Stereoselective Synthesis of (*E*)- and (*Z*)-Disubstituted Vinyl Bromides *via* Organoboranes

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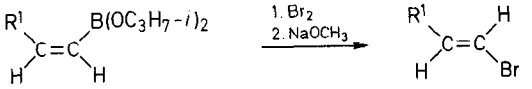
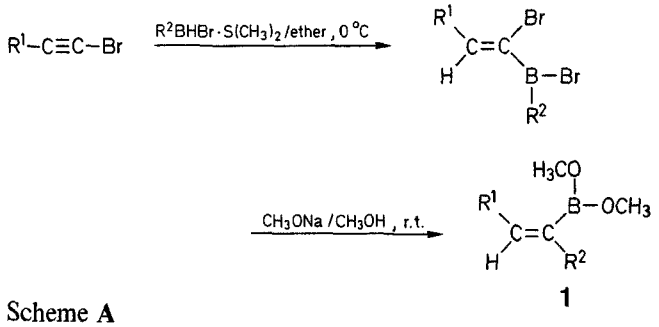
Treatment of [*E*]- and [*Z*]-disubstituted vinyldimethoxyboranes, prepared as described previously, with bromine, followed by a base, produced [*Z*]- and [*E*]-disubstituted vinyl bromides in good yields (61–80%) and excellent stereochemical purities (≥ 97%). In both cases, replacement of the boron moiety with bromine proceeds with inversion.

Vinyl bromides are useful synthetic intermediates[2,3] in organic synthesis. These have been synthesized by a variety of methods. In many cases, a mixture of the (*E*)- and (*Z*)-isomers is obtained. However, stereospecific syntheses have been developed which utilize the reaction of bromine with organoaluminum[4], organosilicon[5], and organoboron[6–9] intermediates. We recently reported[10] the synthesis of (*E*)-1-bromo-1-alkenes *via* organoboranes.

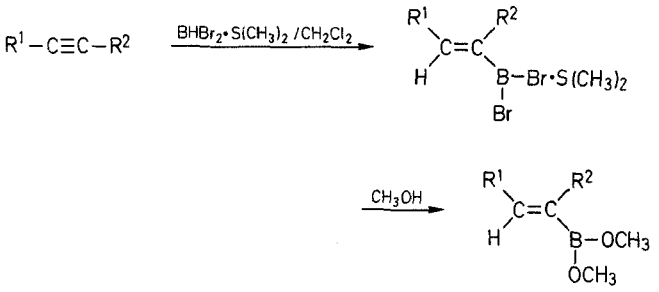


There are not many methods[7,11] available for the stereospecific syntheses of (*E*)- and (*Z*)-disubstituted vinyl

bromides *via* organoboranes. We previously reported[12,13,14] procedures for preparing (*E*)- and (*Z*)-(1-substituted-1-alkenyl)-boronic esters *via* dibromoborane-dimethyl sulfide (Schemes **A** and **B**).



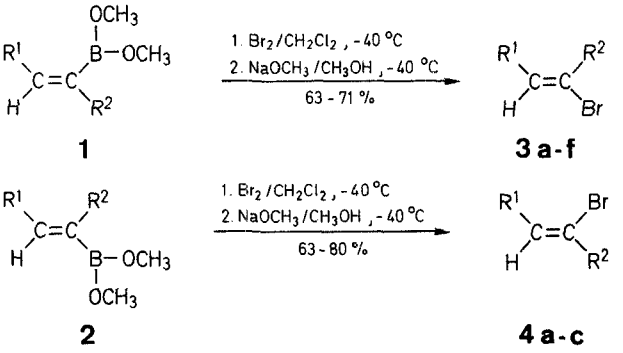
Scheme **A**



Scheme **B**

We now report the convenient syntheses of (*E*)- and (*Z*)-disubstituted vinyl bromides based on these organoboron intermediates, *viz.* **1** and **2**.

Treatment of **1** with bromine followed by base provided the corresponding (*E*)-disubstituted vinyl bromides in good yields (Table 1). Similarly, (*Z*)-disubstituted vinyl bromides were obtained from **2** upon treatment with bromine followed by base (Table 2).



It is possible to account for the inversion of configuration in the present reactions in terms of the usual *trans*-addition of bromine to the double bond[15], followed by a base-induced *trans*-elimination of boron and bromine to give the products[11]. Since these vinyl bromides are readily converted into vinyl Grignard[16] and vinyllithium[17,18,19] derivatives with retention of their stereochemistry, the present developments open up highly practical routes to these vinyl metallics of known stereochemistry. The corresponding reaction of internal alkenyl boronic ester with iodine and base takes another course[20]. We are presently exploring this reaction.

In conclusion, the synthesis of (*E*)-disubstituted vinyl bromides appears to be general, as seen from Table 1. However, the procedure for preparing (*Z*)-disubstituted vinyl bromides is not fully general. It can be applied to symmetrically substituted alkynes, $R^1 = R^2$, and to unsymmetrically substituted alkynes, $R^1 > R^2$. At present it cannot be applied to cases where R^2 is sterically larger than R^1. Nevertheless, both of these procedures are simple and the reactions can be carried out in one pot. Consequently, we are now in a position to synthesize all (*E*)- and many (*Z*)-disubstituted vinyl bromides by convenient procedures.

All boiling points are 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

Table 1. Regio- and Stereoselective Synthesis of (*E*)-Disubstituted Vinyl Bromides **3a–f**

Product[a,b] No.	R^1	R^2	Yield [%]	b.p. [°C]/torr	n_D^{20}	M.S. *m/e* (M^+)
3a	*n*-C_6H_{13}	*n*-C_3H_7	71	52–54°/0.10	1.4705	232, 234
3b	*n*-C_5H_{11}	*n*-C_5H_{11}	68	70–72°/0.01	1.4667	246, 248
3c	*n*-C_4H_9	*c*-C_5H_9	63	66–68°/0.15	1.4894	230, 232
3d	*c*-C_6H_{11}	*n*-C_4H_9	67	64–66°/0.01	1.4967	244, 246
3e	*n*-C_4H_9	*n*-C_4H_9	64	64–66°/0.90	1.4693	218, 220
3f	*n*-C_6H_{13}	*c*-C_6H_{11}	66	80–82°/0.01	1.4924	272, 274

[a] All of the reactions were carried out on a 20-mmol scale; yields of isolated products are based on 1-bromo-1-alkynes.
[b] The stereochemistry of these vinyl bromides was determined by preparation of the lithio derivatives[18,19], followed by protonolysis and identification of the resulting olefin by G.L.C. All of the compounds were ≥ 97% isomerically pure.

Table 2. Stereoselective Synthesis of (*Z*)-Disubstituted Vinyl Bromides **4a–c**

Product[a,b] No.	R^1	R^2	Yield [%]	b.p. [°C]/torr	n_D^{22}	M.S. *m/e* (M^+)
4a	*n*-C_5H_{11}	*n*-C_5H_{11}	80	68–70°/0.01	1.4664	246, 248
4b	*n*-C_4H_9	*n*-C_4H_9	76	62–64°/0.9	1.4645	218, 220
4c	*c*-C_6H_{11}	*c*-C_6H_{11}	63	88–90°/0.07	1.5155	270, 272

[a] All of the reactions were carried out on a 20-mmol scale; yields of isolated products are based on alkynes.
[b] The stereochemistry of these internal alkenyl bromides was established by preparing the corresponding lithio derivatives[18,19], followed by protonolysis and identification of the resulting olefin by G.L.C. All of the compounds were found to be ≥ 97% isomerically pure.

G.L.C. analysis on a Varian 1400 gas chromatograph (column 5 ft × 1/8 in packed with 5% Carbowax on Chromosorb W, 20 M, under isothermal conditions). Both (*E*)- and (*Z*)-alkenyl bromides separated very well. The 1-bromo-1-alkynes were prepared from 1-alkynes (Farchan Labs) by literature procedures[21]. All manipulations of the boron compounds were done under nitrogen using standard procedures[22].

(*E*)-6-Bromo-6-dodecene (3b):

To neat *n*-pentyldibromoborane-dimethyl sulfide (20 mmol), prepared from 1-pentene (22 mmol, 2.4 ml) and dibromoborane-dimethyl sulfide (20 mmol)[12], are added at 0 °C dimethyl sulfide (4.4 ml) and diethyl ether (20 ml), followed by a slow addition of lithium aluminum hydride in diethyl ether (5 mmol, 5.2 ml) with stirring. The reaction is allowed to proceed for 3 h at 0 °C, followed by 1 h at room temperature. To the resulting *n*-pentylbromoborane in diethyl ether is added 1-bromo-1-heptyne (20 mmol, 2.86 ml) at 0 °C. After 1 h at room temperature, sodium methoxide in methanol (40 mmol, 8.25 ml) is added at 0 °C and the mixture stirred at room temperature for 1 h. The solvents are removed under vacuum. To the mixture is added dichloromethane (20 ml). It is then cooled to − 40 °C, bromine (20 mmol, 1 ml) is added slowly with vigorous stirring and the mixture is stirred for 1 h. Sodium methoxide in methanol (40 mmol, 9.25 ml) is added at − 40 °C and the mixture is allowed to stir for 1 h, followed by 0.5 h at room temperature. Water (20 ml) is added and the organic phase is separated. The aqueous phase is extracted twice with dichloromethane (2 × 20 ml), the combined organic phase washed with water (2 × 20 ml), and dried with magnesium sulfate. The dichloromethane is removed and the product on distillation gives pure (*E*)-6-bromo-6-dodecene **(3b)**; yield: 3.3 g (68%); b.p. 70–72 °C/0.01 torr; n_D^{20}: 1.4667; G.L.C. isomeric purity: 98%.

M.S.: *m/e* = 248, 246 (M^+).

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 1.86–2.50 (m, 4H); 5.83 ppm (t, J = 7.5 Hz, 1H).

(*Z*)-6-Bromo-6-dodecene (4a):

To a solution of 6-dodecyne (20 mmol, 4.22 ml) in dichloromethane (20 ml) in a 100-ml round-bottom flask equipped with a magnetic stirrer is slowly added a solution of dibromoborane-dimethyl sulfide (20 mmol, 4.40 ml) at 0 °C. After stirring of the mixture for 2 h at room temperature, pentane (20 ml) is added to it and cooled to − 10 °C. Methanol (80 mmol, 3.2 ml) 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 and the latter is extracted with *n*-pentane (2 × 20 ml). Pentane extracts are combined and the solvent is removed under reduced pressure. Dichloromethane (20 ml) is added and the reaction mixture is cooled to − 40 °C. Bromine (20 mmol, 1 ml) is slowly added and the reaction mixture is stirred for 1 h at − 40 °C. Sodium methoxide in methanol (40 mmol, 8.25 ml) is slowly added to the mixture and the stirring in continued fro 1 h at − 40 °C, followed by 0.5 h at room temperature. Water (20 ml) is then added and the organic layer is separated. The aqueous layer is extracted with dichloromethane (2 × 20 ml) and the combined organic layer is washed with water, dried with magnesium sulfate. Dichloromethane is removed and the distillation affords the pure (*Z*)-6-bromo-6-dodecene **(4a)**; yield: 4 g (81%); b.p. 68–70 °C/0.01 torr; n_D^{22}: 1.4664; G.L.C. isomeric purity: > 98%.

M.S.: *m/e* = 248, 246 (M^+).

^{1}H-N.M.R. ($CDCl_3$/TMS): δ: 0.76–1.63 (m, 18H); 2.0–2.5 (m, 4H); 5.66 ppm (t, J = 7 Hz, 1H).

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