A General, Stereoselective Synthesis of *trans*-Disubstituted Alkenes via Thexylchloroborane

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We recently reported that thexyl-chloroborane/methyl sulfide **(1)** is a versatile reagent for the selective monohydroboration of alkenes of various structural types[1]. The resulting thexyl-alkyl-chloroboranes **(2)**, unlike thexyl-monoalkyl-boranes **(3)**[2], are unusually stable. Consequently, they can be prepared, stored, and used for the synthetic purposes. The hydridation[3] of **2** in the presence of a second alkene produces the corresponding mixed thexyl-dialkyl-borane **(4)**[4]. This sequence represents a stepwise hydroboration wherein two different alkyl groups can be attached to thexylborane (Scheme **A**).

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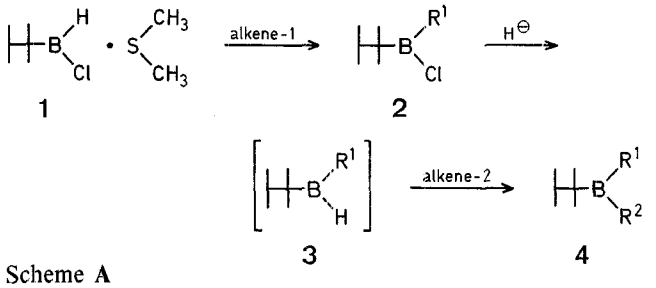
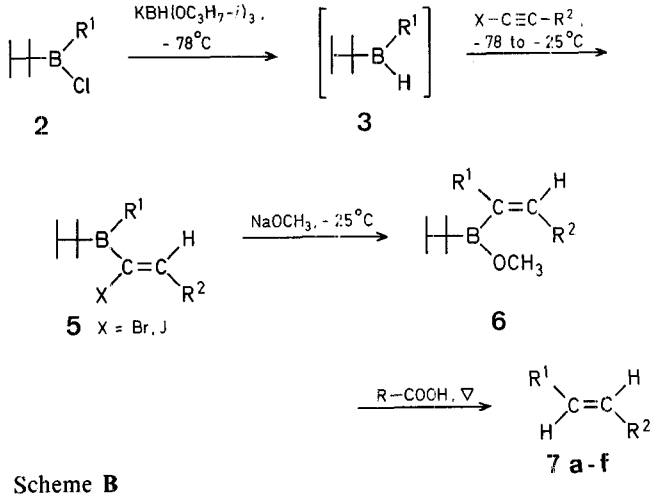


Scheme A

We also reported that the hydroboration of 1-halo-1-alkynes with **3**, generated *in situ* via the hydridation of **2**, produces the corresponding thexylalkyl-α-halovinylboranes in excellent yields. Treatment with sodium methoxide affords the corresponding 1,2-disubstituted vinylboranes[5]. These derivatives have been converted to the unsymmetrical ketones by oxidation with alkaline hydrogen peroxide[5]. Alternatively, the protonolysis of such 1,2-disubstituted vinylboranes should provide the corresponding *trans*-disubstituted alkenes. Therefore, we undertook to explore this aspect of α-halovinylboranes.

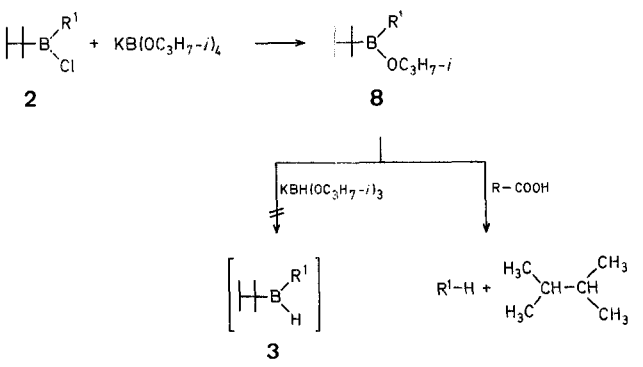
The hydridation with potassium triisopropoxyborohydride of **2** derived from **1** and a terminal alkene provides the corresponding **3**. It is necessary to carry out the hydridation at −78 °C in order to minimize disproportionation or dehydroboration of **3**, both of which are known to be facile[2]. The subsequent treatment with 1-halo-1-alkyne affords the desired thexyl-alkyl-α-halovinyl-borane[6] **(5)**. The action of sodium methoxide induces the migration of R^1 selectively, with the formation of **6**. Protonolysis with 2-methylpropanoic acid produces the desired *trans*-disubstituted alkene **(7)** (Scheme **B**). To test this procedure, a variety of pure *trans*-disubstituted alkenes **(7a–f)** were synthesized from representative terminal alkenes and haloalkynes (Table). The reactions were satisfactory, giving yields of ~90% by G.L.C. and 70–80% of isolated product.



Scheme B

The reaction sequence employed here involves mild conditions capable of tolerating many functional groups. In the case of alkenes carrying acetate groups, the protonolysis with 2-methylpropanoic acid could cause transesterification, forming the corresponding 2-methylpropanoate. However, this could be avoided by carrying out the protonolysis with acetic acid[7].

The G.L.C. analysis of the crude products revealed the presence of 5–10% of impurities, usually the alkane R^1—H or the unreacted haloalkyne. These impurities arise from the side-reaction (Scheme **C**) caused by the presence of 5–10% of potassium tetraisopropoxyborate in the potassium triisopropoxyborohydride.



Scheme C

The haloalkyne corresponding to the amount of **8** remains unreacted[8]. However, a careful distillation provides pure **7** free of such impurities.

It appears that unhindered primary alkyl groups have considerably higher migratory aptitudes relative to the secondary alkyl groups examined earlier[9]. Consequently, the migration of the thexyl group is less (1–2%) when R^1 is a primary alkyl group than it is when R^1 is a secondary alkyl group (2–7%)[9].

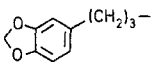
In summary, the limitations associated with the original synthesis of *trans*-disubstituted alkenes[10], largely overcome by the modified procedure[9], have now been completely circumvented with thexylmonochloroborane. The present study has emphasized especially the synthesis of *trans*-disubstituted alkenes carrying unhindered primary alkyl groups, some carrying functionalities, derivatives which could not be handled by the earlier modifications[9,10]. The reaction, however, appears to be general, and it should be possible to introduce other types of alkyl groups as well[11]. The mild reaction conditions that tolerate many common functional groups, coupled with the high yields of both chemically and stereoisomerically pure products, will undoubtedly make it a valuable method in organic synthesis. We are presently exploring applications of this method for the synthesis of insect pheromones.

Melting and boiling points are uncorrected. The G.L.C. analyses were carried out on a Varian 1400 gas chromatograph (column 12 ft × 1/8 in packed with 10% SE-30 on Chromosorb-WHF, temperature 60–200 °C programmed 8 °C/min, carrier gas nitrogen). ^{1}H-N.M.R.- and ^{13}C-N.M.R.-spectra were recorded on Varian T-60 and FT-80A spectrometers, respectively. The alkenes and potassium triisopropoxyborohydride were obtained from Aldrich Chemical Company. Alternatively, potassium triisopropoxyborohydride was prepared from potassium hydride and triisopropoxyborane in tetrahydrofuran[12]. The freshly prepared reagent contains less of the undesired by-product, potassium tetraisopropoxyborate, than the commercial material. The alkynes (from Farchan Division) were converted to the haloalkynes by literature procedures[13].

***trans*-7-Tetradecene (7a):**

To a 2.17 molar solution of **1** in dichloromethane (9.22 ml, 20 mmol) in a 250-ml reaction flask is added 1-hexene (2.5 ml, 20 mmol) at 0 °C under nitrogen[14]. The mixture is stirred for 2 h at 25 °C, cooled to −78 °C, and diluted with tetrahydrofuran (20 ml). To the well-stirred solution is added a 0.86 molar solution of potassium triisopropoxyborohydride (23.2 ml, 20 mmol), also cooled to −78 °C. The mixture is thoroughly stirred for 10 min, 1-bromo-1-octyne[15] (3.1 ml, 19 mmol) is added, and again, mixed well. After 10 min, the flask is brought to −25 °C and maintained at this temperature for 2 h with vigorous stirring. To the reaction mixture is added a 4 molar solution of sodium methoxide in methanol (15 ml, 60 mmol), dropwise, at −25 °C, and

Table. Stereoselective Synthesis of *trans*-Disubstituted Alkenes

Alkene	Haloalkyne	Product[a] No.	R^1	R^2	Yield[b] [%]	b.p. [°C]/torr found	b.p. [°C]/torr reported	n_D^{20} found	n_D^{20} reported
1-hexene	1-bromo-1-octyne	**7a**	n-C_6H_{13}	n-C_6H_{13}	77 (90)	69–71°/0.4	—	1.4385	1.4470[18]
1-octene	1-iodo-1-octyne	**7b**	n-C_8H_{17}	n-C_6H_{13}	(92)	—	—	—	—
1-octene	1-bromo-1-hexyne	**7c**	n-C_8H_{17}	n-C_4H_9	76	56–61°/0.1	—	1.4365	1.4382[18]
4-pentenyl acetate	1-iodo-1-butyne	**7d**[c]	AcO–$(CH_2)_5$–	C_2H_5	74	71–72°/0.5	65–70°/0.3	1.4352	1.4343[19], 1.4386[17] (n_D^{25})
4-pentenyl acetate	1-bromo-1-hexyne	**7e**[c]	AcO–$(CH_2)_5$–	n-C_4H_9	71	82–83°/0.2	—	1.4405	—
safrole	1-iodo-1-butyne	**7f**[d]		C_2H_5	79	106–108°/0.3	—	1.5170	—

[a] Distilled products (from 20 mmol-scale reactions); chemical purities by G.L.C. are >96%, and isomeric purities (^{13}C-N.M.R.) are >99%; ^{1}H-N.M.R. and ^{13}C-N.M.R. spectra are satisfactory.

[b] Yields of isolated products based on 1-halo-1-alkyne; values in the parentheses indicate the G.L.C. yields.

[c] Protonolysis with acetic acid (see experimental).

[d] ^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 0.95 (t, 3H); 1.4–2.4 (m, 6H); 2.50 (t, 2H); 5.4 (m, 2H); 5.78 (s, 2H); 6.4–6.8 ppm (m, 3H).

the mixture is allowed to warm up to room temperature. After 1 h, the solvents are removed completely under the aspirator vacuum, 2-methylpropanoic acid (30 ml) is added, and the mixture heated under reflux for 6 h. The cooled mixture is poured into water (100 ml), neutralized by adding a saturated solution of sodium hydrogen carbonate, the organic layer is separated, and the aqueous layer is extracted with pentane (3 × 50 ml). The combined organic extract is washed with sodium hydrogen carbonate solution (3 × 50 ml), followed by washing with water (100 ml), and dried with anhydrous potassium carbonate. Distillation provides *trans*-7-tetradecene; yield: 2.9 g (77% based on the bromoalkyne); b.p. 69–70°C/0.4 torr; n_D^{20}: 1.4385; G.L.C. purity: >98%.

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 0.7–1.6 (m, 22H); 1.9–2.2 (m, 4H); 5.4 ppm (m, 2H).

^{13}C-N.M.R. ($CDCl_3$/TMS): δ = 13.8; 22.5; 28.7; 29.5; 31.7; 32.5 (alkyl C); 130.1 ppm (C=C). The single vinylic carbon ($\delta \approx 130.1$) reveals the absence of any significant amount of the corresponding *cis*-isomer[16].

***trans*-6-Undecenyl Acetate (7e):**

The preparation of thexylalkylchloroborane **(2)** from **1** and 4-pentenyl acetate, the hydroboration of 1-bromo-1-hexyne with **3**, and the subsequent conversion to **6** by the action of sodium methoxide, are carried out as described in the previous paper[5]. The reaction mixture is cooled to 0°C and water (100 ml) is added slowly with vigorous stirring. The aqueous layer is saturated with sodium chloride and extracted with diethyl ether (3 × 50 ml). The combined organic extract is washed with water (2 × 50 ml) and dried with anhydrous sodium sulfate. The solvents and volatile materials are removed on a rotovapor and the residue is heated under reflux with glacial acetic acid (30 ml) for 20 h. The product is isolated as described for **7a**. Distillation provides *trans*-6-undecenyl acetate **(7e)**; yield: 3.3 g (82%); b.p. 82–84°C/0.3 torr; n_D^{20}: 1.4405; G.L.C. purity: >99%.

^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 0.7–1.7 (m, 13H); 1.7–2.2 (m+s, 7H); 4.03 (t, 2H); 5.4 ppm (m, 2H).

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6 When potassium triisopropoxyborohydride was added to **2** in the presence of 1-halo-1-alkyne, a considerable amount of an undesirable side-product was formed, see Ref.[5].

7 Surprisingly, in the case of **6**, when R^1 was derived from 4-pentenyl acetate, the direct protonolysis following the base-induced migration failed. The borane intermediate had to be separated from the salts prior to protonolysis; see the experimental part.

8 This problem can be partially solved by using 95 mol% of the haloalkyne per mol of **2**.

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13 The bromoalkynes were prepared according to a literature procedure: E. Schulte, M. Goes, *Arch. Pharm. (Weinheim, Ger.)* **290**, 118 (1959); the iodoalkynes were prepared by the action of iodine on the corresponding alkynyllithium derivatives.

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15 When a freshly prepared pure solution of potassium triisopropoxyborohydride is used, 20 mmol of the haloalkyne can be added. The yield of **7** is slightly better.

16 We have observed that in most cases the vinyl carbons of *cis*- and *trans*-isomers have different chemical shifts.

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