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Stereoselective Syntheses of 1,1-Dihalo-1-alkenes

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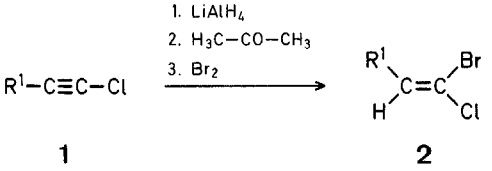
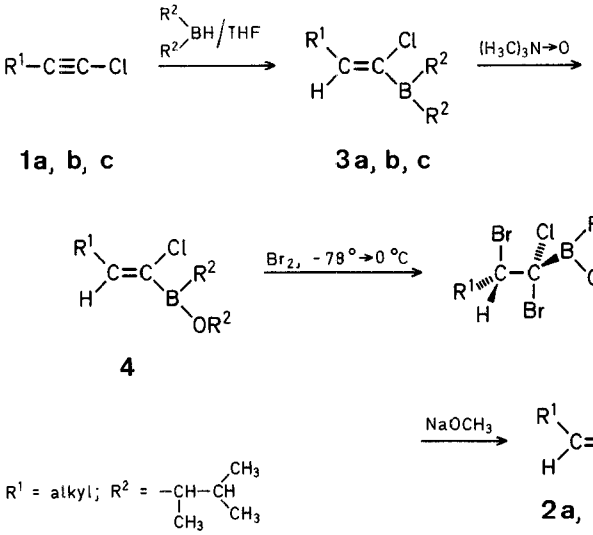
The usefulness of 1-halo-1-alkenes as synthons for preparing substituted olefins and dienes has been amply demonstrated. By contrast, 1,1-dihalo-1-alkenes have not yet played a major role in synthetic methodology. This is probably because most of the currently available methods for their synthesis are confined to the preparation of homo 1,1-dihalo-1-alkenes[1,2]. The prospect that the ready availability of mixed 1,1-dihalo-1-alkenes of defined stereochemistry might open new vistas into the methodology for syntheses of substituted olefins has prompted us to search for convenient procedures for their preparation.

Recently, we reported a stereoselective method for preparing (*Z*)-1-bromo-1-chloro-1-alkenes **(2)** from 1-chloro-1-alkynes **(1)** via a *trans*-hydroalumination-bromination sequence[3].



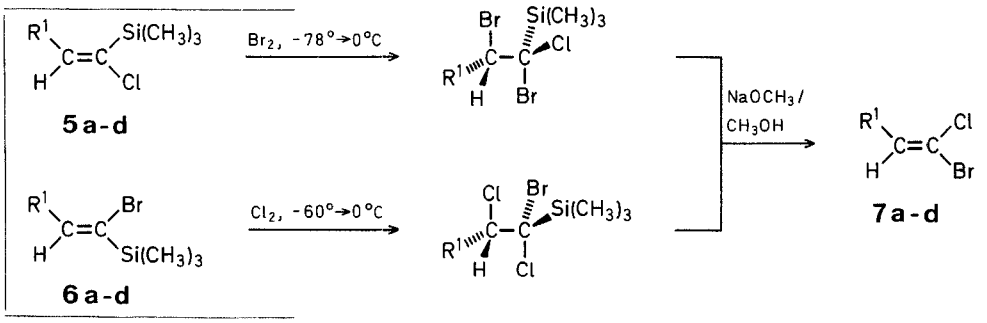
Although this procedure affords mixed (*Z*)-1,1-dihalo-1-alkenes in high isomeric purities and yields, it was of interest to explore whether they might also be obtained from the same precursor **1** but via a sequence of hydroboration-bromination-elimination reactions. Such an alternative method would enable the preparation of 1,1-dihalo-1-alkenes possessing functionalities which are incompatible with the use of lithium aluminum hydride.

The hydroboration of 1-chloro-1-alkynes **(1)** with bis[1,2-dimethylpropyl]-borane places the boron preferentially at the 1-position of the triple bond[4]. Unfortunately, treatment of the resultant 1-chloro-1-alken-1-ylboranes **3** with bromine followed by addition of sodium methoxide in methanol produced the dihaloalkenes **2** in only modest yields owing to competing transfer of one 1,2-dimethylpropyl group from boron to the adjacent C-atom. However, this difficulty was obviated by converting **3** into the borinic ester derivative **4** prior to adding bromine. Thus, **3** was oxidized with 1.1 equivalent of anhydrous trimethylamine oxide[5] and the resultant borinic ester **4** was treated sequentially with bromine and methanolic sodium methoxide. The (*Z*)-1-bromo-1-chloro-1-alkenes **2** produced (see Table 1) contained only small amounts (<2%) of the corresponding 1-chloro-2-bromo-1-alkenes resulting from addition of boron to the 2-position of the triple bond of **1** in the hydroboration step. However, it should be noted that oxidation-bromination-deboronobromination of the 1-chloro-1-alken-1-ylborane **3** containing a *t*-butyl group ($R^1 = t\text{-}C_4H_9$) produced a complex mixture of products.



The stereochemistry of the dihaloalkenes **2** derived from the procedure is compatible with a *trans* addition of bromine to the double bond of the borinic ester **4** followed by base induced *anti*-elimination of the β-Br atom and the boron moiety.

To complement the above syntheses of (*Z*)-1-bromo-1-chloro-1-alkenes, we investigated the possibility that the corresponding (*E*)-isomers might be prepared from the readily available 1-halo-1-alkenylsilanes **5** and **6**[6]. It has been shown that *cis*- and *trans*-1-alkenylsilanes undergo *trans*-halogenation and *anti*-desilicohalogenation when treated successively with halogens and base to furnish the corresponding *trans*- and *cis*-1-alkenyl halides, respectively[7]. Therefore, either bromination-desilicobromination of (*E*)-1-chloro-1-alkenylsilanes **5**[6] or chlorination-desilicochlorination of (*Z*)-1-bromo-1-alkenylsilanes **6**[6] should afford the (*E*)-1-bromo-1-chloro-1-alkenes **7 (a-d)**.



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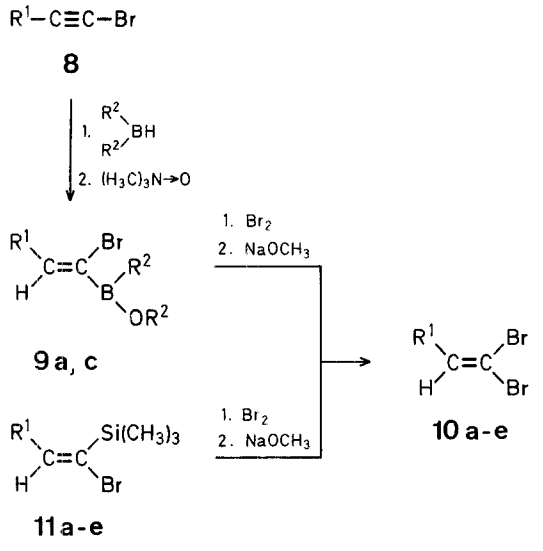
In agreement with the above proposal, addition of bromine or chlorine to **5** or **6**, respectively, containing primary alkyl substituents furnished, after treatment of the reaction mixtures with methanolic sodium methoxide, the desired (*E*)-1,1-dihalo-1-alkenes **7** with better than 98% isomeric purities. However, as it is shown in the Table, increasing the size of the alkyl substituent in **5** and **6** had a detrimental effect on the isomeric purities of the dihaloalkenes **7**. We have not yet established whether the loss in stereospecificity occurs in the halogenation step or in the desilicohalogenation step.

The halogenation-deboronohalogenation and halogenation-desilicohalogenation procedures may also be applied to the preparation of 1,1-dibromo-1-alkenes. Thus, treatment of **9**, derived from hydroboration of 1-bromo-1-alkynes **8**, with bromine and methanolic sodium methoxide afforded the 1,1-dibromo-1-alkenes **10**. Alternatively, the same dibromoalkenes may be obtained from the (*E*)-bromides **11** [or the (*Z*)-bromides **6**] on treatment with bromine and methanolic sodium methoxide.



(*Z*)-1-Bromo-1-chloro-1-octene (2b):
To a stirred 1.5 molar solution (13.34 ml, 20 mmol) of bis[1,2-dimethylpropyl]-borane[8] in tetrahydrofuran is added at −10 °C a solution of 1-chloro-1-octyne[9] (2.893 g, 20 mmol) in tetrahydrofuran (10 ml). The resultant mixture is warmed gradually to 25 °C, stirred for an additional 30 min at this temperature, and treated with anhydrous trimethylamine oxide[10] (1.7 g, 22 mmol) at 0–5 °C. Stirring is continued for 1 h at 25 °C, then tetrahydrofuran and the trimethylamine formed are removed under reduced pressure at room temperature. The resultant borinic ester **4** is diluted with dichloromethane (20 ml), then treated in the dark with a 1 molar solution (22 ml, 22 mmol) of bromine in dichloromethane at −78 °C. The mixture is stirred for 15 min at −78 °C, brought gradually to 0 °C, stirred for 30 min, and then treated with a 1.5 molar solution (26.27 ml, 40 mmol) of sodium methoxide in methanol at −15 °C. The mixture is stirred at this temperature for 15 min, warmed to room temperature, and then diluted with methanol (20 ml). The remaining 1,2-dimethylpropyl group on boron is oxidized with 3 normal sodium hydroxide (4 ml) and 30% hydrogen peroxide (4 ml) at 35–40 °C. The mixture is maintained for 30 min at ambient temperature, then extracted with pentane (3 × 30 ml). The combined pentane extracts are washed with a saturated solution of sodium chloride (60 ml), treated with a few crystals of 2,6-di-*t*-butyl-4-methylphenol (BHT)[11], and then dried with magnesium sulfate. The solvents are removed and the residue is distilled through a short Vigreux column; yield: 2.9 g (66%); b.p. 53 °C/1 torr; n_D^{26}: 1.4782.

$C_8H_{14}BrCl$ (224.0)

M.S.: *m/e* = 223.9968 (M^+).

I.R. (neat): ν = 1610, 840 cm^{-1}.

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.9 (t, 3 H, *J* = 6 Hz); 1.3 (m, 8 H); 2.1 (m, 2 H); 6.0 ppm (t, 1 H, *J* = 7 Hz, C=C<u>H</u>).

(*E*)-1-Bromo-1-chloro-1-hexene (7a, via Bromination):
The crude (*E*)-1-chloro-1-hexenyltrimethylsilane derived from 1-hexynyltrimethylsilane (20 mmol) according to the literature procedure[6] is diluted with dichloromethane (20 ml). To the resultant solution is added at −78 °C in the dark a 1 molar solution (24 ml, 24 mmol) of bromine in dichloromethane while maintaining the temperature during the addition below −60 °C. The mixture is stirred for 30 min at −78 °C, gradually warmed to 0 °C, stirred for 30 min at this temperature, and then treated with a 1.5 molar solution (26.27 ml, 40 mmol) of sodium methoxide in methanol while keeping the temperature during the addition below 10 °C. The resultant white slurry is stirred for 30 min at 0 °C, then for 2 h at 25 °C, and then is poured into water (80 ml). The layers are separated, and the aqueous phase is extracted with pentane (3 × 30 ml). The combined extracts are washed with saturated aqueous sodium chloride (60 ml), treated with a few crystals of BHT, then dried with magnesium sulfate. The filtrate is concentrated and the residue obtained is distilled through a short Vigreux column: yield: 3.1 g (80%); b.p. 57 °C/8.5 torr; n_D^{23}: 1.4809.

$C_6H_{10}BrCl$ (196.0)

M.S.: *m/e* = 195.9655 (M^+).

I.R. (neat): ν = 1610, 840 cm^{-1}.

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.9 (t, 3 H, *J* = 6 Hz); 1.3 (m, 4 H); 2.1 (m, 2 H); 6.0 ppm (t, 1 H, *J* = 8 Hz, C=C<u>H</u>).

(*E*)-1-Bromo-1-chloro-2-cyclohexylethene (7c via Chlorination):
To a solution of pure (*Z*)-1-bromo-2-cyclohexylethenyltrimethylsilane[6] (5.2 g, 20 mmol) in chloroform (10 ml) is added in the dark at −60 °C (chloroform/Dry Ice bath) a 0.6 molar solution (40 ml, 24 mmol) of chlorine in chloroform while maintaining the temperature below −45 °C. The resulting yellow solution is stirred for 30 min at −60 °C, gradually warmed to 0 °C, stirred for 30 min at this temperature, and then treated with a 1.5 molar solution (20.67 ml, 40 mmol) of sodium methoxide in methanol while keeping the temperature during the addition below 10 °C. The resultant white slurry is stirred for 30 min at 0 °C, then for 2 h at 25 °C, and then is poured into water (80 ml). The layers are separated, and the aqueous phase is extracted with pentane (3 × 30 ml). The combined extracts are washed with a saturated aqueous solution of sodium chloride, treated with a few crystals of BHT, then dried with magnesium sulfate. The filtrate is concentrated and the residue obtained is distilled through a short Vigreux column; yield: 3.7 g (84%); b.p. 54 °C/0.8 torr; n_D^{26}: 1.5165.

$C_8H_{12}BrCl$ (222.0)

M.S.: *m/e* = 221.9812 (M^+).

I.R. (neat): ν = 1610, 840 cm^{-1}.

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.5–2.0 (m, 10 H); 2.3 (m, 1 H); 5.8 ppm (d, 1 H, *J* = 9 Hz, C=C<u>H</u>).

1,1-Dibromo-2-cyclohexylethene (10c):
The crude (*E*)-1-bromo-2-cyclohexylethenyltrimethylsilane (20 mmol) prepared according to the literature procedure[6] is diluted with dichloromethane (20 ml). To the resultant solution is added sequentially a solution of bromine (24 mmol) in dichloromethane and a solution of sodium methoxide (40 mmol) in methanol as described above for the preparation of **7a**. Work-up and distillation affords **10c**; yield: 4.7 g (87%); b.p. 66–67 °C/1 torr; n_D^{24}: 1.5403.

$C_8H_{12}Br_2$ (265.9)

M.S.: *m/e* = 265.9306 (M^+).

I.R. (neat): ν = 1610, 840, 820, 770 cm^{-1}.

^{1}H-N.M.R. (CCl_4/TMS): δ = 0.8–2.0 (m, 10 H); 2.3 (m, 1 H); 6.2 ppm (d, 1 H, *J* = 9 Hz, C=C<u>H</u>).

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Table. Yields of 1,1-Dihalo-1-alkenes derived from 1-Halo-1-alkenylboranes or 1-Halo-1-alkenyltrimethylsilanes

Starting material[a]	R[1]	Halogen added	Yield [%] of Product 2	7	10	Isomeric[c] purity [%]	b.p./torr [°C]	n_D [°C]	Molecular formula[b] or Lit. b.p./torr [°C]
3a	*n*-C_4H_9	Br_2	73			97	74–77°/23	1.4777 (23)	$C_6H_{10}BrCl$ (196.0)
3b	*n*-C_6H_{13}	Br_2	65			98	53°/1	1.4782 (26)	$C_8H_{14}BrCl$ (224.0)
3c	*c*-C_6H_{11}	Br_2	74			98	97–99°/10	1.5141 (22)	$C_8H_{12}BrCl$ (222.0)
5a	*n*-C_4H_9	Br_2		80[d]		99	57°/8	1.4809 (23)	$C_6H_{10}BrCl$ (196.0)
5b	*n*-C_6H_{13}	Br_2		69[d]		99	55°/1	1.4791 (24)	$C_8H_{14}BrCl$ (224.0)
5c	*c*-C_6H_{11}	Br_2		96		91[e]	—	—	— —
5d	*t*-C_4H_9	Br_2		82		57[e]	—	—	— —
6a	*n*-C_4H_9	Cl_2		83		98	59–61°/10	1.4798 (24)	$C_6H_{10}BrCl$ (196.0)
6c	*c*-C_6H_{11}	Cl_2		84		95	54°/8	1.5165 (26)	$C_8H_{12}BrCl$ (222.0)
6d	*t*-C_4H_9	Cl_2				73[e]	—	—	— —
9a	*n*-C_4H_9	Br_2			62		68–69°/7	1.5050 (24)	90–92°/22[12]
9c	*c*-C_6H_{11}	Br_2			67		70–72°/2	1.5386 (26)	$C_8H_{12}Br_2$ (265.9)
11b	*n*-C_6H_{13}	Br_2			89[d]		55–56°/1	1.5006 (24)	120–122°/22[12]
11c	*c*-C_6H_{11}	Br_2			87[d]		66–67°/1	1.5403 (24)	$C_8H_{12}Br_2$ (265.9)
11e	C_6H_5	Br_2			76[d]		47–49°/0.02	1.6329 (24)	108°/3.5[13]

[a] The 1-halo-1-alkenylsilanes **(5, 6, 11)** were prepared as described in Ref.[6], except that a 50% excess instead of a 25% excess of bromine was used for the bromination of the alkenylalane precursors of compounds **6** and **11.**

[b] The microanalyses showed the following deviations from the calculated values: C, ±0.07; H, ±0.12; Br, ±0.24; Cl, ±0.28.

[c] The isomeric purities of the (*E*)- and (*Z*)-1-bromo-1-chloro-1-alkenes were determined on a SE-30 glass capillary column (90 m). The differences in chemical shifts of the vinyl protons of the (*E*)- and (*Z*)-isomers are very small (0.6 Hz at 90 MHz), the (*E*)-isomer absorbing at lower field.

[d] The yield is based on crude 1-chloro- *(6)* or 1-bromo-1-alkenylsilane **(11).**

[e] The yield and the isomer distribution were determined by G.L.C. using authentic reference compounds.

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[11] To inhibit isomerization, solutions of 1-bromo-1-chloro-1-alkenes were treated with a few crystals of BHT prior to removal of the solvents. Also, the isolated compounds were stored over a few crystals of BHT.

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