Reaction of 2-isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane with acetonitrile

V. V. Kuznetsov, E. A. Alekseeva, and A. I. Gren'*

A. V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, 86 Chernomorskaya dor., 270080 Odessa, Ukraine.
Fax: +380 (048 2) 65 2012

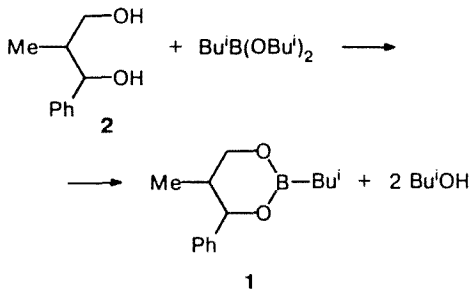
Reaction of 2-isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane (a mixture of *cis*- and *trans*-isomers in a 81 : 19 ratio) with acetonitrile yielded 2,5-dimethyl-4-phenyl-5,6-dihydro-1,3-oxazine as a mixture of *cis*- and *trans*-forms in a 50 : 50 ratio. The possible mechanism of this transformation is discussed.

Key words: 1,3,2-dioxaborinane; 2,5-dimethyl-4-phenyl-5,6-dihydro-1,3-oxazine, *cis*- and *trans*-isomers; mechanism of the reaction, carbocations.

One of the convenient methods for the synthesis of 1,3-aminoalcohols is based on alkaline hydrolysis of 5,6-dihydro-1,3-oxazines.[1] The latter are rather readily formed by the reaction of substituted 1,3-dioxanes[2] or 1,3-dioxa-2-heteracyclohexanes (*e.g.*, 1,3-dioxa-2-silacyclohexanes[3] or six-membered cyclic sulfites[4]) with acetonitrile. Earlier[5] it was shown that such a transformation is also typical of 1,3,2-dioxaborinanes. To elucidate the peculiarities of the mechanism of this reaction, in this work we studied the reaction of 2-isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane (**1**) with acetonitrile.

Compound **1** was obtained by the reaction of an isobutylboronate with 2-methyl-1-phenyl-1,3-propanediol (**2**) (Scheme 1).

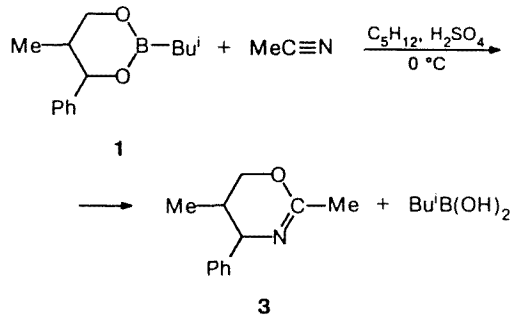
Scheme 1



Diol **2** was synthesized as a mixture of two isomers in a 80 : 20 ratio (judging from the integral intensities of the signals of methyl protons in the ^{1}H NMR spectrum at 0.80 and 0.66, respectively) by the reduction of α-methyl benzoylacetate with lithium alumohydride. According to the published data,[6] the *erythro*-isomer predominates.[2] In the case of cyclic ester **1**, the ratio of isomers determined by GLC corresponds to the ratio of integral intensities of the signals in the ^{13}C NMR spectrum equal to 81 : 19. In the ^{13}C NMR spectrum of the predominant isomer, the signal of the methyl group at the C(5) atom (10.54 ppm) is shifted upfield compared to the corresponding signal of the minor isomer (13.00 ppm), indicating the axial orientation of the methyl group.[7] Thus, the product of the *cis*-configuration predominates.

Ester **1** (as a mixture of isomers) reacts with acetonitrile in pentane and conc. H_2SO_4 to produce 2,5-dimethyl-4-phenyl-5,6-dihydro-1,3-oxazine (**3**) in 83 % yield (Scheme 2).

Scheme 2

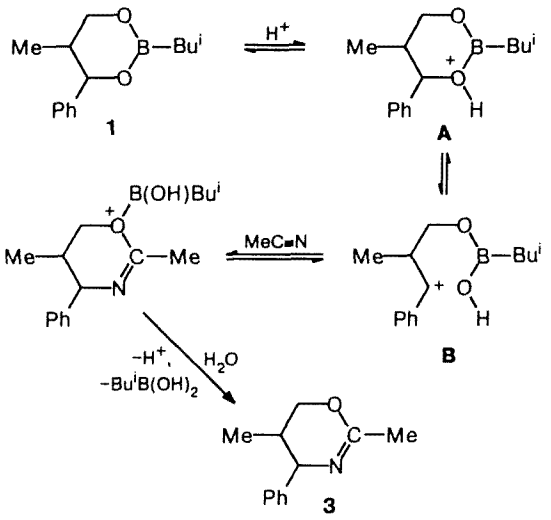


The purity of compound **3** is confirmed by the GC data, and its structure and composition are determined by mass spectrometry and IR spectroscopy. As in the previous case,[5] isobutylboronic acid is also the product of the reaction; it was isolated in 73 % yield and identified by the melting point.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 1297—1298, May, 1996.

According to the GLC data, the ratio of the *cis*- and *trans*-isomers of oxazine **3** is 50 : 50, which does not agree with the isomeric composition of the initial ester **1**. This regularity is apparently caused by the structure of the intermediate, which is similar to the carbocationic one. In accordance with the general concepts on the mechanism of solvolytic reactions of saturated oxygen-containing heterocycles,[8] the reaction of ester **1** with acetonitrile should initially involve the formation of an oxonium ion **A** that undergoes slow isomerization into a carbocation **B** (Scheme 3).

Scheme 3



Since the reaction medium is rather polar (conc. H_2SO_4/pentane = 1 : 1), the stability of the ion **B** is mainly determined by the stabilizing effect of the phenyl group. Subsequent addition of the acetonitrile molecule, which is accompanied by racemization, produces final product **3**. Acetonitrile reacts with 1,3-dioxanes by a similar mechanism.[9]

The studied reaction opens new possibilities for the synthesis of stereoisomeric 5,6-dihydro-1,3-oxazines, which are valuable precursors of 1,3-aminoalcohols, and extends the field of chemical transformations of substituted 1,3,2-dioxaborinanes.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker AM-250 spectrometer (250 and 62.89 MHz, respectively) in $CDCl_3$ with the natural abundance of ^{13}C isotope using $SiMe_4$ as the internal standard. IR spectra were obtained on a Specord-75 IR spectrophotometer in $CHCl_3$ (the thickness of the layer was 0.412 mm). Mass spectra were obtained on an MX-1321 instrument with ionization energy of 70 eV. GLC was carried out on a Tsvet-126 chromatograph on a 3000×4 mm column with a flame-ionization detector, the stationary phase was 5 % OV-17 at a Chromaton N-Super, and argon was a carrier gas.

2-Isobutyl-5-methyl-4-phenyl-1,3,2-dioxaborinane (1) was obtained using the standard procedure[7] by the reaction of the corresponding diol **2** (see Ref. 6) with diisobutyl isobutylboronate.[10] The yield was 84 %, b.p. 141—143 °C (4 Torr), n_D^{20} 1.4926. Found (%): C, 72.25; H, 9.42; B, 4.35. $C_{14}H_{21}BO_2$. Calculated (%): C, 72.41; H, 9.05; B, 4.74.

2,5-Dimethyl-4-phenyl-5,6-dihydro-1,3-oxazine (3). A mixture of pentane (10 mL) and conc. H_2SO_4 (10 mL) was cooled to 0 °C, and acetonitrile (4 mL, 70 mmol) was slowly added with stirring. Then ether **1** (1.7 g, 7.33 mmol) was added, and the reaction mixture was stirred at 0 °C for 3 h and poured on finely crushed ice (100 g). The resulting aqueous solution was washed with chloroform (3×25 mL) and ether (30 mL). The combined organic extracts were concentrated to give 0.52 g (73 %) of isobutylboronic acid, which was identified by the melting point (105—110 °C; *cf.* Ref. 11: m.p. 106—112 °C). Ice (10—15 g) was added to the remaining aqueous solution, and the resulting solution was alkalized with solid NaOH to pH 9—10 (the use of KOH resulted in a decrease in the yield of the final product). The oil formed was extracted with ether (3×50 mL) and chloroform (3×25 mL). The combined organic phases were dried with $MgSO_4$ and the solvents were distilled off to give 1.16 g (83 %) of crude oxazine **3**. IR ($CHCl_3$), ν/cm^{-1}: 1656 (C=N); 1600, 1581 (C—C arom). MS, m/z (I_{rel} (%)): 189 $[M]^+$ (100), 147 $[M-H-MeCN]^+$ (18), 132 $[M-H-MeCN-Me]^+$ (40), 106 $[M-H-MeCN-Me-C_2H_2]^+$ (40).

References

1. M. E. Smith and H. Adkins, *J. Am. Chem. Soc.*, 1938, **60**, 407.
2. USSR Pat. No. 1705290, *Byull. Izobret.*, 1992, No. 2, 100.
3. V. V. Kuznetsov, *XVII Ukrainskaya konf. po organ. khim., Tez. dokl.* [*Proc. XVII Ukrainian Conference on Organic Chemistry*], Khar'kov, 1995, 191 (in Ukrainian).
4. V. V. Kuznetsov, *Khim. Geterotsikl. Soedin.*, 1995, 275 [*Chem. Heterocycl. Compd.*, 1995 (Engl. Transl.)].
5. V. V. Kuznetsov, *Zh. Org. Khim.*, 1994, **30**, 1571 [*Russ. J. Org. Chem.*, 1994, **30** (Engl. Transl.)].
6. J. Canceill and J. Jacques, *Bull. Soc. Chim. Fr.*, 1970, 2180.
7. A. I. Gren' and V. V. Kuznetsov, *Khimiya tsiklicheskikh efirov bornykh kislot* [*The Chemistry of Cyclic Esters of Boron Acids*], Naukova Dumka, Kiev, 1988 (in Russian).
8. I. Ap'ok, M. Bartok, R. A. Karakhanov and N. I. Shuikin, *Usp. Khim.*, 1969, **38**, 72 [*Russ. Chem. Rev.*, 1969, **38** (Engl. Transl.)].
9. A. I. Gren and V. V. Kuznetsov, *19th European Symposium of Organic Chemistry. Abstrs.*, Warszawa, 1995, PA 46.
10. USSR Pat. No. 1220317; *Byull. Izobret.*, 1990, No. 36, 278.
11. A. N. Nesmeyanov and R. A. Sokolik, in *Metody elementoorganicheskoi khimii. Bor, alyuminii, gallii, indii, tallii* [*Methods of Organoelement Chemistry. Boron, Aluminium, Gallium, Indium, Thallium*], Nauka, Moscow, 1964, 28 (in Russian).

Received November 15, 1995;
in revised form January 31, 1996