Reaction of Zirconocene–Alkyne Complexes with $Mo(CO)_6$

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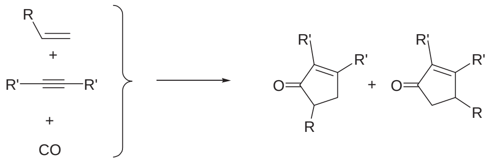
The reaction of zirconocene–alkyne complexes prepared from Cp_2ZrCl_2 with BuLi and an alkyne with $Mo(CO)_6$ yielded 2,3-disubstituted-5-ethylcyclopentenone derivatives by incorporation of once eliminated butene with excellent regioselectivity.

Intermolecular coupling of an alkyne, an alkene and CO using transition-metal complexes is very useful to prepare cyclopentenone derivatives (Eq 1).[1] However, regio-control of the substituted alkenes in the coupling still remains to be studied.

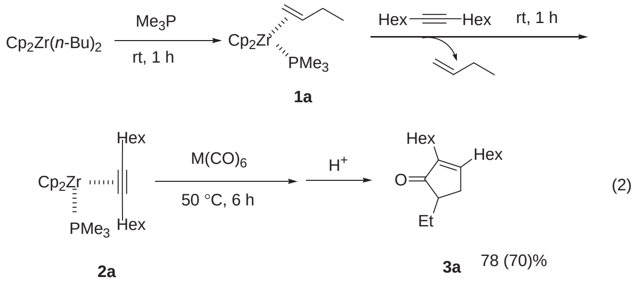


(1)

We have already reported that zircona- or titanacyclopentenes prepared by intermolecular coupling of alkynes and ethylene are very useful intermediate for the formation of cyclopentenones. The reaction of the zircona- or titanacyclopentenes with CO gives the corresponding cyclopentenone derivatives in good yields.[2] However, the coupling of an alkyne and a mono-substituted alkene on zirconocene and titanocene has a critical problem for the orientation of the substituent of the mono-substituted alkene.[3] So far there is no selective method for the formation of metallacyclopentene derivatives with high selectivity in the intermolecular coupling of the mono substituted alkene and an alkyne.

Very recently, we have investigated the reaction of zirconocene–alkyne complexes with CO and found a double carbonylation reaction of alkynes which gave cyclobutenone derivatives.[4] During our further investigation of zirconocene–alkyne complexes with $Mo(CO)_6$ as an easy handled CO source, we found that surprisingly cyclopentenone derivatives were formed as a single product. In this paper, we would like to report that once eliminated butene was incorporated in the cyclopentenone formation with high regioselectivity in the reaction of a zirconocene–alkyne complex, which was prepared from Cp_2ZrCl_2, BuLi, and an alkyne, with $Mo(CO)_6$.

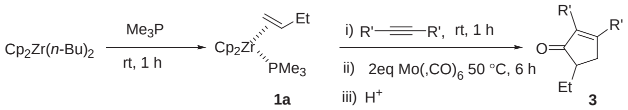
The reaction was carried out as follows. Me_3P was added to a solution of $Cp_2Zr(n\text{-}Bu)_2$ (Negishi reagent) prepared from zirconocene dichloride with 2 equiv. of *n*-BuLi in THF at −78 °C under nitrogen.[5] After the mixture was warmed up to room temperature and stirred for 1 h, zirconocene–butene complex **1a** stabilized with Me_3P, was formed. To this mixture was added 7-tetradecyne and the resulting mixture was stirred for 1 h at the same temperature. Zirconocene–alkyne complex **2a** was prepared in situ. To this was added $Mo(CO)_6$ at 50 °C and the mixture was stirred for 6 h. After hydrolysis 5-ethyl-2,3-dihexylcyclopent-2-en-1-one (**3a**) was obtained in 78% yield (70% isolated yield) as shown in Eq 2.

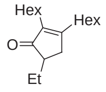
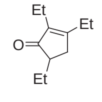
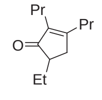
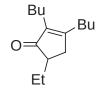
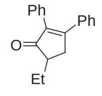


When Ph_2PMe was used as a ligand, 58% of cyclopentenone **3a** was obtained. $Cr(CO)_6$ and $W(CO)_6$ could also be used and gave cyclopentenone **3a** in 46% and 48% yields, respectively. When the amount of $Mo(CO)_6$ was changed to 1.0, 1.5, 2.0, and 3.0 equiv., cyclopentenone **3a** was obtained in 25, 46, 78, and 56% yields, respectively. The best yield was obtained in the case of 2.0 equiv. of $Mo(CO)_6$.

Various alkynes were used instead of 7-tetradecyne as shown in Table 1. In all cases, 2,3-disubstituted-5-ethylcyclopentenones were obtained. Not only dialkylacetylenes but also diphenylacetylene reacted smoothly, and the expected product **3e** was formed (Entry 5).

Table 1. Formation of cyclopentenones from zirconocene–alkyne complexes

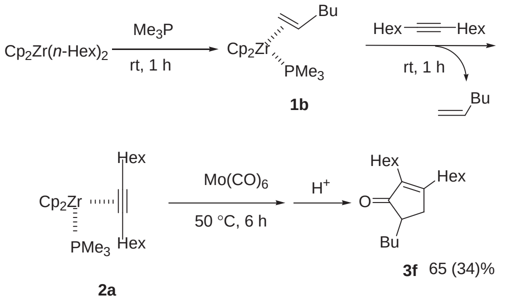


Entry	Alkyne	Product		Yield/%[a]
1	Hex—≡—Hex		**3a**	78 (70)
2	Et—≡—Et		**3b**	58 (41)
3	Pr—≡—Pr		**3c**	55 (37)
4	Bu—≡—Bu		**3d**	61 (42)
5	Ph—≡—Ph		**3e**	49 (31)

[a]GC yields. Isolated yields are in parentheses.

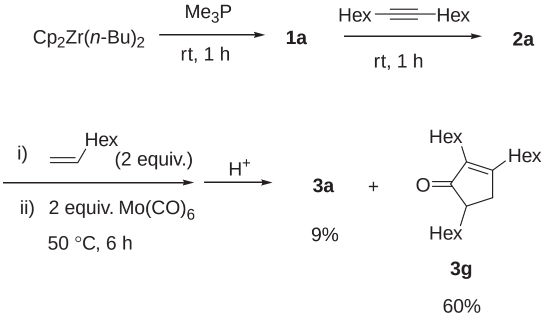
It is noteworthy that the products, 2,3-disubstituted-5-ethylcyclopentenones **3a**–**3e** were formed from an alkyne, 1-butene and CO. It clearly indicated that once eliminated free 1-butene incorporated in the final product. Regiochemistry of the 1-butene in the products was completely controlled. It is well known that zirconium mediated intermolecular coupling of an alkyne and a mono-substituted alkene does not show high regioselectivity of alkenes.[6] Therefore, the zirconacyclopentene is not the intermediate in this reaction.

1-Butene could be free 1-butene which was eliminated from zirconocene–butene complex, when an alkyne replaced 1-butene of **1a**. In order to make clear this point, *n*-hexyllithium was used instead of *n*-butyllithium. As expected, 5-butyl-2,3-dihexylcyclopent-2-en-1-one (**3f**) was obtained (Eq 3).



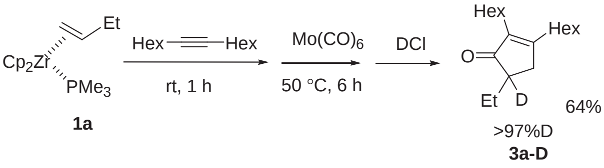
(3)

When 4 equiv. of 1-octene was added to **2a**, a mixture of two products **3a** and **3g**, 5-ethyl- and 5-hexylcyclopentenones, were obtained in 9 and 60% yields, respectively. The ratio of those two compounds depended on the amount of 1-octene. This indicates that the substituent at C5 in the cyclopentenones can be introduced directly from monosubstituted alkenes.



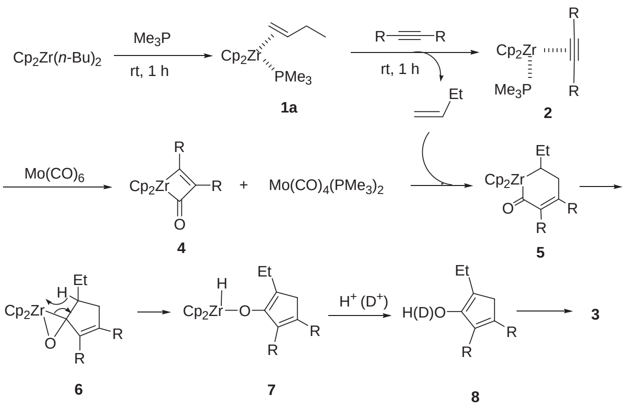
(4)

Deuterolysis of the resulting mixture instead of hydrolysis afforded deuterated **3a-D** in 64% isolated yield with >97% deuterium incorporation at 5-position (Eq 5).



(5)

In the final reaction mixture, the formation of $Mo(CO)_4(PMe_3)_2$ in 45% yield was detected. Based on the results obtained here, a possible mechanism is shown in Scheme 1, although there is no direct evidence for the formation of **5**. A zirconocene–alkyne complex **2** reacts with $Mo(CO)_6$, and PMe_3 is abstracted by $Mo(CO)_6$ to afford $Mo(CO)_4(PMe_3)_2$ and a reactive zirconocene–alkyne complex without PMe_3. The reaction of the reactive zirconocene–alkyne complex with CO liberated from $Mo(CO)_6$ affords zirconacyclobutenone derivative **4** as we reported. It is well known that zirconium complexes react with metal carbonyl complexes to afford stable metal carbene complexes.[7] However, in this reaction, no formation of such stable carbene complex was detected. When an excess of CO is present, the second molecule of CO can react with **4** as we reported. In this reaction, 1-butene in the solution is more reactive than $Mo(CO)_6$, and then selective insertion of 1-butene into the Zr–alkenyl carbon bond of **4** occurs to give **5**. Successive 1,2-shift from **5** to **6** proceeds. β-Hydrogen elimination and three-membered ring opening produces the complex **7** which affords **3** after hydrolysis. As shown here, some steps are still speculative. We must await further investigation to elucidate the reaction mechanism.



Scheme 1. A possible mechanism.

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