Palladium catalyzed hydrocarbonation of olefins

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Abstract: The addition of activated methylene and methynes 5 to monoalkyl- and di-substituted allenes 6 takes place in the presence of catalytic amounts of Pd$_2$(dba)$_3$·CHCl$_3$ in THF under reflux, giving the internal alkenes 7 and 8. The nucleophile attacks the terminal carbon of the allenes. The addition of methylmalononitrile 5b to arylallenes 12 affords the internal adducts 13 and 14 either exclusively or predominantly when an electron withdrawing group is present at the para-position, whereas it gives the terminal adduct 15 exclusively when an electron donating group is present at the para-position. The addition of 5b and 5d to $\alpha$-alkoxyallenes 16 affords the $\alpha$-addition products 17 in good to high yields. The reaction of pronucleophiles with allyltributylstannanes in the presence of catalytic amounts of Pd$_2$(dba)$_3$(4 mole %) and dppe(10 mole %) at room temperature gives the corresponding allylation products in good to high yields.

The addition of carbanionic organometallic compounds 1 to activated alkenes 2a, such as Michael acceptors, is a classical and standard procedure for the C-C bond formation (Type A). In modern organic synthesis, the use of transition metal catalysts enables the addition of 1 to unactivated alkenes 2b (Type B)(1). The additions of activated methylenes and methynes 3 to activated alkenes 2a in the presence of bases are commonly known as Michael reactions, which afford the C-C bond forming product 4 (Type C). More recently, the transition metal catalyzed version of Type C has been discovered(2). We have found the transition metal catalyzed addition of activated methylenes and methynes 3 to allenes(3), which are thought to fall under the category of unactivated alkenes (Type D).

Palladium Catalyzed Addition of Pronucleophiles to Di- and Monoalkyl-substituted Allenes(4)

The addition of activated methylenes and methynes 5 to di- and monoalkyl-substituted allenes 6 proceeded smoothly in the presence of catalytic amounts of Pd$_2$(dba)$_3$·CHCl$_3$ in THF under reflux to give the internal alkenes (7 and/or 8) (eq 1). The addition of malononitrile 5a and methylmalononitrile 5b to 4-phenyl-1,2-butadiene 6a proceeded smoothly to give exclusively the trans alkenes 7a and 7b, respectively. It should be noted that double addition took place in the case of 5a, because the mono-adduct $R^1R^2C=CHCH_2CH(CN)_2$ had a more reactive tertiary C-H bond.
The addition of 5b to 6c proceeded smoothly, but a mixture of the trans and cis alkenes was obtained. Compared to the monosubstituted allenes 6a-e, the disubstituted allenes 6d-g gave higher chemical yields and better material balance. The addition of 5b to 6d and 6e afforded exclusively the trans alkenes 7f and 7g, respectively. However, a mixture of the trans and cis alkenes was obtained in the addition reactions to 6f and 6g.

A mechanistic rationale which accounts for the unprecedented addition of certain activated nucleophiles to allenes is shown in Scheme 1. The oxidative insertion of Pd(0) into the C-H bond of the activated nucleophiles(5) would produce the Pd(I) species 9 (or alternatively a tautomeric structure H₃C(CN)C=C=NPdHLn may be more suitable). The carbopalladation of the allene with 9 would afford the alkenylpalladium(11) complex 10, which would undergo reductive coupling to give the addition product and Pd(0) species. As an alternative mechanism, it may be considered that the hydropalladation of the allene with 9 gives the π-allylpalladium complex 11 which undergoes reductive coupling to afford the adduct and palladium (0) species.

Regioselectivity Reversal in the Palladium Catalyzed Hydrocarbonation of Allenes(6)

Phenyllallene 12a, in which neither an electron-donating nor electron-withdrawing group is present at the para-position, gave the terminal trans adduct 15a in 33% yield. As minor products, the internal adducts 13a (19%) and 14a (6%) were obtained. The ratio of the internal to terminal adducts (32/19) in the case of para-fluorophenylallene 12b was greater than the ratio in the case of 12a (27/33). The reactions of para-chloro (12c), bromo (12d), trifluoromethyl (12e), and trifluoromethoxy (12f) phenylallenes with methylmalononitrile 5b gave the internal adducts (13c-13f, and 14c-14f, respectively) exclusively. No terminal trans adducts 15 were detected. Very interestingly, the terminal trans adducts 15c and 15d were afforded as a single product in good to high yields in the reaction of arylallenes in which electron donating methyl and methoxy (12g, 12h) groups were present at the para-position. Accordingly it is clear that the electron donating group at the para-position directs the "hydrocarbonation" reaction in a way to give the terminal adducts, whereas the electron-withdrawing group to give the internal adducts. A sterically bulky nucleophile 5c behaved differently. Regardless of the electronic effect of the substituent at the para-position of aryllallenes (12b-12h), the terminal trans adducts (7e-7k) were obtained as a sole product. Therefore, the steric effect of nucleophiles 5 also plays an important role to control the regioselectivity of the "hydrocarbonation" reaction.
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The "hydrocarbonation" reaction of allenes with activated methynes (H–Nu), can be explained either by a carbopalladation or by a hydropalladation mechanism; the terminal adduct is produced either via a vinylpalladium intermediate arised from the carbopalladation of the terminal double bond of allenes or via a \( \pi \)-allylpalladium intermediate formed by the hydropalladation of the terminal double bond. The present results (eq 2) may be accounted for also by the hydro- or carbo-palladation mechanism(7).

Palladium Catalyzed \( \alpha \)-Addition of Pronucleophiles to Alkoxy(phenoxy)-allenes(8)

The reactions of phenylpropyloxy-(16a), phenylethoxy-(16b) and benzyloxy-allenes 16c with pronucleophiles (5b and 5d) gave the corresponding \( \alpha \)-adducts 17a - f in good to high yields (eq.3). No regioisomeric adducts were produced. Although the reaction of phenyloxyallene 16d with 5b afforded regioselectively the \( \alpha \)-adduct 17g in 57% yield, the reaction of 16d with 5d gave the \( \gamma \)-adduct 18 in 19% yield along with the \( \alpha \)-adduct 17h (49%). Next, we examined the palladium catalyzed reaction of a sterically more bulky pronucleophile 5c. Very interestingly, the \( \gamma \)-adducts 19 were obtained regioselectively regardless of alkoxy- and phenyloxyallenes 16; 19a in 77%, 19b in 75%, 19c in 62% and 19d in 84% yield. No regioisomeric adducts were produced in these cases. Consequently it is clear that the palladium catalyzed reaction of alkoxy- and aryloxyallenes 16 with pronucleophiles 5b and 5d affords the \( \alpha \)-adducts 17 either exclusively or predominantly, whereas the reaction of 16 with 5c gives the \( \gamma \)-adduct 19. Perhaps the \( \gamma \)-regioselectivity in the case of the reaction using 5c is due to the steric crowding around the nucleophilic carbon center of 5c. It is interesting that pronucleophiles 5b and 5d, less sterically demanding than 5c, exhibit \( \alpha \)-regioselectivity.
It has been known that the palladium catalyzed allylic substitution of 3-alkoxy-2-propenyl acetates and carbonates with various carbonucleophiles occurs \( \alpha \) to the alkoxy group. Furthermore, it was reported that the carbo palladation of alkoxyallenes leads to \( \pi \)-allylpalladium complexes, which react with carbonucleophiles at the position \( \alpha \) to the alkoxy group(9). Accordingly, it seems that an alkoxy group of \( \pi \)-allylpalladium complex directs a nucleophile to the \( \alpha \)-position of \( 20 \). This is reasonable, since an alkoxy group stabilizes positive charge formed at the \( \alpha \)-position and hereby a nucleophilic attack at the \( \alpha \)-position becomes more favorable.

Taken together, the present \( \alpha \)-addition of pronucleophiles (H-Nu) can be accounted for either by the hydropalladation or carbopalladation mechanism (Scheme 2). Irrespective of the precise mechanism, remarkable difference of regioselectivities in the reactions of the substituted allenes may be synthetically useful.

**Palladium Catalyzed Direct Allylation of Pronucleophiles with Allylstannanes(10)**

Conversion of pronucleophiles \( 18 \) to the corresponding allylated derivatives \( 19 \) has been carried out, generally, via the carbanion process a or the free-radical chain procedure b. Pronucleophiles \( 18 \) are once converted to the corresponding carbanions \( 20 \), which are treated either with allyl halides (or related allylic compounds) or with allyl palladium complexes (path a). The reaction of allyltributylstannane with reactive halides \( 21 \), which are obtained from pronucleophiles \( 18 \) via halogenation, in the presence of AIBN affords the allylated derivatives \( 19 \) (path b). An entirely new procedure which enables the direct conversion of \( 18 \) into \( 19 \) (path c) has been developed; the reaction of \( 18 \) with allyl stannanes in the presence of catalytic amounts of \( \text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3 \) at room temperature gives \( 19 \) in high to good yields (Scheme 3).

The results are summarized in Table 1. The reaction of methylmalononitrile \( 5b \) with allyltributyltin (2 equiv) in the presence of 4 mol \% \( \text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3 \) and 10 mol \% dppe in \( \text{CH}_2\text{Cl}_2 \) at room temperature gave the allylated product \( 19a \) in 86 \% yield (entry 1). The reaction of \( 5b \) with crotyltributyltin (2 equiv) under similar conditions as above afforded a 57:43 mixture of straight \( 19b \) and branched \( 19b' \) butenylation products in 98 \% combined yield (entry 2). Similarly, the reactions of ethyl 2-cyano-2-phenylacetate \( 5c \) with allyltin or crotyltin gave the allylated \( 19c \) or butenylated (\( 19d \) and \( 19d' \)) products, respectively, in high yields (entries 3 and 4). Methylene tributyltin also reacted with \( 5c \) to give the corresponding methallyl derivative \( 19e \) in 66 \% yield (entry 5). Not only pronucleophiles bearing CN substituents (\( 5b, 5c \)) but also those having ester and ketone groups (\( 18a-18d \)) underwent the direct
Table 1. Palladium Catalyzed Direct Allylation of Pronucleophiles

<table>
<thead>
<tr>
<th>entry</th>
<th>Pronucleophiles</th>
<th>Allylstannanes (2 equiv)</th>
<th>Product</th>
<th>Isolated yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{CH}_3 \text{CN} )</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CN} \text{CN} )</td>
<td>19a</td>
</tr>
<tr>
<td>2</td>
<td>5b</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CN} \text{CN} )</td>
<td>19b</td>
</tr>
<tr>
<td>3</td>
<td>( \text{Ph} \text{CN} ) ( \text{CO}_2\text{C}_2\text{H}_5 ) 5c</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19d</td>
</tr>
<tr>
<td>4</td>
<td>5c</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19d</td>
</tr>
<tr>
<td>5</td>
<td>5c</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19e</td>
</tr>
<tr>
<td>6</td>
<td>( \text{CH}_3 \text{CO}_2\text{C}_2\text{H}_5 ) 18a</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19f</td>
</tr>
<tr>
<td>7</td>
<td>( \text{CH}_3 \text{CO}_2\text{C}_2\text{H}_5 ) 18a</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19f</td>
</tr>
<tr>
<td>8</td>
<td>( \text{O} \text{CO}_2\text{CH}_3 ) 18c</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{CH}_3 )</td>
<td>19h</td>
</tr>
<tr>
<td>9</td>
<td>( \text{CH}_3 \text{CO}_2\text{C}_2\text{H}_5 ) 18d</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19i</td>
</tr>
<tr>
<td>10</td>
<td>( \text{CN} ) ( \text{CO}_2\text{CH}_3 ) 18e</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{CH}_3 )</td>
<td>19j</td>
</tr>
<tr>
<td>11</td>
<td>( \text{CO}_2\text{CH}_3 ) ( \text{CO}_2\text{C}_2\text{H}_5 ) 18f</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{CH}_3 )</td>
<td>19k</td>
</tr>
<tr>
<td>12</td>
<td>( \text{O} \text{CO}_2\text{C}_2\text{H}_5 ) 18g</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19l</td>
</tr>
<tr>
<td>13</td>
<td>( \text{CO}_2\text{C}_2\text{H}_5 ) ( \text{CO}_2\text{C}_2\text{H}_5 ) 18h</td>
<td>( \text{SnBu}_3 )</td>
<td>( \text{CN} \text{CO}_2\text{C}_2\text{H}_5 )</td>
<td>19m</td>
</tr>
</tbody>
</table>

*aA mixture of a pronucleophile (0.5 mmol), allyltin (1 mmol), Pd_2(dbac)_3CHCl \_3 (0.02 mmol), dppe (0.05 mmol), and dry CHCl \_3 (1 mL) was stirred at room temperature for 2 days under Ar, except where otherwise indicated.  \( 19b : 19b ^{c} = 57:43 \).  \( 19d : 19d ^{c} = 53:47 \).  
*bSince the reaction at room temperature was sluggish, THF was used as a solvent and the mixture was refluxed overnight. The allylation product 19i was isolated in 20 \% yield along with the recovered 18d(43 \%).  
*cThe starting materials 18a and 18b were recovered in 11 \% yields.  
*dFour equiv of allyltritbutylstannane was used.  
*eNo mono-allylation product was obtained even using 2 equiv allyltin.  
*fNo di-allylation product was obtained even using 4 equiv allyltin.

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allylation reaction in the presence of the palladium catalyst to afford the allylation products (19f-19i) (entries 6-9). (R)-BINAP (5 mol %) was used as a ligand, instead of dppe, in the reactions of 5c and 18a with allyltin, and higher chemical yields were achieved; 92 % yield of 19c (cf. entry 3) and 76 % yield of 19f (cf. entry 6). Other catalysts were examined in the reaction of 5c with allyltin (cf. entry 3); the use of 8 mol % PdCl2(CH3CN)2 or PdCl2(PhCN)2 gave 19c in 76-81 % yields. Normally, we performed the allylation with 2 equiv allyltins for 2 days, but the reaction of 5b was rapid; after 1 day, 19a was obtained in 86 % yield with 1.1 equiv allyltin.

Not only methynes but also activated methylenes underwent the allylation to give the di-allylation products in acceptable yields (entries 10-12). No mono-allylation products were obtained even using 2 equiv (or one equiv) allyltin. Very interestingly, the mono-allylation product 19m was produced selectively in the case of 18h (entry 13). In conclusion, the palladium catalyzed direct allylation is applicable to a wide range of pronucleophiles including activated methylenes and methynes.

A mechanistic rationale which accounts for the unprecedented direct allylation of pronucleophiles (H-Nu) is shown in Scheme 4. The oxidative insertion of Pd(0) into the C-H bond of pronucleophiles would produce the Pd(II) intermediate. The transmetallation between this Pd(II) species and allyltin would give the π-allylpalladium–Nu (or σ-allyl) complex and tributyltin hydride. Reductive coupling may produce the allylation product and Pd(0). We followed the reaction of 5c with allyltin in CDCl3 by using 1H NMR and found that a signal at 6 5.28 ppm ascribed to HSnBu3 appeared clearly along with the signals due to the allylation product. Accordingly, it is clear that the proposed transmetallation process is involved in the catalytic cycle. One may consider a possibility that allyltin and palladium complexes reacts with the palladium complex to produce a π-allylpalladium species which undergoes nucleophilic attack of Θ-Nu. In a NMR tube, Pd2(dppe)3(CHCl3) (1 equiv) and 10 mol % dppe were dissolved in CDCl3, and then allyltin (1 equiv) was added at room temperature. Even after 19 h, signals due to the allyl remained unchanged, suggesting that no reaction takes place between the palladium catalyst and allyltin at room temperature in the absence of pronucleophiles. The signals of allyltin disappeared by heating the mixture at 50 °C for 9 h, and those ascribed to a π-allylpalladium species appeared. Then, 5c (1 equiv) was added at room temperature, but no allylation product was obtained even after 2 days.

References and Notes

5. Several rhenium complexes of activated nucleophiles have been isolated. M. Hirano, Y. Ito, M. Hirai, A. Fukuoka, and S. Komiya, Chem. Lett. 2057 (1993). We confirmed a rapid C-H insertion of Pd(0) into methylmalononitrile by using its deuterated derivative. No deuterium exchange took place when MeCN(CD2)2 was treated with dppe (26 mole %) in THF. When Pd2(dppe)3(CHCl3) (5 mole %) was added to this mixture, rapid deuterium exchange occurred to give MeCN(CD2)2.
10. Y. Yamamoto and N. Fujiwara, unpublished results.

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