

Convenient Titration Method for Organometallic Zinc, Magnesium, and Lanthanide Reagents

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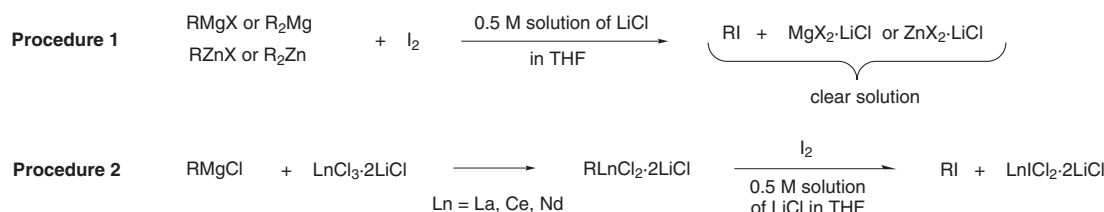
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Abstract: A convenient and reliable procedure for the titration of various organometallic compounds, such as magnesium, zinc, and lanthanides by using 0.5 M THF solutions of LiCl as the titration medium has been developed.

Key words: titration, magnesium reagents, zinc reagents, organolanthanide reagents, lithium chloride



Scheme 1

Introduction

The rapid and accurate determination of the concentration of organomagnesium and organozinc reagents has become increasingly important with the wide use of these reagents in organic synthesis.¹ Colorimetric single-titration methods² are useful and eliminate the need for a conventional double titration.³ Most of these methods are very convenient for the analysis of strongly basic organolithium reagents, but they are usually not applicable to the determination of the concentration of organomagnesium and organozinc reagents due to their weaker basicity. The titration method using diphenyl ditelluride as a colored indicator, developed by Ogura,⁴ could be used for the titration of organolithium and organomagnesium reagents, but it cannot be recommended because of the toxicity problems associated with the waste solutions. The development of a simple procedure for the analysis of reactive organomagnesium and especially organozinc reagents, without interference from any metal alkoxide or hydroxide base which might be present as a result of adventitious oxidation or hydrolysis, would be highly desirable. Herein, we report a practical procedure for such titrations.

Scope and Limitations

During our work with Grignard reagents complexed with LiCl,⁵ we observed the formation of clear solutions during quenching experiments with iodine. In the absence of LiCl, in most cases the precipitation of mixed magnesium halides was observed. Based on these observations we have developed a new protocol for the titration of organomagnesium and organozinc reagents taking advantage of the rapid reaction between organometallic compounds and iodine in THF saturated with LiCl (ca. 0.5 M). A sharp color change from the brown color of the iodine solution in THF to a colorless, completely transparent solution at the end point of the titration could be easily observed, indicating the complete consumption of iodine. The concentration of the organometallic reagent is determined from the amount of iodine consumed. Not only alkyl, alkenyl, and aryl magnesium reagents, but also less basic mono- and diorganozinc compounds can be successfully titrated (Procedure 1). The values obtained by our procedure were reproducible within $\pm 2\%$ over three titrations and were in fair agreement with those obtained by other methods.⁶ The addition of one equivalent of LiCl or *t*-BuOLi did not change these results, indicating that this method is also applicable to the titration of Grignard reagents complexed with LiCl and that there is no interaction of iodine with lithium alkoxides. These titrations can be done even at low temperature (-78°C) which makes the analysis of unstable organometallic compounds possible.

Recently, we have developed a new procedure for the preparation of various organolanthanides.⁷ We also applied our titration method to these reagents, thus, after transmetalation of *i*-PrMgCl and PhMgCl with LnCl₃·2LiCl (Ln = La, Ce, Nd), the resulting organolanthanide reagents *i*-PrLnCl₂ and PhLnCl₂ were accurately titrated by our method (Procedure 2). The resulting values were in good agreement with the molarity of the starting Grignard reagents before transmetalation minus the amount of protic impurities present in the lanthanide solutions (LnCl₃·2LiCl).

In summary, we have developed a simple and reliable method for the titration of organomagnesium, organozinc, and organolanthanide compounds.⁸ The procedure is environmentally friendly, convenient to perform, and the end point is easy to observe. The precision of the method is limited by the accuracy of syringe graduation (ca. 0.5 mol% for a 1-mL syringe).

Saturated Solution of LiCl in THF

Anhyd LiCl (100 mmol) was placed in an argon-flushed flask and dried under high vacuum (1×10^{-2} mbar) for 4 h at 140 °C. After cooling to r.t., anhyd THF (200 mL) was added and the mixture was stirred for 24 h at r.t. until the LiCl was completely dissolved, resulting in the formation of a 0.5 M solution of LiCl.

Titration Using I₂

A 10-mL round-bottom flask equipped with a magnetic stirring bar and a septum was heated with a heat gun under reduced pressure and cooled to r.t. under an argon atmosphere. The dry flask was charged with accurately weighed I₂ (254 mg, 1 mmol), fitted with a rubber septum, and flushed with argon. The sat. solution of LiCl in THF (3–5 mL) was added and stirring was started. After the iodine was completely dissolved, the resulting brown solution was cooled to 0 °C in an ice bath and the organometallic reagent was added dropwise via a 1.00-mL syringe (0.01-mL graduations) until the brown color disappeared. The amount consumed contains 1 equiv of the organometallic reagent relative to iodine in the case of monoorganometallic reagents and 0.5 equiv for diorganometallic reagents.

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- (8) It is possible to determine the concentration of most organolithium compounds using our procedure with the exception of some secondary and tertiary alkyl lithiums in which a facile elimination of HI from the alkyl iodide formed during titration is possible (for example *s*-BuLi and *t*-BuLi).