The Mechanism of Reaction of Benzophenone with Grignard Reagent Prepared from Propargyl Bromide

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ABSTRACT

The most possible reaction pathway in the mechanism was suggested that benzophenone ketyl might react with allenyl magnesium bromide to form the homopropargyl alcohol.

Keyword: Grignard reagent, Propargyl bromide, Benzophenone ketyl, Homopropargyl alcohol.

INTRODUCTION

The preparation of Grignard reagent from propargyl bromide was very difficult at first for dimerization often being observed.1 The first preparation of Grignard reagent from propargyl bromide was proposed by Newman and Watz in 1949. In general, the Grignard reagent prepared from propargyl bromide afford mixtures of propargylic Grignard reagent (HC≡CCH₂MgBr) and allenic Grignard reagent (H₂C=C=CHMgBr), with allenic Grignard reagent as major product.3 Moreau and Gaudemar4 suggested that there is fast equilibrium between propargylic Grignard reagent and allenic Grignard reagent. The preparation of allenyl magnesium bromide from propargyl bromide was also reported by several groups.5

The reactions of allenyl magnesium bromide with electrophilic reagents in principle gave the mixture of propargylic and allenic product, while only propargylic products for the reaction with aldehydes or ketones.5c,6 The allenyl magnesium bromide reacted with tributyltin chloride(ClSnBu₃) yielded a mixture of allenic and propargylic derivative in a ratio 7:93.7 The acetylenic product is obtained predominantly for the reaction of trimethyl-chlorosilane with allenyl magnesium bromide.8 The results of the reaction of Grignard reagent prepared from propargylbromidewith tin halide, chlorosilane, mercuric halide, ketone and aldehyde are summarized in Table 1.

Table 1

The distribution of propargyl product / allenyl product of reaction of H₂C=C=CHMgBr with different substances.
The mechanism of the alkyl Grignard reagents addition to ketone or benzophenone has become much clear owing to the effort of the past several decades, the formation of corresponded radical is a consensus. The allenic Grignard reagent prepared from propargyl bromide should generate the allenic radical. The addition of allenic radical to benzophenone would led to the formation of product 2 not product 1 as shown Scheme 1. This is not coincided with the data in the Table 1. This intrigues us to investigate the mechanism of allenyl magnesium bromide addition to benzophenone.

![Scheme 1](image)

**RESULTS and DISCUSSIONS**

In order to confirm the structure of Grignard reagent prepared from propargyl bromide, the allenyl magnesium bromide was prepared according to the literature methods and the products were analysis by FTIR. There is no new peak was observed when the solvent was anhydride ether, indicated that no allenyl magnesium bromide was formed. The reaction was repeated with additional 10 mg HgCl₂ as catalyst, a new peak was detected at 1881 cm⁻¹ which is consisted with literature (1880 and 1885 cm⁻¹) and therefore can be easily assigned as the vibration mode of allenyl group of allenyl magnesium bromide. When the anhydride THF was used as a solvent, a new absorption was appeared at 1956 cm⁻¹, a characteristic vibration mode of C=C=C stretching mode, suggested only the formation of allenlylic Grignard reagent. The results are agreed with the conclusion of Moreau and Gaudemar.

The mechanism of the alkyl Grignard reagents addition to benzophenone involved the initial single
electron transfer process first was proposed by several group. The alkyl Grignard reagent proceeds one electron transfer to benzophenone with the formation of the alkyl radical and benzophenone ketyl radical as eq.3.

\[
\text{RMgX} + \text{Ph}_2\text{C}=\text{O} \xrightarrow{\text{SET}} \text{R} \cdot + \text{PhC}-\text{O-MgBr} \quad (3)
\]

If the allenyl magnesium bromide addition to benzophenone also follows the single electron transfer process first, then the allenyl radical and ketyl radical anion intermediate should form as eq.3. The 2, 2, 6, 6-tetramethyl-1-piperidinyloxy (TEMPO) was used to trap any possible radicals generated from eq.3. Ten mmol of propargyl bromide was added slowly to mixtures of Mg (5 mmol)/ TEMPO (5 mol)/HgCl₂ (7.4 mmol) in anhydride ether (10 mL) under nitrogen. The solution was stirred for 24 hours at room temperature. After working up, the products were analyzed by GCMS, a peak of m/z at 196 was detected, indicated that there is C₃H₃ radical was trapped by TEMPO. Unfortunately the trapped product was unable to be isolated. This implies that the radical might generated from the electron transfer process.

The possible mechanisms of allenyl Grignard reagent addition to benzophenone are shown on Scheme 2. After the electron transfer has been occurred between allenyl Grignard reagent and benzophenone, the allenyl radical and the intermediate 3 are created. There are three possible pathways to produce the product 1, the first is the allenyl radical resonates to form propargyl radical which might couple with the intermediate 3 to form the product 1 (path A); the second possible path is the intermediate 3 reacts with allenyl Grignard reagent via a S₈₂’ process to form the product 1 (path B); and the last possible pathway is the allenyl radical couples with the intermediate 3 to give the product 2 which might rearrange to the product 1 (path C).

\[\text{Scheme 2}\]

\[
\begin{align*}
\text{C=C=CH} + \text{PhC}-\text{O-MgBr} &\rightarrow \text{C=C=CH} \\
\text{PhC-O-MgBr} &\rightarrow \text{PhC-OH}
\end{align*}
\]
Propargyl radical and allenyl radical are generally considered as resonance hybrid structural isomer. Many experimental and theoretical studies have given varying pictures regarding the relative contributions of these forms to the resonance structure.\(^1\)

\[
\text{H}_3\text{C}=\text{C} = \text{C} + \text{C}^* \quad \leftrightarrow \quad \text{H}_3\text{C}=\text{C} = \text{H}_2
\]

It is hard to determined that the relative population of the propargyl radical/the allenyl radical, the propargylic structure are favor in the esr\(^{1\text{a-d}}\), electronic absorption spectra studies\(^{1\text{e-g}}\), and the theoretical calculation studies\(^{1\text{h-i}}\), however, both forms contribute equally to a resonance structure from microwave spectroscopy study\(^{1\text{j}}\) and the theoretical calculation studies\(^{1\text{k}}\). A well resolved isotropic spectrum was observed by Fessenden and Schuler\(^{1\text{l}}\) in the liquid phase from high-energy irradiation of a solution of allene in propane; splitting constants of 18.9 and 12.6 Gauss for the CH\(_2\) and CH groups, respectively, were observed. By use of Q\(_{\text{sp}2}\)= 23.7 G and Q\(_{\text{sp}}\) = 34.7 G. Although the exact values of spin densities are in doubt, esr spectra do demonstrate greater spin density on the propargylic carbon atom and the relative population of the propargyl radical/the allenyl radical might estimate rough near 2.25 from the spin density of esr. Therefore, it seems reasonable to assume that the value of the relative population of the propargyl radical/the allenyl radical would be between 2.25 and 1. If the path A is a major pathway for this mechanism, then, the significant amount of the product 2 would be expected, owing to the low value of the relative population of the propargyl radical/the allenyl radical, however, only a trace amount of the product 2 was detected by GC. This might imply that the path A might be not the major pathway for formation of the product 1 on Scheme 2. If the reaction follows path C, the product 2 would form first, then the product 2 rearranged to the product 1. However, it seems difficult that the product 2 rearranged to the product 1, because the allenic product in this case is thermodynamically more stable than the propargylic product.\(^{1\text{m}}\)

The reaction of allenyl magnesium bromide with benzophenone gave the 48\% yield of the product 1 and a trace amount of the product 2. However, the reaction of benzophenone ketyl with allenyl magnesium bromide also gave the 68\% yield of the product 1 and a trace amount of the product 2. The yield of product 1 of the latter reaction is higher than that of the former reaction. It seems plausible that the yield of product 1 of the latter reaction is higher than that of the former reaction owing to the electron transfer between allenyl magnesium bromide and benzophenone in the former reaction caused the concentration of allenyl magnesium bromide decreased. This implies that the path B might be the major pathway for the formation of the product 1 on Scheme 2. This means that benzophenone ketyl reacts with allenyl magnesium bromide via S\(_{\text{H}}\)2 reaction might be a major pathway in the mechanism. However, the path Acould not be excluded by the data we have,
it might be a minor pathway in the mechanism. Based on the above discussion, the reaction of allenyl magnesium bromide with benzophenone is most possible proceed via path B.

CONCLUSION

The reaction of benzophenone with freshly prepared allenyl Grignard reagent from propargyl bromide produced compound 1 (homopropargylalcohol) with trace amount of compound 2 (allenyl alcohol). The possible \( \text{C}_3\text{H}_3 \) radical intermediate was trapped by TEMPO with GC/MS peak of m/z at 196. Three possible pathways have been discussed and the most possible reaction pathway was suggested that benzophenone ketyl intermediate reacted with allenyl magnesium bromide via a \( \text{S}_2\text{Hi}2' \) process to form the homopropargyl alcohol (path B).

EXPERIMENTAL DETAIL

All chemical are analytical grades. Propargyl bromide (Fluka) was purified by trap to trap distillation before use. TEMPO (2, 2, 6, 6-tetramethyl-1-piperidinyloxy, free radical) (Aldrich) was purified by vacuum sublimation. Benzophenone (R. D. H.) was refluxed and recrystallized in diethyl ether. Solvents, diethyl ether and THF (R. D. H.), were added sodium and refluxed until the solution is deep blue color and freshly distilled before use. Magnesium sulfate anhydrous (Mallinckrodt), mercury (II) chloride (Wako), and magnesium (R. D. H.) were used as received.

GC/MS were recorded on a HP 5890 Series II Gas Chromatograph with HP 5972A MSD and Carbowax capillary column (60 m*0.25 mm id. and 0.25 μ thickness). GC spectra were also performed on PE with Carbowax column (15 m *0.53 mm id. and 1.25 μ thickness). \( ^1\text{H} \)-NMR spectra were recorded on a 300 MHz Vax FT-NMR spectrometer. CI spectra were run with Quattro GC/MS 5022 with Carbowax column (60 m *0.25 mm id. and 0.25 μ thickness). All the glassware system was purged with \( \text{N}_2 \) gas during experimental process.

Grignard Reagent Preparation

\[
\text{HC} \equiv \text{C} = \text{CH}_2 - \text{Br} + \text{Mg} \rightarrow \text{H}_2\text{C} = \text{C} = \text{CH} - \text{Mg} - \text{Br}
\]

Fresh ground 10 mmol magnesium trips and 37 mmol mg mercury (II) chloride were quickly poured into a round flask; 10 mL anhydrous diethylether was added from side arm of flask and then stirred 6 hrs. at room temperature. Five mmol purified propargyl bromide was slowly added to flask and stirred 24 hrs. at room temperature. Infrared spectra indicated the formation of allenyl magnesium Grignard reagent. FTIR: 1881 (allenyl group), 1880, 1885 cm\(^{-1}\).
Trapping of Free Radical

\[ \text{Mg + TEMPO + HC} \rightleftharpoons \text{C - CH}_2 - \text{Br} \rightarrow \]
\[ \text{H}_2\text{C} = \text{C} = \text{CH} - \text{TEMPO} + \text{HC} \rightleftharpoons \text{C - CH}_2 - \text{TEMPO} \]

Fresh ground 5 mmol magnesium trips, 5 mmol TEMPO, and 7.4 mmol mercury (II) chloride were quickly transfer to round flask, then added 10 mmol anhydrous diethylether and stirred 5 min. Ten mmol purified propargyl bromide was slowly added to flask and stirred 24 hrs at room temperature. The sample was extracted with diethylether and washed with water three times, and then added magnesium sulfate anhydrous to remove water. A new peak with m/z 196 was observed on GC/MS spectra indicated that the C₃H₃ radical was trapped by TEMPO.

The reaction of allenyl magnesium bromide with benzophenone

\[ \text{Ph}_2\text{C} = \text{O} + \text{H}_2\text{C} = \text{C} = \text{CH}_2 - \text{Mg} - \text{Br} \rightarrow \]
\[ \text{H}_2\text{C} = \text{C} = \text{CH}_2 - \text{CPh}_2 - \text{OH} + \text{HC} \rightleftharpoons \text{C - CH}_2 - \text{CPh}_2 - \text{OH} \]

The freshly prepared allenyl magnesium bromide (0.5 M, 10 mL) was added slowly to the 0.5 M solution of benzophenone in anhydride diethylether (10 mL), the reaction was stirred at 0 °C ice bath for 6 hours. Slowly added 50 mL 0.1 M NH₄Cl solution, half hour later, the solution was extracted with diethylether three times and washed with saturated NaCl solution three times. Finally, the solution was added magnesium sulfate anhydrous to remove water, filtrated, and condensed. Two products were observed on GC, the compound 1 was the major product (48 %) and atrace amount of the compound 2 was also detected by GC. The product 1 was isolated and identified by GCMSand ¹HNMR and the spectra were all consistent with the literature data. 5(c)

GC/MS: (EI) m/z: 223 (M+1⁺, 0.05), 222 (M⁺, 0.2), 184 (27), 183 (100), 105 (98), 77 (98). H¹-NMR (300 MHz, CDCl₃): □ 7.5-7.2 (m, 10H), 3.1 (s, 2H), 2.9 (s, 1H), 2.0 (s, 1H). FTIR: 3400 cm⁻¹.

The reaction of allenyl magnesium bromidewith benzophenone ketyl

\[ \text{Na + Ph}_2\text{C} = \text{O} + \text{Ether} \rightarrow \text{Ph}_2\text{C}^\cdash\text{O}^- \]
\[ \text{Ph}_2\text{C}^-\text{O}^- + \text{H}_2\text{C} = \text{C} = \text{CH}_2 - \text{Mg} - \text{Br} \rightarrow \text{HC} \rightleftharpoons \text{C - CH}_2 - \text{CPh}_2 - \text{OH} \]

A blue color of benzophenone ketyl (0.5 M) was prepared from the reaction of benzophenone (5 mmol) with sodium (10 mmol) in 10 mL anhydride ether under nitrogen. The solution was refluxed until the solution became blue, then the blue solution was filtered under nitrogen. The freshly prepared allenyl
magnesium bromide (0.5 M, 10 mL) was then added slowly to the filtrated blue solution in ice bath, the reaction was then stirred for 6 hours at 0 °C. Slowly added 50 mL 0.1 M NH₄Cl solution, half hour later, the solution was extracted with diethylether triple times and washed with saturated NaCl solution three times. Finally, magnesium sulfate anhydrous was added to remove water. The solution was filtrated and condensed. After working up, two products were detected by GC, the compound 1 was the major product (68 %) and a trace amount of the compound 2 was found.

REFERENCES
8. Reference 6, p127.


13. The energies of the product 1 and 2 are -693.45323516 au and -693.45785338 au, respectively, which are calculated by the method of B3LYP/6-311g(d,p).