Pergamon

Tetrahedron Letters 41 (2000) 109–112

TETRAHEDRON
LETTERS

Copper(I)-catalyzed cross-coupling reaction of acylzirconocene complexes with allylic and/or propargylic halides

Yuji Hanzawa,* Kensuke Narita and Takeo Taguchi *

School of Pharmacy, Tokyo University of Pharmacy and Life Science 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

Received 22 September 1999; revised 18 October 1999; accepted 22 October 1999

Abstract

Efficient cross-coupling reaction of acylzirconocene chloride with allylic and/or propargylic halides was attained by utilizing a catalytic amount of a Cu(I) salt to give allylic and/or allenic ketones, respectively, in good yields. The mild Cu(I)-catalyzed reaction of acylzirconocene chloride offered an alternative protocol for the generation of an 'unmasked' acyl anion. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: zirconium; zirconium compounds; coupling reactions; copper catalyst.

The cross-coupling reaction of an acylmetal species with organic halides has attracted attention for the synthesis of the unsymmetrical ketone derivatives. However, the instability and/or toxicity of the starting acylmetal species sometimes restricts its practical use for the synthesis.[1] Our recent studies[2] on the reactivity of the stable acylzirconocene chloride complex **1**,[3] which is easily accessible through hydrozirconation of alkene or alkyne with $Cp_2Zr(H)Cl$ (Schwartz reagent)[4] and subsequent insertion of carbon monoxide, have indicated a promising use of **1** as an 'unmasked' acyl anion donor (Scheme 1). In these studies, the Pd-catalyzed cross-coupling reaction with organic halides showed the usability of **1** for the preparation of unsymmetrical ketones.[2c]

However, in the Pd-catalyzed coupling reactions of **1** with allylic halides and/or acetate, the purification of the coupling product, β,γ-unsaturated ketone, was sometimes hampered by the formation of a side product, α,β-unsaturated ketone, which is derived from the isomerization of the β,γ-double bond. For practical purposes, exclusive formation of the β,γ-unsaturated ketones is desirable. In this communication, we describe Cu(I)-catalyzed cross-coupling reactions of **1** with allylic and propargylic halides under mild reaction conditions. Reactions of the acylzirconocene chlorides **1** [R; $Ph(CH_2)_4$ (**1a**) or R; (*E*)-$Ph(CH_2)_2CH{=}CH$ (**1b**)] with allyl halides in the presence of a catalytic amount (10 mol%) of Cu(I) in DMF or THF were completed within 1 h at 0°C to give acyl–allyl coupled products **2** in good yields, and no isomerized side product **3** was obtained (Eq. (1)). The results are listed in Table 1. Most of the examined Cu(I) salts except $CuBr\cdot SMe_2$ (entry 6) can be used as an efficient catalyst. Allyl tosylate is also an excellent reactant in the present reaction (entry 4) while allyl acetate is not. Not only **1a** but also

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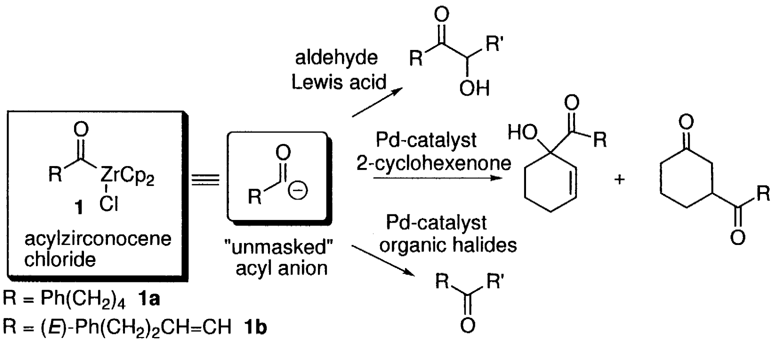
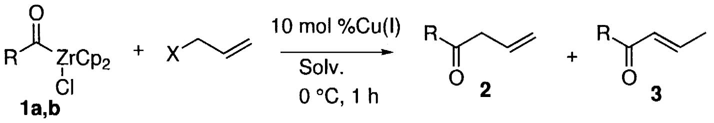
* Corresponding authors. Tel: +81 426 76 3274; fax: +81 426 76 3257; e-mail: hanzaway@ps.toyaku.ac.jp (Y. Hanzawa)

PII: S0040-4039(99)02015-8



Scheme 1. Reactions of acylzirconocene chloride **1** as an ‘unmasked’ acyl anion

α,β-unsaturated acylzirconocene **1b** gave **2** in a good yield (entry 9). Thus, the mild reaction conditions of Cu(I)-catalyzed coupling reactions of **1** compared to the previously reported Pd-catalyzed reactions[2c] exert a desirable influence on the formation of **2**.



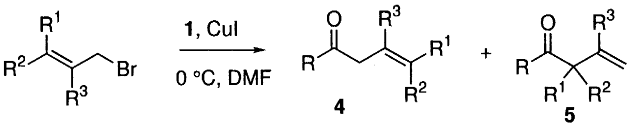
(1)

Table 1
Cu(I)-catalyzed coupling reaction of **1** with allyl compounds

Entry	**1**	X	Cu(I)	Solvent	Yields / %[b]	
					2	**3**
1	**1a**	Br	CuI	DMF	91	0
2	**1a**	Cl	CuI	DMF	44	0
3	**1a**	I	CuI	DMF	76	0
4	**1a**	OTs	CuI	DMF	77	0
5	**1a**	Br	CuI•2LiCl	THF	88	0
6	**1a**	Br	CuBr•SMe$_2$	THF	trace	0
7	**1a**	Br	CuBr	DMF	78	0
8	**1a**	Br	CuCl	DMF	84	0
9	**1b**	Br	CuI	DMF	78	0
10	**1a**	Br	CuCN•2LiCl	THF	87	0

[a] 1.5 Equiv. of **1** vs allyl compounds was used.
[b] Yieds are calculated from allylic compounds.

Substituted allylic bromides also reacted with **1** under identical conditions to give a mixture of regioisomers (**4** and **5**) (Eq. (2) and Table 2). In the reaction of prenyl bromide, it required a longer reaction time (10 h) for the completion of the reaction (entries 1 and 2). Reactions of propargyl bromide and/or tosylate derivatives **6** with **1** afforded allenyl ketone derivatives **7** as the sole product, and propargyl ketone **9** was not detected in the reaction mixture (Eq. (3)).

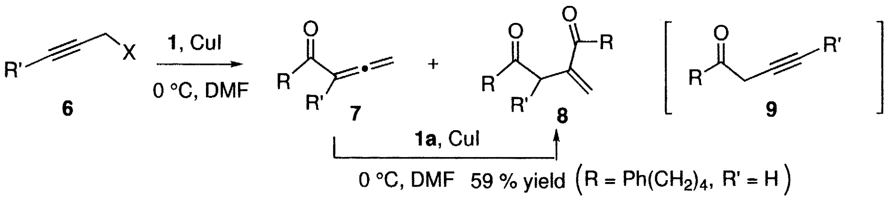


(2)

Table 2
Cu(I)-catalyzed coupling reaction of **1a** with substituted allylic halides

Entry	**1**	R^1	R^2	R^3	Reaction Time	Yields/%[a] **4**	**5**	total
1	**1a**	CH_3	CH_3	H	1	13	24	37
2	**1a**	CH_3	CH_3	H	10	29	62	91
3	**1b**	CH_3	CH_3	H	10	18	29	47
4	**1a**	CH_3[b]	H[b]	H	1	20	52	72
5	**1a**	H	H	CH_3	10	84		

[a] Calculated from allylic bromide.
[b] (*E*)-crotyl bromide : (*Z*)-crotyl bromide : 3-bromo-1-butene = 73 : 14 : 13.



(3)

It is interesting to note that the utilization of an increased amount (3 equiv.) of **1a** versus **6** gave a significant amount of 1,4-dicarbonyl compound **8** together with **7** (entry 2, Table 3). The observation that the independent reaction of **7** (R′=H) with **1a** under identical conditions afforded **8** in 59% yield indicates

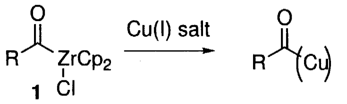
Table 3
Cu(I)-catalyzed coupling reaction of **1** with propargylic compounds

Entry	**1**	Equiv of **1** vs **6**	R'	X	Time	Yields/% **7**	**8**	**9**
1	**1a**	1.5	H	Br	1	65[a]	< 5[a]	0
2	**1a**	3.0	H	Br	1	24[a]	48[a]	0
3	**1a**	0.5	H	Br	1	55[b]	0	0
4	**1a**	0.5	H	OTs	10	21[b]	0	0
5	**1a**	0.5	Me	Br	10	61[b]	0	0
6	**1b**	0.5	H	Br	1	52[b]	0	0
7	**1b**	0.5	Me	Br	1	47[b]	0	0

[a] Calculated from **6**.
[b] Calculated from **1**.

the Cu(I)-catalyzed Michael addition of **1a** to **7**.[5] The formation of **7** as the sole product was attained by utilizing an excess amount (2 equiv.) of propargyl bromide versus **1** (entries 3–7). The attempted reactions of **1** with alkyl, vinyl, homoallyl and aryl halides failed to yield the coupling products. [6]

Although the exact role of the Cu(I)-catalyst in the present reaction is, as yet, unclear, it has been reported that the transmetalation of an acyl group from zirconium to aluminum occurs to yield acylaluminum.[7] It has also been reported that the transmetalation of an alkyl or vinyl group from zirconium to copper has been applied to carbon–carbon bond formations.[8] Thus, in the present reactions, the transmetalation of the acyl group from zirconium to copper giving an 'acyl–Cu' species as a transient species might have been involved (Eq. (4)).[9]



(4)

In summary, this paper describes an efficient coupling reaction of acylzirconocene chlorides with allyl and/or propargyl halides in the presence of a Cu(I) salt. The methodology opened further possibility of acylzirconocene chloride as an 'unmasked' acyl anion. Further studies towards an actual reactive species of this process are under current investigation in our laboratory.

General experimental procedure: **1** (1.5 mmol) in DMF or THF (10 mL) was prepared through: (i) a reaction of 4-phenyl-1-butene (1.5 mmol) and $Cp_2Zr(H)Cl$ (1.5 mmol) in CH_2Cl_2 (5 mL) at ambient temperature for 0.5 h followed by the insertion of CO (stirring at ambient temperature for 2 h using a CO balloon); (ii) concentration of the solvent to dryness in vacuo and addition of THF or DMF. To the solution of **1** was added a solution of allylic or propargylic halide (1 mmol) in THF or DMF (2 mL) at 0°C. After addition of Cu(I) (10 mol%) at 0°C, the mixture was stirred for 1–10 h at the same temperature. The reaction mixture was filtered through a short dry silica gel pad and the filtrate was concentrated to dryness to give a crude oil. Purification by silica gel column chromatography (hexane:ethyl acetate) gave a pure product.

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