

$\text{Cp}_2\text{TiCl}_2$ -CATALYZED GRIGNARD EXCHANGE REACTIONS WITH ACETYLENES.  
A CONVENIENT METHOD FOR PREPARATION OF E-ALKENYL GRIGNARD REAGENTS

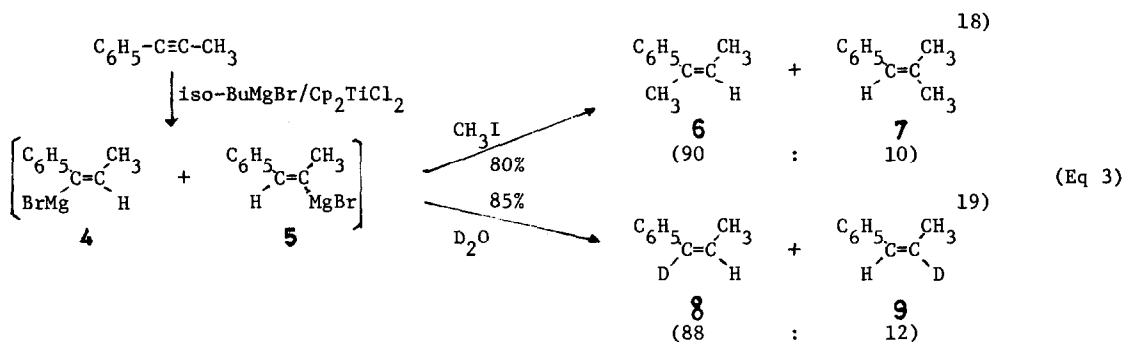
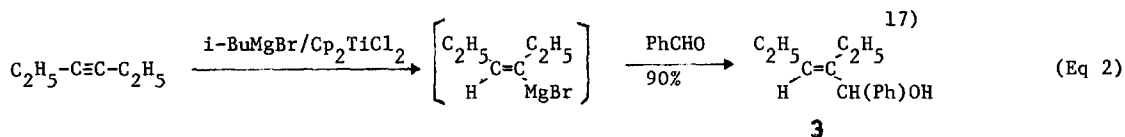
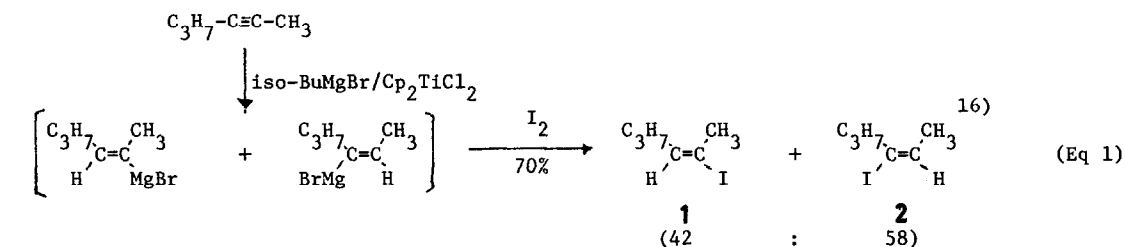
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Summary: Disubstituted acetylenes react with isobutylmagnesium halide in the presence of a catalytic amount of  $\text{Cp}_2\text{TiCl}_2$  in ether to afford E-alkenyl Grignard reagents selectively and in almost quantitative yields. The regiochemistry of this hydromagnesation reaction is high for alkylarylacetylenes and silylacetylenes giving E-ArC(MgBr)=CHR from alkylarylacetylenes, E-ArC(MgBr)=CH(SiMe<sub>3</sub>) from arylsilylacetylenes, and E-CHR=C(MgBr)(SiMe<sub>3</sub>) from alkylsilylacetylenes, respectively. Thanks to the high reactivity of the Grignard reagent, the present reaction offers a novel, selective and operationally simple route for preparation of trisubstituted olefins.

Over the past few decades, several hydrometalation reactions of acetylenes, such as B<sup>1</sup>, Al<sup>2</sup>, Si<sup>3</sup>, Sn<sup>4</sup> and Zr<sup>5</sup>, have been developed and are finding increasing acceptance as methodology for preparation of disubstituted and trisubstituted olefins. Grignard reagents are more reactive towards inorganic and organic electrophiles than organo borane, aluminum, silicon, tin or zirconium compounds. Therefore, though in principle hydromagnesation of acetylenes is very attractive, it is not yet well-developed.<sup>6</sup> Recently, Snider and his co-workers reported the nickel-catalyzed regio- and stereo-selective hydromagnesation reaction of silylacetylenes with ethylmagnesium bromide.<sup>10</sup> This reaction appears to be essentially the only known hydromagnesation of reasonable generality to be useful in synthesis, although the reaction co-produces 20-30% of the dimerization product of silylacetylene.<sup>11</sup> Colomer and Corriu showed that diphenylacetylene reacts with 5 equiv of isopropylmagnesium bromide in the presence of 5 mol% of  $\text{Cp}_2\text{TiCl}_2$ , affording a 70% yield of trans-stilbene and 30% of a mixture composed of cis-stilbene and 1,2-diphenylethane after hydrolysis.<sup>13</sup> These results, showing the low stereoselectivity of the  $\text{Cp}_2\text{TiCl}_2$ -catalyzed hydromagnesation reactions, discouraged work to apply the reaction to other disubstituted acetylenes.

We now wish to report our findings, which are in marked contrast to the results of Colomer and Corriu, that disubstituted acetylenes reacted with isobutylmagnesium bromide in the presence of a catalytic amount of  $\text{Cp}_2\text{TiCl}_2$  producing selectively the E-alkenylmagnesium bromides.<sup>14</sup>

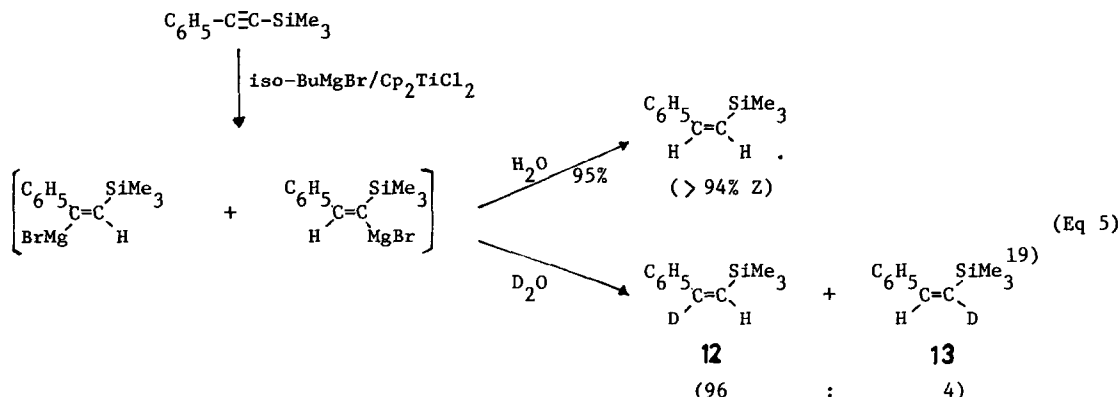
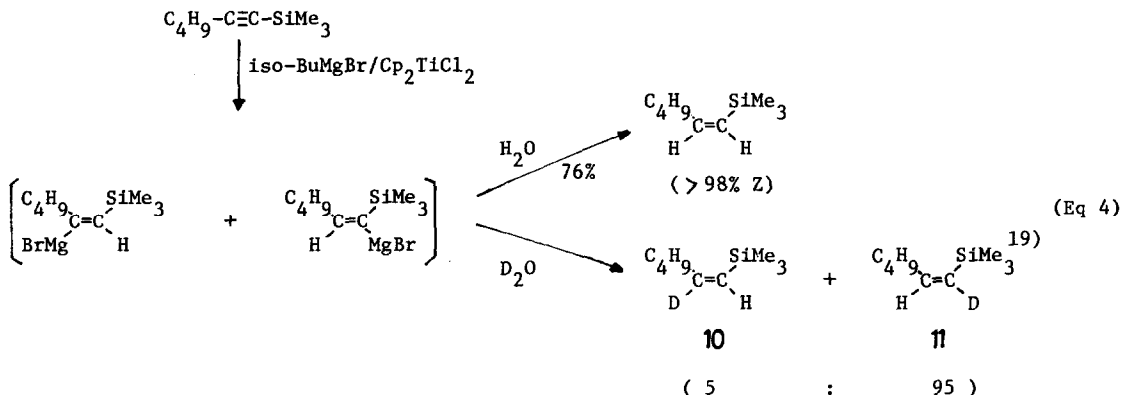
Internal acetylenes such as 2-hexyne, 3-hexyne, phenylmethylacetylene and diphenylacetylene reacted with 1.2 equiv of isobutylmagnesium bromide in the presence of 3 mol%  $\text{Cp}_2\text{TiCl}_2$  in ether to afford after workup 2-hexene (100% Z), 3-hexene (>99% Z), 1-phenyl-1-propene (>99% Z) and 1,2-diphenylethylene (96% Z) in 92-100% yield (GLC), respectively.<sup>15</sup> These results strongly indicate that the hydromagnesation of acetylenes proceeds with cis stereoconfiguration to afford E-alkenyl Grignard reagents. Not only to confirm the production of E-alkenyl Grignard reagents but also to establish the regiochemistry of the reaction, the reaction mixture was quenched with  $\text{D}_2\text{O}$ ,  $\text{CH}_3\text{I}$  or  $\text{PhCHO}$ . The results shown in eqs. 1, 2 and 3 clearly support the formation of E-alkenyl Grignard reagents. Noteworthy here is the fact that the reaction with phenylmethylacetylene proceeds regioselectively putting the magnesium atom at the carbon substituted with the phenyl group, whereas the hydromagnesation of unsymmetrically substituted dialkylacetylenes showed low regioselectivity.



It is clear that the present reaction provides a convenient preparational method for the synthesis of E-alkenyl Grignard reagents from symmetrically disubstituted acetylenes and the Grignard reagents of type **4** from phenylalkylacetylenes.

The usefulness of the present hydromagnesation reaction is further enhanced when one considers the examples of eqs 4 and 5, showing that silylacetylenes can also be stereoselectively hydromagnesated.<sup>20</sup> In particular, it is noteworthy that the reaction proceeds with high regioselectivity as indicated by the results of the deuterolysis of the reaction mixture.

However, the site where the magnesium atom is attached is different for alkyl- and aryl-silyl-acetylenes. On hydromagnesation of 1-trimethylsilyl-1-alkyne, the magnesium atom is placed at the 1-position, whereas in the case of phenylsilylacetylene, it is placed at the carbon bonded to the phenyl group.



As we noted for the  $\text{Cp}_2\text{TiCl}_2$ -catalyzed hydromagnesation reaction of conjugated dienes or styrene<sup>8</sup>, the reaction very likely proceeds as follows.  $\text{iso-BuTiCp}_2$ , initially from  $\text{Cp}_2\text{TiCl}_2$  and 2 equiv of isobutylmagnesium bromide, undergoes  $\beta$  hydride elimination giving isobutene and  $\text{Cp}_2\text{TiH}$  intermediate.  $\text{Cp}_2\text{TiH}$  can then add to the acetylene giving a vinyltitanium species. Then vinyl group transmetalates to magnesium by reaction with isobutylmagnesium bromide to afford the vinylmagnesium species and regenerates  $\text{iso-BuTiCp}_2$ .

While the full scope and mechanistic details remain to be further explored, it is clear that a novel, selective and operationally simple route to various vinyl Grignard reagents is now at our disposal.

## References and Notes

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11.  $(Ph_3P)_2NiCl_2$ -catalyzed hydromagnesation of acetylenes with isopropylmagnesium bromide<sup>12</sup>, and  $Cp_2TiCl_2$ -catalyzed addition reaction of  $MgH_2$  with acetylenes<sup>9</sup> were reported. Unfortunately, however, these reactions did not appear to be useful in organic synthesis because of low yields and low selectivity.
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14. We have noted that the reaction is highly dependent on Grignard reagents and solvent. Isobutylmagnesium chloride can be used instead of isobutylmagnesium bromide. Ethylmagnesium bromide did not give hydromagnesation products. Hydromagnesation was observed for reaction of isopropylmagnesium bromide with phenylmethylacetylene, but the yield was low ( $\approx 20\%$ ). Hydromagnesation reaction did not proceed in tetrahydrofuran.
15. Representative procedure: 125 mg (0.5 mmol) of  $Cp_2TiCl_2$  was added to a mixture of 3-hexyne (1.5 g, 18 mmol) and isobutylmagnesium bromide (22 mmol) in 20 ml of ether at room temperature under argon, and the reaction mixture was stirred for 1 h.
16. The ratio of **1** and **2** was determined from integration of methyl NMR peaks.
17. **3** shows satisfactory  $^1H$  NMR and IR spectra, in accord with the assigned structure.
18. After reaction, the ether was evaporated and  $CH_3I$  was added to a solution prepared in THF. Exothermic reaction occurred smoothly to give **6** and **7** in 80% yield (by distillation). The ratio was determined from GLC and  $^1H$  NMR peaks of vinyl protons.
19. The ratio was determined from the areas of vinyl proton peaks.
20. The reaction procedure, which is given below, is a little different to that for the reaction with alkyl or aryl disubstituted acetylenes. The same procedure gave the alkenyl Grignard reagents with a little bit lower regioselectivity. 4 mol%  $Cp_2TiCl_2$  was added to an ether solution of isobutylmagnesium bromide (8.6 mmol) at 0°C and the reaction mixture was stirred for 30 min under argon. Silylacetylene (7.2 mmol) was then added and stirred for 6 h at room temperature.