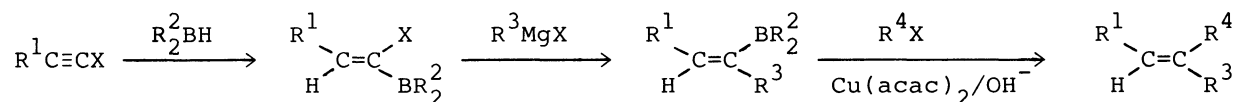# THE SYNTHESIS OF REGIO- AND STEREOSPECIFICALLY SUBSTITUTED 1,4-DIENES OR CONJUGATED ENYNES FROM INTERNAL ALKENYLDIALKYLBORANES

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Internal alkenyldialkylboranes give regio- and stereospecifically designed 1,4-dienes or conjugated enynes, bearing a substituent at the internal alkenyl carbon atom, by a coupling reaction with allyl bromide or 1-bromo-1-alkynes.

Recently, the authors reported a synthesis of internal (E)-alkenyl-dialkylboranes by coupling reactions of 1-halo-1-alkenyldialkylboranes with Grignard reagents.[1] Regio- and stereospecifically designed internal alkenyldialkylboranes, thus obtained, seem to have a wide variety of application to organic synthesis.

On the other hand, several methods have been reported for coupling reactions of alkenyldialkylboranes with organic halides.[2]

$$R^1C{\equiv}CX \xrightarrow{R^2_2BH} {}^{R^1}_{\;H}{>}C{=}C{<}^{X}_{BR^2_2} \xrightarrow{R^3MgX} {}^{R^1}_{\;H}{>}C{=}C{<}^{BR^2_2}_{R^3} \xrightarrow[Cu(acac)_2/OH^-]{R^4X} {}^{R^1}_{\;H}{>}C{=}C{<}^{R^4}_{R^3}$$

Scheme 1.

An application of the above cross-coupling reactions to such internal alkenyldialkylboranes expected to be a simple synthetic method for 1,4-dienes or conjugated enynes substituted at the internal alkenyl carbon atom.

To examine above, two methods involving catalytic coupling reaction, in which tetrakis(triphenylphosphine)palladium[3] and bis(acetylacetonato)copper[4] were used as catalysts, were chosen because of their simplicity of the procedures.

1-Iodo-1-hexyne was employed as a substrate, and it was successively treated with dicyclohexylborane or bis(1,2-dimethylpropyl)borane and Grignard reagents. 1-Substituted 1-hexenyldialkylboranes, thus obtained, were allowed to react with allyl bromide in the presence of catalytic amount of alkaline tetrakis(triphenylphosphine)palladium or alkaline bis(acetylacetonato)copper (Scheme 1).

Alkaline tetrakis(triphenylphosphine)palladium did not show any catalytic property for the reaction. However, in the presence of alkaline bis(acetyl-

acetonato)copper, corresponding 4-substituted 1,4-nonadienes were obtained in good yields. Particularly, in the case that both $R^3$ and $R^4$ (in Scheme 1) were allyl, a high yield (90% based on 1-iodo-1-hexyne) was obtained.

In similar reactions using 1-bromo-1-alkynes instead of allyl bromide as $R^4X$, corresponding substituted enynes were obtained.

These results are shown in Table 1.

Table 1.  Products and yields of substituted 1,4-dienes and conjugated enynes

| $\begin{array}{c} n-C_4H_9 \\ \quad \diagdown C=C \diagdown \\ H \quad\quad R^3 \end{array} \begin{array}{c} BR^2_2 \end{array}$ a) | | | | Products and yields/% b) $\quad n-C_4H_9\diagdown C=C\diagup R^4 \diagdown R^3 \; (over\,H)$ | $n-C_4H_9\diagdown C=C\diagup R^4 \diagdown R^2 \;(over\,H)$ |
|---|---|---|---|---|---|
| $R^2$ | $R^3$ | $R^4$ of $R^4Br$ | | (Compd. no) | |
| $c\text{-}C_6H_{11}$ | $CH_3$ | $CH_2CH=CH_2$ | 80 | (1) | 2 |
| | $CH_2CH=CH_2$ | $CH_2CH=CH_2$ | 90 | (2) | 0 |
| $\begin{array}{c}CHCHCH_3\\CH_3\;\;CH_3\end{array}$ | $CH_3$ | $CH_2CH=CH_2$ | 84 | (1) | 4 |
| | $n\text{-}C_3H_7$ | $CH_2CH=CH_2$ | 85 | (3) | 3 |
| $c\text{-}C_6H_{11}$ | $CH_2CH=CH_2$ | $C{\equiv}CC_4H_9\text{-}n$ | 34 | (4) | 3 |
| $\begin{array}{c}CHCHCH_3\\CH_3\;\;CH_3\end{array}$ | $n\text{-}C_3H_7$ | $C{\equiv}CC_4H_9\text{-}n$ | 70 | (5) | 3 |
| | $n\text{-}C_3H_7$ | $C{\equiv}CC_4H_9\text{-}n$ | 66 | (6) | 3 |

a) Prepared by the successive reactions of 2 mmol of 1-iodo-1-hexyne with 2 mmol of dialkylborane at 0 °C and 2 mmol of Grignard reagent at -50 °C.
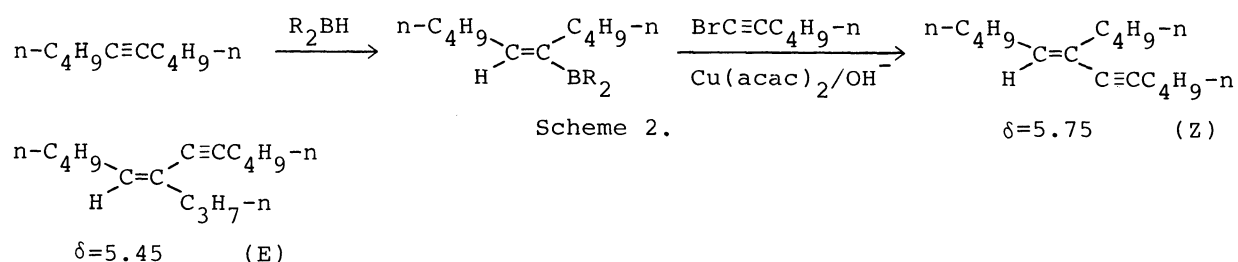b) Determined by VPC.

In the bis(acetylacetonato)copper-catalyzed cross-coupling reactions of alkenyldialkylboranes with allyl halides or 1-halo-1-alkynes, allyl or 1-alkynyl groups were introduced to $\alpha$-alkenyl carbon atom in a complete retention of configuration giving internal alkenes.[4] From the analogy, $R^4$ is suggested to be stereospecifically introduced in retention of configuration giving the 1,4-dienes or the conjugated enynes as depicted in Scheme 1.
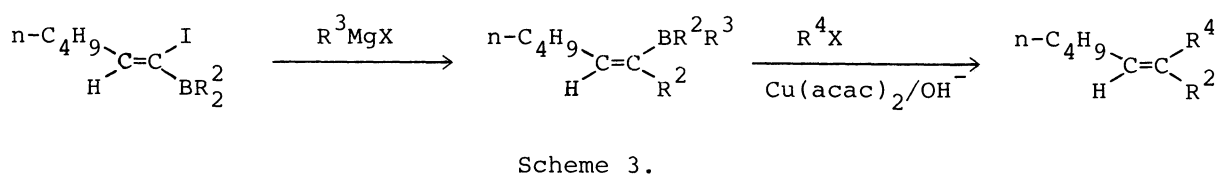
On the other hand, the $\delta$ value of alkenyl proton's absorption in the ^{1}H NMR spectrum of 7-propyl-7-dodecen-5-yne ($\delta$=5.45), obtained by the present reaction, differs markedly from that of (Z)-7-butyl-7-dodecen-5-yne ($\delta$=5.75), obtained by the reaction in Scheme 2. This fact supports above suggestion (the configuration of the former compound is E).

Examinations of the products by ^{1}H NMR spectra and by vapor phase chromatography using a glass capillary column revealed that the present products were isomerically pure.

One disadvantage of the present reaction is the contamination of the products by a small amount of by-product, 1,4-dienes or conjugated enynes whose internal alkenyl carbon atom are substituted by cyclohexyl or 1,2-dimethyl-
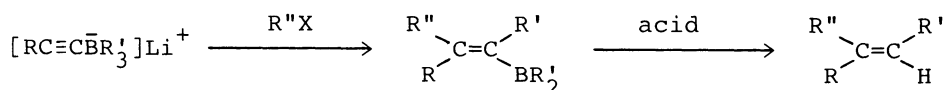
$$
\text{n-C}_4\text{H}_9\text{C}{\equiv}\text{CC}_4\text{H}_9\text{-n} \xrightarrow{\text{R}_2\text{BH}} \underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{BR}_2}{\overset{\text{C}_4\text{H}_9\text{-n}}{}} \xrightarrow[\text{Cu(acac)}_2/\text{OH}^-]{\text{BrC}{\equiv}\text{CC}_4\text{H}_9\text{-n}} \underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{C}{\equiv}\text{CC}_4\text{H}_9\text{-n}}{\overset{\text{C}_4\text{H}_9\text{-n}}{}}
$$

Scheme 2.                    $\delta = 5.75$       (Z)

$$
\underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{C}_3\text{H}_7\text{-n}}{\overset{\text{C}{\equiv}\text{CC}_4\text{H}_9\text{-n}}{}}
$$

$\delta = 5.45$       (E)

propyl group, (except for the case that both $\text{R}^3$ and $\text{R}^4$ are allyl). This by-product may be derived from an internal alkenyldialkylborane, formed as a minor product in the Grignard reaction stage (Scheme 3). However, in most cases

$$
\underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{BR}_2^2}{\overset{\text{I}}{}} \xrightarrow{\text{R}^3\text{MgX}} \underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{R}^2}{\overset{\text{BR}^2\text{R}^3}{}} \xrightarrow[\text{Cu(acac)}_2/\text{OH}^-]{\text{R}^4\text{X}} \underset{\text{H}}{\overset{\text{n-C}_4\text{H}_9}{}}\text{C}{=}\text{C}\underset{\text{R}^2}{\overset{\text{R}^4}{}}
$$

Scheme 3.

it is removed from the reaction mixture by careful column chromatography or by preparative vapor phase chromatography.

Pelter et al. reported a synthesis of trisubstituted ethylenes, whose three substituents were defined arbitrarily to a certain extent, by reactions of lithium trialkylalkynylborates with organic halides followed by protonolysis with acid.[5] In these reactions, R" of organic halide attacks at the β-carbon atom and R' on boron atom migrates to the α-carbon atom.

$$
[\text{RC}{\equiv}\text{C}\bar{\text{B}}\text{R}_3']\text{Li}^+ \xrightarrow{\text{R"X}} \underset{\text{R}}{\overset{\text{R"}}{}}\text{C}{=}\text{C}\underset{\text{BR}_2'}{\overset{\text{R'}}{}} \xrightarrow{\text{acid}} \underset{\text{R}}{\overset{\text{R"}}{}}\text{C}{=}\text{C}\underset{\text{H}}{\overset{\text{R'}}{}}
$$

Like above synthesis, the present reaction is also a synthetic method for trisubstituted ethylenes using organoboranes and organic halides. However, in our reaction no alkyl group on the boron atom migrates to the α-carbon atom, but both alkyl groups of Grignard reagents and allyl or 1-alkynyl group are introduced into the α-carbon atom. Thus, such highly unsaturated compounds as 4-(2-propenyl)-1,4-nonadiene (2) and (E)-7-(2-propenyl)-7-dodecen-5-yne (4), which cannot easily be prepared by other methods, are synthesized by a relatively simple procedure and in a one-pot manner.

The following procedure for the synthesis of 4-(2-propenyl)-1,4-nonadiene is representative. A dry 25-ml flask equipped with a gas inlet for argon, a septum inlet with a serum cap and a magnetic stirring bar was flushed with argon. In the flask, 2 mmol of $\text{BH}_3$ in THF was successively treated with 4 mmol of cyclohexene (added at 0 °C and stirred at this temperature for 2 h) and 2 mmol of 1-iodo-1-hexyne (added at -10 °C and stirred at 0 °C). After removal of THF under reduced pressure, 3 ml of dry diethyl ether was added, and then 2 mmol

of allyl magnesium bromide in diethyl ether, prepared in another flask, was transferred into the solution at -50 °C by using a syringe.  The solution was stirred at this temperature for 1 h and then allowed to warm up to room temperature.  After removal of diethyl ether under reduced pressure, 3 ml of THF was added as the solvent.  The reaction mixture was successively treated with 2 ml of 3 mol $dm^{-3}$ aqueous sodium hydroxide (added at 0 °C and stirred for 0.5 h at room temperature), 0.1 mmol of $Cu(acac)_2$ (added at -15 °C), and 2 mmol of allyl bromide (added at -15 °C and stirred for 1 h at the same temperature). After an additional 20 h of the reaction at room temperature, the residual organoborane was decomposed by oxidation with alkaline hydrogen peroxide.  The reaction mixture was extracted three times with hexane and the combined extracts were washed with NaCl-saturated water and dried over anhydrous magnesium sulfate.  The reaction mixture was analyzed by VPC (5%-FFAP, supported on Diasolid M) using the internal standard method.

In the preparative scale reaction, the amounts of reagents and solvents were 10 times those in the analytical reaction.  4-(2-Propenyl)-1,4-nonadiene was isolated, in 81% yield, from the worked up reaction mixture by column chromatography using a neutral aluminium oxide column and hexane as eluent.
$^1$H NMR (CDCl , TMS) δ=0.89 (t, J=7 Hz, 3H), 1.24-1.42 (m, 4H), 1.90-2.15 (m, 2H), 2.69-2.78 (m, 4H), 4.95-5.06 (m, 4H),5.24 (t, J=7 Hz, 1H), and 5.62-5.87 (m, 2H);  IR (film) 1640, 990, and 910 $cm^{-1}$;  MS (m/z) 164 ($M^+$).

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