Reduction of Cp$_2$ZrCl$_2$ with Mischmetall: A New Method for Generating an Efficient "Cp$_2$Zr" Equivalent

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ABSTRACT
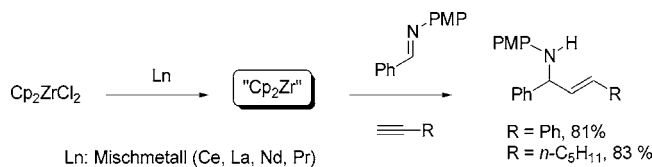
A "Cp$_2$Zr" equivalent is generated under mild conditions (THF, room temperature) by reducing Cp$_2$ZrCl$_2$ with cheap and readily available mischmetall (an alloy of Ce, La, Nd, and Pr). Coupling reactions, including those of terminal alkynes, can efficiently be achieved by using this reagent.

Important applications of zirconium in organic synthesis[1] particularly involve Cp$_2$Zr(II) species, the so-called zirconocene. Although 14-electron Cp$_2$Zr has never been observed in a monomeric form, "Cp$_2$Zr" equivalents, that is, species that effectively act as Cp$_2$Zr(II), can typically be generated by reduction of Cp$_2$ZrCl$_2$ in the presence of stabilizing ligands.

Early attempts to produce Cp$_2$Zr(II) employed Na–naphthalene[2] or Na and Mg in the presence of alkynes or bipyridine.[3] More recently, a large excess of Mg (10 equiv)

and HgCl$_2$ (1 equiv) was frequently used as reductant.[4] Rosenthal's reagent, Cp$_2$Zr(Me$_3$SiCCSiMe$_3$), formed from Cp$_2$ZrCl$_2$/Mg and bis(trimethylsilyl)acetylene,[5] has also been shown to be useful. In 1986, Negishi reported a convenient method for generating Cp$_2$Zr–butene by treatment of Cp$_2$-ZrCl$_2$ with 2 equiv of *n*-BuLi.[6] The Negishi reagent has proved to act effectively as a zirconocene equivalent in a number of synthetically useful reactions,[1] and its introduction largely contributed to the extensive development of zirconocene chemistry in the 1990s. However, some limitations in the use of Cp$_2$Zr–butene have been encountered, among them the fact that terminal alkynes cannot be employed with this reagent. An alternative procedure for generating Cp$_2$Zr equivalents would be useful. Mild and selective reducing

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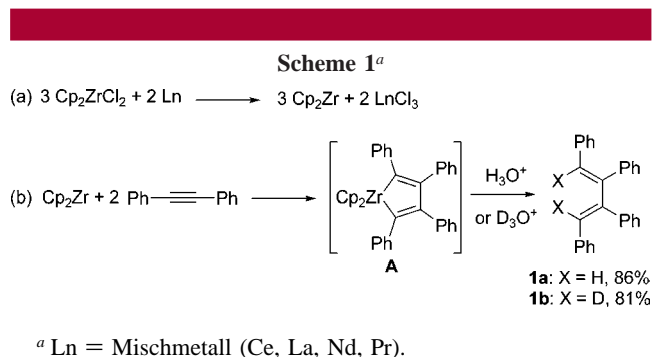
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agent and conditions would be the major advantages of such a method, with the aim of forming unstable $Cp_2Zr(II)$ species in the presence of a substrate.

Herein, we report on a practical and efficient experimental protocol for the formation of a zirconocene equivalent by employing mischmetall as reductant. Mischmetall, an alloy of rare earths (Ce 48−50%, La 32−34%, Nd 13−14%, Pr 4−5%, and ca. 1% others), is a cheap material, commercially available as ingots which can easily be powdered with a rasp.[7] After scraping, the mischmetall powder can be stored under argon for several weeks. The use of mischmetall in various synthetically useful reactions has recently been reviewed.[8] Mischmetall has been employed as a co-reductant in Sm(II)-mediated Barbier and Grignard reactions,[9] as well as pinacol coupling reactions,[10] or in SmI_2/Pd(0)-catalyzed coupling of allylic esters with ketones.[11] Interestingly, in the absence of another metal component, it appeared to be rather unreactive toward esters, ketones, and the majority of alkyl and aryl halides. These features as well as its availability made mischmetall an interesting candidate for generating $Cp_2Zr(II)$ species from Cp_2ZrCl_2.

Initially, when the mixture of mischmetall powder (1−2 mmol,[12] based on its average molecular weight of 140 $gmol^{-1}$) and Cp_2ZrCl_2 (1 mmol) in THF (5 mL) was stirred under argon at room temperature for about 1 h, there was a change of color from pale yellow to deep red. By carrying out the reaction in the presence of 2 mmol of diphenylacetylene for 4 h, the dimer, (E,E)-1,2,3,4-tetraphenyl-1,3-butadiene (1a), was obtained after a hydrolytic workup, in moderate yield of about 50%. Furthermore, the deuterated analogue 1b was obtained after deuteriolysis, thus demonstrating the formation of zirconacyclopentadiene intermediate (A) (Scheme 1, eq b). To determine the specific reactivities

In each case, 1 mmol of Cp_2ZrCl_2, 0.66 mol of the metal, and 2 mmol of diphenylacetylene were used. This stoichiometry corresponded to the hypothetical transformations as depicted in Scheme 1 (eq a). The reactions were carried out as described previously at room temperature for 4 h. When using La or Ce,[13] the reaction mixtures turned deep red after 45 min and 1 h, and the dimer 1a was formed in 78 and 60% yields, respectively. In contrast, the use of Nd[13] proved to be inefficient. The reaction did not occur even by warming the reaction mixture to 50 °C.

In the next experiments, 0.86 mmol of mischmetall was used to reduce 1 mmol of Cp_2ZrCl_2. Since only about 80−85% of mischmetall has to be considered to take part in the reaction, this corresponded to the stoichiometric amount of the active reductant (Ce, La) according to Scheme 1 (eq a). Two alternative experimental approaches have been developed and can be used to efficiently form a zirconocene equivalent. In the first, the color turned red within 10 min, when the mixture of mischmetall powder, Cp_2ZrCl_2, and diphenylacetylene in THF was warmed at 50 °C. The reaction was next carried out at room temperature for the additional 4 h. In the second, a rapid color change (5−10 min) was induced at room temperature by the addition of a few crystals of iodine, and the reaction was then continued as previously. By using the two experimental protocols above, the diene 1a was obtained, respectively, in 84 and 86% yields.[14]

By applying the latter procedure, several reactions have been demonstrated to occur smoothly under mild conditions (Scheme 2). Similarly to diphenylacetylene, also di(n-

Scheme 1[a]

(a) $3\ Cp_2ZrCl_2 + 2\ Ln \longrightarrow 3\ Cp_2Zr + 2\ LnCl_3$

(b) $Cp_2Zr + 2\ Ph{-\!\!\equiv\!\!-}Ph \longrightarrow$ ... A ... $\xrightarrow{H_3O^+ \text{ or } D_3O^+}$ ...

1a: X = H, 86%
1b: X = D, 81%

[a] Ln = Mischmetall (Ce, La, Nd, Pr).

of the main mischmetall components, Ce, La, and Nd, the reactions using pure lanthanide metals were next performed.

Scheme 2[a]

1a: R = Ph, 86%
1c: R = n-Pr, 93%

2   3
R = Ph, 81%, 2a/3a = 2.5:1
R = n-C_5H_{11}, 79%, 2b:3b = 1:1.5

6a: R = Ph (81%),
6b: R = n-C_5H_{11} (83%)

"Cp_2Zr"

4a: R = H, 75%
4b: R = SiMe$_3$, 72%, Z/E = 6:1

5a: n = 1, 71%, dr = 1:1
5b: n = 2, 66%, dr > 10:1

[a] Reaction conditions: THF, 2 crystals of I_2, Cp_2ZrCl_2, Ln (0.86 mmol). PMP = 4-methoxyphenyl; PMB = 4-methoxybenzyl.

propyl)acetylene coupled to afford the dimer 1c in 93% yield. Interestingly, the title reagent proved to be compatible with the use of terminal alkynes. Thus, the reaction with phenyl-

(7) Caution: mischmetall is pyrophoric and sparks can come out from ingot when scraped.

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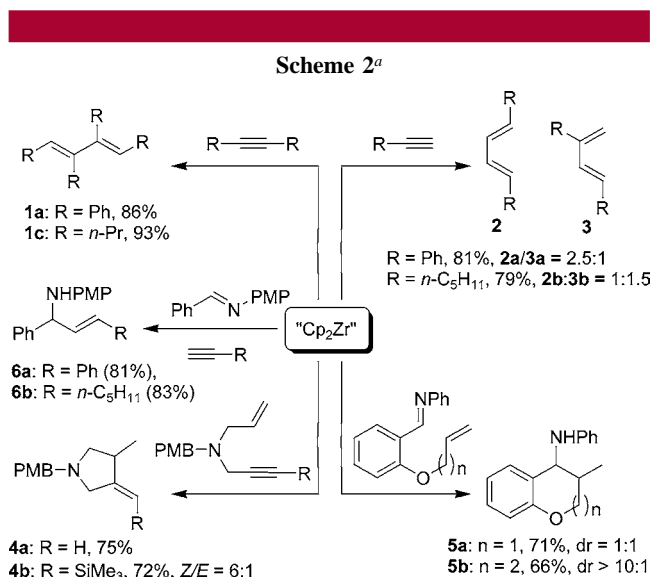(10) Hélion, F.; Lannou, M.-I.; Namy, J.-L. *Tetrahedron Lett.* **2003**, *44*, 5507−5510.

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(12) Mischmetall ingots were purchased from Fluka or Alfa Aesar−Johnson Matthey (minimum rare earth content is 99.0%).

(13) La, Ce, and Nd ingots (Aldrich, 99.9% purity) were powdered with a rasp under Ar.

acetylene gave a mixture of dienes **2a** and **3a** in a 2.5:1 ratio, in a good combined yield. By using 1-heptyne, a 1:1.5 mixture of **2b** and **3b** was formed. Although these reactions appeared to be only moderately "pair"-selective in the aforementioned conditions, a possible use of terminal alkynes is noteworthy. The use of terminal alkynes would open the way to a number of synthetically useful reactions through zirconacyclopentadiene intermediates.[15]

Bicyclization of enynes by cyclic carbozirconation is a well-known reaction, leading to versatile subsequent transformations.[1a,e] Particularly, Pauson−Khand-type reactions are concerned, which would possibly compete with the well-established cobalt-promoted processes. A marked restriction for the development of such reactions is, however, the lack of procedures which would allow the concomitant use of substrates containing terminal alkynes and a zirconocene equivalent.[16] An example of a bicyclization reaction which overcomes this limitation is now shown in Scheme 2. In fact, the use of a starting enyne with the terminal alkyne moiety, together with the title zirconocene equivalent, proved successful, providing the heterocyclic compound **4a** in 75% yield. Additionally, the compound **4b** was obtained from a silylated enyne.

Little is known about zirconocene-mediated cyclization of ene- or yne-imine. Whereas some intramolecular coupling reactions have been reported,[17] the direct intermolecular coupling remains unknown, to our knowledge.[18] Remarkably, not only intra- but also intermolecular reactions of this type have been noticed to occur smoothly by using the described procedure. The intramolecular reaction starting from ene-imines is exemplified by the synthesis of the cyclic compounds **5a,b**. Two examples of intermolecular reactions leading to **6a** and **6b** are shown. These high-yielding reactions represent a simple one-pot access to allylamines from terminal alkynes and imines.

In summary, we have presented a new method for the formation of Cp$_2$Zr(II) species which act as an efficient zirconocene equivalent. Several reactions, including an unprecedented coupling of terminal alkynes as well as intermolecular coupling of alkynes with imines, were efficiently carried out. Simplicity of the procedure, selective reducing character of mischmetall, and mild reaction conditions are noteworthy, offering the possibility of employing functionalized starting materials. Studies aimed at further exploring the formation, structure, and the synthetic potential of this new reagent are currently underway.

Supporting Information Available: Experimental procedures and spectral data for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) When phenylacetylene was added only 15 or 30 min after the reaction mixture turned red, the yield of **1a** decreased to 68 and 43%, respectively.

(15) Various selective transformations from tetrasubstituted zirconacyclopentadienes have been developed by Negishi, Takahashi, Whitby. and others. See: Takahashi, T.; Li, Y. Zirconacyclopentadienes in Organic Synthesis. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, Germany, 2002; Chapter 2.

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