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Palladium–Catalyzed Reactions of Acylzirconocene Chloride with Organic Halides

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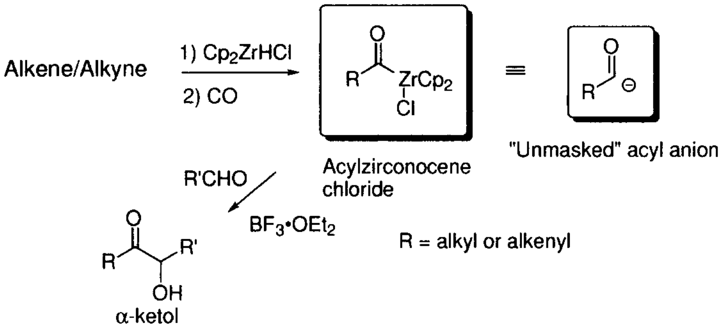
Abstract: Palladium–catalyzed reactions of nonanoylzirconocene chloride **1** with aryl halide, acid halides, and allylic halides gave the acylated compounds through a nucleophilic attack of an "unmasked" acyl anion in fair to excellent yields. In an analogous way, allylic acetate gave an acyl substituted product through the reaction of **1**.

Keywords: Complexes; Coupling reactions; Palladium and compounds; Zirconium and compounds

Acylzirconocene chloride, which is a stable and easily available complex through hydrozirconation of alkene/alkyne with zirconocene hydrochloride (Cp_2ZrHCl) and subsequent insertion of carbon monoxide, is an important intermediate for the preparation of aldehyde and carboxylic acid derivatives from alkene and/or alkyne.[1] Among extensive research work on the acylzirconocene chloride, its transformation to a zirconocene (Cp_2Zr)–ketene complex and the following reactions with unsaturated compounds are noteworthy in the sense of a carbon-carbon bond forming reaction.[2] Recently, we disclosed the Lewis acid-mediated reactions of the acylzirconocene chloride with aldehydes to give α-ketol derivatives.[3] In these reactions, the acylzirconocene chloride reacts as an "unmasked" acyl anion under mild reaction conditions. The results of our findings of the acylzirconocene chloride as an "unmasked" acyl anion[3] and the palladium-catalyzed carbon-carbon bond forming reaction of an acyltin species[4] with organic halide led us to examine the palladium-catalyzed coupling reaction of the acylzirconocene chloride with organic halide.



In this communication, we describe the further utilization of the acylzirconocene chloride as an "unmasked" acyl anion in organic synthesis: a palladium–catalyzed coupling reaction of nonanoylzirconocene chloride **1** with organic halide and allylic acetate derivatives (Scheme 1). The reaction of **1** with organic halide without any catalyst did not give the desired product. In the presence of a palladium catalyst, the nucleophilic acylation products are obtained in modest to good yields. The results of $PdCl_2[P(C_6H_5)_3]_2$-catalyzed reactions in toluene at 100 °C (oil bath temperature) are shown in Table 1.

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Scheme 1

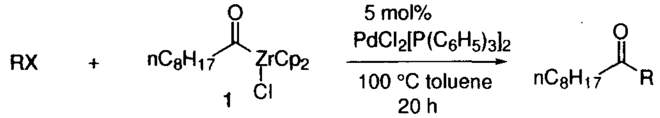
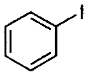
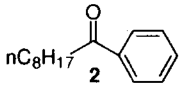
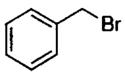
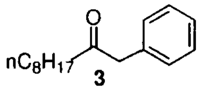
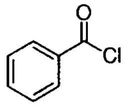
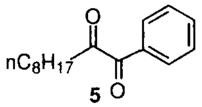
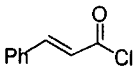
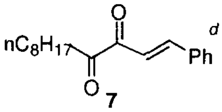
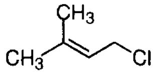
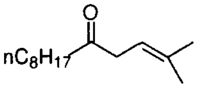
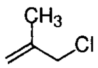
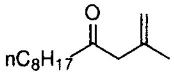
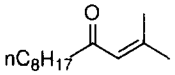
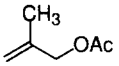
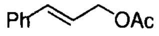
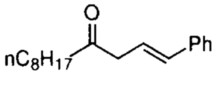
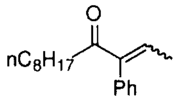
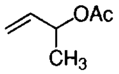
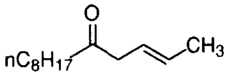
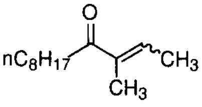
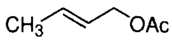


Table 1.PdCl$_2$[P(C$_6$H$_5$)$_3$]$_2$-catalyzed reactions of nonanoylzirconocene chloride **1**

Entry	RX	Product	Yield (%)[a]
1		 **2** [b]	32
2		 **3** [b]	27
3		 **5** [c]	38
4		 **7** [d]	65
5			62
6		 **8** 1.7 : 1 10 : 1[e]  **9**	60
7		3 : 1	86
8		  1 : 5	91
9	 **10**	  1 : 1	56
10	 **11**	1.2 : 1	80

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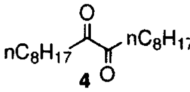
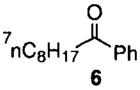
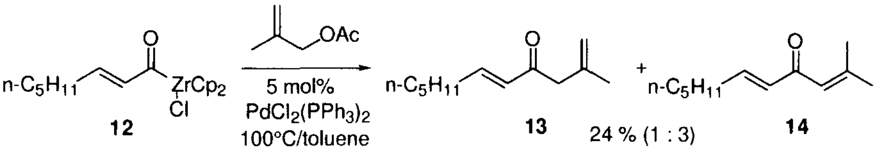
[a] Isolated yield. [b] Diketone **4** (15% yield) was formed as side product. [c] Ketone **6** was formed in 11 % yield. [d] Reaction conditions; rt for 48 h. [e]Reaction conditions; 50 °C for 48 h.

 **4**

 **6**

Iodobenzene and benzyl bromide gave **2** and **3** in 32 and 27 % yields along with a considerable amount of self-coupled α-diketone **4** (15 %) derived from **1** (entries 1, 2). The reaction of alkyl halide did not give an appreciable amount of the acylated product. Changing the catalyst to $[(C_6H_5)_3P]_4Pd$,[5] $PdCl_2[P(C_6H_5)_3]_2$–DIBAL-H or $(CH_3CO_2)_2Pd$–triphenylphosphine resulted in the formation of the products (**2** and **3**) in lower yields (less than 10 %) compared to $PdCl_2[P(C_6H_5)_3]_2$. Reaction of **1** with benzoyl chloride gave α-diketone **5** and ketone **6**, which is a decarbonylated product of **5**, in 38 % and 11 % yields, respectively (entries 3). Although the reaction of cinnamoyl chloride also gave a diketone **7**, a higher yield (65 %) of **7** was obtained by reacting cinnamoyl chloride at ambient temperature for 48 h under otherwise identical reaction conditions (entry 4). These observations indicate that acylzirconocene chloride can be used as an acyl anion source in the palladium–catalyzed nucleophilic substitution reactions.[6] The reaction was also effected by treating a toluene solution of allylic halides (entries 5, 6). Thus, the reactions of methallyl chloride with **1** gave a mixture of β,γ-unsaturated ketone **8** and the isomerized α,β-unsaturated ketone **9** in 60 % yield (entry 6). The frequently used catalysts for the allylic substitution, $[(C_6H_5)_3P]_4Pd$ (30% yield) and/or $Pd_2(dba)_3{\cdot}CHCl_3$-$(C_6H_5)_3P$ (55% yield) turned out to be less effective catalysts in the present reactions of **1**.[7] The formation of the isomerized α,β-unsaturated ketone **9** was significantly suppressed (**8** : **9** = 10 : 1) by lowering the reaction temperature to 50 °C although it took a longer reaction time (48 h) for the completion. It has been well established that the allylic acetate species is an excellent precursor for the generation of a π-allylic palladium complex.[8] In our present cases, **1** reacts with allylic acetate derivatives to give a mixture of β,γ- and α,β-unsaturated ketones **8** and **9** in even better yields than in the cases of allylic halides under the same catalytic conditions (entries 7~10). The results of the reactions of **1** with the isomeric allylic acetates (**10**, **11**) were consistent with the nucleophilic attack of an acyl anion to a common π-allylic palladium complex intermediate since an almost identical ratio of the products was obtained through the reactions of isomeric allylic acetates **10** and **11**, respectively (entries 9, 10). It should be mentioned that the present palladium-catalyzed reaction of acylzirconocene chloride is applicable to an unsaturated acylzirconocene complex **12** (Scheme 2). Thus, the reaction of α,β-unsaturated acylzirconocene chloride **12** with methallyl acetate gave acylated products (**13**, **14**) in somewhat lower yield under the same reaction conditions.

Scheme 2



Typical experimental procedure: Under an argon atmosphere, 1-octene (0.47 mL, 3 mmol) was added to a suspension of Cp_2ZrHCl (387 mg, 1.5 mmol) in CH_2Cl_2 (8 mL) at ambient temperature and the mixture was stirred for 0.5 h. After the argon balloon was changed to a CO balloon, the mixture was stirred for 2 h at ambient temperature, the mixture was concentrated to dryness *in vacuo* and the residue was dissolved in toluene (15 mL). To the toluene solution was added $PdCl_2[P(C_6H_5)_3]_2$ (35 mg, 5 mol%) and methallyl acetate (114 mg, 1 mmol) at ambient temperature, and the mixture was stirred at 100 °C for 20 h. After adding aq. $NaHCO_3$, the reaction mixture was extracted with ether. The crude product was purified by silica gel column chromatography (hexane–EtOAc = 75 : 1) to give a mixture of **8** and **9** in 86 % combined yield. The mixture was finally separated by medium-pressure column chromatography (hexane–EtOAc = 100 : 1) to give pure products.

The chemistry of acylzirconocene chloride has been developed by many research groups; however, there is no example which shows that the acylzirconocene chloride behaves as an acyl anion in nucleophilic substitution reactions. Thus, the present paper shows the further possibility of acylzirconocene chloride as an "unmasked" acyl anion in organic synthesis.

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References and Notes

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3. Harada, S.; Taguchi, T.; Tabuchi, N.; Narita, K.; Hanzawa, Y. *Angew. Chem. Int. Ed. Engl.* in press.
4. It has been reported that the palladium–catalyzed reactions of an acyltin species with acid halide and allylic halide gave α-diketone and allylketone, respectively.
   a) Verlhac, J.; Chanson, E.; Jousseaume, B.; Quintard, J. *Tetrahedron Lett.* **1985**, *26*, 6075. b) Kosugi, M.; Naka, H.; Harada, S.; Sano, H.; Migita, T. *Chem. Lett.* **1987**, 1371.
5. In the $[(C_6H_5)_3P]_4Pd$-catalyzed reaction of iodobenzene, an addition of 1 equiv of $ZnCl_2$ to the reaction mixture improved the yield of **2** from less than 5 % to 28 %. Although the exact role of $ZnCl_2$ is unclear in our case, this additive effect of $ZnCl_2$ might suggest one possibility of the transmetalation process of an acylzirconocene derivative to an acylzinc species. Similar observation has been reported in the Pd-catalyzed reaction of vinylzirconocene chloride derivatives with vinyl halide by Negishi et al. Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254.
6. Structures of new compounds were determined unambiguously by spectroscopic (1H-, 13C-NMR, IR, MS) and combustion analyses.
7. $Ni[COD]_2$ (10 mol%) catalyst in the presence of $ZnCl_2$ (1 equiv) can also be used as a less efficient catalyst.
8. Tsuji, J. *"Palladium Reagents and Catalyst: Innovations in Organic Synthesis"* John Wiley & Sons, **1995**.