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Zirconium Catalyzed or Mediated Regioselective C-C Bond Formation Reactions of α,β-Unsaturated Acetals

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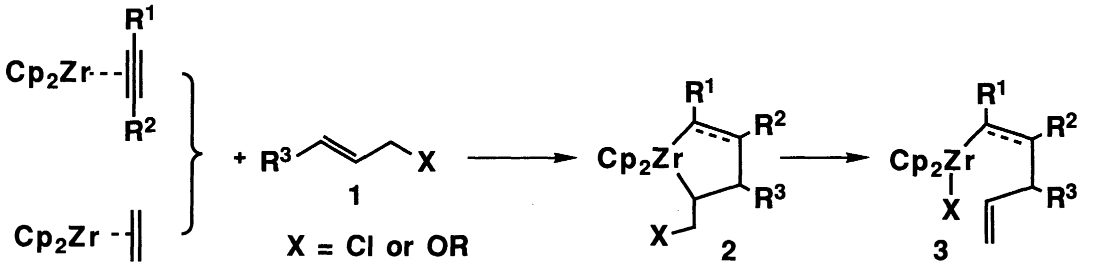
Zirconium-alkyne complexes or zirconacyclopentenes, which were easily prepared in situ from alkynes, reacted with acrolein diethylacetal to afford vinyl ether derivatives. The C-C bond formation proceeded exclusively at β-position of the α,β-unsaturated acetal. Zirconium catalyzed C-C bond formation reactions of α,β-unsaturated acetals with EtMgBr also proceeded at β-position exclusively.

Recently we have reported novel type of allylation reactions catalyzed or mediated by zirconium (eq 1).1) These reactions proceeded exclusively at γ-position of allylic moiety via zirconacyclopentanes or zirconacyclopentenes. In order to extend this type of allylation reactions we investigated the reactions of alkynes or alkenes with α,β-unsaturated acetals. We would like to describe here the highly regioselective C-C bond formation reactions with α,β-unsaturated acetals catalyzed or mediated by zirconium.



(1)

Allylmetalation reactions of unsaturated compounds are very useful reactions.2) However, these reactions using allylmetals have the following critical limitations. (i) Metals available for the allylation reaction are limited. For example, only Li, Mg, B, Zn and Al have been used for the allylmetalation of alkynes.2,3) (ii)There are two regioisomers formed. This is due to allylic rearrangements of allymetals such as allylmagnesium compounds4) or due to the mechanism involving four-centered or six-centered intermediates.2) (iii) It is relatively difficult to use the functionalized allylmetals.

Novel type allylmetalation reactions that we reported recently1) employed a combination of a zirconocene(II)-alkyne complex and an allylic compound. These results represent an expansion in the number of the metals useful for the allylmetalation. In fact, this method provided allylzirconation products, which is in contrast to the allylzirconium compound which does not react with an alkyne. The key point of our method was elimination of the leaving group. This elimination occurred only when CH_2X moiety was in α-position of zirconacyclopentenes or zirconacyclopentanes. The C-C bond formation occurred exclusively at γ-position of allylic compounds. In order to investigate the scope of our new method, we used here α,β-unsaturated acetals which could afford a functionalized allylic moiety in the products.

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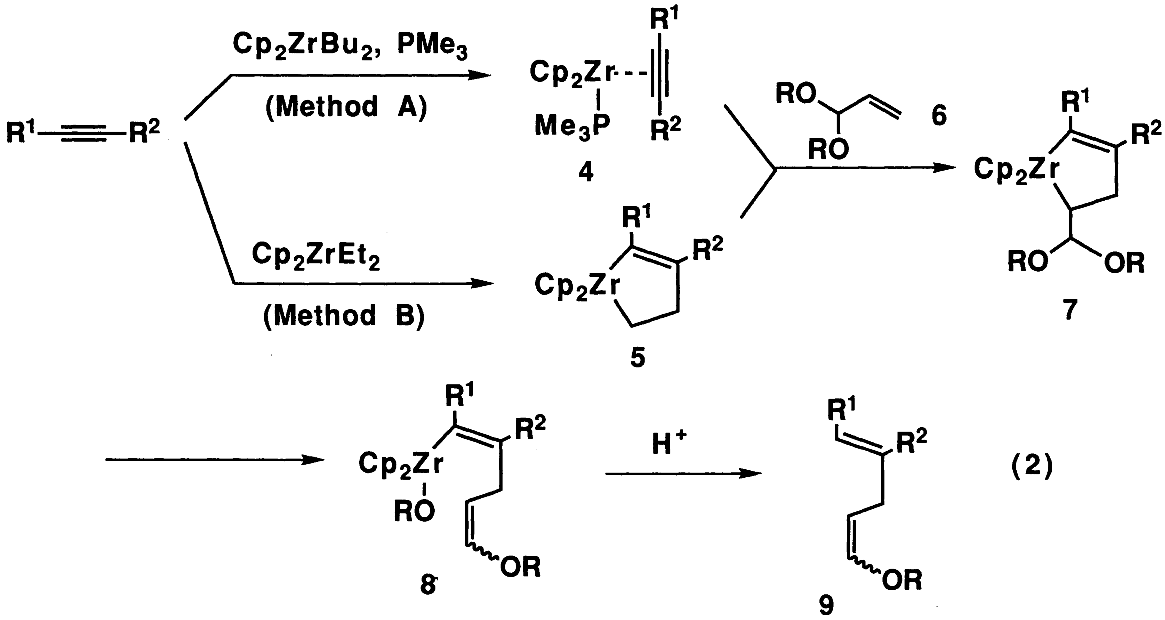
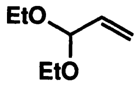
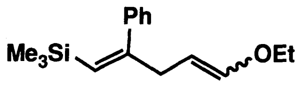
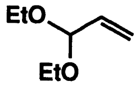
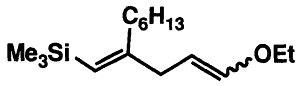
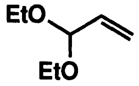
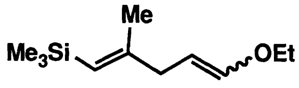
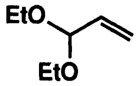
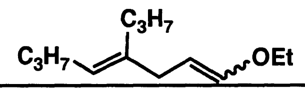


(2)

In this work we used two methods for the reaction of an alkyne with a α,β-unsaturated acetal. One is the reaction of zirconocene-alkyne complexes stabilized with trimethylphosphine5) (Method A). The other is the reaction of zirconacyclopentenes (Method B).

Typical procedure of Method A for the reaction of a zirconocene-alkyne complex with acrolein diethyl acetal is as follows. To a solution of Cp_2ZrCl_2 (1.0 mmol, 0.29 g) in THF (5 cm^3) was added *n*-butyllithium (hexane solution, 1.6 mol dm^{-3}, 1.3 cm^3, 2.0 mmol) at -78 °C and stirred for 1 h. After adding trimethylphosphine (THF solution, 1.0 mol dm^{-3}, 1.1 cm^3, 1.1 mmol) the reaction mixture was warmed up to room temperature and was stirred for 2 h. Addition of 1-trimethylsilyl-1-octyne (1.0 mmol, 0.18 g) gave

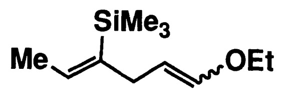
Table 1. Reactions of Alkynes with α,β-Unsaturated Acetals Promoted by Zirconium

Alkyne	α,β-Unsaturated Acetals	Temp /°C	Time /h	Products	Yield /% a)	Regio-selectivity for alkyne/%	cis:trans for vinyl ether
$Ph{\equiv}SiMe_3$		35	1		71b)	>98	53:47
$C_6H_{13}{\equiv}SiMe_3$		35	1		75b)	>98	48:52
$CH_3{\equiv}SiMe_3$		35	24		81b)	89	41:59
$C_3H_7{\equiv}C_3H_7$		r.t.	24		61c)	-	49:51

a) Yields were determined by GC after hydrolysis. b) Method A; Cp_2ZrCl_2 : n-BuLi : Alkyne : PMe_3 : Acetals = 1.0 : 2.0 : 1.0 : 1.1 : 2.0; Solvent THF (5 cm^3). c) Method B; Cp_2ZrCl_2 : EtMgBr : Alkyne : Acetals= 1.25 : 2.5 : 1.0 : 2.0; Solvent THF (5 cm^3).

zirconocene-1-trimethylsilyl-1-octyne phosphine complex in 90-95% yield. To this reaction mixture, acrolein diethyl acetal (2.0 mmol, 0.26 g) was added and the mixture was stirred at 35 °C for 1 h. After hydrolysis 5-trimethylsilyl-4-hexyl-1,4-pentadienyl ethyl ether **9** (R^1 = Me_3Si, R^2 = C_6H_{13}, R = Et) was obtained in 75% yield with >98% of regioselectivity for Me_3Si and C_6H_{13} groups. This reaction proceeded in a syn fashion (>98%) as usually observed for the carbometalation of an alkyne. The cis-trans ratio for vinylether moitey was 48 : 52. For Method B, the zirconacyclopentene was prepared by the procedure we reported⁶⁾ using Cp_2ZrEt_2 and 4-octyne. To this zirconacyclopentene in THF was added acrolein diethyl acetal. Further treatment of the reaction mixture was carried out in the same way as in the typical procedure of Method A.

The results are shown in Table 1. The C-C bond formation proceeded exclusively at the terminal carbon of acrolein diethyl acetal. For unsymmetrical alkynes such as trimethylsilylphenylacetylene and trimethylsilyl-1-octyne, the regioselectivity was very high (>98%). In the case of trimethylsilyl-1-propyne, about 10% of regioisomer **10** was obtained. The cis:trans ratio for vinyl ether moiety was approximately 1:1. β-Substituted acetals such as **11** and **12** did not give the desired products even at 60 °C.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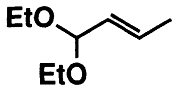
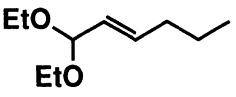

11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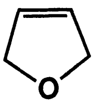
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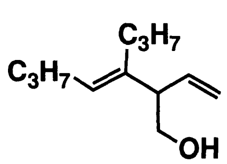
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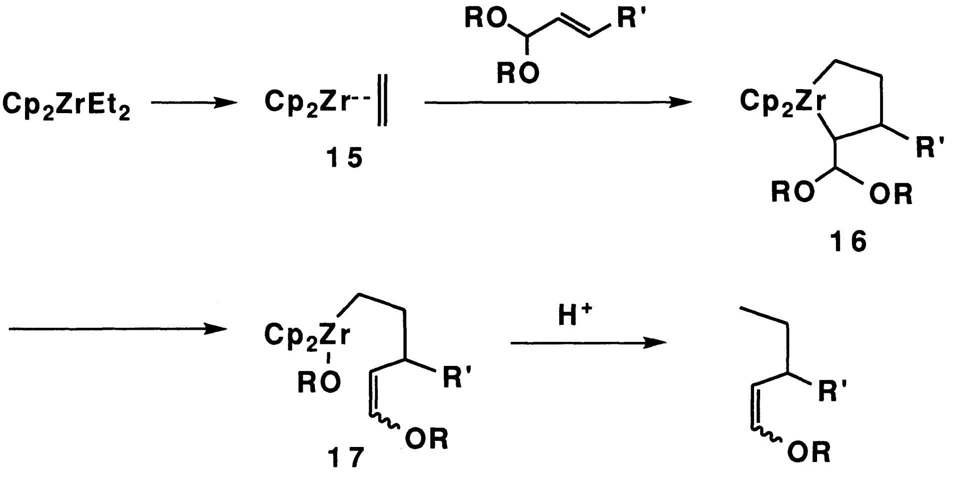
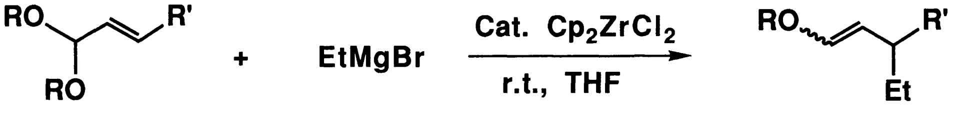
As described above, functionalized allyl moiety such as a vinyl ether group was introduced for the allylzirconation of an alkyne. When 1,4-dihydrofuran is used as an allylic compound for the reaction with a zirconacyclopentene **5** (R^1=R^2=C_3H_7), a homoallylic alcohol **14**⁷⁾ resulted after hydrolysis (yield 75%). Method A also gave a similar result for 1,4-dihydrofuran. Product **14** was obtained in 53% yield after stirring the mixture for 24 h at room temperature.

Zirconocene-ethylene complex $Cp_2Zr(CH_2{=}CH_2)$⁸⁾ **15**, prepared from Cp_2ZrEt_2, reacted with acrolein diethyl ether to give a vinyl ether product **18** in 64% yield. A catalytic cycle could be developed for this reaction



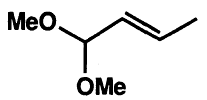
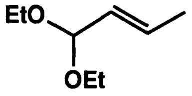
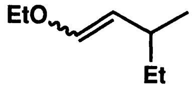
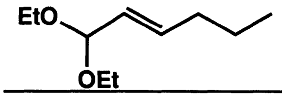
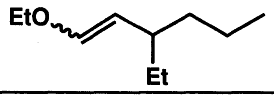
(3)

18: R = Et, R' = H 64%
R = Et, R' = Me 66%



(4)

Table 2. Zirconium Catalyzed C-C Bond Formation of α,β–Unsaturated Acetals with EtMgBr

Substrate	Equiv of EtMgBr	Time /h	Product	Yield /%	trans:cis
	2	24		81	66:34
	2	24		79	75:25
	2	6		61	78:22

a) Conditions; Cp_2ZrCl_2:Acetals = 0.1 : 1; room temperature in THF.

using EtMgBr as we reported for the reaction of allylic ethers (eq 4).[1b] The results for catalytic reactions are shown in Table 2. The C-C bond formation occurred exclusively at the β-carbon of α,β–unsaturated acetals. A plausible mechanism for this catalytic reaction is the same as that we reported for the reactions of allylic ethers.[1b] The key reaction is the regeneration of ethylene complex **15** by the reaction of product **17** with EtMgBr in the reaction mixture.

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7) **14** ($R^1 = R^2 = C_3H_7$) ^1H NMR ($CDCl_3$, Me_4Si): δ 0.90 (t, J = 7.3Hz, 6H), 1.30-1.46 (m, 4H), 1.48-1.60 (m,1H), 1.95-2.07 (m, 4H), 2.80-2.90 (m, 1H), 3.49-3.70 (m, 2H), 5.08-5.15 (m, 2H), 5.22 (t, J = 7.3Hz, 1H), 5.66-5.81 (m, 1H) ; ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.87, 14.29, 22.23, 23.11, 29.90, 32.40, 53.01, 63.95, 116.31, 127.40, 138.25, 138.70 .

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