Synthesis and Reactions of Pyridinylcalcium Bromides

Lara Pryor and Anthony Kiessling
Department of Chemistry
Wilkes University
PO Box 111
Wilkes-Barre, Pennsylvania 18766 USA

Received January 17, 2002 Accepted February 21, 2002

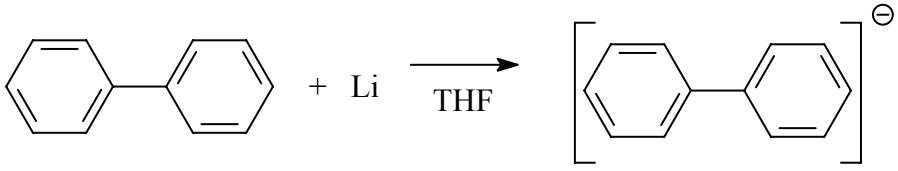
ABSTRACT

Pyridinylcalcium bromide was synthesized by reacting activated calcium with 3-bromopyridine. Since the pyridinylcalcium bromide would be difficult to isolate, the compound were trapped by acetone in Grignard-like reactions. The subsequent products were identified by GC/MS to confirm the synthesis of the pyridinylcalcium bromide.

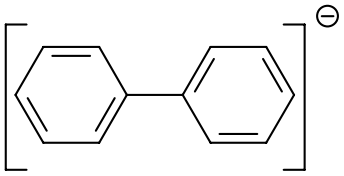
I. INTRODUCTION

Organometallic compounds are compounds that contain carbon-metal bonds (C–M). Although the organic portions of the structure can effect the overall nature of the compound, the identity of the metal itself has a much more significant impact on the compound's properties. Organometallic synthetic studies conducted over the past thirty years have focused on the formation of novel organometallic reagents from reactive metals such as copper, magnesium, zinc and calcium [1]. For example, highly reactive magnesium has the ability to react with organic dihalides to yield four, five or six membered ring compounds, and the metal will readily form organomagnesium halides, or Grignard reagents. Comparatively, calcium differs in redox potential and ionic radius (*i.e.*, calcium has a larger ionic radius than magnesium). Therefore, corresponding calcium metallocycles will behave differently with respect to reactivity and selectivity [2]. High reactivity usually pertains to oxidative addition reactions and the extent to which the formed compounds will undergo them [3].

In theory, organocalcium chemistry should be quite extensive; however, advances in this chemistry have been hindered by the lack of an easy preparation for organocalcium products. Reacting the calcium metal with organic substrates results in reduced activity due to surface poisoning factors, which restrict the oxidative addition [2]. Rueben D. Rieke et al. of the University of Nebraska have developed a relatively easy preparation of organocalcium compounds, and has reported that the resulting calcium compounds have a higher reactivity than that of their magnesium analogues [2]. Rieke has found that organocalcium compounds can be prepared from activated calcium and organic halides through Grignard-like reactions. Reactive calcium is prepared by the reduction of calcium halides with preformed lithium biphenylide or lithium naphthalenide in dry tetrahydrofuran (THF) under an argon atmosphere as depicted in equations (1) and (2) [3]. The reaction will occur at room temperature.



(1)



$$Li^{+} + CaBr_2 \xrightarrow[THF]{} Ca(BPh)_2 \qquad (2)$$

The calcium halide and lithium biphenyl reaction creates a species that is soluble in the solvent [2]. The activated calcium will now react with a variety of organic substrates to form the organocalcium compounds. In general, primary, secondary and tertiary halides will react rapidly with activated calcium. The reaction will be very exothermic; therefore, a significant amount of heat will be released. The reaction vessel is cooled to –78ºC to counteract the temperature increase [2]. Highly reactive calcium complexes will react readily with substrates to generate excellent yields [2]. According to Rieke, the activated calcium successfully reacts with all types of organohalides. Nevertheless, there is no documented evidence of the activated calcium reacting with bromopyridines to form pyridinylcalcium bromides.

II. EXPERIMENTAL

Activated calcium was prepared via the method proposed by Rieke et al. [3]. All glassware, needles, and cannulae used in the following reactions were dried in an oven for at least 24 hours. The tetrahydrofuran (THF) used in the following reactions was dried with sodium benzophenone mixture and freshly distilled prior to use. Calcium bromide, 3-bromopyridine and lithium metal were used as supplied from Aldrich. In a 25 mL reaction flask, lithium (83.4 mg, 12.02 mmol), biphenyl (2.040 g, 13.22 mmol) and 30 mL of dry THF were combined under argon. The mixture was stirred vigorously at room temperature under argon for 2.5 hours until all of the lithium metal had dissolved. The resulting solution of lithium biphenylide was a dark blue/green color. The preformed lithium biphenylide was transferred via cannula to a suspension of calcium bromide (2.426 g, 12.14 mmol) in 30 mL of dry THF and mixed under argon for an hour to produce the activated calcium. The activated calcium solution was cooled to –78˚C using an acetone/dry ice bath. Then 3-bromopyridine (1.918 g, 12.15 mmol) was diluted in 10 mL of dry THF and subsequently added to the cooled solution under argon via cannula. The solution was stirred for twenty minutes after which the reaction flask was removed from the acetone/dry ice bath and allowed to warm up to –20˚C. To the pyridinylcalcium bromide solution, an excess of ketone or aldehyde (*i.e.*, acetone, butanone, acetaldehyde) was added. After thirty minutes of mixing, the reaction is quenched with 40 mL of deionized water.

Once the solution was warmed to room temperature, the mixture was filtered through a Celite pad. The Celite was washed with copious amounts of diethyl ether. The filtrate was then acidified to pH paper with 10% hydrochloric acid. The layers were then separated, and the aqueous layer was washed with two 20 mL portions of ether. The acidified aqueous layer was then made basic to pH paper with 10% sodium hydroxide. The resulting precipitate was removed via gravity filtration, and the remaining liquid was extracted with three 20 mL portions of methylene chloride. The organic layer was dried with anhydrous magnesium sulfate, and the solvent was removed with the assistance of the roto-vaporator. The crude product was then analyzed via nuclear magnetic resonance, mass spectroscopy and thin layer chromatography.

III. RESULTS AND DISCUSSION

The actual pyridinylcalcium bromides – like a typical Grignard reagent – cannot be isolated because of their instability in the presence of moisture and atmospheric compounds. In effect, the additional reaction of the pyridinylcalcium bromide with a ketone or aldehyde was

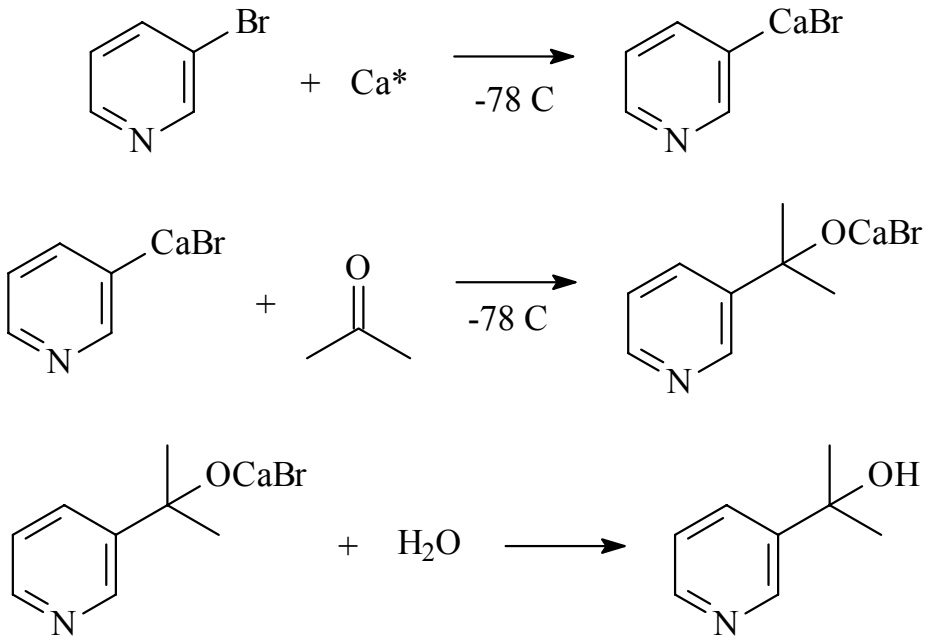
necessary to assist in confirming the synthesis. Thin layer chromatography and nuclear magnetic resonance spectroscopy were used to determine whether any starting materials remained in the mixture. The prepared samples for these tests came from the crude product; in effect, the resulting data was not helpful in confirming the synthesis of the desired product. Ultimately, gas chromatography of the crude product mixture was much more illuminating since the desired product was separated from the other side products.

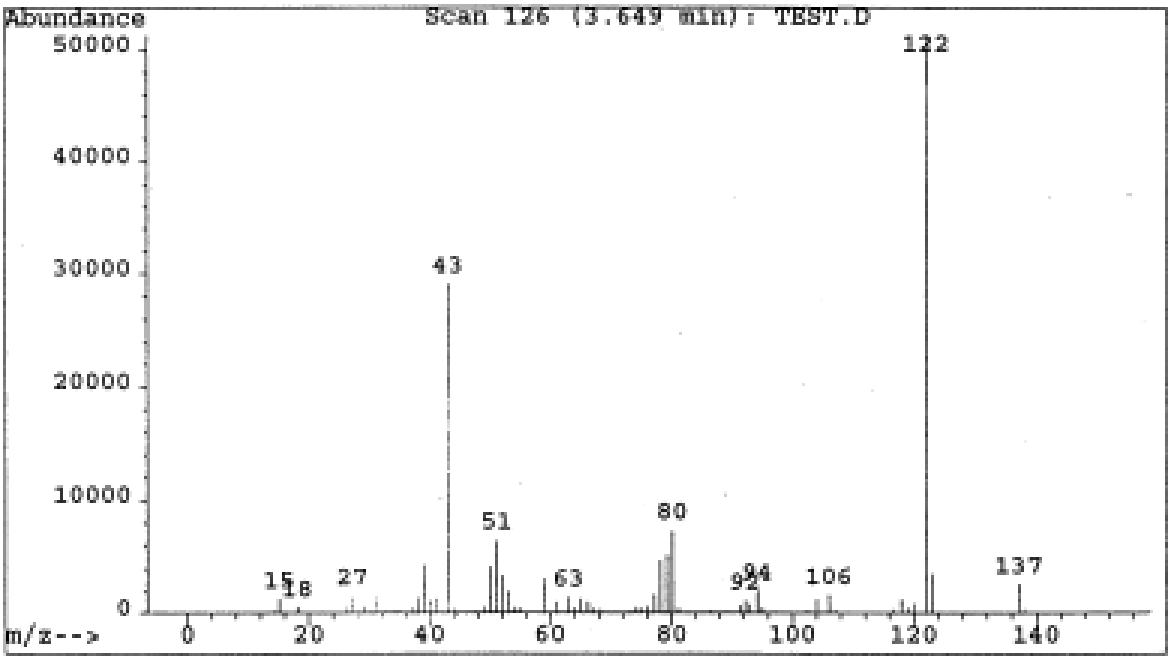
For example, scheme (1) depicts the reaction of 3-bromopyridine with the activated calcium (Ca*) followed by reaction with excess acetone then water. The mass spectrum for the desired product of this reaction was obtained by GC/MS analysis of the crude product mixture and can be seen in figure (1). The resulting product, 2-(3-pyridyl)-2-propanol, has a molecular weight of 137 grams per mole and a corresponding mass-to-charge ratio (*m/z* value) of 137 which is present in the spectrum. Also in the spectrum, there is a peak of high intensity at m/z of 122. Structurally, this *m/z* value arises from the loss of a methyl group by □-cleavage of 2-(3-pyridyl)-2-propanol.

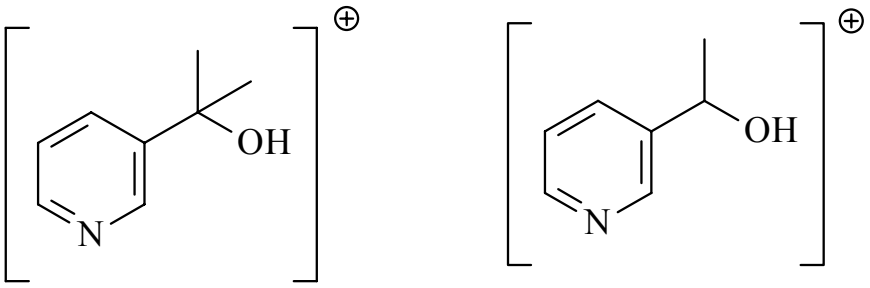
IV. CONCLUSION

Ultimately, it has been shown that 3-pyridinylcalcium bromides can be synthesized by first synthesizing active calcium from lithium biphenylide and calcium bromide, and then, adding 3-bromopyridine. The resulting 3-pyridinylcalcium bromide will undergo Grignard-like reactions. The products from these reactions can be identified using mass spectroscopy. The preparation of these compounds is virtually straightforward. Failure to get the desired product usually arises from the compound's exposure to water or atmospheric conditions. The most common sign of failure is an abundance of the bromopyridine reactant in the crude product analysis, which is revealed via thin layer chromatography.

Scheme 1







$m/z = 137$ $m/z = 122$

Figure 1. The Mass Spectrum of 2-(4-Pyridal)-2-Propanol and Corresponding Structures

REFERENCES

1. Rieke, Reuben D. *Aldrichimica Acta*. *33* (2), 52-60 (2000).
2. Wu, Tse-Chong; Xiong, Heping; Rieke, Reuben D. *J. Org. Chem*. *55* (17), 5045-5051 (1990).
3. Rieke, Reuben D.; Wu, Tse-Chong; Rieke, Loretta I. *Org. Synth*. *72*, 147-153 (1995).