Pergamon

Tetrahedron Letters 41 (2000) 2911–2914

TETRAHEDRON
LETTERS

Palladium-catalyzed cyanoallylation of activated olefins

Hiroyuki Nakamura, Hitoshi Shibata and Yoshinori Yamamoto *

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-8578, Japan

Received 5 January 2000; accepted 14 February 2000

Abstract

The three-component coupling reaction of the activated olefins **1**, allylic chlorides **2**, and trimethylsilyl cyanide proceeded very smoothly in the presence of $Pd_2dba_3\cdot CHCl_3$–2dppf catalyst in THF to give the corresponding cyanoallylation products **3** in good to high yields. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: palladium; cyanoallylation; activated olefins; π-allylpalladium cyanide complex.

Trimethylsilyl cyanide has been known as a versatile reagent to introduce a cyano group into organic molecules.[1] Recently, it was reported that allylic carbonates and acetates undergo cyanation with trimethylsilyl cyanide in the presence of palladium catalysts to afford the corresponding allylic cyanides in high yields.[2,3] The detailed mechanistic study revealed that the cyanation proceeded via a π-allylpalladium cyanide complex, which was isolated and characterized by X-ray analysis.[4] We previously reported that a bis-π-allylpalladium complex, which is formed in situ from allyl chloride and an allylstannane, reacts with certain Michael acceptors in a catalytic amphiphilic manner to give the corresponding α,β-dialkylated adducts in high yields (three-component coupling, Fig. 1(a)).[5]

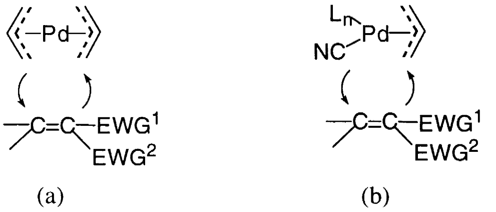

Fig. 1. Amphiphilic reactivity of π-allylpalladium complexes

It occurred to us that, by proper choice of amphiphilic substrates, similar three-component coupling reactions[6,7] may proceed between a π-allylpalladium cyanide complex and Michael acceptors (Fig. 1(b)). Actually, the reaction of the activated olefins **1** with the allylic chlorides **2** and trimethylsilyl cyanide took

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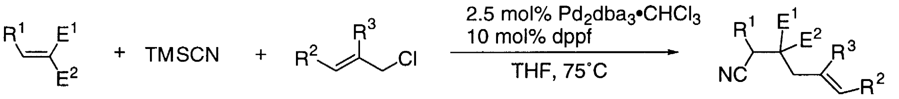
* Corresponding author.

PII: S0040-4039(00)00284-7

place in the presence of a $Pd_2dba_3 \cdot CHCl_3$–4dppf catalyst in THF to give the three-component coupling products **3** in good to high yields (Eq. (1)).



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1a: R^1=Ph, E^1=E^2=CN
b: R^1=*p*-$MeOC_6H_4$, E^1=E^2=CN
c: R^1=*p*-MeC_6H_4, E^1=E^2=CN
d: R^1=*p*-$MeO_2CC_6H_4$, E^1=E^2=CN
e: R^1=*n*-Pentyl, E^1=E^2=CN
f: R^1=*t*-Bu, E^1=E^2=CN
g: R^1=*i*-Pr, E^1=E^2=CN
h: R^1=Ph, E^1=CN, E^2=CO_2Et
i: R^1=*n*-Pen, E^1=CN, E^2=CO_2Et

2a: R^2=R^3=H
b: R^2=H, R^3=Me
c: R^2=Me, R^3=H
d: R^2=Ph, R^3=H
e: R^2=H, R^3=Cl

(1)

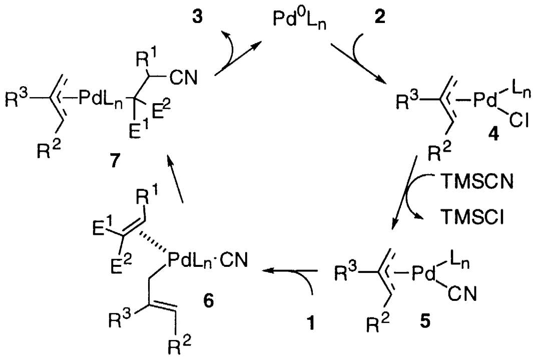
The results are summarized in Table 1. The reaction of benzylidene malononitrile **1a**, allyl chloride **2a**, and trimethylsilyl cyanide proceeded very smoothly in the presence of $Pd_2dba_3 \cdot CHCl_3$–4dppf catalyst in THF at 75°C to give the corresponding cyanoallylation product **3a** in 89% yield (entry 1). Although allyl acetate and carbonate are effective for the palladium-catalyzed cyanation, allyl chloride gave the best result for the cyanoallylation. The use of $Pd(PPh_3)_4$ gave **3a** in lower yield. Not only the activated olefins derived from malononitrile with aromatic aldehydes (**1a**–**d**) but also those derived from malononitrile with aliphatic aldehydes (**1e**–**g**) underwent the cyanoallylation (entries 1–7). The reaction of the activated olefins (**1h**–**i**) prepared from ethyl cyanoacetate gave the cyanoallylation products in lower yields (entries 8 and 9). Next, various allylic chlorides were examined for the reaction. The reaction of **1f** with methallyl chloride **2b** proceeded quantitatively (entry 10). Although the reaction of crotyl chloride **2c** gave the α-adduct **3k** in 74% yield along with the γ-adduct **3l** in 25% yield, the reaction of cinnamyl chloride **2d** afforded the α-adduct **3m** exclusively (entry 11 versus 12). The reaction of 2,3-dichloropropene **2e** with **1f** gave **3n** in 40% yield. The vinylation product was not obtained in this case.[8]

Table 1
Palladium-catalyzed cyanoallylation of activated olefins **1** with allylic chlorides **2** and TMSCN

entry	olefin **1**	allylic chloride **2**	product **3**	yield of **3** (%)[a]
1	**1a**	**2a**	**3a**	89
2	**1b**	**2a**	**3b**	80
3	**1c**	**2a**	**3c**	84
4	**1d**	**2a**	**3d**	82
5	**1e**	**2a**	**3e**	77
6	**1f**	**2a**	**3f**	>99
7	**1g**	**2a**	**3g**	86
8[b]	**1h**	**2a**	**3h**	34 (67/33)
9	**1i**	**2a**	**3i**	48 (64/36)
10	**1f**	**2b**	**3j**	>99
11	**1f**	**2c**	**3k**	74[c]
12	**1f**	**2d**	**3m**	74
13	**1f**	**2e**	**3n**	40

[a] Isolated yields based on **1**. Diastereomer ratios are indicated in the parenthesis. [b] The reaction was carried out at 100°C. [c] The γ-adduct, *t*-Bu(CN)$CHC(CN)_2CH(Me)CH{=}CH_2$ (**3l**), was also obtained in 25% yield.

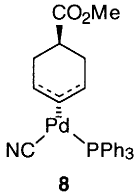
A mechanistic rational which accounts for the cyanoallylation of activated olefins is shown in Scheme 1. The oxidative addition of Pd(0) to the allyl chloride **2** would produce the π-allylpalladium chloride complex **4**. The ligand exchange of Cl with CN would produce the π-allylpalladium cyanide complex **5**, which would react with the activated olefins **1** to give the π-allylpalladium intermediate **7** via the σ-allylpalladium cyanide-olefin complex **6**. The reductive coupling from **7** would give the corresponding cyanoallylation products **3** and a Pd(0) species. In the amphiphilic π-allylpalladium cyanide complex **5**, CN reacts in a nucleophilic manner and the π-allyl ligand in an electrophilic manner.



Scheme 1.

A representative procedure for the cyanoallylation is as follows: To a solution of benzylidene malononitrile **1a** (0.5 mmol, 77 mg), $Pd_2dba_3{\cdot}CHCl_3$ (0.013 mmol, 12 mg), and dppf (0.05 mmol, 28 mg) in THF (2.5 mL) were added allyl chloride **2a** (1.0 mmol, 60 μL) and TMSCN (1.0 mmol, 100 μL) under Ar, and the mixture was stirred at 75°C for 1 day. The reaction progress was monitored by TLC and at this stage the starting material **1a** was consumed completely. The reaction was quenched by filtering the mixture through a short silica gel column. Purification by silica gel column chromatography (hexane:ethyl acetate=9:1) gave the cyanoallylation product **3a** as a colorless liquid (98 mg, 89% yield).

The key for the cyanoallylation is the stability of the π-allylpalladium cyanide complex **5** during the reaction pathway. If the reductive coupling of the allyl and cyanide groups is very fast, allyl cyanide must be produced. However, this is not the case. Actually, 1-methoxycarbonyl-3,4,5-η-cyclohexyl(triphenylphosphine)palladium cyanide **8** was isolated and characterized by X-ray analysis.[4] Therefore, the π-allylpalladium cyanide complex **5** is stable enough to undergo further insertion of activated olefins **1**, giving the cyanoallylation products **3** via **7**. We also confirmed that the reaction of allyl cyanide with **1a** under palladium catalysis did not take place at all. Further extension of the catalytic cyanoallylation is now in progress.



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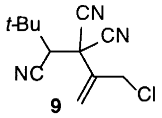

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