Pure & Appl. Chem., Vol. 68, No. 1, pp. 9–14, 1996.
Printed in Great Britain.

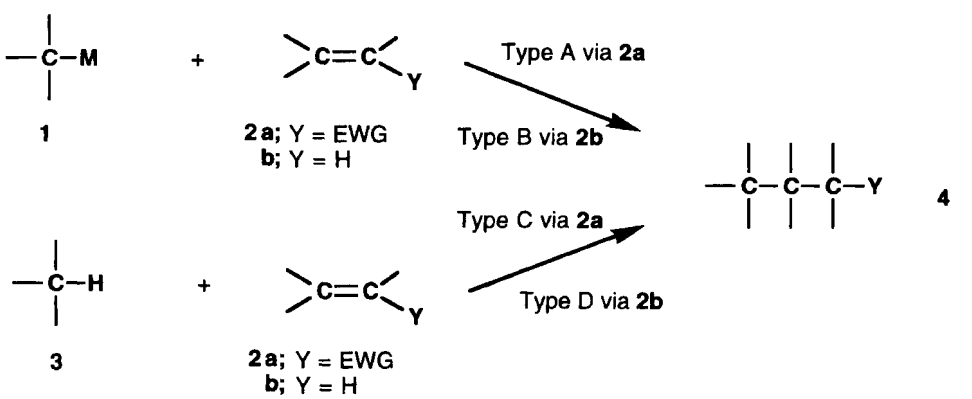
Palladium catalyzed hydrocarbonation of olefins

Yoshinori Yamamoto

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-77, Japan

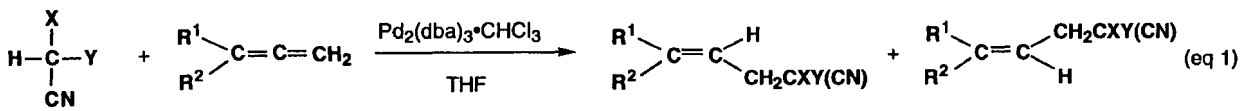
Abstract: The addition of activated methylene and methynes **5** to monoalkyl- and di-substituted allenes **6** takes place in the presence of catalytic amounts of $Pd_2(dba)_3 \cdot CHCl_3$ in THF under reflux, giving the internal alkenes **7** and **8**. The nucleophile attacks the terminal carbon 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 α-alkoxyallenes **16** affords the α-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 methynes and methylenes **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 $Pd_2(dba)_3 \cdot CHCl_3$ 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.



5

a; X=H, Y=CN
b; X=CH_3, Y=CN
c; X=Ph, Y=CO_2Et

6

a; R^1=CH_2Ph, R^2=H
b; R^1=*c*-C_6H_{11}, R^2=H
c; R^1=Ph, R^2=H
d; R^1=Ph, R^2=Me
e; R^1=Ph, R^2=Et
f; R^1=CH_2Ph, R^2=Me
g; R^1=Ph, R^2=CH_2Ph

7a-k

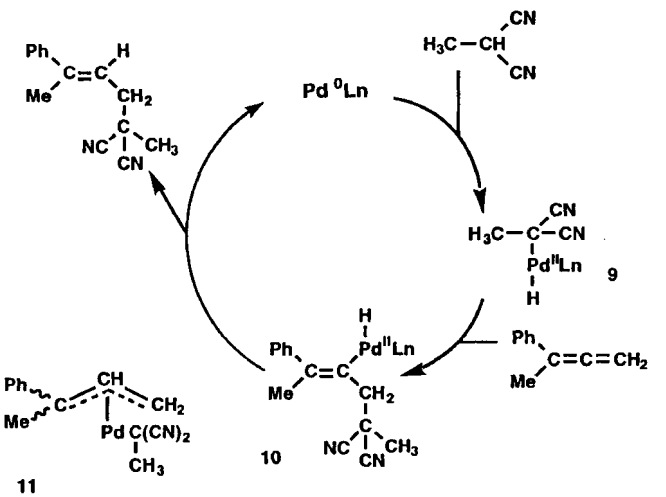
a; R^1=CH_2Ph, R^2=H, X=CH_2CH=$CHCH_2Ph$, Y=CN
b; R^1=CH_2Ph, R^2=H, X=Me, Y=CN
c; R^1=*c*-C_6H_{11}, R^2=H, X=Me, Y=CN
d; R^1=Ph, R^2=H, X=CH_2CH=CHPh, Y=CN
e; R^1=Ph, R^2=H, X=Me, Y=CN

8a - k

f; R^1=Ph, R^2=Me, X=Me, Y=CN
g; R^1=Ph, R^2=Et, X=Me, Y=CN
h; R^1=$PhCH_2$, R^2=Me, X=Me, Y=CN
i; R^1=Ph, R^2=Me, X=Ph, Y=CO_2Et
j; R^1=$PhCH_2$, R^2=Me, X=Ph, Y=CO_2Et
k; R^1=Ph, R^2=$PhCH_2$, X=Ph, Y=CO_2Et

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** - **c**, 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**.

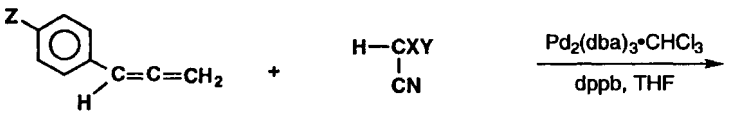
Scheme 1



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(II) species **9** (or alternatively a tautomeric structure $H_3C(CN)C$=C=NPdHLn may be more suitable). The carbopalladation of the allene with **9** would afford the alkenylpalladium (II) 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.

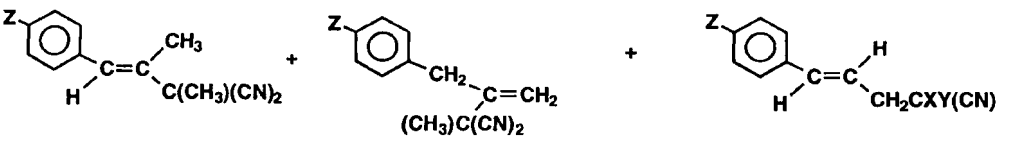
Regioselectivity Reversal in the Palladium Catalyzed Hydrocarbonation of Allenes(6)

Phenylallene **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 arylallenes (**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.



12a - h; Z = H, F, Cl, Br, CF_3, OCF_3, CH_3, OCH_3

5b; X = CH_3, Y = CN
c; X = Ph, Y = CO_2Et



(eq 2)

internal adducts

13a ; Z = H
b; Z = F
c; Z = Cl
d; Z = Br
e; Z = CF_3
f; Z = OCF_3

14a ; Z = H
b ; Z = F
c ; Z = Cl
d ; Z = Br
e ; Z = CF_3
f ; Z = OCF_3

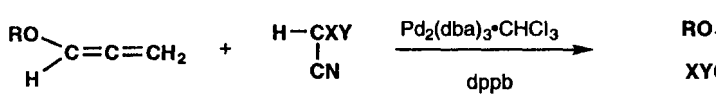
terminal adduct

15a ; X = CN, Y = CH_3, Z = H
b ; X = CN, Y = CH_3, Z = F
c ; X = CN, Y = CH_3, Z = CH_3
d ; X = CN, Y = CH_3, Z = OCH_3
e ; X = CO_2Et, Y = Ph, Z = F
f ; X = CO_2Et, Y = Ph, Z = Cl
g ; X = CO_2Et, Y = Ph, Z = Br
h ; X = CO_2Et, Y = Ph, Z = CF_3
i ; X = CO_2Et, Y = Ph, Z = OCF_3
j ; X = CO_2Et, Y = Ph, Z = CH_3
k ; X = CO_2Et, Y = Ph, Z = OCH_3

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 π-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 α-Addition of Pronucleophiles to Alkoxy(phenoxy)-allenes(8)

The reactions of phenylpropyloxy-(**16a**), phenylethyloxy-(**16b**) and benzyloxy-allenes **16c** with pronucleophiles (**5b** and **5d**) gave the corresponding α–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 α-adduct **17g** in 57% yield, the reaction of **16d** with **5d** gave the γ–adduct **18** in 19% yield along with the α-adduct **17h** (49%). Next, we examined the palladium catalyzed reaction of a sterically more bulky pronucleophile **5c**. Very interestingly, the γ–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 α-adducts **17** either exclusively or predominantly, whereas the reaction of **16** with **5c** gives the γ-adduct **19**. Perhaps the γ–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 α-regioselectivity.

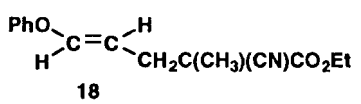


(eq 3)

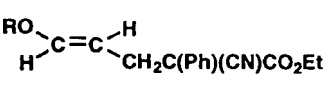
16a; R=$(CH_2)_3Ph$
b; R=$(CH_2)_2Ph$
c; R=CH_2Ph
d; R=Ph

5b; X=CH_3, Y=CN
c; X=Ph, Y=CO_2Et
d; X=CH_3, Y=CO_2Et

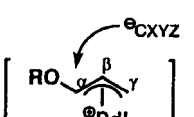
17a; R=$(CH_2)_3Ph$, XY=$(CH_3)CN$
b; R=$(CH_2)_3Ph$, XY=$(CH_3)CO_2Et$
c; R=$(CH_2)_2Ph$, XY=$(CH_3)CN$
d; R=$(CH_2)_2Ph$, XY=$(CH_3)CO_2Et$
e; R=CH_2Ph, XY=$(CH_3)CN$
f; R=CH_2Ph, XY=$(CH_3)CO_2Et$
g; R=Ph, XY=$(CH_3)CN$
h; R=Ph, XY=$(CH_3)CO_2Et$



18



19a; R=$(CH_2)_3Ph$ **c**; R=CH_2Ph
b; R=$(CH_2)_2Ph$ **d**; R=Ph

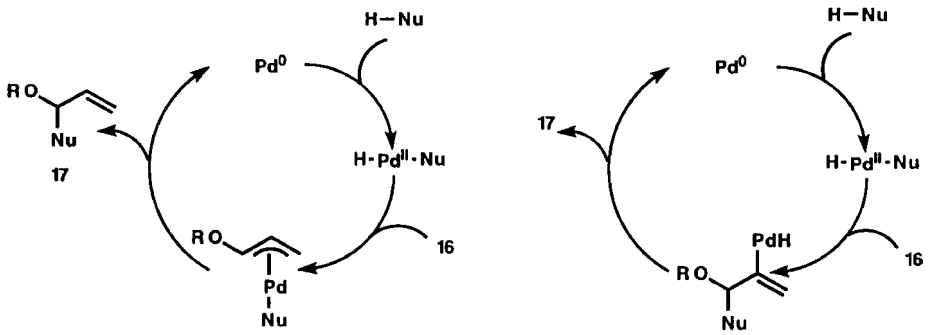


20

It has been known that the palladium catalyzed allylic substitution of 3-alkoxy-2-propenyl acetates and carbonates with various carbonucleophiles occurs α to the alkoxy group. Furthermore, it was reported that the carbopalladation of alkoxyallenes leads to π-allylpalladium complexes, which react with carbonucleophiles at the position α to the alkoxy group(9). Accordingly, it seems that an alkoxy group of π-allylpalladium complex directs a nucleophile to the α-position of **20.** This is reasonable, since an alkoxy group stabilizes positive charge formed at the α-position and hereby a nucleophilic attack at the α–position becomes more favorable.

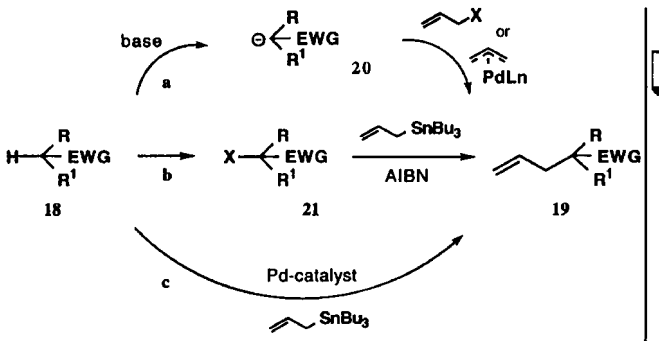
Taken together, the present α-addition of pronucleophiles (H-Nu) can be accounted for either by the hydropalladation or carbopalladation mechanism (Scheme 2). Irrespective of the precise mechanism, remarkable difference of regioselectivities in the reactions of the substituted allenes may be synthetically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

Scheme 2

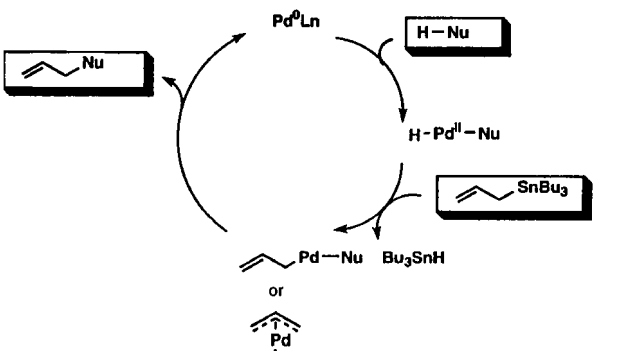


Palladium Catalyzed Direct Allylation of Pronucleophiles with Allylstannanes(10)

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 allylic stannanes in the presence of catalytic amounts of $Pd_2(dba)_3$•$CHCl_3$ at room temperature gives **19** in high to good yields (Scheme 3).



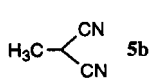
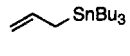
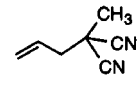
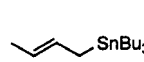
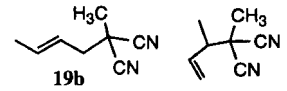
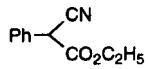
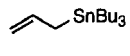
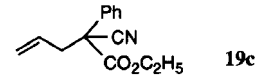
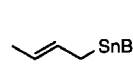
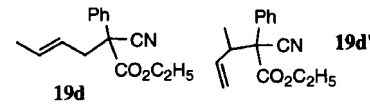
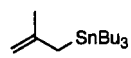
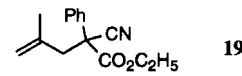
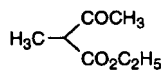
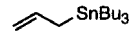
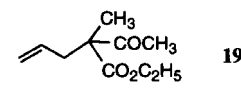
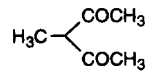
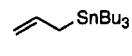
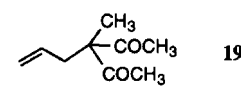
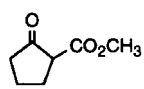
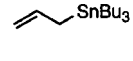
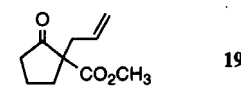
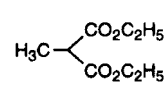
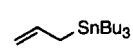
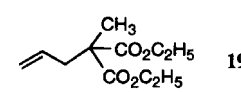
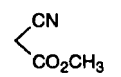
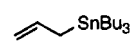
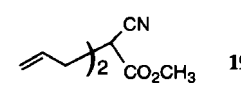
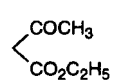
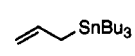
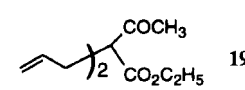
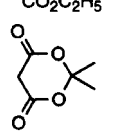
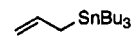
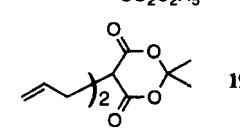
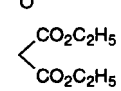
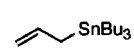
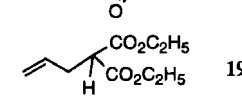
Scheme 3



Scheme 4

The results are summarized in Table 1. The reaction of methylmalononitrile **5b** with allyltributyltin (2 equiv) in the presence of 4 mol % $Pd_2(dba)_3$•$CHCl_3$ and 10 mol % dppe in CH_2Cl_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). Methallyltributyltin 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 [a]

entry	Pronucleophiles	Allylstannanes (2 equiv)	Product	Isolated yield (%)
1	 **5b**		 **19a**	86
2	**5b**		 **19b** **19b'**	98[b]
3	 **5c**		 **19c**	89
4	**5c**		 **19d** **19d'**	90[c]
5	**5c**		 **19e**	66
6	 **18a**		 **19f**	65[e]
7	 **18b**		 **19g**	65[e]
8	 **18c**		 **19h**	70
9	 **18d**		 **19i**	20[d]
10	 **18e**		 **19j**	50[f,g]
11	 **18f**		 **19k**	41[f,g]
12	 **18g**		 **19l**	45[f,g]
13	 **18h**		 **19m**	47[f,h]

[a]A mixture of a pronucleophile (0.5 mmol), allyltin (1 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 mmol), dppe (0.05 mmol), and dry CH_2Cl_2 (1 mL) was stirred at room temperature for 2 days under Ar, except where otherwise indicated. [b]**19b**:**19b'** = 57:43. [c]**19d**:**19d'** = 53:47. [d]Since 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 %). [e]The starting materials **18a** and **18b** were recovered in 11 % yields. [f]Four equiv of allyltributylstannane was used. [g]No mono-allylation product was obtained even using 2 equiv allyltin. [h]No di-allylation product was obtained even using 4 equiv allyltin.

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 allyltributyltin, 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 allyltributyltin (cf. entry 3); the use of 8 mol % $PdCl_2(CH_3CN)_2$ or $PdCl_2(PhCN)_2$ 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 allyltributyltin.

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 methynes and methylenes.

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 allyltributyltin 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 allyltributyltin in $CDCl_3$ by using ^1H NMR and found that a signal at δ 5.28 ppm ascribed to $HSnBu_3$ 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 allyltributylstannane reacts with the palladium complex to produce a π-allylpalladium species which undergoes nucleophilic attack of $^{\ominus}Nu$. In a NMR tube, $Pd_2(dba)_3{\cdot}CHCl_3$ (1 equiv) and 10 mol % dppe were dissolved in $CDCl_3$, and then allyltributyltin (1 equiv) was added at room temperature. Even after 19 h, signals due to the allyltin 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

1. a) L.S Hegedus, *in Comprehensive Organic Synthesis*; B.M. Trost and I. Fleming, Eds. *Pergamon Press.* **vol.4**, p571, Oxford, U.K. (1990). b) For carbometallation, P. Knochel, *in Comprehensive Organic Synthesis*; B.M. Trost and I. Fleming, Eds. *Pergamon Press.* **vol.4**, p.865, Oxford, U.K. (1990).
2. Michael and aldol reactions. a) T. Naota, H. Taki, M. Mizuno, and S.-I. Murahashi, *J. Am. Chem. Soc.* **111**, 5954 (1989). Michael reactions. b) S. Paganelli, A. Schionata, and C. Batteghi, *Tetrahedron Lett.* **32**, 2807 (1991). c) M. Sawamura, H. Hamashima, and Y. Ito, *J. Am. Chem. Soc.* **114**, 8295 (1992). Imine addition. d) Y. Yamamoto, N. Kubota, Y. Honda, H. Fukui, N. Asao, and H. Nemoto, *J. Am. Chem. Soc.* **116**, 3161 (1994).
3. Transition metal catalyzed reactions of allenes, see (a) B. Cazes, *Pure & Appl. Chem.* **62**,1867 (1990). (b) V. Gauthier, B. Cazes, and J. Gore, *Tetrahedron Lett.* **32**, 915 (1991). (c) N. Chaptal, V.C. Gotleland, C. Grandjean, B. Cazes, and J. Gore, *Tetrahedron Lett.* **32**, 1795 (1991). (d) L. Besson, J. Bazin, J. Gore, and B. Cazes, *Tetrahedron Lett.* **35**, 2881 (1994). (e) I. Shimizu and J. Tsuji, *Chem. Lett.* 233 (1984). (f) I. Shimizu, T. Sugiura, and J. Tsuji, *J. Org. Chem.* **50**, 537 (1985). (g) R.C. Larock, S.Varaprath, H.H. Lau, and C.A. Fellows, *J. Am. Chem. Soc.* **106**, 5274 (1984). (h) R.C. Larock, N.G. Berrios-Pena, and C.A. Fried, *J. Org. Chem.* **56**, 2615 (1991). (i) S. Ma and E. Negishi, *J. Org. Chem.* **59**, 4730 (1994). (j) B.M. Trost and G. Kottirsh, *J. Am. Chem. Soc.* **112**, 2816 (1990). (k) M. Yamaguchi, K. Omata, and M. Hirama, *Tetrahedron Lett.* **35**, 5689 (1994).
4. Y. Yamamoto, M. Al-Masum, and N. Asao, *J. Am. Chem. Soc.* **116**, 6019 (1994).
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 $MeCD(CN)_2$ was treated with dppe (26 mole %) in THF. When $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mole %) was added to this mixture, rapid deuterium exchange occurred to give $MeCH(CN)_2$.
6. Y. Yamamoto, M. Al-Masum, N. Fujiwara, and N. Asao, *Tetrahedron Lett.*, **36**, 2811 (1995).
7. More recently , hydropalladation mechanisum has been proposed in the related reactions. B. M. Trost and V. J. Gerusz, *J. Am. Chem. Soc.* **117**, 5156 (1995).
8. Y. Yamamoto and M. Al-Masum, *Synlett.* in print (1995).
9. N. Vicart, B. Cazes, and J. Gore, *Tetrahedron Lett.*, **36**. 535 (1995). N. Chaptal, V. C.-Gotteland, C. Granjean, B. Cazes, and J. Gore, *ibid.*, **32**, 1795 (1991).
10. Y. Yamamoto and N. Fujiwara, unpunlished results.