Convenient Procedure for the Synthesis of (*E*)-1-Bromo-1-alkenes and (*Z*)-1-Iodo-1-alkenes

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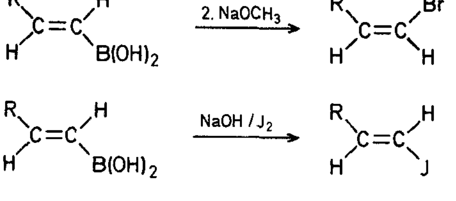
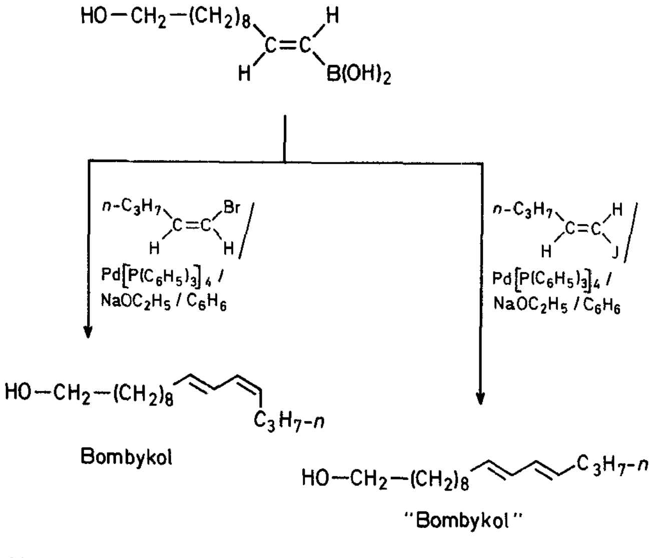
We have earlier described the synthesis of (*E*)-1-iodo-1-alkenes[1] and (*Z*)-1-bromo-1-alkenes[2] in excellent stereochemical purities from (*E*)-1-alkenylboronic acids, readily available via the hydroboration of 1-alkynes.



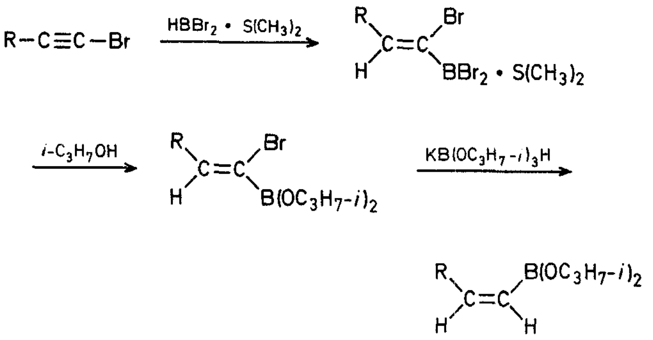
These vinyl halides find extensive application in the stereospecific synthesis of biologically important molecules such as sex pheromones containing the 1,3-diene grouping. For example, bombykol [(10*Z*,12*E*)-10,12-hexadecadien-1-ol] and its three geometrical isomers have been synthesized by the palladium-catalyzed cross-coupling between the 1-alkenylboronic acids and the 1-alkenyl halides[3] [(*Z*)-bromide and (*E*)-iodide].



Similarly, other sex pheromones with (*E,E*)- or (*E,Z*)-diene configuration have been prepared[4].

In view of the synthetic importance of these vinyl halides, it was desirable to have available a convenient synthesis of (*Z*)-1-iodo-1-alkenes and (*E*)-1-bromo-1-alkenes. We have now developed such a synthesis.

Recently, we established a convenient synthetic route to the (*Z*)-boronic esters[5].



These (*Z*)-1-alkenylboronic esters exhibit properties very similar to those of (*E*)-1-alkenylboronic esters. For example, treatment of this (*Z*)-ester with sodium hydroxide and iodine gives pure (*Z*)-1-iodo-1-alkene (Table 1).

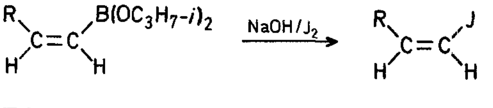


Table 1. Synthesis of (*Z*)-1-Iodo-1-alkenes

R	b.p. [°C]/ torr[a]	n_D^{25} [a]	Yield [%]	Isomeric Purity[b] [%]	M⁺ m/e
n-C_4H_9	60–61°/10[9]	1.5021	80	98	210
c-C_6H_{11}[c]	52–53°/0.3	1.4911	81	99	236
t-C_4H_9	50°/20[10]	1.5008	83	100	210
Cl—$(CH_2)_3$	64–65°/0.5	1.5031	78	96	230

[a] The values agree with literature values.

[b] Determined by gas chromatographic analysis.

[c] $C_8H_{13}J$ (236.1) calc. C 40.70 H 5.55 J 53.75; found 40.56 5.32 53.56

On the other hand, the corresponding (*E*)-1-bromo-1-alkene is formed on treatment with bromine followed by base (Table 2).

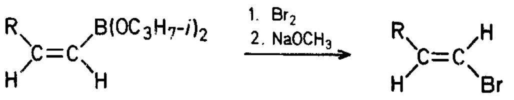


Table 2. Synthesis of (*E*)-1-Bromo-1-alkenes

R	b.p. [°C]/ torr[a]	n_D^{25} [a]	Yield [%]	Isomeric Purity[b] [%]	M$^+$ *m/e*
n-C_6H_{13}	59–60°/6[11]	1.4620	81	99	190, 192
c-C_6H_{11}	50–52°/4[9]	1.5043	80	98	188, 190
t-C_4H_9	48°/50[12]	1.4625	79	100	162, 164
Cl—$(CH_2)_3$	66–68°/6	1.4774	80	97	182, 184

[a] The values agree with literature values.

[b] Determined by gas chromatographic analysis.

These reactions appear to be general, as seen from the Tables. An advantage of this present method is that both bromination and iodination reactions may be carried out without the actual isolation of the (*Z*)-1-alkenylboronic ester, since the by-product, triisopropyl borate, does not interfere with the reactions. Consequently, we are now in position to synthesize both (*E*)- and (*Z*)-vinyl iodides and (*E*)- and (*Z*)-vinyl bromides by simple procedures.

Boiling points were uncorrected. ^{1}H-N.M.R. spectra were recorded on a Varian T-60 instrument. All of the compounds gave satisfactory N.M.R. data. The isomeric purities were determined by G.C. analysis on an HP 5730A instrument using methylsilicone glass capillary column (50 meter) under isothermal conditions. The 1-bromo-1-alkynes were prepared from 1-alkynes (Farchan Labs) by literature procedure[6]. Potassium triisopropoxyborohydride (Aldrich) was used as such. All manipulations of the boron compounds were done under nitrogen using standard procedures[7].

Diisopropyl (*Z*)-1-Bromo-1-hexenylboronate:

To a solution of 1-bromo-1-hexyne (25 mmol) in dichloromethane (15 ml) in a 100-ml round-bottom flask equipped with a septum inlet and a magnetic stirrer surrounded by a water bath (room temperature) is slowly added a solution of dibromoborane/dimethyl sulfide (25 mmol). After stirring of the reaction mixture for 8 h at room temperature, pentane (25 ml) is added to it and the water bath is replaced with an ice/water bath. Isopropyl alcohol (100 mmol) is slowly introduced to the flask and the stirring is continued for an additional 15 min. The almost colorless pentane layer is separated from the heavier alcohol layer (containing dissolved hydrogen bromide) and the latter is extracted with fresh pentane (2 × 10 ml)[8]. The combined pentane extracts on solvent evaporation and fractionation give diisopropyl (*Z*)-1-bromo-1-hexenylboronate; yield: 87%; b.p. 64°C/0.2 torr; n_D^{20}: 1.4448.

Diisopropyl (*Z*)-1-Hexenylboronate:

To a solution of diisopropyl (*Z*)-1-bromo-1-hexenylboronate (25 mmol) in ether (20 ml) in a 100-ml round-bottom flask cooled to 0°C with an ice/water bath, is introduced slowly a solution of potassium triisopropoxyborohydride in ether (25 mmol). Potassium bromide starts precipitating out at this stage. After stirring of the reaction mixture for 15 min at 0°C, it is allowed to come to room temperature (0.5 h). The clear ethereal solution is removed after centrifugation, the solid is washed with ether (2 × 10 ml), and the combined ether solutions on solvent evaporation and fractionation give diisopropyl (*Z*)-1-hexenylboronate; yield: 90%; b.p. 70–71°C/6 torr; n_D^{20}: 1.4158.

(*Z*)-1-Iodo-1-hexene:

The reaction of diisopropyl (*Z*)-1-hexenylboronate (25 mmol) with potassium triisopropoxyborohydride (25 mmol) is carried out as described above. The combined ether solution after centrifugation is cooled to 0°C and 5 normal sodium hydroxide solution (15 ml) is added to it followed by a solution of iodine (30 mmol) in ether (~40 ml). Stirring is continued for 1 h and the excess iodine is destroyed with aqueous sodium thiosulfate. The ethereal layer is separated, washed with brine, dried with anhydrous magnesium sulfate, and the ether removed under reduced pressure. The product on distillation gives pure (*Z*)-1-iodo-1-hexene; yield: 80%; b.p. 60–61°C/10 torr.

(*E*)-1-Bromo-1-octene:

The reaction of diisopropyl (*Z*)-1-octenylboronate (25 mmol) with potassium triisopropoxyborohydride (25 mmol) is carried out as described. Ether and most of the triisopropyl borate are removed from the centrifugate under reduced pressure and the residue is dissolved in dichloromethane (20 ml) and cooled to −25°C. Bromine (25 mmol) in dichloromethane (10 ml) is added to it and the reaction mixture is stirred for 1 h at −25°C. Sodium methoxide in methanol (25 mmol) is then introduced into the reaction flask and stirring is continued for 1 h at −25°C and an additional 0.5 h at room temperature. Pentane (25 ml) is added to the reaction mixture and the product is worked up as usual. Fractionation gives pure (*E*)-1-bromo-1-octene; yield: 81%; b.p. 59–60°C/6 torr.

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