Zirconocene-catalysed cyclobutene formation by reaction of alkynyl halides with EtMgBr

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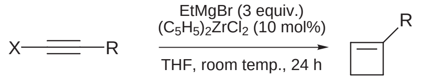
Zirconium-catalysed reaction of alkynyl halides with EtMgBr produced cyclobutene derivatives in which two carbon–carbon bonds were formed on the ethyl moiety of EtMgBr *via* an ethylene group in a catalytic cycle.

The zirconium-catalysed reaction of olefins with EtMgBr was first reported as an ethylmagnesation reaction by Dzhemilev.[1] Recently, we found that the reaction proceeds *via* a zirconocene–ethylene complex and a zirconacycle.[2,3] However, so far the ethyl moiety of EtMgBr has only been incorporated in products as an ethyl group in the catalytic reaction with olefins[1–4] or acetylenes.[5] There has been no example in which two carbon–carbon bonds were formed on the ethyl moiety in the catalytic cycle in the strict sense, even though it is converted into an ethylene group in the cycle. We report here the first example of the formation of two carbon–carbon bonds to the ethyl moiety of EtMgBr in a catalytic cycle.

Typically, when 1 mmol of 1-chlorooct-1-yne **1a** was treated with a catalytic amount of $(C_5H_5)_2ZrCl_2$ (10 mol%) and 3 equiv. of EtMgBr in THF (5 ml) at room temperature for 24 h, 1-hexylcyclobutene **2a** was formed in 61% yield [eqn. (1)].

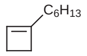
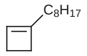
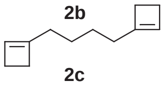
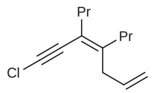
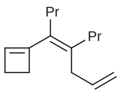


1 **2** (1)

Table 1 shows the results of cyclobutene formation reactions under the catalytic conditions. The choice of halogen on the terminal carbon of the alkynes was important. 1-Bromo- and 1-iodo-alkynes did not give cyclobutenes under these conditions; only metal–halogen exchange products were formed. The yields were also dependent on the amount of EtMgBr, and the use of 3 equiv. was found to be suitable in all the cases for the catalytic reactions. Interestingly, when a diyne dichloride **1c** was treated under similar conditions, a bridged dicyclobutenyl product **2c** was obtained.

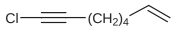
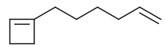
This reaction was interesting due to the fact that an alkynyl chloride and ethylene derived from EtMgBr reacted formally in a [2 + 2] cycloaddition with the loss of halogen. In order to understand this catalytic reaction, we also carried out stoichiometric reactions.[6] The results are shown in Table 2. A typical procedure is as follows. To a solution of $(C_5H_5)_2ZrCl_2$ (0.37 g, 1.25 mmol) in THF (6 ml) was added EtMgBr (1.0 M THF solution, 2.5 mmol) at −78 °C. The reaction mixture was warmed up to −40 °C and stirred for 1 h. To the mixture was added 1-chlorooct-1-yne at −78 °C. The mixture was stirred for 1 h at room temperature. After stirring for 1 h, the reaction mixture was quenched with 3 M HCl and the usual workup gave 1-hexylcylobutene in 80% yield. The same products were obtained under both catalytic and stoichiometric conditions; however, under the latter conditions the reaction proceeded much faster. It is noteworthy that the intermolecular coupling of the chloroalkyne moieties with ethylene derived from EtMgBr

Table 1 Formation of cyclobutenes under catalytic conditions[a]

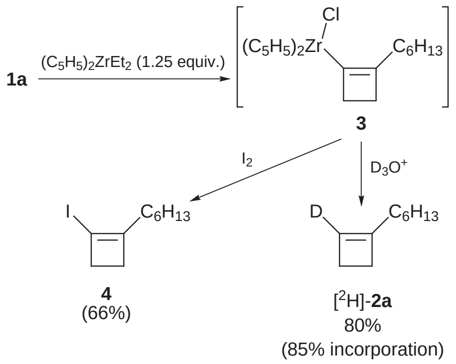
XC≡CR	Product	Yield[b] (%)
$Cl{-}{\equiv}{-}C_6H_{13}$ **1a**	 **2a**	61
$Cl{-}{\equiv}{-}C_8H_{17}$ **1b**	 **2b**	51
$Cl{-}{\equiv}{-}(CH_2)_4{-}{\equiv}{-}Cl$ **1c**[c]	 **2c**	54
 **1d**	 **2d**	50

[a] Unless otherwise noted, $(C_5H_5)_2ZrCl_2$ (10 mol%) and EtMgBr (3 equiv.) were used for the catalytic reactions. Conditions: room temperature, 24 h. [b] Yields were determined *via* GC using hydrocarbons as internal standards. [c] $(C_5H_5)_2ZrCl_2$ (20 mol%) and EtMgBr (6 equiv.) were used.

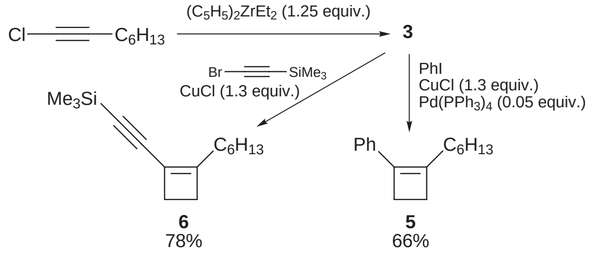
Table 2 Formation of cyclobutenes under stoichiometric conditions[a]

XC≡CR	Product	Yield[b] (%)
1a	**2a**	80 (80)
$Br{-}{\equiv}{-}C_6H_{13}$	**2a**	66
$I{-}{\equiv}{-}C_6H_{13}$	**2a**	60
1b	**2b**	83
1c[c]	**2c**	89[d] (60)
1d	**2d**	80[d] (50)
 **1e**	 **2e**	40

[a] Unless otherwise noted, $(C_5H_5)_2ZrCl_2$ (1.25 equiv.) and EtMgBr (2.5 equiv.) were used for the stoichiometric reactions. Conditions: room temperature, 1 h. [b] Unless otherwise noted, yields were determined *via* GC using hydrocarbons as internal standards. [c] $(C_5H_5)_2ZrCl_2$ (2.5 equiv.) and EtMgBr (5 equiv.) were used. [d] Yield was determined by NMR analysis. Isolated yields are given in parentheses.



Scheme 1



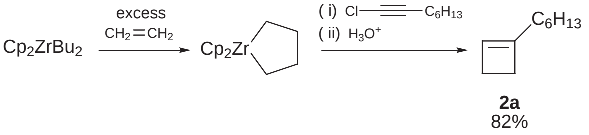
Scheme 2

predominated over the intramolecular coupling of an alkynyl group with an olefin moiety, or the second alkynyl group when **1c**–**e** were used.

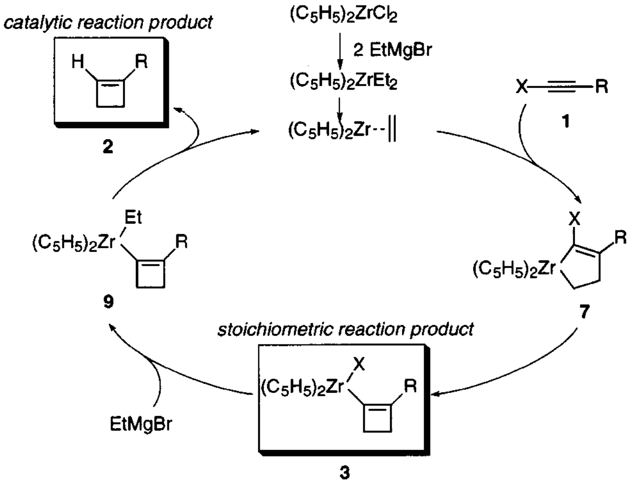
Deuterolysis of the stoichiometric reaction mixture gave [^{2}H]-**2a** in 80% yield with 85% deuterium incorporation. Iodinolysis gave a 66% yield of iodocylobutene **4**. These results suggest that the intermediate is cyclobutenylzirconium **3** (Scheme 1).

Since the intermediate **3** contains a zirconium–carbon bond, the further carbon–carbon bond formation reactions of alkenylzirconium compounds were examined (Scheme 2). To a stoichiometric reaction mixture of **1a** and $(C_5H_5)_2ZrEt_2$ prepared *in situ* from $(C_5H_5)_2ZrCl_2$ and 2 equiv. of EtMgBr were added iodobenzene, CuCl (1.3 equiv.) and $Pd(PPh_3)_4$ (0.05 equiv.). The mixture was stirred at 50 °C, and 1-hexyl-2-phenylcyclobutene **5** was obtained in 66% overall yield based on **1a**. Similarly, treatment of **3** with 1-bromo-2-trimethylsilylacetylene and CuCl (1.3 equiv.) gave alkynylcyclobutene **6** in 78% yield. This procedure is a convenient preparative method for various 1,2-disubstituted cyclobutenes.

Introducing ethylene gas to a solution of the Negishi reagent (Cp_2ZrBu_2)[7] and subsequent addition of a 1-chloroalkyne also gave cyclobutene **2a** in good yield as expected [eqn. (2)]. This clearly showed that ethylene and the ethyl moiety of EtMgBr are equivalent in the carbon–carbon bond formation described above.



(2)



Scheme 3

A plausible mechanism of the catalytic cyclobutene ring formation is shown in Scheme 3. The zirconocene–ethylene complex reacts with haloalkyne **1** to form α-halozirconacyclopentene **7**, which undergoes a ring-closing reaction to give cyclobutenyl–zirconocene complex **3**. This ring-closing reaction might proceed *via* reductive elimination of zirconacyclopentenes[6] and oxidative addition of the alkenyl chloride moiety to zirconocene.[8] The ethylene complex is regenerated by the reaction of **3** with EtMgBr to complete the catalytic cycle.

Notes and References

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Received in Cambridge, UK, 22nd June 1998; 8/04697B