

STUDIES OF SONOCHEMICALLY ENHANCED GRIGNARD REACTIONS

MATTHEW D. CANTRELL

Department of Physical Science

Abstract: The Grignard reagent, an organometallic compound, was prepared using ultrasonic irradiation (sound waves) to initiate the reaction. Significantly reduced initiation times, compared to initiation times using traditional methods, were produced--most on the order of less than 20 seconds. Reaction product yields of traditional and ultrasonic methods of preparing Grignard reagents were compared by individually performing reactions with and without ultrasound, however, no increase in product yield was reported using ultrasound. Finally, an alkyl halide coupling mechanism using ultrasound and lithium wire was modified using magnesium metal instead of the lithium wire. No significant amounts of coupling product were detected in reactions carried out using a high power ultrasonic processor.

Over the past 10 to 15 years a considerable amount of research has been done involving the use of high frequency sound waves to induce various scientifically interesting phenomenon. Most of the interest lies in the field of chemistry and how ultrasound affects various elements, compounds, and reactions. Some of the work done in previous years includes the breaking of molecular bonds (Suslick et al., 1983; Hart and Fischer, 1990) and chemical syntheses (Lindley and Mason, 1987). Much of the research on synthetic techniques involves organometallic reactions in which organic molecules interact directly with metals (Anonymous, 1980; Lindley and Mason, 1987; Han and Boudjuok, 1981).

The complete mechanism for some of the interaction that ultrasound promotes is not fully understood. However, it is known that ultrasound causes tiny bubbles to form and cavitate creating extremely high localized temperatures in liquids without significantly affecting the overall temperature of the liquid. These localized temperatures are high enough to cause reactions similar to combustion or pyrolysis without the extreme temperature requirements. The bubbles are also believed to act as a cleaning agent for the surface of metals.

The primary objective of this research was to study the effects of replacing the lithium metal in an alkyl halide coupling mechanism with the magnesium used in the Grignard reaction by ultrasound as suggested by Han and Boukjuok (1981).

MATERIALS AND METHODS

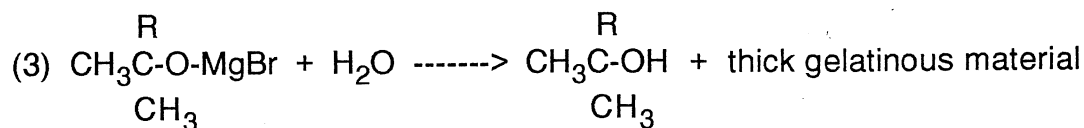
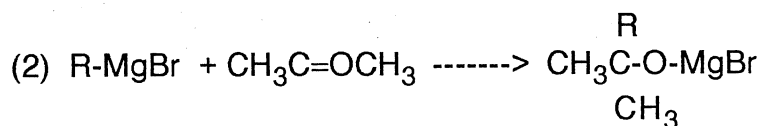
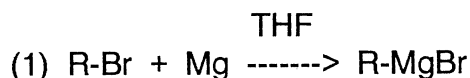
Experimental preparations of the solvent to be used in the syntheses, tetrahydrofuran (THF), required the removal of as much water as possible. This was accomplished by placing considerable quantities of freshly cut sodium metal and benzophenone into a 1000-mL flask half full of THF and warming for several hours on a hot plate until the mixture

showed a deep blue/purple color, at which time the solvent was raised to the boiling point and distilled under positive nitrogen atmosphere. The drying of this solvent was necessary for the easy facilitation of the Grignard reaction since it is extremely sensitive to water.

To substitute magnesium for lithium in the alkyl halide coupling reaction 0.01 mol of magnesium 50 mesh powder, 0.02 mol of the organic halide (n-butyl bromide, 2-bromobutane, and bromobenzene) and 10 mL of THF were placed in a Suslick type pressure cell fitted to a direct immersion sonic horn (Vibra cill model VT-600W) and irradiated with ultrasound for a period of usually 8 hours (Han and Boudjouk, 1981). Notice that this procedure promotes the coupling mechanism of the organic halide since it is in large excess. Upon completion of the reaction, the products were analyzed on a Perkin-Elmer Sigma 3 B gas chromatograph (G. C.) with a Supelco 10% SP-2100 column 1/8" x 10', and the chromatograms were compared with those of the starting materials injected under the same conditions.

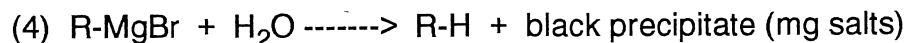
The next section of studies undertaken were comparisons of reaction initiation times, completion times, and product yields between the standard Grignard reactions, involving equimolar ratios of magnesium metal and the organic halide, carried out with and without sonication. Reactions were prepared identically in every respect: equimolar amounts of the halide and magnesium (0.01 mol) were placed in 5 mL THF. Initiation times were measure as the first visible sign of exothermic behavior, boiling, or characteristic opaqueness of solution as reaction begins. In some cases, where ultrasound was not utilized, it was necessary to add a small crystal of iodine to the mixture or to crush the metal with a glass stirring rod to promote the start of the reaction. These methods reduced induction times but to a lesser degree than ultrasonic irradiation. Induction times were also studied for magnesium pretreated for one hour with ultrasound in THF by using both an ultrasonic cleaning bath and a direct immersion sonic horn to ultrasonically irradiate the metal. Neither method provided any reduction in induction periods. Completion times for the synthesis of the Grignard reagent were also taken into account and the ultrasonically promoted reactions went to completion quickly and violently when compared to the conventional methods for carrying out the reaction.

Since the Grignard reagent is quite unstable and very reactive, it is generally used *in situ*. However, several attempts were made to convert the reagent to a higher alcohol by reaction with a carbonyl group such as is found in acetone according to the following reactions:



where R represents is primary, secondary, and benzyl. Analysis by G. C. indicated that this

synthesis was feasible except for the fact that the last step released a magnesium hydroxide complex into the solution in the form of a thick gel which I was unable to eliminate and could have clogged the G. C. with repeated injections. A second method was then chosen that eliminated the halide from the organic molecule leaving the parent alkane structure, and is depicted in the following reaction:



where R represents is primary, secondary, and benzyl. This method was chosen after careful observation of earlier work where the chromatograms showed a gaseous material forming a peak before the solvent peak. It was hypothesized that this gaseous material must be the parent alkane formed by the removal of the halogen atom. This method proved to be quite simple, yet effective. A mixture of water and THF, containing a sufficient molar quantity of water to fully react with the Grignard reagent prepared, was carefully added to the mixture just fast enough to keep the mixture boiling. The products of the reaction performed with and without sonication were analyzed by G. C.

RESULTS

The product yield comparisons between the reactions with and without sonication showed no increase in yield from using ultrasound in the reaction. In fact, the reactions using ultrasound yielded starting material peaks on the chromatograms whereas the reaction without ultrasound did not. Desired coupling products were obtained in quantities of less than 50% of the total product, however, because of failed reactions, the data in Table 1 may not accurately reflect the entirety of the effects of sonication upon the coupling mechanism. Reactions carried out in the high intensity ultrasound processor produced a low yield of coupling products. However, the last reaction, which was carried out in the sonicating bath for only a short period of time, showed considerable promise in yielding the coupling product.

Table 1. Approximate percentages of products produced in reactions with coupling promoted equilibrium.

Alkyl halide	Coupling product (%)	Other (%)
n-bromobutane	25	75
2-bromobutane	---	---
2-bromobutane*	~50	~50

* - Data regenerated, after reactions had failed, through use of a Branson Ultrasonic Laboratory cleaning bath [similar to that used by Han and Boudjouk (1981)].

The rates of initiation and completion of the reaction proved to be quite positive. The

use of ultrasound dramatically reduced the induction period for the process to get underway (Table 2). Another important observation that I made was that the reaction went to completion much faster using ultrasound throughout the process. The reactions performed without ultrasound would not spontaneously start unless interacted with iodine crystals or crushing with a glass rod. It is also interesting to note that magnesium pretreated with ultrasound while in THF did not reduce the induction period once the halide was added.

Table 2. Induction times for evidence of beginning reactions with and without ultrasound.

Organic halide	With sonication	Without sonication*
n-bromobutane	< 15 sec	2.0 h
2-bromobutane	< 20 sec	2.0 h
2-bromobutane	< 10 sec	2.0 h

* - Reactions began only after crushing metal with a glass stirring rod.

DISCUSSION

Ultrasound dramatically reduced the induction period and the completion time of the reactions. This may or may not have been beneficial for the standard Grignard reaction studies since the reaction may have stopped early due to by-product formation. The fact that pretreatment of magnesium with ultrasound did not reduce the induction period indicates that sonication plays a more complicated role than simply cleaning the metal surface.

Sonication did not significantly increase the product yield in the reactions carried out in this experiment. In fact, the ultrasound enhanced reactions may have actually had an inhibitory effect on these reactions. This may be due, in part, to the fact that the reaction completed very rapidly and may have promoted by-product formation. However, other outside factors could also have caused problems, since reactions carried out with an excess of alkyl halide typically yielded total consumption of the magnesium metal which would indicate that the starting materials were being consumed in the desired manner. Similar reactions without ultrasound did not consume all the magnesium metal; a small amount of metal was invariably left at the bottom of the flask, which indicated more by-product formation.

The reaction products were not found in the amounts I had hoped for and were low enough to possibly be just accidental by-products when the reaction was done in the Suslick vessel with the direct radiating horn. I assumed from there that the reaction would not go in a similar way to Han and Boudjouk's work (1981) and sought results for other areas of the project. However, upon repeating the process at the last minute using the ultrasound cleaning bath, it appeared that the coupling may have occurred to a greater extent than first observed. The power of the direct radiating horn may have been too great to facilitate a reaction of this nature and could be why the low intensity sonicating bath produced similar results to what was desired. However, sufficient data were not generated to make a general

interpretation and I regret giving up on the idea so early on.

ACKNOWLEDGEMENTS

I wish to thank Dr. R. Zerger for several fruitful discussions about the project and life in general. Special thanks are also extended to Midwest Oilseeds for providing financial support for this project.

LITERATURE CITED

Anonymous. 1980. Ultrasounds in organic synthesis. 1. Effect on the formation of lithium organometallic reagents. *Journal of the American Chemical Society*, 102:7926-7927.

Han, B. H. and P. Boudjouk. 1981. Organic sonochemistry: Ultrasound-promoted coupling of organic halides in the presence of lithium wire. *Tetrahedron Letters*, 22:2757-2758.

Hart, E. J., C. H. Fischer, and A. Henglein. 1990. Pyrolysis of acetylene in sonolytic cavitation bubbles in aqueous solution. *Journal of Physical Chemistry*, 94:284-290.

Lindley, J. and T. J. Mason. 1987. Sonochemistry part 2 - synthetic applications. *Chemical Society Review*, 16:275-311.

Suslick, K. S., J. J. Gawlenowski, P. F. Schubert; and H. H. Wang. 1983. Alkane sonochemistry. *Journal of Physical Chemistry*, 87:2299-2301.