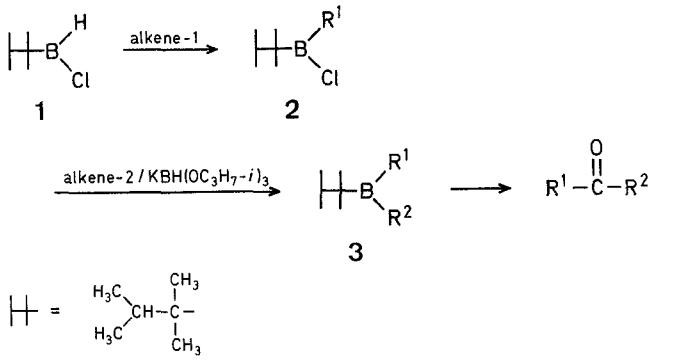
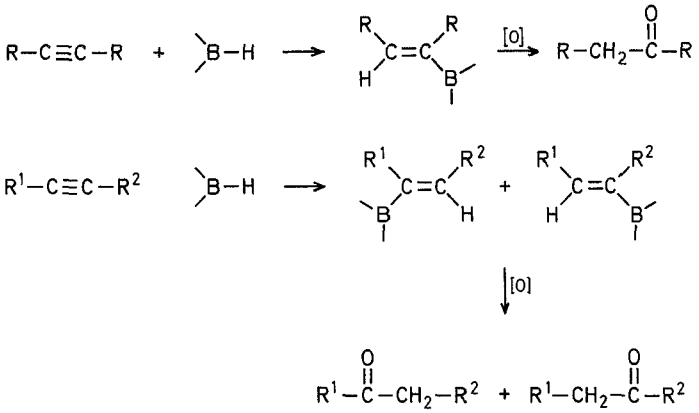


Scheme A

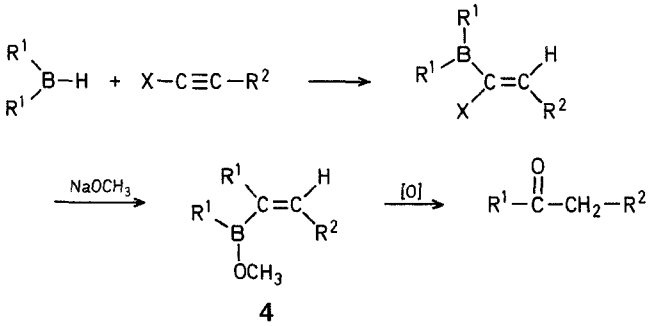
Alternatively, the ketones can also be prepared by the oxidation of vinylboranes, which, in turn, are obtained via the hydroboration of alkynes (Scheme **B**).



Scheme B

However, unsymmetrical alkynes usually form a mixture of two isomeric ketones. Development of a convenient method for the preparation of pure unsymmetrically substituted vinylboranes would open a simple route for the general, regioselective synthesis of ketones.

One method presently available for the synthesis of unsymmetrically substituted vinylboranes consists of the hydroboration of 1-halo-1-alkyne by dialkylboranes, followed by the base-induced migration of an alkyl group from boron to the vinylic carbon atom (Scheme **C**)[6].



Scheme C

There are two difficulties with the original procedure for the preparation of disubstituted vinylboranes. First, it requires dialkylboranes, whose availability by simple hydroboration is relatively limited[7]. Second, one of the two alkyl groups ($R^1$) from the dialkylborane is not utilized. The latter problem was solved by using thexylmonoalkylboranes for the hydroboration of haloalkynes with the thexyl moiety serving as a blocking group[8]. The low migratory aptitude of the thexyl group, as compared with that of primary and secondary alkyl groups,

## A Regioselective Synthesis of Ketones from Alkene and Haloalkyne Precursors via Thexylchloroborane

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The hydroboration reaction readily converts alkenes and alkynes into the corresponding organoboranes[1]. These organoboranes can be conveniently transformed into a variety of organic functional derivatives[2]. Carbonyl derivatives constitute one such class of compounds that has received considerable attention. Such ketones have been prepared from organoboranes via carbonylation, cyanidation, or carbenoidation reactions[1].

Thexylborane provides an elegant route for the conversion of two alkenes into the corresponding ketone[3]. However, there are some serious limitations, which have been recently circumvented by the use of a new reagent, thexylchloroborane (**1**)[4]. The mixed thexyldialkylboranes (**3**), prepared conveniently from **1**, can be readily converted into the corresponding unsymmetrical ketones (Scheme **A**)[5].

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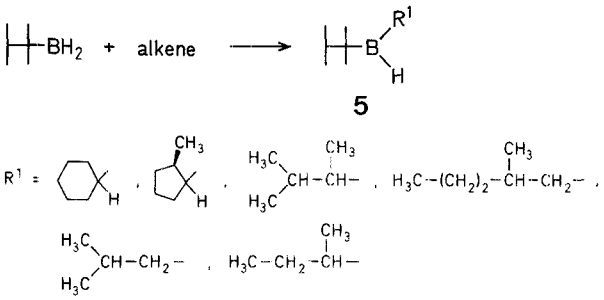
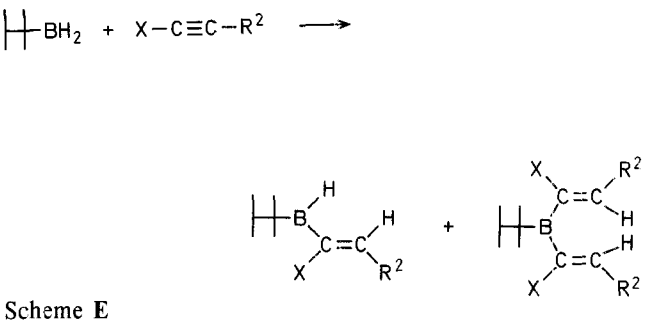
permits selective migration of such groups[8]. However, the scope of this approach is limited by the availability of suitable thexylmonoalkylboranes **(5)**. Only alkenes with intermediate steric requirements form **5** cleanly (Scheme **D**)[8,9].



Scheme **D**

In order to solve this problem, we tried to hydroborate the haloalkyne with thexylborane in the first step[10], so that the unhindered primary alkyl group could be introduced in the second stage. However, a competing dialkenylation of thexylborane decreases the yield of the desired vinylborane (Scheme **E**)[11].



Scheme **E**

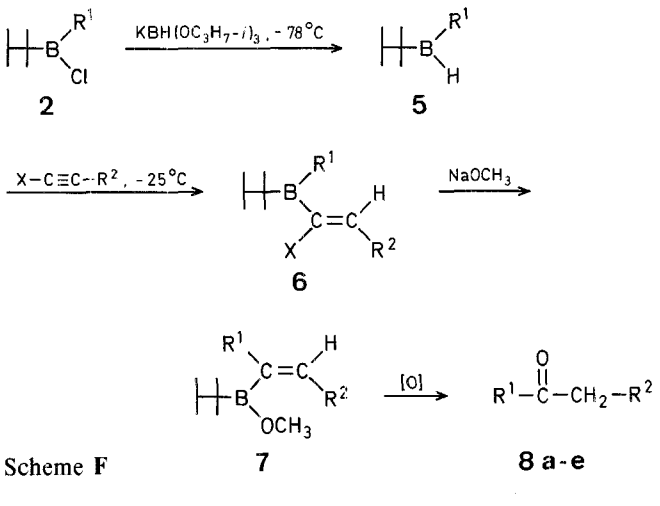
Consequently, we undertook to explore the possibilities of bringing together an alkene with a haloalkyne using **1**, followed by a selective migration of the alkyl group to the adjacent vinyl carbon to obtain the desired 1,2-dialkylvinylborane.

Simple oxidation of such an intermediate would provide the corresponding ketone. However, we encountered a number of difficulties.

When the alkyl-chloro-thexylborane was treated with potassium triisopropoxyborohydride in the presence of 1-halo-1-alkyne, an undesirable side-product was formed[12]. Fortunately, this difficulty could be overcome by first adding potassium triisopropoxyborohydride to generate **5** at low temperature, followed by rapid addition of the haloalkyne.

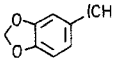
We examined the hydroboration of chloro-, bromo-, and iododooctyne with thexyl-*n*-octylborane in order to establish the effect of the halogen atom. It appears that 1-bromo-1-octyne and 1-iodo-1-octyne react with approximately the same ease, providing, after treatment with base and oxidation, comparable yields of the desired ketone (Table). The hydroboration of 1-chloro-1-octyne was relatively slow and it provided a lower yield of ketone upon similar work-up. Consequently, bromo- or iodoalkynes are preferable for this synthesis.

Thus, the preparation of **2** via simple hydroboration of alkene[4], followed by hydridation with potassium triisopropoxyborohydride at −78 °C, affords the corresponding thexylmonoalkylborane **5**. Subsequent hydroboration of 1-halo-1-



Scheme **F**

**Table.** The Synthesis of Ketones from Alkenes and Haloalkynes via Thexylchloroborane

| Alkene | Haloalkyne | Product[a] No. | $R^1$ | $R^2$ | Yield[b] [%] | m.p. [°C] or b.p. [°C]/torr found[c] | m.p. [°C] or b.p. [°C]/torr reported | $n_D^{20}$ found | $n_D^{20}$ reported |
|---|---|---|---|---|---|---|---|---|---|
| 1-octene | 1-iodo-1-octyne | **8** | $n$-$C_8H_{17}$ | $n$-$C_6H_{13}$ | (91) | — | — | — | — |
| | 1-bromo-1-octyne | | | | (88) | | | | |
| | 1-chloro-1-octyne | | | | (74) | | | | |
| 1-decene | 1-iodo-1-octyne | **8a** | $n$-$C_{10}H_{21}$ | $n$-$C_6H_{13}$ | 81 | 44–45° | 44.8–46°[19] | — | — |
| 1-decene | 1-iodo-1-butyne | **8b** | $n$-$C_{10}H_{21}$ | $C_2H_5$ | 80 | 24–25° | 24.5–25.7°[20] | — | — |
| 2-methyl-1-pentene | 1-bromo-1-octyne | **8c**[d] | $n$-$C_3H_7$-CH($CH_3$)-$CH_2$- | $n$-$C_6H_{13}$ | 87 | 85–87°/0.3 | 136.5°/10[21] | 1.4353 | 1.4358[21] |
| 4-pentenyl acetate | 1-bromo-1-octyne | **8d** | HO-$(CH_2)_5$- | $n$-$C_6H_{13}$ | 81[e] | 49–50.5° | — | — | — |
| safrole | 1-bromo-1-hexyne | **8e**[f] |  | $n$-$C_4H_9$ | 86[g] | 130–132°/0.1 | — | 1.5090 | — |

[a] The structures were confirmed by $^1$H-N.M.R. analyses.

[b] Yields of pure (>98% by G.L.C.) products isolated (from 20 mmol-scale reactions) by distillation or crystallization (pentane, −78 °C); based on the haloalkyne used; values in parentheses indicate the G.L.C. yields.

[c] Further recrystallization did not increase the m.p.

[d] Contained ~2% of the thexyl-migrated ketone; in other cases, the corresponding impurities were < 1%.

[e] Recrystallized twice from pentane. The hydroxy ketone was obtained.

[f] $^1$H-N.M.R. ($CDCl_3$/TMS): $\delta$ = 0.7–2.1 (m, 11H); 2.1–2.8 (m, 6H); 5.81 (s, 2H); 6.5–6.8 ppm (m, 3H).

[g] Recovered as a solid at low temperature, dried in dessicator; distillation provides lower yields.

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alkyne with **5** proceeds cleanly at −25 °C with the formation of the desired α-halovinylborane **6**. The base-induced migration of the alkyl group to the adjacent carbon atom (→ **7**), followed by oxidation with alkaline hydrogen peroxide, provides the ketones **8** (Scheme F and Table).

The G.L.C. analysis of the crude products **8**, prior to distillation or crystallization, indicated 5–10% impurities (usually $R^1$—OH and X—C≡C—$R^2$), attributed to the presence of potassium tetraisopropoxyborate in potassium triisopropoxyborohydride[13]. However, these impurities can be removed during distillation or crystallization, providing >98% pure ketones. A small amount (<2%) of thexyl-migrated ketone was present (**8**; $R^1$ = thexyl) in some cases[14]. In contrast, the ketones prepared via cyanidation of thexyldialkylboranes[5] invariably contain small amounts of the corresponding symmetrical ketones[15].

We have emphasized the synthesis of ketones where $R^1$ is an unhindered primary alkyl group because the corresponding vinylboranes have not been available previously. However, the synthesis appears general[16], with no restrictions as to the nature of $R^1$ and $R^2$.

In summary, we now have a method for a general synthesis of ketones from alkene and alkyne components. The excellent yields of pure ketones realized by a reaction sequence involving such mild conditions should make this procedure quite valuable for complex organic syntheses. We are presently exploring the feasibility of applying this method to alkenes and alkynes carrying common functional groups. The 1,2-disubstituted vinylboranes prepared during this investigation are also readily converted to the corresponding *trans*-alkenes[13].

Melting and boiling points were uncorrected. G.L.C. analyses were carried out on 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. spectra were recorded on Varian T-60 instrument. The alkenes were obtained from Aldrich Chemical Company. The alkynes (from Farchan Division) were converted to the haloalkynes by literature procedures[17].

**6-Oxo-tridecan-1-ol (8d):**

To 4-pentenyl acetate (2.82 ml, 20 mmol) in a 100-ml reaction flask[18], is added a 2.17 molar solution of thexyl-chloroborane/dimethyl sulfide complex in dichloromethane (9.22 ml, 20 mmol) at 0 °C, under nitrogen. The mixture is stirred for 2 h at 25 °C, cooled to −78 °C, and diluted with tetrahydrofuran (20 ml). This solution is added to a 250-ml reaction flask containing 1.0 molar potassium triisopropoxyborohydride solution (20 ml, 20 mmol) at −78 °C, the mixture is stirred for 10 min, and 1-bromo-1-octyne (3.1 ml, 19 mmol) is added. The mixture is thoroughly stirred, maintained at −78 °C for 10 min, and finally brought to −25 °C, where it is maintained for 2 h with vigorous stirring. Then, 4 molar sodium methoxide solution in methanol (15 ml, 60 mmol) is added dropwise, and the mixture is allowed to warm up to room temperature where it is maintained for 1 h with stirring. The reaction mixture is then oxidized by adding tetrahydrofuran (50 ml), 3 normal sodium hydroxide (25 ml, 75 mmol) and 30% hydrogen peroxide (25 ml, excess) at 0 °C, followed by stirring at 25 °C for 1 h and under reflux for 10 h. The organic layer is separated, the aqueous layer is extracted with pentane (3 × 50 ml), the combined organic extract is washed with water (2 × 50 ml), and dried with anhydrous potassium carbonate. The solvents are removed on a rotovapor and the residue is crystallized from pentane at −78 °C. 6-Oxotridecan-1-ol is obtained; yield: 3.3 g (81%); m.p. 49–50.5 °C; G.L.C. purity: >99%.

$^1$H-N.M.R. ($CDCl_3$/TMS): $\delta$ = 0.7–1.8 (m, 19 H); 2.11 (t, $J$ = 5 Hz, 1 H); 2.40 (t, $J$ = 6 Hz, 4 H); 3.6 ppm (m, 2 H).

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