# A NOVEL, CONTINUOUS HIGH-YIELD SYNTHESIS OF GRIGNARD REAGENTS *

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## Summary

A continuous process for the production of Grignard reagents, in particular, allylmagnesium chloride is described. The yield and purity of the Grignard reagent are both significantly higher than those normally obtained by use of conventional batch procedures. Disproportionation of the Grignard reagent to insoluble magnesium chloride presented the major technical problem in the process, though, of course, the yield of active "allyl" is unaffected.

## Introduction

Although Grignard reagents are the most commonly used alkylating agents for the preparation of metal allyls, aryls, and alkenyls [1,2,3], the methods by which they are made and used have hardly changed since the time of Grignard himself. Their batchwise synthesis in the laboratory may require ingenuity to get the reaction started, especially with chlorides. Yields are often disappointing, particularly where coupling reactions may occur, and the scale in the laboratory is limited to a few litres of molar solution. Such shortcomings, rarely acknowledged in the literature, are particularly acute in the preparation of allylmagnesium chloride, which can rarely be prepared in > 30% yield by the batch procedure. We describe here a new continuous procedure by which allylMgCl solution at a pre-determined concentration can be prepared in yields approaching 100%, and virtually free from impurities.

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* Dedicated to Professor G.E. Coates on the occasion of his 70th birthday. The author's interest in organometallic chemistry stems from the seven years he spent at Durham during the period 1960–1967, a particularly fertile period for Main Group organometallic chemistry, and has continued undiminished in his subsequent industrial career. A paper illustrating some of the difficulties that large-scale preparation of Grignard reagents can pose, and how they may be circumvented, appeared an appropriate vehicle for expressing his appreciation in view of G.E. Coates' evident long-term interest in all aspects of magnesium chemistry.
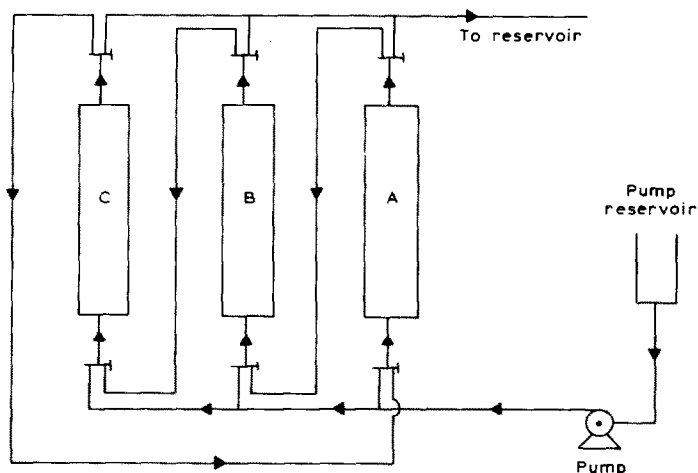
Fig. 1. Scheme for continuous Grignard reagent synthesis.

## Experimental

### Equipment description

A number of process designs were investigated, and a diagram of the most successful is shown in Fig. 1. It consists of a reservoir containing allyl chloride solution, a positive displacement flame-proof metering pump, three water cooled glass columns (volume approx. 300 ml) containing activated magnesium turnings, and an integrated series of two-way taps which allowed sequential isolation of each of the magnesium columns for replenishment.

### Column packing

The column consisted of a Pyrex tube fitted with a cooling jacket. Each column contained 60 g of commercial magnesium turnings, uniformly dispersed by shaking with an equal volume of glass beads. The column was then packed in layers as follows: a 1/2″ layer of glass beads supported on a gauze constituted the foundation of the column. Above this, 2–3″ layers of magnesium and beads alternated with 1/4″ layers of beads alone. The upper surface of the top magnesium layer was kept below the level of the water jacket to prevent boiling of the ether. It was found that a final upper layer of glass beads induced significant crystallisation of magnesium chloride etherate in this region, where it could be cleared during column regeneration without shutting down the apparatus, and this consequently reduced crystallisation in other parts of the apparatus.

### Magnesium activation

Although Grignard reagent preparations may begin spontaneously when the reagents are of sufficient purity, it is much more usual for an initiation procedure to be necessary [4]. Commonly used initiators include elemental iodine [5] or 1,2-di-bromoethane [6]. The preferred method recommended here is the use of di-bromoethane, because the products, ethylene and magnesium bromide are inert and

colourless, and the use of iodine tends to give rise to coloured solutions. The most effective method of magnesium activation for this continuous process is described below.

Magnesium turnings were activated by vigorous agitation under nitrogen [7] for a minimum period of 3 h, until the magnesium became dark grey in colour, presumably due to surface nitride formation. The activated magnesium thus prepared was loaded, in layers as described previously, into the nitrogen-filled tube against a counterflow of nitrogen. The activator solution (5 ml dibromoethane in 400 ml 0.55 molar solution of allyl chloride in diethyl ether) was blown rapidly by nitrogen pressure through the pump head into the column until all the magnesium was covered. The pump was switched off and the reaction was allowed to proceed, with cooling, to completion ( ~ 20 min). The metering pump was then switched on and allyl chloride solution, free from dibromoethane, was circulated through the column at the desired rate. As a general rule, within ten minutes of switching on the pump, the concentration of Grignard reagent taken from the column was at least 0.5 molar, corresponding to a minimum yield of about 90%. Exceptions to this generalisation could always be traced to either insufficient agitation of the magnesium in nitrogen, or ingress of air into the column during charging. However, yields in excess of 95% were common by the time the reaction had reached the steady state.

The traditional method for the batch initiation of the Grignard reaction, namely adding the activator to magnesium turnings suspended in ether, is unsuitable for this continuous application. When the allyl chloride solution is pumped into the apparatus there is considerable delay before the Grignard reagent reaches full strength because of dilution caused by back-mixing with the ether/dibromoethane solution.

*Working procedure*

It was found that to get complete reaction it was necessary for the allyl chloride solution to have a residence time of ca. 1 h in contact with the magnesium turnings. This required a flow rate of 250 ml h$^{-1}$ in the apparatus used and about 80% of the magnesium was consumed in 16 h. Unreacted allyl chloride passed through the magnesium column before this stage was reached, and consequently methods for rapid changeover of columns enabling full utilisation of magnesium were developed, as shown in Fig. 1, and described below.

Column A was filled with "activator solution" as described above, and when the initiation reaction subsided the pump was started. Allyl chloride was then pumped into Column A, displacing the Grignard reagent into Column B which acted as the secondary column, incidentally further activating the magnesium metal at the same time. When all magnesium in Column A had reacted the flow of allyl chloride was diverted from Column A into Column B which then became the primary column. The flow of Grignard reagent was diverted into Column C, which thus became the secondary column. Column A was removed from the system to be replenished with "activated" magnesium as described previously, ready for use when Column B became spent. Thus each column in turn starts off as the secondary column ending up as the primary column, ensuring maximum usage of magnesium. Yields approaching 100% on magnesium were generally obtained, and the lines from one column to another were cleaned out during column changes, virtually eliminating

serious build-up of crystalline magnesium chloride etherate *.

Although the process was designed for the preparation of allylmagnesium chloride solution, its versatility was also tested extensively for the preparation of benzylmagnesium chloride, and virtually quantitative yields based on both magnesium and benzyl chloride were obtained.

In subsequent work to make the process fully continuous, with no time lost during column changes, it was found necessary to use a second pump to fill the newly charged columns with activator solutions so that time was not lost in filling the dead space in the column.

## Discussion

The structure of the Grignard reagent in solution has been the subject of much research, and many such reagents are oligomeric $(RMgX)_n$ in ether solution [8] with halogen and occasionally alkyl bridges. The ether solvent itself satisfies the vacant coordination sites on the terminal magnesium atoms. It was proposed earlier by Schlenk [9] that the solution contained an equilibrium proportion of magnesium halide and dialkylmagnesium as shown in eq. 1. In most situations, the equilibrium

$$2RMgX \rightleftharpoons MgR_2 + MgX_2 \qquad (1)$$

lies largely in favour or RMgX with little free $MgX_2$ being formed, and the Grignard reagent is quite stable to crystallisation from solution. However, in the case of allylmagnesium chloride, crystallisation of magnesium chloride formed by disproportionation of the Grignard reagent, occurred to an unusual extent and proved to be a significant problem. Analysis of the resulting solution showed the composition to be $(allyl)_{1.3}MgCl_{0.7}$, reflecting the degree of disproportionation. Even this solution, after filtration, continued to deposit further magnesium chloride, though the active allylMg content of the solution remained constant. This effect appears to be particularly pronounced with the allyl derivative. (For example, disproportionation, with consequent magnesium chloride crystallisation, did not present any problem in the preparation of benzylmagnesium chloride.) The reason for this behaviour is not fully understood, but may well reflect a relatively facile transfer of allyl groups between magnesium atoms in the oligomer $(allylMgCl)_n$.

### Grignard reagent yield and purity

The yield of allylmagnesium chloride from the normal batch procedure [10] rarely exceeds 30% (based on allyl chloride) and the product is contaminated by varying amounts of 1,5-hexadiene formed by coupling of allyl chloride with the Grignard reagent:

$$CH_2=CHCH_2MgCl + CH_2=CHCH_2Cl \rightarrow CH_2=CH(CH_2)_2CH=CH_2 + MgCl_2$$

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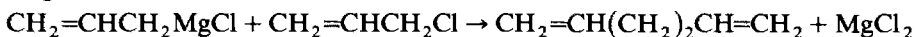
* An alternative procedure, consisting of two interchangeable primary columns backed up by a single secondary column proved to be only partly successful. Crystallisation of magnesium chloride etherate from allylmagnesium chloride solution occurred progressively, mainly in the manifold between the primary and secondary columns. Gradual accumulation over the duration of a few column changes ultimately led to a complete blockage, resulting in an enforced shutdown. Also, to avoid significant consumption of the secondary column it was necessary to use only part of the magnesium in the primary column. It was found that up to 80% of the magnesium could be used without appreciable break-through of allyl chloride. The method described above was therefore devised to meet these objections.

One of the advantages of a column method for the preparation of Grignard reagents is that once formed the Grignard reagent passes through the column to be replaced by allyl chloride solution. Thus the contact between allyl magnesium chloride and allyl chloride is kept to a minimum, as is reflected in the yield and purity of the product. Yields of 90–95% based on allyl chloride used are commonplace and on occasions effectively quantitative yields were obtained. Similarly, 1,5-hexadiene was only detected in trace quantities, if at all. High yields based on magnesium were also obtained. Since the reaction is performed in a sealed system of small volume which is completely filled with ether, the product obtained is very pure and free from hydroxide, alkoxide, peroxide or any other oxygenated species.

*Magnesium chloride crystallisation*

Using the experimental procedure previously described, crystallisation of magnesium chloride etherate was controlled at a workable level. However, should larger columns be used, and the change-over periods substantially lengthened, then blockages are more likely to occur as the run proceeds. Reduction of the allyl chloride concentration did not eliminate the problem of crystallisation even when yields of active allylMg approached 100%. However, some success was obtained by replacing a small amount (ca. 5%) of allyl chloride by the more expensive allyl bromide. Not only does magnesium bromide have a higher solubility than the chloride in ether but the adverse Schlenk equilibrium apparent with the chloride did not appear to affect allylmagnesium bromide; similarly, there is much less precipitation of mixed chloride/bromide complexes. An alternative possibility, not tested in this work, is the substitution of diethyl ether by tetrahydrofuran in applications where removal of THF would not present difficulties.

## Acknowledgements

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