

The first example of γ -chloromagnesian γ -lactones: their generation from γ -tolylsulfinyl γ -lactones with isopropylmagnesium chloride, stability, and reaction with electrophiles

Shimpei Sugiyama, Hitomi Shimizu and Tsuyoshi Satoh*

Department of Chemistry, Faculty of Science, Tokyo University of Science, Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162-0826, Japan

Received 12 September 2006; revised 28 September 2006; accepted 29 September 2006
Available online 20 October 2006

Abstract—The treatment of γ -lactones having a sulfinyl group at the γ -position, which were synthesized from 1-chlorovinyl *p*-tolyl sulfoxides with lithium enolate of carboxylic esters, with isopropyl magnesium chloride in THF at -78 °C gave γ -chloromagnesian γ -lactones by the sulfoxide–magnesium exchange reaction in high yields. The generated γ -chloromagnesian γ -lactones were found to be stable at below -50 °C for at least 2 h. The reaction of these γ -chloromagnesian γ -lactones with electrophiles and the stereochemistry of the reactions were investigated.

© 2006 Elsevier Ltd. All rights reserved.

Organomagnesium compounds, the Grignard reagents, are one of the most important reagents for the formation of a carbon–carbon bond with carbonyl compounds or alkyl halides.¹ As the carbon–magnesium bond is highly reactive, it has long been generally recognized that the presence of electrophilic functional groups, such as esters, nitriles, and ketones, cannot be compatible in the Grignard reagents. However, recently, the preparation of functionalized Grignard reagents and their properties have been studied and reported by Knochel² and some other chemists.

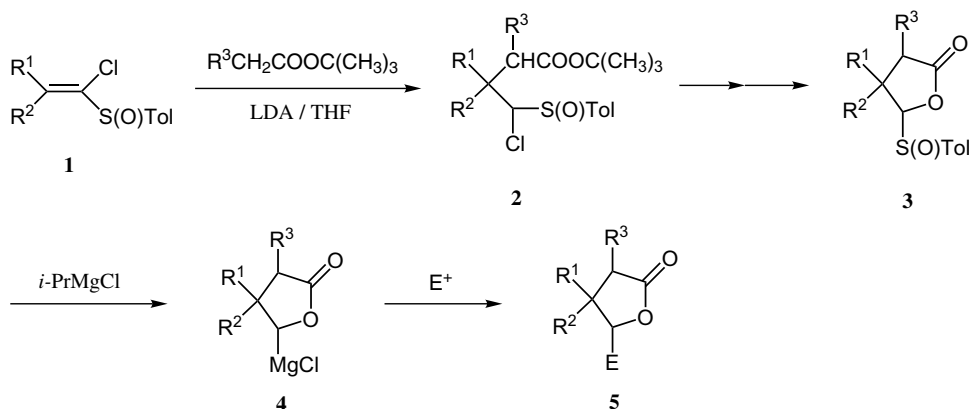
The functionalized Grignard reagents are those for functionalized arylmagnesium reagents,³ polyfunctional heteroaryl-magnesium reagents,⁴ functionalized alkenyl-magnesium reagents.⁵ These functionalized magnesium reagents have ester, nitrile, halogen, and amide as the functional groups. However, those functional groups are usually present directly on the aromatic ring or on the sp^2 -carbon, which means that there is no acidic α -hydrogen, although some exceptions are also reported.⁶

In previous studies, we have found that various ester lithium enolates reacted with 1-chlorovinyl *p*-tolyl sulfoxides **1** to give adducts **2** in high yields. Furthermore, we also reported a novel method for the synthesis of lactones having a sulfinyl group at γ -position **3** from adducts **2** in two steps in high overall yields.⁷ We thought that if Grignard reagents react with the sulfinyl group in lactones **3**, γ -chloromagnesian γ -lactone **4** could be generated via sulfoxide–magnesium exchange reaction.⁸ We also anticipated that the continuous reaction of **4** with various electrophiles would afford lactones **5** having a carbon–carbon bond at the γ -position. Herein, we report the generation of the first example of γ -chloromagnesian γ -lactones and investigation of their property and the reaction with electrophiles (Scheme 1).

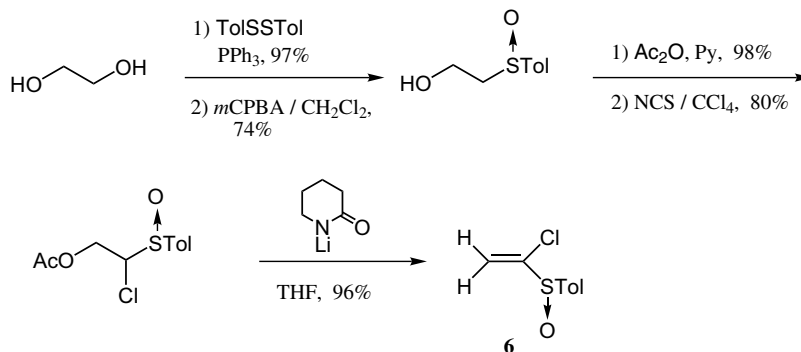
First, 1-chlorovinyl *p*-tolyl sulfoxide **6** was selected as a representative example of the 1-chlorovinyl *p*-tolyl sulfoxide in this study and was synthesized from ethylene glycol in five steps in a 54% overall yield (Scheme 2). Lithium ester enolate of *tert*-butyl 4-phenylbutyrate was generated in THF at -78 °C and to this solution was added 1-chlorovinyl *p*-tolyl sulfoxide **6**. The desired addition reaction took place within 5 min to afford adduct **7** in a quantitative yield. Adduct **7** has three chiral centers and theoretically four diastereomers would be

Keywords: Sulfoxide; Sulfoxide–magnesium exchange; Grignard reagents; γ -Chloromagnesian γ -lactone; γ -Lactone.

* Corresponding author. Tel.: +81 3 5228 8272; fax: +81 3 3235 2214; e-mail: tsatoh@ch.kagu.tus.ac.jp



Scheme 1.



Scheme 2.

produced; however, adduct **7** was obtained as a single diastereomer.⁹

Next, trifluoroacetic anhydride (TFAA) was added to a solution of adduct **7** in the presence of NaI in acetone to give γ -lactone **8** having a tolylsulfanyl group at the γ -position (Scheme 3).⁷ γ -Lactone **8** has two chiral centers and, theoretically, two diastereomers are possible. On silica gel TLC, two products could be observed and they could be separated by silica gel column chromatography as a less polar (expressed as **8a**; 31%) and a more polar product (expressed as **8b**; 52%).

In order to determine the configuration of **8a** and **8b**, the NOESY spectrum of both lactones was measured. From the detailed inspection of the spectra, we were able to determine unambiguously the *cis*-structure of **8b** as shown in Scheme 3. The main isomer **8b** was used in the following studies. Sulfide **8b** was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA) at -50 °C to give sulfoxide **9b** as a mixture of two diastereomers in a good yield.

Finally, **9b** was treated with 1.6 equiv of *i*-PrMgCl at -78 °C for 10 min (a solution of **9b** in THF was added to a solution of *i*-PrMgCl in THF) to give the desulfenylated product **11b** in a 91% yield via sulfoxide–magne-

sium exchange reaction without a trace of the starting sulfoxide **9b**. Quenching this reaction with CH_3OD gave γ -lactone deuterated at γ -position **11b** with 99% deuterium incorporation. This result showed that the intermediate of this reaction was γ -chloromagnesium γ -lactone **10b** (see Scheme 3).

At this stage, we were worried about an intermolecular or an intramolecular proton abstraction, because **10b** has a relatively acidic hydrogen on the α -position. However, no deuterium incorporation at the α -position of γ -lactone **11b** was observed on its ^1H NMR.

Next, we investigated the stability of γ -chloromagnesium γ -lactone **10b** by the chemical yield and the rate of deuterium incorporation and the results are summarized in Table 1. The γ -sulfinylated lactone **9b** was treated with 1.6 equiv of *i*-PrMgCl and the reaction mixture was stirred at -78 °C for 1 h, and the reaction was quenched with CH_3OD (Table 1, entry 1). The result was almost the same as the result in Scheme 3. Next, the reaction mixture was stirred at -78 °C for 2 h and the reaction was quenched with CH_3OD (entry 2). The result was almost the same compared with that in entry 1. These results show that γ -chloromagnesium γ -lactone **10b** is stable at -78 °C for at least 2 h. Next, the reaction mixture was slowly allowed to warm to -50 °C for over 50 min and

Download English Version:

<https://daneshyari.com/en/article/5282031>

Download Persian Version:

<https://daneshyari.com/article/5282031>

[Daneshyari.com](https://daneshyari.com)