Chemistry of Heterocyclic Compounds, Vol. 31, No. 9, 1995

CONFIGURATION AND ISOMERIZATION OF 2,4,5-SUBSTITUTED 1,3,2-DIOXABORINANES

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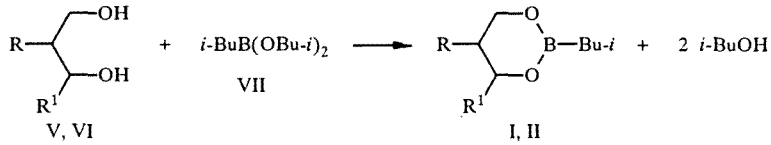
Reaction of esters of isobutylboronic acid with 2-methyl-1-phenyl-1,3-propanediol and 2-benzyl-1,3-butanediol gave 2-isobutyl-5-methyl-4-phenyl- and 4-methyl-5-benzyl-1,3,2-dioxaborinanes respectively, with a preponderance of the cis*-isomers in the mixtures.* Cis*-2-isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane was converted to the* trans *isomer on heating to 150°C with a catalytic amount of $ZnCl_2$.*

It is known that, unlike their close non-boron analogs (the 1,3-dioxanes), configurational stereoisomers of 2,4- and 2,5-derivatives in the 1,3,2-dioxaborinane series involving two,or three carbon atoms of the ring are not possible [1]. A peculiarity of molecules of 2,4,5- and 2,4,6-substituted six-membered cyclic esters of boric acid is their ability for configurational isomerization, which is unknown for 4,5- and 4,6-substituted 1,3-dioxanes [2]. We have studied the isomerization of 2-isopropyl-4,6- and -4,5-dimethyl-1,3,2-dioxaborinanes previously [3, 4]. In the latter case we observed the slow conversion of the *cis* isomer into the more stable *trans* form. The present work is concerned with the configurational assignment and the isomerization of the previously undescribed 2-isobutyl-5-methyl-4-phenyl- (I) and 4-methyl-5-benzyl-(II) 1,3,2-dioxaborinanes.



V, VI I, II

I, V R = Me, R^1 = Ph; II, VI R = $PhCH_2$, R^1 = Me

These compounds were synthesized as a mixture of *cis* and *trans* isomers by the general method [1] of treating esters of isobutylboronic acid with the corresponding 1,3-diols.

Configurational assignment was based on the ^{13}C NMR spectra of esters I and II and those of reference substances: individual stereoisomers of 2-isopropyl-4,5-dimethyl-1,3,2-dioxaborinane (III) and 4-methyl-5-benzyl-1,3-dioxane (IV) (mixture of isomers) together with the ^1H NMR spectra of the starting materials 2-methyl-1-phenyl-1,3-propanediol (V) and 2-benzyl-1,3-butanediol (VI). Diol V was prepared by reduction of ethyl α-methylbenzoylacetate with lithium tetrahydroaluminate to give a mixture of isomers in a ratio of ~80:20 (from the integrated intensities of the methyl resonances at δ = 0.80 and 0.66 ppm respectively in the ^1H NMR spectrum). According to [5] the *erythro* form predominates in this case. In the case of diol VI, synthesized by lithium tetrahydroaluminate reduction of ethyl benzylacetoacetate the isomer ratio was 62:38 (from the integrated intensities of the methyne proton on the carbon atom bonded to the benzyl group at δ = 2.01 and 1.73 ppm in the ^1H NMR spectrum). Since reduction of substituted acetoacetate esters is controlled by the cyclic model of 1,2-asymmetric induction (Cram's rule) [6, 7], the *erythro* form predominates in this case also.

The parameters of the ^{13}C NMR spectra of compounds I-IV are give in Table 1. Firstly note the similarity of the $C_{(7)}$ signals in the spectra of the minor isomer of compound I and the *cis* and *trans* isomers of the reference ester III. Isomerization in the latter arises from the different orientation of the methyl group at $C_{(5)}$, which in the *cis*-isomer is pseudo-axial and in the

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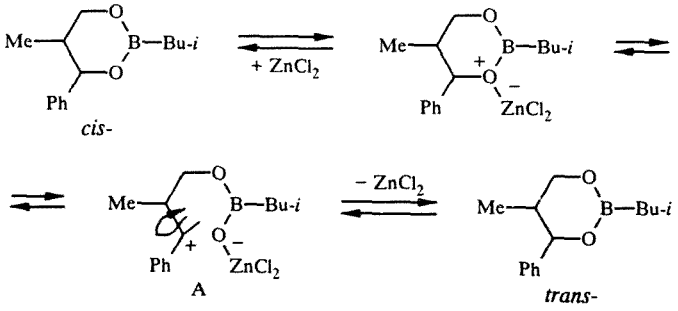
trans-form is equatorial [1, 8]. It is not difficult to see that in the spectrum of the predominant isomer the $C_{(7)}$ signal is at higher field than that of the minor isomer which indicates that it is axial or pseudoaxial in orientation [9]. Thus the predominant isomer in this case is *cis* and the minor isomer is *trans*. The ratio of the integral intensities in the spectrum of compound I agree approximately with GLC results. A comparison with the 1,3-diol (V) starting material shows that their stereoisomeric constitutions correspond: *erythro*-/*threo*-forms = *cis*-/*trans*-isomers = 80:20 (81:19), which provides a basis for considering that formation of the ester I is stereospecific.

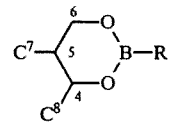
The signals of the methylene carbon of the benzyl group in compound II and the reference compound IV serve to assign the configuration: a high field shift indicates an axial or pseudoaxial orientation resulting from the large effect of steric deformation [9]. In the spectra of the model 1,3-dioxane IV and the boron ester II the higher intensity signal is at higher field which shows that the predominant isomer in the mixtures is *cis* in both cases. GLC results show that the isomer ratios in II and IV are identical (66:34) and close to the results from the ^{13}C NMR method (Table 1).Since the formation of 4,5-substituted 1,3-dioxanes from the corresponding 1,3-diols is strictly stereospecific [6, 7], then the correspondence of the stereoisomeric composition of the 1,3-diol (VI) starting material and with those of compounds II and IV indicates that the formation of the boron ester II is stereospecific.

Configurational isomerization was studied by heating samples of compounds I and II to 150°C in the presence of a catalytic amount of $ZnCl_2$ and monitoring by GLC. Under these conditions the stereoisomers of compound II underwent no detectable change during 7 hours and remained constant within the limits of error (±3%) of the GLC method. In contrast the isomeric composition of compound I changed to give an increase in the amount of the *trans* isomer. The rate was considerably higher than for the 4,5- and 4,6-dimethyl derivatives: after 1 h the *cis*-/*trans*- ratio was 66:34, after 5 h 35:65 and after 7 h 26:74 (the initial ratio was 81:19). Partial resinification and destruction of the compound was also observed. Comparable changes in the isomeric composition of 2-isopropyl-4,5- and 4,6-dimethyl-1,3,2-dioxaborinanes with the same catalyst concentration required 12-50 h [3, 4]. The kinetics of the isomerization confirm the mechanism proposed previously [3, 4] in which, in distinction from the 1,3-dioxanes [2, 10, 11], it was proposed that breaking of the C−O bond at the chiral center $C_{(4)}$ occurred, followed by rotation about the C−C bond and reformation of the ring:



The bipolar structure A with a phenyl groups at $C_{(4)}$ is more stable than the analogous structure with a 4-methyl group which explains the considerable increase in the rate of isomerization of compound I. It is also clear that the molecule of the *trans*-isomer is the more thermodynamically stable because of the absence of strain between the axial or pseudo-axial methyl group at $C_{(5)}$ and the heteroatoms in the sofa conformation which is standard for this type of heterocycle [8].

TABLE 1. Parameters of the ^{13}C NMR Spectra of 2-Isobutyl-5-methyl-4-phenyl- (I), 4-Methyl-5-benzyl- (II), 2-Isopropyl-4,5-dimethyl-1,3,2-dioxaborinanes (III) (individual stereoisomers) and 4-Methyl-5-benzyl-1,3-dioxane (IV)



Compound	Chemical shifts, δ, ppm					Isomer ratio
	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	
I						
cis-	75,44	34,96	65,84	10,54	139,90	83
trans-	79,50	38,12	66,77	13,00	141,13	17
III						
cis-	64,91	33,82	69,14	10,32	17,10	—
trans-	64,72	36,73	70,71	12,90	20,41	—
II						
cis-	69,01	32,45	62,30	41,48	17,71	66
trans-	70,87	35,54	63,34	43,52	21,78	34
IV						
cis-	75,05	29,93	68,46	40,57	18,16	69
trans-	77,39	34,65	70,55	42,60	19,16	31

Evidently these interactions in the *cis*-isomer of the 4-methyl-5-benzyl compound II are somewhat smaller and consequently no noticeable change in stereoisomeric composition was observed in the reaction time used.

These results open up new possibilities for the study of stereoisomeric regularities in the substituted 1,3,2-dioxaborinanes.

EXPERIMENTAL

GLC analysis was carried out with Tsvet-126 machine equipped with a flame-ionization detector, a 3000 × 4 mm column filled with 5% OV-17 on Chromaton N-Super carrier and with argon as carrier gas. ^1H and ^{13}C NMR spectra were measured with an AM-250 spectrometer (250 MHz for protons, 62.89 MHz for ^{13}C) in solutions in $CDCl_3$ containing the natural abundance of ^{13}C and with TMS as internal standard.

Diisobutyl isobutylboronate VII was prepared by method [12] and 2-methyl-1-phenyl-1,3-propanediol V and 2-benzyl-1,3-butanediol VI by methods [5] and [13] respectively. The model 1,3-dioxane IV was synthesized by method [14].

2-Isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane (I). Equimolar amounts (0.05 mol) of ester VII and diol V were boiled in benzene (70 cm^3) for 2 h, the benzene was evaporated and the residue was fractionated in vacuum. Yield 70%, bp 141-143°C (4 mmHg), n_D^{20} 1.4926.

2-Isobutyl-4-methyl-5-benzyl-1,3,2-dioxaborinane (II) was synthesized by the same method by the reaction of 1,3-diol VI and the boron ester VII in 84% yield, mp 150-151°C (4 mmHg), n_D^{20} 1.4876.

Configurational Isomerization of Compound I. Ester I (1 g) and anhydrous $ZnCl_2$ (0.1 g) were mixed in a glass reactor and kept in a thermostat at 150°C under argon. Samples were taken periodically for GLC analysis.

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