REACTIONS OF FENCHONE WITH ORGANO MAGNESIUM AND ORGANO LITHIUM COMPOUNDS

A. N. Nesmeyanov, V. A. Sazonova, and R. B. Materikova

We have shown previously [1] that in the reaction of a Grignard reagent with a carbonyl compound it is not possible to isolate a complex compound of the type,

\[ R'\text{C} = O - R''\text{Mg}X \cdot \text{Ether} \]

and that the intermediate compounds described by Hess [2], Meisenheimer [3], and others as complexes are of the alkoxide type,

\[ R'\text{C} - \text{OMg}X \cdot \text{Ether} \]

as supposed by Grignard.

Klages [4] was in error in affirming the existence of the complex,

\[ \text{C} - \text{CH} = \text{CH} \cdot \text{C}_2\text{H}_5\text{MgI} \cdot (\text{C}_2\text{H}_5\text{O}) \]

Fison and coworkers [5] showed that in this case the substance formed was the enolate of 2', 4', 6'-trimethylacetophenone

\[ \text{C} = \text{CH}_2 \cdot \text{OMgI} \]

and not a complex formed with an organomagnesium compound. There remains the complex of a carbonyl compound with a Grignard reagent described by Lerode [6], namely, the addition product formed by fenchone with phenylmagnesium bromide

\[ \text{C}_6\text{H}_5\text{MgBr} + \text{C} \rightarrow \text{C}_6\text{H}_5\text{MgBr} \cdot \text{C} \]

As this case was in conflict with our results and there were independent reasons for doubting it, we set ourselves the task of determining the structure of this compound, the study of which we had undertaken previously but had not completed.

Lerode writes: "Fenchone reacts with aromatic organomagnesium compounds to give addition products that are insoluble in ether and hydrocarbons. When these derivatives are treated with water, fenchone is regenerated and the hydrocarbon corresponding to the organomagnesium compound used is formed. The following compounds were prepared:

\[ \text{C}_6\text{H}_5\text{MgBr} \cdot \text{C}_10\text{H}_16\text{O}; \; \text{o-CH}_3\text{C}_6\text{H}_4\text{MgBr} \cdot \text{C}_10\text{H}_16\text{O}; \; \text{p-CH}_3\text{C}_6\text{H}_4\text{MgBr} \cdot \text{C}_10\text{H}_16\text{O}. \]

By prolonged heating in presence of a large amount of solvent these compounds were converted into magnesium derivatives of tertiary alcohols."".

As the author does not give any analysis, does not discuss the separation of these precipitates, and apparently worked with the reaction mixture, the hydrocarbon that he found in the decomposition products can be accounted for by unchanged organomagnesium compound present in the solution, especially when we take into account the
fact that very little precipitate was obtained; there can be no doubt that fenchone also would then be obtained. When the reaction mixture was heated for a long time (60 hours in a mixture of ether and toluene for the phenyl derivative), Lerolde succeeded in obtaining small amounts of tertiary alcohols (7% for 2-phenylfenchyl alcohol). There is no proof, however, that these alcohols were formed from the precipitate and not from the fenchone and phenylmagnesium bromide present in the solution.

In our work we tried to avoid the errors made by Lerolde. All experiments requiring the absence of oxygen and moisture were carried out in an atmosphere of pure dry nitrogen. The precipitate was filtered off through a starched glass filter, washed repeatedly with absolute ether, dried in a current of nitrogen, and analyzed. The further work was carried out solely with this precipitate.

Experiment showed that the analysis of the precipitate was far moved from that required by Lerolde's formula and also from that required by the magnesium derivative of the tertiary alcohol. The Mg:Br ratio found was 1:1.4 (Br 40.6%, Mg 8.8%); but for the complex postulated by Lerolde we ought to have obtained Br 24.02%, Mg 7.27% (Mg:Br ratio, 1:1). The yield of precipitate was very low (3.0%, was calculated as C₆H₅MgBr·C₁₆H₁₈O). When the solution filtered from the precipitate was rapidly poured into another vessel in the open air, a further small amount of the same precipitate separated after a short time. The small amount in which this substance was formed, the slow formation of further precipitate when the filtrate was allowed to stand in the air, and the pressure of appreciable amounts of biphenyl in the solution all these facts suggested that the formation of the precipitate was associated with oxidative processes. In fact, when the reaction was carried out under the usual conditions, without the use of nitrogen, considerably more precipitate was obtained and, moreover, its separation was gradual.

When the substance was decomposed with water, ether and fenchone were obtained, and no benzene was detected. It was found that fenchone could be displaced from the complex by means of benzophenone, but no triphenylmethanol was then formed, though this would be the product of the reaction of benzophenone with the phenylmagnesium bromide considered by Lerolde to be present in the complex. Benzil also displaced fenchone from the complex, but again no 2-hydroxy-2,2-diphenylacetophenone was detected (benzilic acid was unexpectedly obtained). It was found that, under similar conditions, benzil rearrangement occurred also when benzil was treated with the basic magnesium salt MgBr₂·MgBrOH·2(C₆H₅O). The occurrence of the benzil rearrangement under the action of such weakly alkaline reagents has not been reported in the literature.

The evident absence of phenylmagnesium bromide in the precipitate, the complex nature of the precipitate as indicated by the ease with which fenchone is separated from it by the action of substituting reagents (water, ketones), and the association of the formation of the precipitate with oxidative processes— all these facts point to the conclusion that the precipitate is a complex of fenchone with a basic magnesium salt MgBr₂·MgBrOH·2C₆H₅O(C₆H₅)₂O and not with phenylmagnesium bromide as maintained by Lerolde. It was found, in fact, that treatment of fenchone with a salt of composition MgBr₂·MgBrOH·2C₆H₅O, prepared by careful oxidation of an ethereal solution of phenylmagnesium bromide with atmospheric oxygen, results in the formation of a complex containing fenchone which is identical in properties with the precipitate studied.

As stated at the beginning, in the reactions of fenchone with phenylmagnesium bromide, o-tolylmagnesium bromide, and p-tolylmagnesium bromide, the corresponding tertiary alcohols are obtained only in very low yield. In 1946 in connection with investigations on the properties of terpenes, Namekina and Obtemperanskaya [7] improved the procedure for the Grignard reaction by replacing diethyl ether by dibutyl ether, so that the reaction temperature could be raised to 110°C; also, they used a twofold excess of phenylmagnesium bromide in the reaction. In this way they succeeded in raising the yield of tertiary alcohol from 7% to 30%.

For the synthesis of 2-phenyl- and 2-p-tolyl-fenchyl alcohols we used organolithium compounds:

Very mild reaction conditions were used: fenchone was added gradually at room temperature to an ethereal solution of phenyl- or p-tolyl-lithium, the mixture was stirred for 30 minutes, and the reaction mixture was decomposed with water. The arylfenchyl alcohols were obtained in good yield (70%).

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