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The bromination of vinylboronic acids on alumina

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Abstract

The reaction of a series of vinylboronic acids with Br_2 on alumina has been examined. A mixture of (*E*)- and (*Z*)-vinyl bromides was formed in every case by competing mechanisms: (1) $S_E{}^2$ reaction of the surface-complexed vinylboronic acid with Br_2 to form the *E* isomer and (2) anti-elimination of $B(OH)_3$ and Br from the surface-complexed adduct arising by the reaction of vinylboronic acid and Br_2 in solution, which affords the *Z* isomer. As was the case with the comparable iodination reactions, the bromination of the vinylboronic acids synthesized from phenylacetylene and 3,3-dimethyl-1-butyne gave inordinately large amounts of (*E*)-vinyl halides. Because of steric factors in these examples the anti elimination described above is retarded and a syn elimination occurs preferentially. Experiments were performed to test the mechanisms.

Keywords: Boron; Boronic acids; Alumina; Bromine; Substitution reaction

1. Introduction

Brown and coworkers have shown that one can synthesize (*E*)- and (*Z*)-1-halo-1-alkenes by the reaction of terminal (*E*)-vinylboronic acids with halogen and base in solution [1,2]. Remarkably, the selectivity of the reaction is dictated by the order in which the halogen and base are added to the vinylboronic acid. When the halogen is iodine, for example, addition of the iodine first to the boronic acid favors the formation of (*Z*)-vinyl iodide except in sterically demanding cases where the (*E*)-vinyl iodide is favored (Eq. (1)) [1]. When the base is added first, however, the (*E*)-vinyl iodide is favored in all cases (Eq. (1)) [2].

$$(E)\text{-RCH=CHI} \xleftarrow[(2)\,I_2]{(1)\,OH^-} (E)-\text{RCH=CHB(OH)}_2 \xrightarrow[(2)\,OH^-]{(1)\,I_2} (Z)-\text{RCH=CHI} \qquad (1)$$

It is also possible to iodinate vinylboronic acids on the surface of alumina where the surface hydroxyl groups now function as the base [3]. Unlike the examples in solution where the reaction is ordinarily highly selective, the reaction on the surface yields both (*E*)- and (*Z*)-vinyl iodides by competing mechanisms.

In continuation of our work on the halogenation of unsaturated compounds on alumina [4–8] and, specifically, on the iodination of vinylboronic acids on alumina, we report herein our results on the bromination of vinylboronic acids on alumina. Because of the higher reactivity of Br_2 with alkenes than I_2 [9], and because the addition of Br_2 to double bonds is irreversible, unlike that of I_2 [9], the selectivity of surface-catalyzed bromination reactions should be different than the corresponding iodination reactions.

2. Experimental details

^1H NMR spectra were recorded on Bruker 250 MHz and 400 MHz spectrometers in $CDCl_3$ with 1% tetramethylsilane ($\delta = 0$ ppm) as internal standard. GC/MS were recorded on a Hewlett-Packard 5970 series instrument and gas chromatography was carried out on a Hewlett-Packard 5890A instrument using a 30 m by 1/8 inch column packed with 30% by weight SE-30 on Chromasorb W. Product yields were determined from GC and GC/MS peak areas using an internal standard. (*E*)-alkenylboronic acids were pre-

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pared via the procedure of Brown et al. [1,2] by reacting alkynes with catecholborane followed by hydrolysis of the resulting organoborane with water. Phenylboronic acid was purchased from Aldrich and used as received. Unactivated Brockmann neutral activity I alumina (Aldrich) was ordinarily used as base in the reactions. Activated alumina, when needed, was prepared by a literature procedure. [11] The alumina–boronic acid complexes were also prepared by a literature procedure. [3]

2.1. *Reaction of alumina–boronic acid complex with bromine*

The following is representative of the bromination reactions. To the free-flowing solid complex (2.0 mmol (*E*)-1-octenylboronic acid + 20 g alumina) was added first decane (1.0 mmol; internal standard) in anhydrous ether (30 ml) and then bromine (2.0 mmol) in anhydrous ether (30 ml). The mixture was stirred at RT for 24 h. After removing the solid by filtration, the ether was removed by careful evaporation. The (*E*)-1-bromo- and (*Z*)-1-bromo-1-octene were separated by GC and characterized by GC/MS and ^{1}H NMR spectroscopy. These compounds (and all of the other bromides prepared in this study) are known compounds and gave the appropriate spectral parameters. The 1-bromooctenes were formed in 53% yield and in a 25:75 *E*:*Z* ratio.

When the reaction was performed on alumina activated at 400° under the conditions described above, the 1-bromooctenes were only formed in 29% yield and in a 43:57 ratio.

When the reaction was performed on unactivated alumina using 2, 4 and 6 equivalents of Br_2, the following results were obtained: yield (*E*:*Z*) 65% (33:67); 56% (21:79); and 65% (22:78).

3. Results and discussion

As was the case with the iodination reactions, the bromination reactions were first carried out on unactivated alumina which has a polar surface [11] consisting of hydroxyl groups capable of functioning as bases in the reaction [12]. After adsorption of the vinylboronic acid (1 equiv.), which was prepared in two steps by treatment of the appropriate alkyne with catecholborane followed by hydrolysis, onto alumina from ether, the resulting free-flowing powder was exposed to a solution of bromine (1 equiv.) in ether for 24 h at ambient temperature (normal addition). The results of these reactions (% yield; *E*:*Z* ratio) are shown in Table 1, column 3. For comparison purposes, the results of our earlier study on the iodination of vinylboronic acids [3] are shown in column 5.

Note first that phenylboronic acid (entry 11) and the internal vinylboronic acid derived from 4-octyne (entry 10) both yielded the corresponding bromide on alumina, with the latter product only formed in low yield. Iodination of the same substrates on alumina failed [3]. All of the vinylboronic acids including the internal one just mentioned afforded mixtures of (*E*)- and (*Z*)-vinyl bromides with the *Z* isomer predominating in each case except for the sterically demanding phenyl and *tert*-butyl cases (entries 1 and 3) where the *E* isomer predominated. The three terminal vinylboronic acids that possess straight chain alkyl groups attached to the double bonds, interestingly, all gave virtually identical ratios of products (entries 4, 5 and 7). Surprisingly, in every case where a comparison of the bromination and iodination reactions can be made, the brominated products were significantly enriched in the *Z* product relative to the iodinated products.

The product ratios reported in Table 1 reflect kinetic control. When the reactions of (*E*)-1-octenyl-

Table 1
Product yields and *E*:*Z* ratios in the reaction of vinylboronic acids with bromine and iodine on unactivated alumina [a]

Entry	Substrate, $RB(OH)_2$ R =	% yield (*E*:*Z*)		
		Br_2		I_2
		Normal addition [b]	Reverse addition [b]	Normal addition [c]
1	(*E*)-$C_6H_5CH{=}CH-$	65 (81:19)	52 (78:22)	96 (> 99:1)
2	(*E*)-$C_6H_5CH{=}CH-$		75 (74:26) [d]	
3	(*E*)-$(CH_3)_3CCH{=}CH-$	40 (80:20)	37 (58:42)	55 (100:0)
4	(*E*)-$CH_3(CH_2)_3CH{=}CH-$	31 (25:75)	51 (18:82)	
5	(*E*)-$CH_3(CH_2)_5CH{=}CH-$	53 (25:75)	63 (18:82)	61 (56:44)
6	(*E*)-$CH_3(CH_2)_5CH{=}CH-$		90 (11:89) [d]	
7	(*E*)-$CH_3(CH_2)_7CH{=}CH-$	57 (24:76)	69 (19:81)	66 (60:40)
8	(*E*)-$ClCH_2(CH_2)_2CH{=}CH-$	56 (20:80)	66 (11:89)	82 (74:26)
9	(*E*)-$HOCH_2(CH_2)_8CH{=}CH-$			59 (58:42)
10	(*E*)-*n*-PrCH=C(*n*-Pr)-	5 (20:80)	8 (15:85)	0
11	C_6H_5-	38		0

[a] $RB(OH)_2$: halogen: alumina = 1 mmol: 10 g. [b] Run for 24 h at room temperature. [c] Ref. [3]; optimum yields; [d] Br_2 and $RB(OH)_2$ stirred for 24 h before contacted with alumina.

Table 2
Percentage yield and $E:Z$ ratio as a function of time

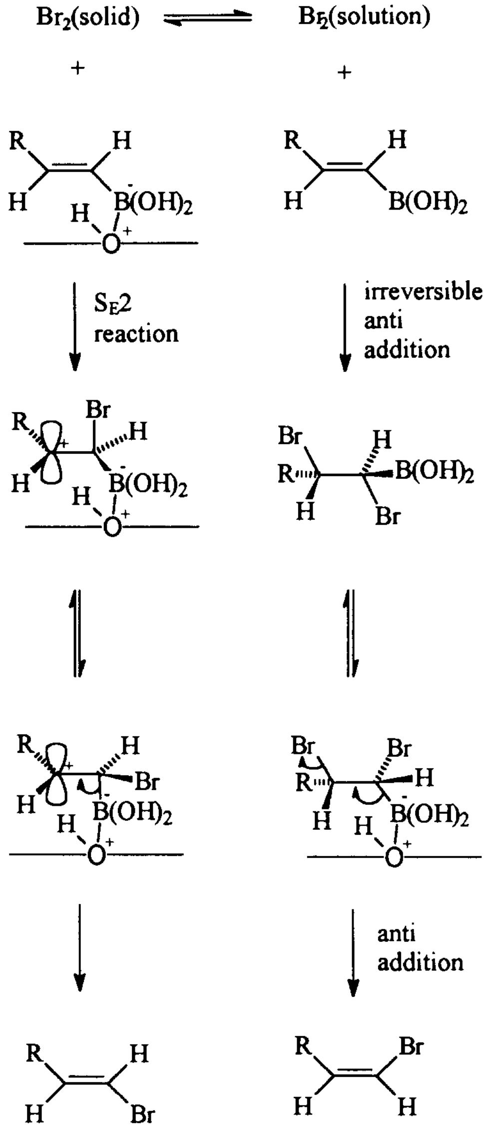
(*E*)-1-octenylboronic acid			(*E*)-3,3-dimethyl-1-butenylboronic acid		
Time (h)	% yield	$E:Z$	Time (h)	% yield	$E:Z$
0.5	45	23:77	0.25	23	79:21
1.0	47	26:74	0.50	21	78:22
1.5	48	24:76	0.75	34	74:26
2.0	49	25:75	1.00	35	76:24
2.5	51	24:76	1.25	38	76:24
3.0	53	25:75	1.50	38	78:22
24.0	53	25:75	24.0	40	80:20

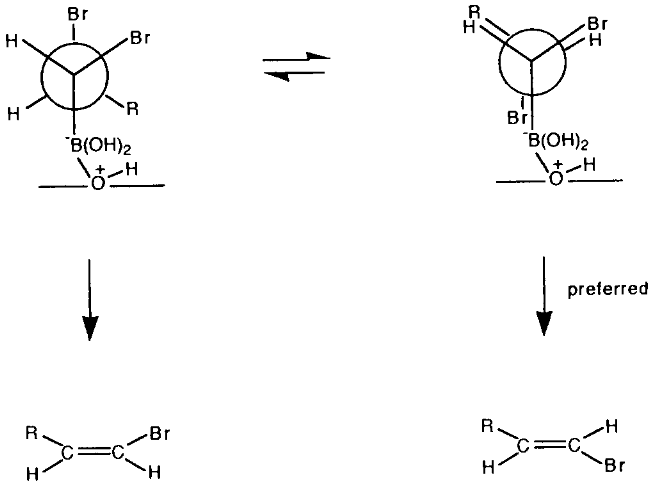
boronic acid, which gives more of the less stable (*Z*)-vinyl bromide, and (*E*)-3,3-dimethyl-1-butenylboronic acid, which gives more of the thermodynamically more stable (*E*)-vinyl bromide, with bromine were examined as a function of time (Table 2), the product yields increased, as expected, but the $E:Z$ ratios remained essentially constant in both cases through 24 h [13].

The mechanism by which the (*E*)- and (*Z*)-vinyl bromides were formed is shown below. Several features of this mechanism are noteworthy. Because the reactions were run as slurries in ether, the two reactants partition themselves between the surface of the solid and solution. The extent to which the reactants exist in each phase is dictated by their respective adsorption isotherms. The adsorbed Br_2 reacts with the adsorbed and complexed boronic acid by an $S_E{}^2$ mechanism with retention of configuration to yield the (*E*)-vinyl bromide. $S_E{}^2$ reactions occurring with retention of configuration are known [14]. The Br_2 in solution, on the other hand, undergoes *irreversible* anti addition to the double bond of the vinylboronic acid in solution to form an adduct which, after adsorption and complexation to the surface, undergoes anti elimination of $B(OH)_3$ and Br to yield the (*Z*)-vinyl bromide.

Based on this scheme alone, it is hard to see why the bromination and iodination of the phenyl- and *tert*-butyl-substituted vinylboronic acids on alumina yield so much more of the (*E*)-vinyl halides than do the other vinylboronic acids. If anything, the opposite should be true. Because of the large size of the phenyl and *tert*-butyl substituents, complexation of the respective vinylboronic acids to the "large" surface of alumina should be disfavored. In these cases then, the vinylboronic acids should prefer to be in solution, thus facilitating halogenation in solution which leads ultimately to the (*Z*)-vinyl halides [15]. This will be true, of course, if each product is formed by anti elimination of $B(OH)_3$ and Br^- from the appropriate gauche conformation of the complexed adduct. A Newman projection suggests, however, that this gauche conformer is sterically congested when a phenyl or *tert*-butyl substituent is present. If anti-elimination is suppressed for this reason, syn elimination of $B(OH)_3$ and Br^- from the sterically less congested eclipsed conformer may occur which will yield the observed (*E*)-vinyl halide. Any differences in the $E:Z$ ratios of products observed in the bromination and iodination of the phenyl- and *tert*-butyl-substituted vinylboronic acids may reflect how the differing sizes of bromine and iodine atoms in the adducts influence the stability of the respective gauche and eclipsed conformations [15].

If the proposed mechanism for the bromination of vinylboronic acids in the presence of alumina is correct, including the modification for the phenyl and *tert*-butyl cases, one should see an increase in the proportion of the (*Z*)-vinyl bromide if the bromination of the vinylboronic acids is allowed to occur before the alumina is added to the mixture (reverse addition). As shown in Table 1, column 4, this is true in every case. If the Br_2/vinylboronic acid solution is allowed to stand for 15 minutes prior to the addition of the alumina, the





R = C_6H_5 and $(CH_3)_3C$

Z content of the product mixture goes up. If the solution is allowed to stand for 24 h before the alumina is added (entries 2 and 6), the Z content goes up even more. The reason that these reactions do not give the Z isomer exclusively is due to the fact that the addition of Br_2 to the electron deficient vinylboronic acids is very slow. Even after 24 h, there is still a significant amount of unreacted Br_2 and vinylboronic acid present in the solution when the alumina is added [16].

If the bromination reaction were run in the absence of solvent, only the (*E*)-vinyl bromide should be generated because all of the vinylboronic acid will be complexed to the surface of alumina. When the vinylboronic acid derived from 1-octyne (1 mmol) was adsorbed to alumina (10 g), as described before, and then the Br_2 (1 mmol) was added directly to this powder, (*E*)- and (*Z*)-1-bromo-1-octene were formed in 10% overall yield after 24 h, and in a 44:56 ratio. With solvent, the same reaction afforded a 25:75 *E*:*Z* ratio of octenes in 53% yield. The low yield obtained from the "dry" reaction can be attributed to the slow rate of diffusion of Br_2 on the surface of the solid to sites where the complexed vinylboronic acid, which likely does not diffuse, resides. When ether is present, on the other hand, the transport of both reactants to and from the surface via the solution acts as a conduit for rapid net surface diffusion. Reaction in solution will, of course, also contribute to the enhanced product yield [17,18].

Although the product mixture is enriched in the *E* isomer when the reaction is run in the absence of solvent, there is still an excess of the *Z* isomer which is contrary to the expectation of the proposed mechanism. Based on previously published data on the bromination of alkenes on alumina [5,8], it is likely that the slow reaction on the dry surface does afford the *E* isomer exclusively, but when solvent is added during workup, the reaction proceeds in the normal way to afford both products until the alumina is removed by filtration [15].

In comparing the bromine and iodine data in Table 1, one may wonder why the iodination reactions give so much more of the (*E*)-vinyl halide than do the bromination reactions. This is most likely a consequence of the fact that the addition of Br_2 to alkenes is irreversible and that of I_2 is reversible. If a vinylboronic acid is brominated in solution, the resulting adduct will in due course always undergo the elimination reaction on the surface to give exclusively, except in the phenyl and *tert*-butyl examples, the (*Z*)-vinyl bromide. The competing reaction of surface-complexed vinylboronic acid, of course, gives the (*E*)-vinyl bromide. When the vinylboronic acid is iodinated in solution, however, the resulting adduct has the choice of undergoing the surface-catalyzed elimination reaction to give the (*Z*)-vinyl iodide or to regenerate the vinylboronic acid which in part will yield the (*E*)-vinyl iodide via the S_E2 mechanism.

Acknowledgements

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[13] When a 25:75 mixture of (*E*)- and (*Z*)-1-bromo-1-octene was contacted with unactivated alumina for 24 h, the resulting mixture was enriched in the *E* isomer ($E:Z = 36:64$). The meaning of this result is unclear because the surface of alumina in this experiment is unlike that during the course of the bromination reaction.

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[15] Because of the Curtin-Hammett principle, one must be cautious in making these arguments.

[16] A referee has suggested that the reaction of vinylboronic acids with Br_2 in solution is fast. When (*E*)-1-decenylboronic acid is treated with Br_2 in CH_2Cl_2 at room temperature, the Br_2 color disappears instantly. When the reaction is repeated in ether, the color persists for indefinite periods of time. When (*E*)-1-decenylboronic acid is treated with Br_2 in CH_2Cl_2 and ether for a given period of time and then with cyclohexene to remove any unreacted Br_2, (*Z*)-bromo-1-decene is formed exclusively in both cases (GC analysis of residue after removal of solvent), with the reaction in CH_2Cl_2 giving a considerably higher yield of product than the reaction in ether. The difference in behavior in the two solvent may be due to the presence of a solvent-vinylboronic acid complex in ether.

[17] A simple calculation shows that 25% of the reaction occurs on the dry surface and 75% during workup.

[18] When (*E*)-1-octenylboronic acid was brominated in a slurry of ether and alumina activated at 400°, more (*E*)-1-bromo-1-octene was formed (44 relative %) than when the reaction was performed on unactivated alumina (25 relative %). The adsorption of the vinylboronic acid to the surface may be enhanced on activated alumina because of the presence of oxide anions on the surface. Enhanced adsorption should favor the formation of the (*E*)-vinyl bromide.