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CuCl-catalyzed reaction of zirconacyclopentenes with oxalyl chloride: a new pathway for the preparation of cyclopentenones

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Dedicated to Professor John M. Birmingham
on the occasion of his 80th birthday

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ABSTRACT

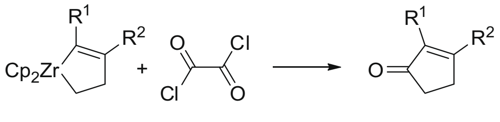
Zirconacyclopentenes, which are easily prepared from alkynes and EtMgBr (or ethylene) and Cp_2ZrCl_2, reacted with oxalyl chloride in the presence of catalytic amount of CuCl to give cyclopentenones in high yields. The reaction was performed conveniently in one pot from alkynes, EtMgBr, oxalyl chloride, and Cp_2ZrCl_2.

Cyclopentenones are particularly useful precursors for the synthesis of various cyclopentyl compounds due to their versatility. Many methods are available for their synthesis.[1–5] Among them, coupling of an alkyne, an alkene, and CO using transition-metal complexes is most attractive for the direct synthesis of a wide variety of cyclopentenones.[3] However, the use of gaseous and highly poisonous carbon monoxide represents a drawback of this procedure. The application of this reaction in most cases is also restricted by the demand for highly toxic carbonyl complexes (e.g., $Co_2(CO)_8$ and $Mo(CO)_6$) and/or nobel metal as the catalysts (e.g., Ru or Rh). A carbonylation reaction in a mild and convenient condition without carbon monoxide would make the reaction more desirable.[6]

Oxalyl chloride, as carbonylated reagent, had been reported previously to undergo condensation reactions with 2 equiv of mono-functional organometallic compounds, such as Grignard reagents, organolithium, organocopper, and organotin compounds, to form 1,2-diones.[7] Recently we found that oxalyl chloride reacted with zirconacyclopentadienes to afford cyclopentadienones, in which the carbon-carbon bond of 1,2-dicarbonyl was cleaved and oxalyl chloride finally served as a source of CO.[8] More recently, Müller et al reported one consecutive three-component synthesis of alkynones by coupling of heterocycles and oxalyl chloride as a source of the CO building block followed by Sonogashira reaction.[9] Prompted by these results, we envisioned that the reaction of oxalyl chloride with zirconacyclopentenes could afford cyclopentenones (Scheme 1), although a convenient procedure for the preparation of cyclopentenones via the reaction of zirconacyclopentenes with CO gas has been reported.[3e,5a,h,i]

Initial experiment showed that the reaction of zirconacyclopentene **1a**, generated by the reaction of 3-hexyne and Cp_2ZrEt_2 in THF[10] with oxalyl chloride in the presence of 2 equiv of CuCl led to the formation of a complex, inseparable mixture. This result was surprising, since such an amount of CuCl was the choice in the reaction of zirconacyclopentadienes with oxalyl chloride to give high yields of cyclopentadienones.[8] Without CuCl, the reaction did not proceed. Surprisingly, when catalytic amount of CuCl (10 mol %) was added, the reaction proceeded smoothly and the cyclopentenone **2a** was obtained in 85% isolated yield. Meanwhile, the generated gas was collected and detected by GC. Only CO gas was observed[11] (Scheme 2).

To extend the reaction, we tried out various substituted monocyclic as well as bicyclic zirconacyclopentenes[12] bearing alkyl, aryl, and TMS groups. In all cases, the corresponding products were formed in high yields. When terminal alkyne was used, the corre-



Scheme 1.

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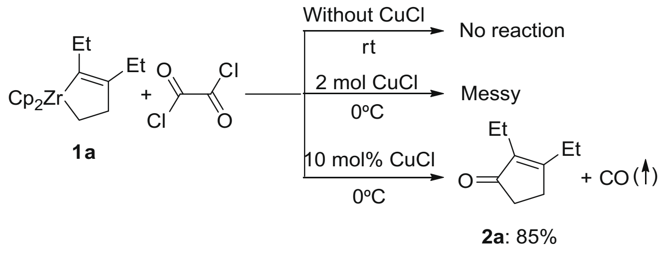
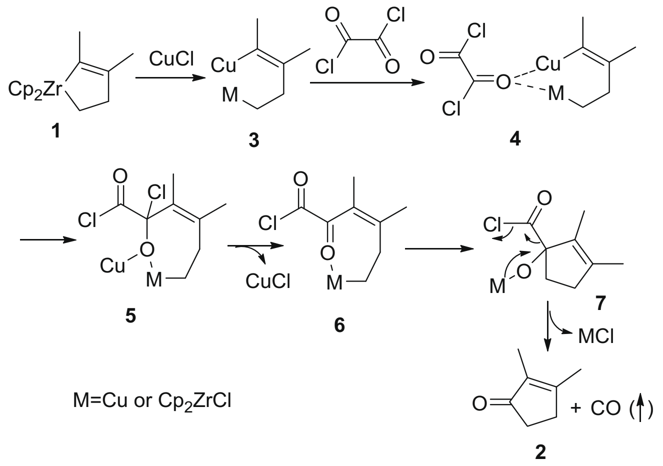


Scheme 2.

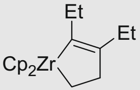
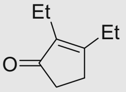
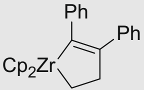
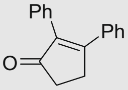
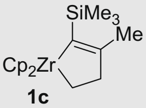
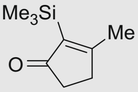
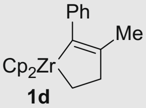
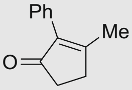
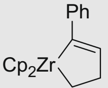
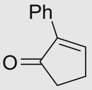
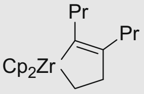
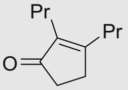
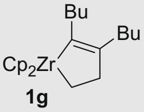
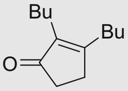
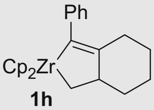
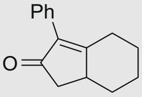


Scheme 3.

sponding products were obtained in moderate yields (entry 5). It is noteworthy that when unsymmetrical alkynes were used two regioisomers were observed (entries 3–5). The ratio of the two isomers depended on the selectivity of the formation of zirconacyclopentenes.[10] The representative results are summarized in Table 1.

According to these results and the literature report,[8,9,13] we propose a possible mechanism for this reaction (Scheme 3). Firstly, the zirconacyclopentene **1** undergoes transmetallation with CuCl to form the intermediate **3**.[14] Secondly, the coordination of one of the two carbonyl groups to copper metals or copper and zirconocene moieties of the intermediate **3** affords seven-membered ring **4**.[8,13] The alkenylcopper moiety reacts with the chelated carbonyl group to form **5**.[7] Then the elimination of CuCl recovers coordinated C=O bond to form **6**, which then undergoes an intramolecular nucleophilic attack by the remaining alkylcopper or alkylzirconium moiety to give five-membered carbocycle **7**. Finally elimination of the MCl (M = Cu or Cp$_2$ZrCl) accompanying decarbonylation gives product **2**. This result is in sharp contrast to the case of other dianionic reagent reactions with oxalyl chloride, which usually gives complex and inseparable products.[15] The chelating effect of the copper moieties and/or zirconocene moiety and the formation of cyclopentenone derivatives and CO gas were assumed to be the driving force in this reaction.

Table 1
Reaction of zirconacyclopentene with oxalyl chloride

Entry	Zirconacyclopetene	Cyclopentenone	Yield[a] (%)
1	 **1a**	 **2a**	85
2	 **1b**	 **2b**	82
3	 **1c**	 **2c**	69[b]
4	 **1d**	 **2d**	93[c]
5	 **1e**	 **2e**	50[d]
6	 **1f**	 **2f**	88
7	 **1g**	 **2g**	83
8	 **1h**	 **2h**	71

[a] Isolated yields.
[b] A mixture of two isomers in a ratio of 25:1, the ratio of two isomers was detected by GC.
[c] A mixture of two isomers in a ratio of 20:1.
[d] A mixture of two isomers in a ratio of 2:1.

We conclude that the reaction of zirconacyclopentenes with oxalyl chloride in the presence of catalytic amount of CuCl gives cyclopentenones. This reaction represents a new and convenient pathway to substituted cyclopentenones using oxalyl chloride as the carbon monoxide source without the need of CO.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.07.065.

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11. *Typical experimental procedure*: Reactions were carried out as follows: A 25-mL Schelenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.350 g, 1.2 mmol) and THF (5 mL). To this solution was added ethylmagnesium bromide (1.0 M, THF solution 2.4 mL, 2.4 mmol) at −78 °C. After stirring for 1 h, 3-hexyne (113μL, 1 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. To this solution were added 10 mol % of CuCl (10 mg) and oxalyl chloride (85 μL, 1.0 mmol) at −30 °C in turn. The reaction mixture was stirred at 0 °C for 1 h. The mixture was quenched with 3 N HCl and extracted with 20 mL of ether thrice. The extract was washed with NaHCO$_3$ and brine, and dried over MgSO$_4$. The solution was filtered and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/CH$_2$Cl$_2$ = 4:1 as eluent) to afford 2,3-diethylcyclopentene-1-one **2a** as light yellow oil (115 mg, 85% isolated yield).
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