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ORGANOBORON COMPOUNDS

CDV *. BROMINATION OF 2-ISOPROPYL-2-BORAADAMANTANE

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Summary

Bromination of 2-isopropyl-2-boraadamantane in CH_2Cl_2 proceeds simultaneously by both radical and electrophilic mechanisms. The first involves elimination of HBr and formation of 2-(2-bromo-2-propyl)-2-boraadamantane; this rearranges, under the action of nucleophilic reagents, to a derivative of 4-borahomoadamantane, which converts, on oxidation, to 3α-hydroxy-7α-(2-hydroxy-2-propyl)bicyclo[3.3.1]-nonane. The second direction includes cleavage of a B–C(isopropyl) bond with formation of i-PrBr and 2-bromo-2-boraadamantane, oxidation of which leads to 3α, 7α-dihydroxybicyclo[3.3.1]nonane. In the presence of H_2O, a solvated Br^+ also takes part in the bromination, which results in formation of hydroxy (3-noradamantyl)isopropylborane, which is oxidized to 3-noradamantanol. Depending on the reaction conditions one of the three possible directions may predominate.

Introduction

The investigation of the reactions of organoboron compounds with bromine represents a problem which is of great importance for organic chemistry. The problem includes the questions of the regiospecifity of the bromination, its mechanism, and the molecular rearrangement processes of the α-bromoorganoboranes and of boron-containing carbonium ions. The bromination of organoboron compounds was first studied by Johnson, Snyder, and Van Campen [1]. The authors found that tributylborane reacted with Br_2, in the absence of a solvent, forming HBr, C_4H_{10}, C_4H_9Br and $(C_4H_9)_2BBr$. Based on the composition of the products, the authors concluded that the reaction involves the cleavage of the boron–carbon bonds by an

* For part CDIV see ref. 22.

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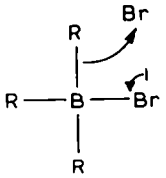
electrophilic mechanism and also replacement of an alkyl group hydrogen by bromine (eq. 1).



(1)

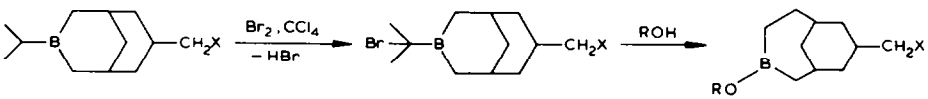
The reaction of organoboranes with Br_2 proceeding by an electrophilic mechanism, is promoted by polar solvents. Thus, 1-butylboracyclopentane reacts smoothly with Br_2 in the presence of pyridine with cleavage of a cyclic B–C bond to produce bromo (4-bromobutyl)butylborane [2,3] in 93% yield, while tributylborane under the same conditions forms bromodibutylborane in 81% yield [3]. By studying the kinetics of the gas-phase bromination of triethylborane, it was shown that the reaction proceeds by a free radical chain mechanism consisting mainly of the substitution of an α-hydrogen atom in the ethyl group by bromine according to eq. 2 [4].

$$CH_3CH_2B(C_2H_5)_2 + Br\bullet \xrightarrow{-HBr} CH_3\dot{C}HB(C_2H_5)_2 \xrightarrow{Br_2} CH_3CHBrB(C_2H_5)_2 + Br\bullet \quad (2)$$

Pasto and coworkers have found that liquid-phase bromination of phenylethylborinates also proceeds by the radical mechanism, the orienting effect of the boron atom being suppressed by that of the phenyl group, as a result of which, in 2-phenylethylboronic acid, a hydrogen atom in the α-position with respect to aromatic nucleus is replaced by bromine [5]. Liquid-phase bromination of triethylborane also proceeds by the radical mechanism to form 1-bromoethyldiethylborane [6].

According to the data of ref. 7, in bromination of 9-sec-alkyl-9-borabicyclo[3.3.1]-nonanes in the dark, substitution of an α-hydrogen in the side chain takes place. According to some data [8], 9-isopropyl-9-borabicyclo[3.3.1]nonane reacts with Br_2 to form 9-(2-bromo-2-propyl)-9-borabicyclo[3.3.1]nonane, which, under the action of water, rearranges to 9,9-dimethyl-10-hydroxy-10-borabicyclo[3.3.2]decane. Unfortunately, no experimental data are reported, therefore it is not clear whether the reaction proceeds unambiguously.

3-Isopropyl-7-methyl- and 3-isopropyl-7-bromomethyl-3-borabicyclo[3.3.1]nonanes are brominated smoothly in the α-position of the side chain [9]. The bromides thus formed, under the action of alcohols, undergo a rearrangement to produce 3-alkoxy-4,4,8-trimethyl- and 3-alkoxy-8-bromomethyl-4,4-dimethyl-3-borabicyclo[4.3.1]decanes, respectively, in 75–85% yield.

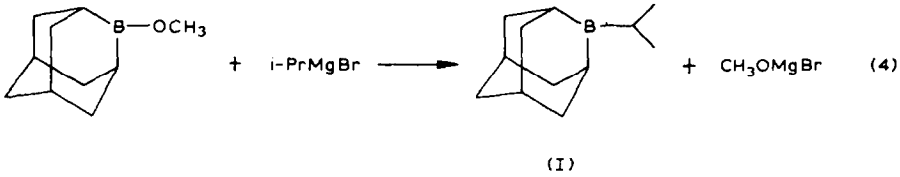


(3)

(X = H, Br)

Developing the 2-boraadamantane chemistry [10,11] we have investigated the

bromination of 2-isopropyl-2-boraadamantane (I) obtained by the action of i-PrMgBr on 2-methoxy-2-boraadamantane.



Results and discussion

It turned out that the bromination of 2-isopropyl-2-boraadamantane proceeds in a complicated manner to result in a complex mixture of products, the ratio of which being dependent on the degree of exposure of the reaction mixture to light. At first, bromination under usual laboratory lighting was studied. The reactions were carried out in a hood with natural illuminance of 20–30 luxes and additional lighting from two 100 W bulbs at a distance of 1.5 m from the reaction flask. The reactions and the analyses of the products formed were carried out as follows. A solution of Br_2 in CH_2Cl_2 was added with intense stirring to a solution of I in CH_2Cl_2 at $-10°C$, with the pressure in the reaction vessel being kept at about 200 mmHg. The addition was accomplished at such a rate that the reaction mixture had time to decolourize. For complete removal of HBr formed, a slight stream of argon was blown through the mixture. HBr evolved was absorbed by a NaOH solution. After adding the Br_2, the reaction mixture was heated to room temperature. The amount of HBr in the alkaline solution was determined by titration; its quantity was 23% of the theoretical amount (Table 1). In the volatiles compounds distilled off from the reaction mixture, isopropylbromide (38%) was found and quantitatively estimated by GLC. To determine the composition of the boron-containing compounds formed, the mixture of reaction products was oxidized with hydrogen peroxide in alkaline medium with subsequent analysis by GLC. The products comprised 3α,7α-dihydroxybicyclo[3.3.1]nonane (II) (53% yield), 3α-hydroxy, 7α-(2-hydroxy-2-propyl)bicyclo-[3.3.1]nonane (III) (21%), oxaadamantane (IV) (16%), along with traces of 3-noradamantanol (V) (~ 1%).

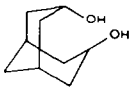
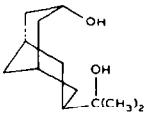
Further, we have found that, if bromination is carried out under additional lighting with a 200 W bulb at a distance of 10 cm from the reaction flask, the ratio of the major products changes sharply. Under these conditions, a considerable amount of HBr (73%) is formed while that of i-PrBr falls from 38% to 4%; the main component among the oxidation products becomes the diol III (71%), with the amount of the diol II falling from 53% to 8% (see Table 1).

Alterations in the ratio of the reaction products observed with different degrees of lighting indicate that the formation of HBr and of the organoboron compound, which yields the diol III on oxidation, is the result of a photochemical reaction. In the first stage of this process, an α-hydrogen of the isopropyl group is replaced by bromine. 2-(2-Bromo-2-propyl)-2-boraadamantane (VI) thus formed, under the action of ethanol (used as a solvent in the oxidation), undergoes the Matteson-Pasto rearrangement [9] * with cycle expansion to form 4-alkoxy-5,5-dimethyl-4-bora-

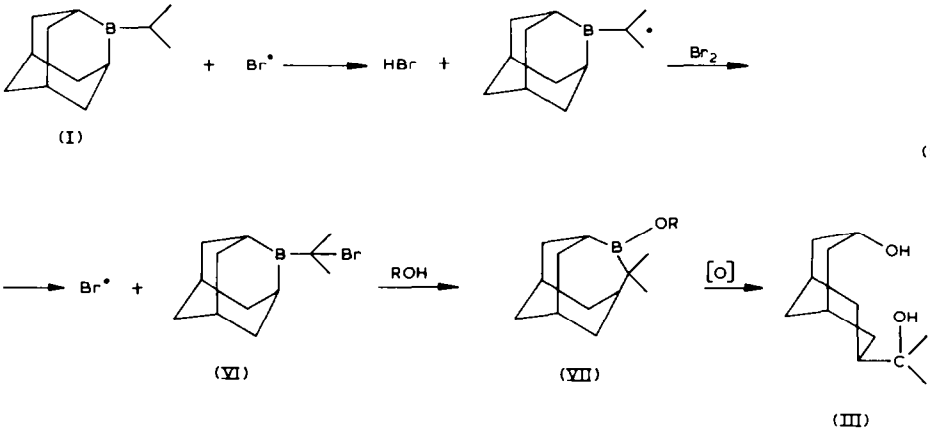
* See also references therein.

TABLE 1

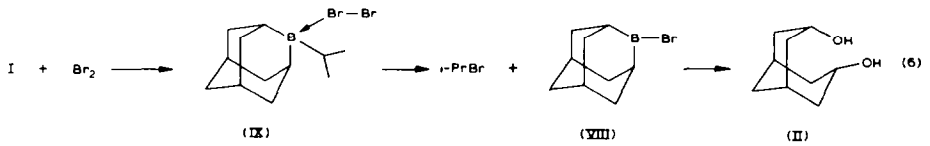
BROMINATION OF 2-ISOPROPYL-2-BORAADAMANTANE IN CH_2Cl_2

Reaction conditions			Yield of the products, %				
Quantity of initial comp. (mmol)	Light	Reaction time (h)	HBr	i-PrBr	(IV)	 (II)	 (III)
15	200 W	1	73	4	7	8	71
14	Normal	2.5	23	38	24	53	21
15	Dark	5.5	14	65	16	59	13

homoadamantane (VII). The latter compound gives the diol III on oxidation (eq. 5).

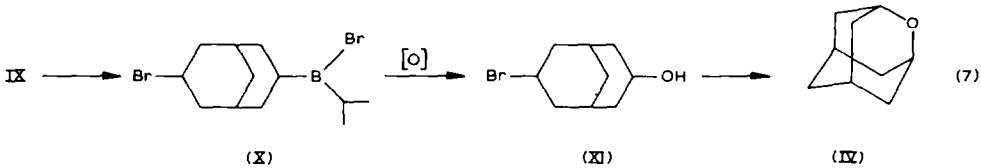


Comparison of the yields of i-PrBr with those of 2-bromo-2-boraadamantane (VIII), which converts into the diol II, in experiments with different degrees of lighting, demonstrates that the processes forming these products are not free radical ones. These substances are apparently formed by an electrophilic mechanism which includes a nucleophilic coordination at the boron atom and is described by the symbol S_EC [12]. According to this mechanism, the reaction of 2-isopropyl-2-boraadamantane starts with the nucleophilic coordination at the boron atom (IX) followed by an electrophilic attack on the carbon connected to the boron. Cleavage of the B–C(isopropyl) bond results in the formation of i-PrBr and 2-bromo-2-boraadamantane (VIII) which is oxidized to the diol II.



Besides this major reaction in the electrophilic substitution, cleavage of the

B–C(cycl.) bond takes place, although to a lesser extent, which results in the formation of 3α-bromo-7α-[(2-propyl)bromoboryl]bicyclo[3.3.1]nonane (X). The latter compound is oxidized to 3α-bromo-7α-hydroxybicyclo[3.3.1]nonane (XI) which further cyclizes to oxaadamantane (IV).



An effect of light on the bromination of 2-isopropyl-2-boraadamantane has been also found in the experiments which were carried out under low lighting, namely with no electric light in the hood (see Table 1). In this case, yields of the products of electrophilic substitution, i-PrBr and compound VIII, increase as compared with experiments under usual lighting conditions, while yields of the compounds formed in the radical process, HBr and the bromide VI, decrease. Hence it follows that the bromination of I in CH_2Cl_2 may proceed by both radical and electrophilic mechanisms.

The next stage of our work involved a study of the bromination of I in CH_2Cl_2 in the presence of an excess of water, which was previously reported in brief [13]. Brown and coworkers [6], who accomplished the bromination of organoboron compounds in the presence of water, assumed that the role of water consists of absorbing HBr, thereby preventing protonolysis of the α-bromo derivatives of organoboron compounds formed with hydrogen bromide. It is known, however, that bromine in water forms a solvated Br^+ which is a very reactive brominating agent, much more active than Br_2 [14,15], and is able to take part in the bromination of organoboron compounds.

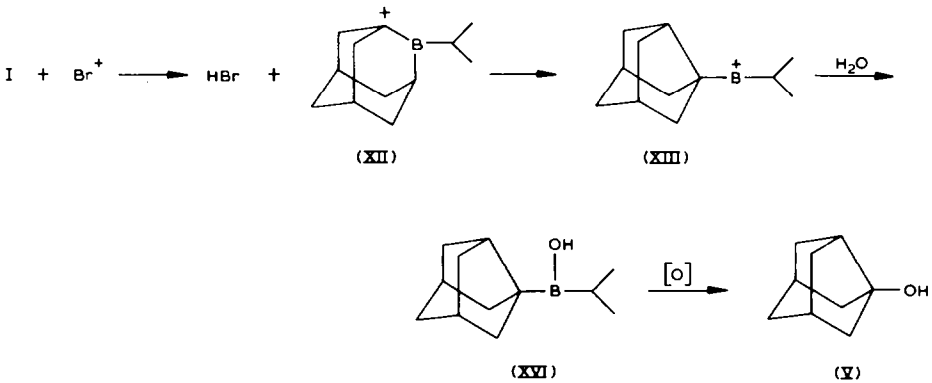
The reaction was carried out as follows. A solution of I in CH_2Cl_2 was mixed with water and to the two-phase mixture formed was added at 0–5°C with stirring a solution of bromine at such a rate that the reaction had time to decolourize. After completing the addition, the mixture was heated to room temperature, the water layer was separated and the amount of HBr therein was estimated by titration. Organoboron compounds obtained from the organic layer by distilling off the solvent were oxidized and the oxidation products were analyzed by GLC. The data obtained are presented in Table 2. As can be seen bromination under these conditions proceeds in different directions. The composition of the products formed also depends on lighting conditions, however it differs considerably as compared with the experiments carried out without water. Thus, the main component of the mixture obtained by the dark bromination is the organoboron compound XIV which is oxidized to 3-noradamantanol (V). The formation of XIV is accounted for by the fact that Br^+ attacks the C–H bond in the α-bridgehead position. The carbonium ion (XII) formed rearranges with cycle contraction to the boryl cation (XIII) which forms 3-noradamantylisopropylborinic acid (XIV) under the action of water. The compound XIV is then oxidized to 3-noradamantanol (V).

The increased reactivity of the C–H bond in the α-bridgehead position of the 2-isopropyl-2-boraadamantane nucleus towards Br^+ is in accord with the behaviour of adamantane in electrophilic halogenation reactions [16,17], resulting mainly in 1-haloadamantanes (e.g. the ratio of 1-chloro- to 2-chloroadamantane is equal to

TABLE 2

BROMINATION OF 2-ISOPROPYL-2-BORAADAMANTANE IN THE PRESENCE OF H_2O

Reaction conditions			Yield of the products (%)					
Quantity of initial comp. (mmol)	Lighting	Reaction time (h)	HBr	i-PrBr	(IV)	(V)	(II)	(III)
12	Dark	3	88	4	3	65	10	10
16	Normal	1.5	88	5	3	45	2	32
16	200 W	1	83	1	1	6	4	82



32 : 1), whereas in the photochemical chlorination of adamantane both isomers are formed in about equal quantities (depending on the nature of the solvent, the ratio between the isomers alters within a range of 0.6–2.1) [18].

The formation of the diols II and III corresponding to the bromides VI and VIII indicates that, under these conditions, substitution of a hydrogen in the side chain (according to eq. 5) and cleavage of the B–C(isopropyl) bond (according to eq. 6) also take place, although to a considerably lesser degree than the attack on the α-bridgehead position of the nucleus (eq. 8). The bromination of I in the presence of water under usual laboratory light proceeds to an almost equal degree in two directions: according to eq. 8 with the formation of 3-noradamantylborane XIV which is oxidized to 3-noradamantanol (V), and also according to eq. 5, as a result of which the bromide VI is formed which is oxidized to the diol III. This indicates that the rate of bromination in the side chain increases with an increasing of lighting, i.e. the replacement of an α-hydrogen of the isopropyl group by bromine in the presence of water is a free radical process. When a 200 W bulb is used, this process becomes predominating.

The investigation of the bromination of 2-isopropyl-2-boraadamantane demonstrates that bromine can react with organoboron compounds in the form of $Br^{\cdot}$, Br_2, or Br^+. The characteristic of the compound that we have chosen consists in the fact that each of these brominating reagents reacts in a specific manner. Thus, $Br^{\cdot}$ attacks

the C–H bond of the isopropyl group, Br_2 reacts mainly with the B–C(isopropyl) bond and to a considerably lesser degree with the B–C(cycl.) bond, while Br^+ attacks the C–H bond in the bridgehead position of the nucleus. Depending on the conditions of the bromination, one or another direction can be predominating.

Experimental

All manipulations with organoboron compounds were carried out under dry argon. GLC analyses of the reaction products were accomplished on a Chrom-4 instrument. Stainless steel columns (3 mm I.D.) were used. A column 2.4 m long packed with Carbowax 20 M on Chromaton was used for determining i-PrBr (60°C), while the oxidation products were analyzed on a column (1 m) packed with silicon OV-225 on Chromosorb W (100–160°C).

Three authentic compounds: 3α,7α-dihydroxybicyclo[3.3.1]nonane (II), oxaadamantane (IV), and 3-noradamantanol (V) were previously synthesized by us [11,19]. The fourth compound, 3α-hydroxy-7α-(2-hydroxy-2-propyl)bicyclo[3.3.1]nonane (III), was isolated in analytically pure state from the reaction mixture in one of the experiments by column chromatography on Al_2O_3 (neutral, act. grade II) with the use of a hexane-chloroform mixture (1 : 1) as eluent, m.p. 129–132°C (lit. m.p. 133–134°C [20]). The ^{1}H NMR and IR spectral data correspond to those available in the literature [20].

Contents of the compounds IV and V in a reaction mixture were estimated by direct GLC analyses. Diols were determined as their trimethylsilyl derivatives which were obtained by treatment of the reaction mixture with trimethylchlorosilane and pyridine [21]. To determine the diols quantitatively, dimethylphthalate was used as an internal standard, while adamantanol-1 was used for the determination of oxaadamantane and 3-noradamantanol.

^{1}H NMR spectra were recorded on a Tesla BS-497 spectrometer relative to TMS. ^{13}C NMR spectra were measured on a Bruker WP-60 instrument also relative to TMS.

2-Isopropyl-2-boraadamantane (I)

To a stirred solution of 0.1 mol of i-PrMgBr in 60 ml of ether was added a solution of 12.9 g (78 mmol) of 2-methoxy-2-boraadamantane in 25 ml of ether (a slight warming-up is observed). The mixture was refluxed for 7 h. After cooling, a precipitate was filtered off and washed with isopentane. Removal of volatile substances from the filtrate and subsequent distillation of the residue afforded 10.9 g (80%) of I, b.p. 60–61°C (1.5 mmHg), n_D^{20} 1.4934. Found: C, 81.00; H, 11.72; B, 5.83. $C_{12}H_{21}B$ calcd.: C, 81.81; H, 12.02; B, 6.14%.

^{1}H NMR ($CHCl_3$, δ, ppm): 1.04 and 1.26 (d, $J = 6$ Hz, CH_3, 6H), 1.81–2.09 (m, $\geqslant$CH and $>CH_2$, 15H).

^{13}C NMR (CH_2Cl_2, δ, ppm): 16.9 (q, CH_3), 23.9 (d, CH – B), 28.6 (d, $\geqslant$CH), 37.0 and 38.5 (t, CH_2).

Bromination of 2-isopropyl-2-boraadamantane

a) Under usual laboratory lighting. The bromination device consisted of a four-necked flask equipped with a magnetic stirrer, thermometer, capillary, and a dropping funnel with capillary end which is inserted in the liquid layer. The flask is

connected in consecutive order to a drying tube, a vessel with alkaline solution (for absorption of HBr), and a cooled trap connected to a water-jet pump. The reaction was carried out at −10°C under a pressure of 170–200 mmHg, blowing a constant stream of argon through the reaction mixture from the capillary. A solution of bromine was added in portions of 0.2–0.5 ml at such a rate that bromine colour had time to vanish.

Into the flask was added a solution of 2.4 g (14 mmol) of 2-isopropyl-2-boraadamantane in 12 ml of CH_2Cl_2, to which was then added a solution of 2.4 g (15 mmol) of Br_2 in 8 ml of CH_2Cl_2 during 2.5 h. The reaction mixture became gradually yellow in colour and was not decolourized further. The mixture was stirred for 30 min at −10°C, afterwards it was heated under vacuum to 17°C, the main part of volatile substances was caught in the cooled trap. The reaction mixture was cooled to −70°C, then 5 ml of ethanol were added and volatile substances was distilled off under vacuum with no heating. The liquid collected in the trap contained 0.6 g (5.3 mmol, 38%) of i-PrBr (GLC). 3.2 mmol of HBr was determined by titration of the alkaline solution in the absorbing vessel (23%).

While cooling and stirring, the residue was oxidized by consecutive addition of 5 ml of C_2H_5OH, 12 ml of 5 *N* NaOH, and 6 ml of 30% H_2O_2. The reaction mixture was then heated for 1 h at 40–50°C with increasing temperature to 70–75°C during the last 10 min, whereupon it was cooled to room temperature, saturated with NaCl, and extracted with $CHCl_3$. After removing volatile substances (2.6 g), the residue was analyzed by GLC.

The bromination in the dark as well as that under additional lighting with a 200 W bulb were carried out analogously. The results are presented in Table 1.

b) Under usual laboratory light in the presence of H_2O. To a three-necked flask equipped with a magnetic stirrer, thermometer, condenser and a dropping funnel, while cooling (0–2°C) and stirring vigorously, were added consecutively 2.8 g (16 mmol) of I in 20 ml of CH_2Cl_2, 17 ml of H_2O, and then, over 1.5 h, a solution of 2.6 g (16 mmol) of Br_2 in 10 ml of CH_2Cl_2. After stirring the mixture for an additional 30 min with subsequent heating to room temperature, the aqueous layer was removed and the organic one was washed with water. The aqueous solution thus obtained was titrated to provide a quantity of HBr (29 mmol, 90%).

Volatiles were removed from the organic layer by condensing them in a cooled trap. According to GLC data, they contained 0.1 g of i-PrBr (0.8 mmol, 5%). The residue was dissolved in 5 ml of ethanol and oxidized (3.2 ml of 5 *N* NaOH and 4 ml of 30% H_2O_2). Oxidation products thus formed were extracted from the aqueous solution with $CHCl_3$ and, after removing the latter (2.8 g), analyzed by GLC.

Both the reaction without lighting and that with additional lighting from a 200 W bulb were accomplished in an analogous manner. The results are listed in Table 2.

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