction of *trans*-**1** with each of the boron substrates is greater than for *cis*-**1**. This finding implies that structure **B** should not be considered as close to the transition state since it has characteristics of an intermediate on the reaction coordinate. Thus, ΔE_{AB} is not equal to the activation energy. On the other hand, our calculation showed that the differences in stability for the most stable conformers of the *cis* and *trans* isomers of dioxane **1** are slight (0.9 kcal/mol in favor of *cis*-**1**). This value for the final 1,3,2-dioxaborinane with hydrogen or a methyl group at the boron atom is even less (0.1 kcal/mol in favor of the *trans* isomer [11]). Hence, the greater reactivity of *cis*-**1** with an acyclic borate ester should be attributed either to the lower activation energy of this reaction or, assuming that the ΔE^* values for both isomers are similar, to the lower barrier on the pathway for conversion of the *cis*-B ion (due to a less pronounced local minimum) into final product **2**.

These results are in accord with the relative reactivities of the *cis* and *trans* isomers of dioxane **1** in their reaction with ethylboron dichloride [12] and indicate a rather marked effect of configuration on the course of the heterocyclic transformations of stereoisomeric formals.

EXPERIMENTAL

The gas-liquid chromatographic analysis was carried out on a Tsvet-126 chromatograph with a flame ionization detector using a 3000×4-mm column packed with 5% OV-17 as the stationary phase on Chromaton N-Super and argon as the gas carrier. The quantitative ratios between 1,3-dioxane **1** and 1,3,2-dioxaborinane **2** were determined by internal normalization with calibration coefficients according to Vyakhirev [13]. The required index, cyclic borate ester **2**, was obtained by convergent synthesis according to our previous procedure [14]. The configurational assignment of this compound was carried out in a separate study [11]. The precision in determining the ratio of stereoisomers of **1** and **2** by gas-liquid chromatography is ±3% [13]. The synthesis of the starting 1,3-dioxane with different *cis/trans* isomer ratios was described by Bogatsky et al. [7, 8]. The calculation in this work was carried out using the HyperChem 5.02 package [15].

Reaction of 1,3-Dioxanes 1a and 1b with Diisobutyl Ester of Isobutylboric Acid. Equimolar amounts (0.5 mmol) of the starting reagents were stirred at room temperature for 24 h. After the gas-liquid chromatographic analysis, 2 mass % $ZnCl_2$ or boron trifluoride etherate was added as the catalyst and the mixture was heated at 110°C for 30 min and resubjected to gas-liquid chromatographic analysis.

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