Catalytic Amphiphilic Allylation via Bis-π-allylpalladium Complexes and Its Application to the Synthesis of Medium-Sized Carbocycles

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Abstract: The reaction of certain activated alkenes **3** with allyltributylstannane (**4**) and allyl chloride (**5a**) in the presence of palladium catalyst gave the bis-allylation products, 1,7-octadiene derivatives **6a**−**k**, in good to high yields. The reaction of certain imines **9** with **4** and **5a** under similar conditions as above afforded the bis-allylated amines, *N*-allyl-*N*-3-butene-1-amine derivatives **10a**−**f**, in good to high yields. The bis-allylation reactions most probably proceed through bis-π-allylpalladium intermediate **2**. The above intermolecular bis-allylation was extended to the intramolecular reaction. The reaction of 8-chloro-2,6-octadienyltributylstannane (**17a**) with activated alkenes **3** gave a mixture of regioisomeric cycloadducts, [8+2] and [4+2] cycloaddition products. The regioisomeric ratio was dependent on solvent and the electron density at the β-position of activated alkenes. In general, the [8+2] cycloadducts **18** were obtained predominantly in CH_2Cl_2, whereas the [4+2] adducts **24** and **25** were produced predominantly in DMF. The reaction of 7-chloro-2,8-nonadienyltributylstannane (**17b**) with activated alkenes gave selectively the [9+2] cycloadducts **19** and **22**: the regioisomeric [5+2] and [7+2] adducts were not obtained at all. The reaction of 10-chloro-2,8-decadienyltributylstannane (**17c**) with activated alkene **3a** afforded the [10+2] cycloadducts **20** and **23** in low yields. The mechanism on the intramolecular bis-allylation reaction is discussed.

Introduction

Palladium-catalyzed allylation with various nucleophiles (Tsuji−Trost-type reaction) is now a very important modern organic transformation for the construction of carbon−carbon or carbon−heteroatom bonds.[1] It is widely accepted that π-allylpalladium complexes **1**,

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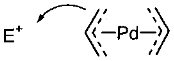

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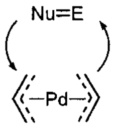
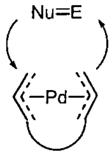
which are key intermediates for the Tsuji−Trost reaction, have an electrophilic character and react with nucleophiles to afford the corresponding allylation products. Recently, we found that bis-π-allylpalladium complex **2** reacts with electrophiles such as aldehydes and imines to produce the carbon−carbon bond in a manner different from the reaction via **1**.[2−4] In this reaction, one of the two allyl groups of the bis-π-allylpalladium complex reacted with electrophiles and the other stayed on the palladium atom. Furthermore, we communicated that, in the reaction with certain α,β-unsaturated carbonyl compounds, bis-π-allylpalladium complex **2** acts as the first amphiphilic catalytic allylating agent (Scheme 1).[5] It occurred to us that bis-π-allylpalladium complexes, in which two π-allyl units are bonded through a carbon tether, may react with certain Michael acceptors in an amphiphilic manner (Scheme 2) to produce the corresponding carbocycles. We now report the full account for the previous

Scheme 1



Scheme 2



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(1) (a) Tsuji, J. In *Palladium Reagents and Catalysts*; John Wiley and Sons: Chichester, 1995; p 61. (b) Codleski, S. A. In *Comprehensive Organic Synthesis*; Semmelhack, M. F., Ed.; Pergamon Press: Oxford, 1991; Vol. 4, p 585. (c) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, 1987; p 417.

(2) (a) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun*. **1996**, 1459. (b) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc*. **1996**, *118*, 6641 and references therein.

(3) Although π-allylpalladium-X complexes **1** in which X is an electron-withdrawing group react with nucleophiles, it is also known that certain π-allyl transition metal complexes react with electrophiles. π-Allylmolybdenum complexes: (a) Faller, J. W.; Nguyen J. T.; Ellis, W.; Mazzieri, M. R. *Organometallics* **1993**, *12*, 1434. (b) Faller, J. W.; DiVerdi, M. J.; John, J. A. *Tetrahedron Lett*. **1991**, *32*, 1271. (c) Faller, J. W.; Linebarrier, D. L. *J. Am. Chem. Soc*. **1989**, *111*, 1937. π-Allylnickel complexes: (d) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. *J. Org. Chem*. **1975**, *40*, 593. π-Allyltitanium complexes: (e) Sato, F.; Iijima, S.; Sato, M. *Tetrahedron Lett*. **1981**, *22*, 243. (f) Collins, S.; Kuntz, B. A.; Hong, Y. *J. Org. Chem*. **1989**, *54*, 4154. For recent papers on the oxidative addition of allylic halides to Pd(0) see: (g) Kurosawa, H.; Kajimaru, H.; Ogoshi, S.; Yoneda, H.; Miki, K.; Kasai, N.; Murai, S.; Ikeda, I. *J. Am. Chem. Soc*. **1992**, *114*, 8417. Kurosawa, H.; Ogosi, S. *Bull. Chem. Soc. Jpn*. **1998**, *71*, 973. For the (η^1-allyl)(η^3-allyl)palladium complex see: (h) Kuhn, O.; Mayr, H. *Angew. Chem., Int. Ed*. **1999**, *38*, 343.

(4) (a) Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc*. **1998**, *120*, 4242. (b) Nakamura, K.; Nakamura, H.; Yamamoto, Y. *J. Org. Chem*. **1999**, *64*, 2614. (c) Bao, M.; Nakamura, H.; Yamamoto, Y. *Tetrahedron Lett*. **2000**, *41*, 131.

(5) Nakamura, H.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc*. **1997**, *119*, 8113.

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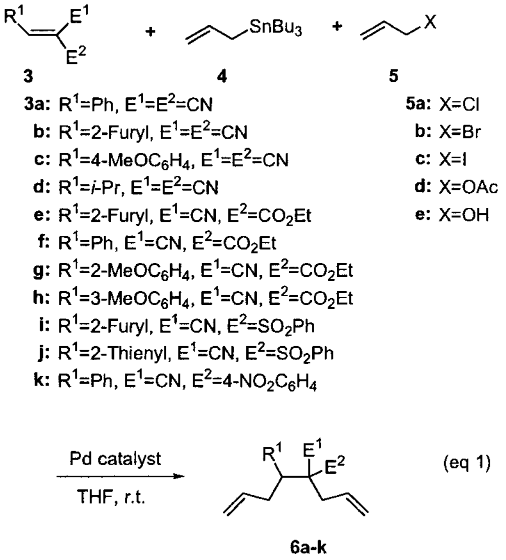
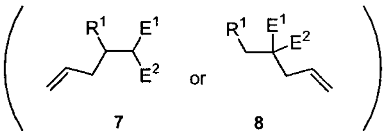
results on the intermolecular amphiphilic bis-allylation reactions (Scheme 1) together with new findings on the intramolecular version of the bis-allylation (Scheme 2).

Results and Discussion

Intermolecular Amphiphilic Bis-Allylation Reaction. The reaction of phenylethylidene malononitrile (**3a**, 1 equiv), allyltributylstannane (**4**, 1.2 equiv), and allyl chloride (**5a**, 1.2 equiv) in THF was carried out in the presence of $PdCl_2(PPh_3)_2$ (3 mol %) under Ar atmosphere at room temperature (eq 1), giving 4,4-dicyano-5-phenyl-1,7-octadiene (**6a**) in 99%. The use of 5 mol % and 1.5 mol % of the catalyst also gave **6a** in 99% and 98% yields, respectively. Allyl bromide (**5b**), iodide (**5c**), acetate (**5d**), and alcohol (**5e**) were less effective compared to allyl chloride (**5a**). The solvent effect was also examined: acetonitrile and *N*,*N*-dimethylformamide (DMF) as well as THF were effective, nitromethane was less effective, and nonpolar solvents such as toluene and CH_2Cl_2 were not effective. Tetrakis(triphenylphosphine)palladium as well as dichlorobis(triphenylphosphine)palladium were efficient catalysts. The use of tetrakis(triphenylphosphine)palladium catalyst gave **6a** in 99% yield under the same reaction conditions. In all cases the monoallylated products **7** and **8** were not obtained. Other palladium catalysts, such as $Pd(dba)_2$, $Pd(OAc)_2$, and $PdCl_2(PBu_3)_2$, were not effective for this reaction and the use of $Ni(PPh_3)_4$ as a catalyst in THF gave the monoallylated product **7a** (R^1 = Ph, E^1 = E^2 = CN) in 70% yield along with small amounts (~9%) of **6a**.





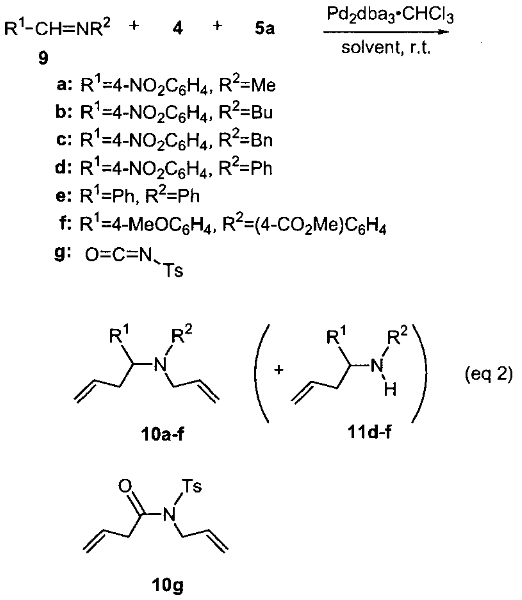
Various activated olefins were examined and the results were reported in the previous communication.[5] The activated olefins (**3b**−**d**) underwent the double allylation very smoothly to give the corresponding 1,7-octadienes (**6b**−**d**) in high yields. Not only the activated olefins having two CN groups (**3a**−**d**) but also those bearing CN and CO_2Et (**3e**−**h**) or CN and SO_2Ph (**3i**−**j**) underwent the double allylation reaction, giving the corresponding octadienes (**6e**−**j**) in 43−80% yields, although the diastereoselectivities of the reactions were not high. Even the olefin **3k** activated by a single CN group gave the amphiphilic allylation product **6k** in an allowable yield.

Table 1. Palladium-Catalyzed Bis-Allylation of the Imines **9a**−**f** and *p*-Toluenesulfonyl Isocyanate **9g** with Allyltributylstannane (**4**) and Allyl Chloride (**5a**)[a]

entry	9	solvent	products	yield (%)[b]
1	**9a**	DMF	**10a**	81
2	**9b**	DMF	**10b**	74
3	**9c**	DMF	**10c**	53
4	**9d**	DMF	**10d** + **11d**	84 (46/54)
5	**9e**	DMF	**10e** + **11e**	78 (44/56)
6	**9f**	DMF	**11f**	98
7[c]	**9g**	THF	**10g**	86

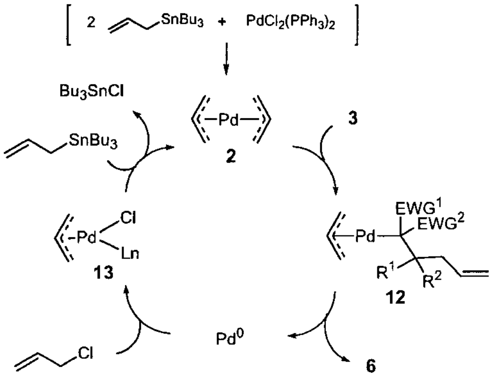
[a] The reactions were carried out in the presence of Pd2dba$_3$•CHCl$_3$ catalyst (5 mol %) in DMF at room temperature. [b] Isolated yields based on **9**. The product ratios of **10** and **11** are indicated in parentheses. [c] Tricyclohexylphosphine (20 mol %) was used as a ligand in the reaction.

Not only the C−C activated unsaturated compounds **3**, but also certain activated C−N unsaturated compounds, such as the imines **9a**−**f** and isocyanate **9g**, underwent the amphiphilic bis-allylation reaction (eq 2). The results are shown in Table 1.



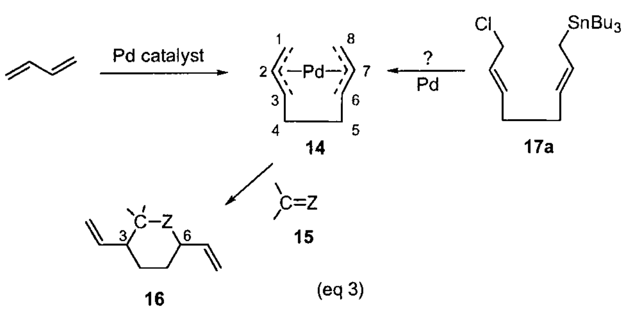
The reaction of imine **9a**, derived from 4-nitrobenzaldehyde and methylamine, with allyltributylstannane (**4**) and allyl chloride (**5a**) proceeded very smoothly in the presence of Pd_2dba_3•$CHCl_3$ catalyst in DMF at room temperature, giving *N*-allyl-*N*-methyl-1-(4-nitrophenyl)-3-buten-1-amine (**10a**) in 81% yield (entry 1). Imines **9b** and **9c**, derived from *n*-butylamine and benzylamine, respectively, also underwent the amphiphilic bis-allylation to afford **10b** and **10c** in good yields (entries 2 and 3). However, the reactions of imines **9d** and **9e**, derived from aniline, gave approximately 1:1 mixtures of the mono- (**11d** and **11e**, respectively) and bis-allylated products (**10d** and **10e**, respectively) in good to high yields (entries 4 and 5), whereas only the mono-allylated product **11f** was obtained in almost quantitative yield in the case of imine **9f**, derived from the electron-deficient amine methyl 4-aminobenzoate (entry 6). Tosyl isocyanate (**9g**) also underwent the amphiphilic bis-allylation very smoothly to give *N*-tosyl-*N*-allyl-3-butenamide (**10g**) in 86% yield (entry 7).

Scheme 3

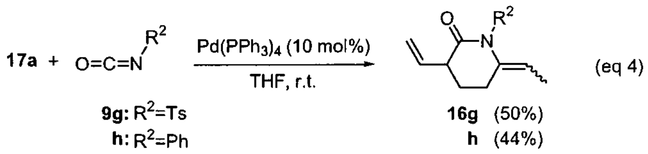


A mechanistic rationale which accounts for the unprecedented amphiphilic bis-allylation of activated olefins **3** is shown in Scheme 3. The transmetalation of allyltributylstannane to palladium would produce bis-π-allylpalladium complex **2**,[6] which would react with activated olefins **3** to give the π-allylpalladium intermediate **12**. The reductive coupling from **12** would give the corresponding 1,7-octadienes **6** and palladium(0) species. At this stage, the π-allyl group of **12** reacts with a nucleophilic carbon center. The oxidative insertion of Pd(0) into allyl chloride would produce the π-allylpalladium chloride complex **13**. When $Pd(PPh_3)_4$ was used as a catalyst instead of $PdCl_2(PPh_3)_2$, the catalytic cycle would start from the Pd(0) species. The reaction of **13** with allyltributylstannane would produce **2** and Bu_3SnCl.

[n+2] Cycloaddition via the Intramolecular Amphiphilic Bis-Allylation Reaction. Several useful transition metal-catalyzed synthetic methods for medium-sized rings have been developed recently: for example, the ring-closing metathesis,[7] the ring-expansion reactions,[8] and the intramolecular cyclizations.[9] However, to the best of our knowledge, very few examples for the [n+m] cycloaddition method are known.[10] Accordingly, we extended the intermoleculer amphiphilic bis-allylation reaction to the intramolecular bis-π-allylpalladium system (Scheme 2). Palladium-catalyzed reactions of 1,3-butadiene with carbon−heteroatom unsaturated compounds **15**, such as aldehydes,[11−13] ketones,[13b] imines,[14] and isocyanates,[15] are well-known as a novel method for the synthesis of the six-membered heterocycles (eq 3). It is thought that in these reactions the bis-π-allylpalladium complex **14** is a key intermediate and reacts with the carbon−heteroatom double bond of **15** at the C3 and C6 positions regioselectively (exo−exo cycloaddition mode) to afford the corresponding heterocyclic products **16**.[16] If the bis-π-allylpalladium mechanism, which is operative in the intermolecular palladium-catalyzed allyl stannane−allyl chloride reaction (Scheme 3), is also operative for **17a**, the intermediate **14** must be generated (eq 3). From 1,3-butadiene, bis-π-allylpalladium (**14**) having only a tether of two carbon chain is obtained. However, the intramolecular version of the allylic stannane−allyl chloride reaction makes it feasible to obtain bis-π-allylpalladiums bearing tethers of three and four carbon chains (**17b** and **17c**) as well as tethers of the two carbon chain. The syntheses of **17a**−**c** are shown in the Supporting Information.



We first examined the reactions of **17a** with isocyanates **9g** and **9h** in the presence of $Pd(PPh_3)_4$ catalyst (10 mol %) in THF at room temperature. It was expected that **17a** would produce **14** as a reactive intermediate, which would react with **9** at the C3 and C6 positions, as observed previously (see eq 3). Actually, the reaction proceeded in an exo−exo cyclization mode to give the corresponding divinylpiperidones **16g** and **16h**[15] in 50% and 44% yields, respectively (eq 4).



Next, we examined the reactions of **17a** with the activated olefins **3** (eq 5). The results are summarized in Table 2. The reaction of **17a** with **3a** proceeded smoothly in the presence of $Pd(PPh_3)_4$ catalyst (10 mol %) in THF at room temperature to give, as expected, the corresponding [4+2] cycloaddition (exo−exo mode) products **24a** and **25a** in 19% and 10% yields, respectively (entry 1). Very interestingly, a trace amount of the [8+2] cycloaddition (endo−endo mode) product **18a** (n = 1) was also obtained (entry 1). The combined yield of the products increased up to 65% when the reaction was carried out in DMF at room temperature (entry 2). When the reaction was carried out in dichloromethane under reflux, **18a** was obtained in 34% yield along with **24a** (34%) and **25a** (18%), and the combined yield of the products increased to 80% (entry 3). The structure of **18a** was determined unambiguously by X-ray analysis as shown in Figure 1 in the Supporting Information. The stereochemistry of the C4−C5 double bond was cis and that of the C8−C9 was trans. The reaction of the activated olefins, **3c** and **3l**, having an electron-donating group at the para position of the benzene ring gave **18c** and **18l**, respectively, as a minor

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(6) It has been confirmed that the reaction between allyltributylstannane and $PdCl_2(PPh_3)_2$ produces bis-π-allylpalladium complex. See ref 2.

(7) Recent examples using the ring-closing metathesis see: (a) Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 5653. (b) Fürstner, A.; Seidel, G.; Kindler, N. *Tetrahedron* **1999**, *55*, 8215. (c) Winkler, J. D.; Holland, J. M.; Kasparec, J.; Axelsen, P. H. *Tetrahedron* **1999**, *55*, 8199. (d) Oishi, T.; Nagumo, Y.; Hirama, M. *Chem. Commun.* **1998**, 1041. (e) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413.

(8) Cr(0)-promoted [6π+4π] cycloaddition: (a) Rigby, J. H. *Tetrahedron* **1999**, *55*, 4521. Rh(II)-catalyzed three-carbon-ring enlargement: (b) Oku, A.; Ohki, S.; Yoshida, T.; Kimura, K. *Chem. Commun.* **1996**, 1077.

(9) Intramolecular Nozaki-Hiyama reaction: (a) Luker, T.; Whitby, R. J. *Tetrahedron Lett.* **1996**, *37*, 7661. Pd-Catalyzed cyclization: (b) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345. $Co_2(CO)_8$-promoted ether ring formation: (c) Isobe, M.; Yenjai, C.; Tanaka, S. *Synlett* **1994**, 916.

(10) Ni(0)-catalyzed [8+2] cycloaddition: (a) Brenner, W.; Heimbach, P.; Ploner, K.-J.; Thömel, F. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 753. $BF_3{\cdot}OEt_2$-promoted [7+3] cycloaddition: (b) Guo, R.; Green, J. R. *Chem. Commun.* **1999**, 2503.

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(12) Manyik, R. M.; Walker, W. E.; Atkins, K. E.; Hammack, E. S *Tetrahedron Lett.* **1970**, 3813.

(13) (a) Ohno, K.; Mitsuyasu, T.; Tsuji, J. *Tetrahedron Lett.* **1971**, *12*, 67. (b) Ohno, K.; Mitsuyasu, T.; Tsuji, J. *Tetrahedron* **1972**, *28*, 3705.

(14) Kiji, J.; Yamamoto, K.; Tomita, H.; Furukawa, J. *Chem. Commun.* **1974**, 506.

(15) Ohno, K.; Tsuji, J. *Chem. Commun.* **1971**, 247.

(16) Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, B.; Schenker, G.; Schick, K.-P.; Schroth, G. *Organometallics* **1985**, *4*, 1945. The stoichiometric reaction of bis-π-allylpalladium complex with CO_2 and SO_2 was reported: Hung, T.; Jolly, P. W.; Wilke, G. J. *J. Organomet. Chem.* **1980**, *190*, C5.

Table 2. Palladium-Catalyzed [*n*+2] Cycloadditions (*n* = 4, 8, 9, and 10) of the Activated Olefins **3** with **17a**−**c**[a]

17a

				yields of products (%)[b]			
				[8+2] adducts		[4+2] adducts	
entry	**3**	catalyst	solvent/temp	**18**	**21**	**24**	**25**
1	**3a**	$Pd(PPh_3)_4$	THF/rt	1		19	10
2	**3a**	$Pd(PPh_3)_4$	DMF/rt	7		40	18
3	**3a**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	34		34	18
4	**3c**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	10		32	12
5	**3l**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	26		36	19
6	**3m**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	53		10	14
7	**3n**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	53		4	23
8	**3o**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	53		24	10
9	**3p**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	66		7	9
10	**3q**	$Pd(PPh_3)_4$	CH_2Cl_2/reflux	61		2	23

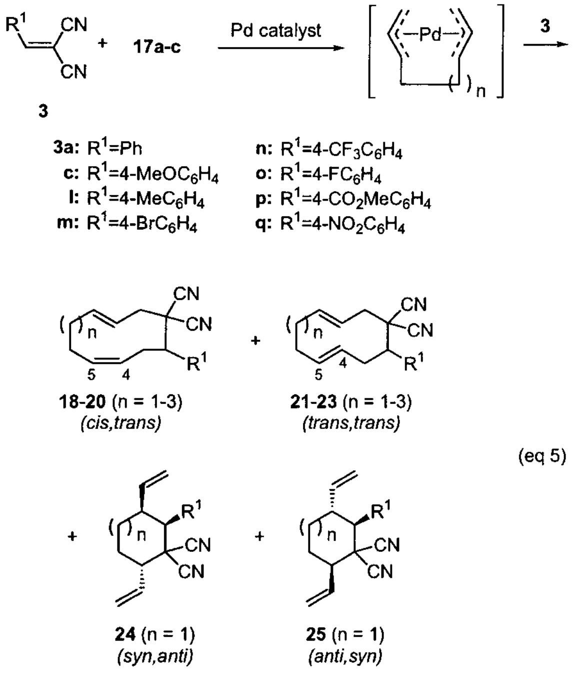
17b

				[9+2] adducts	
entry	**3**	catalyst	solvent/temp	**19**	**22**
11	**3a**	$Pd(PPh_3)_4$	THF/reflux	19	41
12[c]	**3a**	$Pd_2dba_3{\cdot}CHCl_3/4\ P(OPh)_3$	THF/0 °C	trace	35
13[c]	**3a**	$Pd_2dba_3{\cdot}CHCl_3/4\ P(OPh)_3$	THF/rt	6	58
14[c]	**3a**	$Pd_2dba_3{\cdot}CHCl_3/4\ P(OPh)_3$	THF/reflux	17	54
15[c]	**3c**	$Pd_2dba_3{\cdot}CHCl_3/4\ P(OPh)_3$	THF/reflux	14	47
16	**3l**	$Pd(PPh_3)_4$	THF/reflux	24	48
17	**3p**	$Pd(PPh_3)_4$	THF/reflux	20	41

17c

				[10+2] adducts	
entry	**3**	catalyst	solvent/temp	**20**	**23**
18	**3a**	$Pd(PPh_3)_4$	THF/reflux	13	2
19[c]	**3a**	$Pd_2dba_3{\cdot}CHCl_3/4\ P(OPh)_3$	THF/reflux	trace	

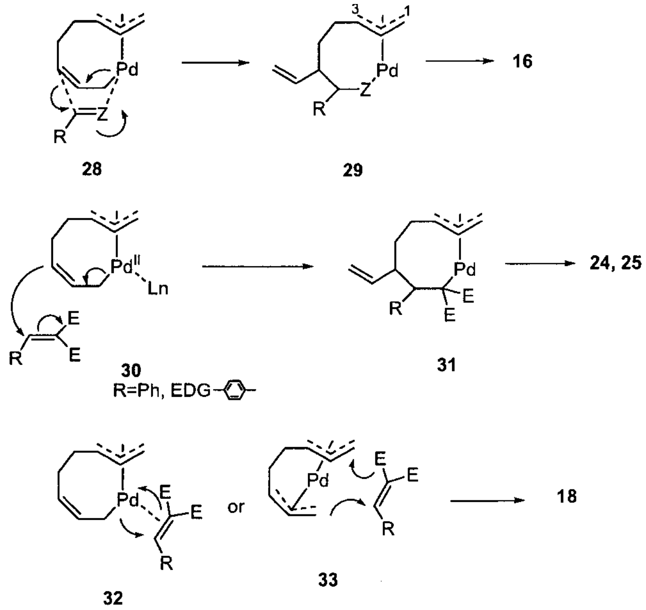
[a] The reactions of the activated olefins **3** with **17a**−**c** (1.3 equiv) were carried out in the presence of the palladium catalysts (10 mol %). [b] Isolated yields based on **3**. [c] The reaction was carried out in the presence of the palladium catalyst (5 mol %) and the phosphine ligand (20 mol %).



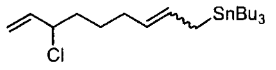
(eq 5)

product, and the [4+2] cycloadducts **25c**−**l** and **31c**−**l** became major products (entries 4 and 5). On the other hand, the activated olefins **3m**−**q**, having an electron-withdrawing group at the para position of the benzene ring, produced the [8+2] cycloadducts **18m**−**q** in 53−66% yields, as major products (entries 6−10). In all the cases, the stereoisomeric (*trans*,*trans*)-[8+2] cycloadducts **21** (*n* = 1) were not obtained.

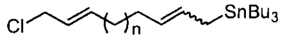
Scheme 4



Interesting observations in the reaction of **17a** with **3a**,**c**,**l**−**g** are as follows: (i) in polar and coordinative solvents such as THF and DMF, the [4+2] adducts were obtained almost exclusively or very predominantly as observed in the previous reactions of **14** with hetero C═Z compounds **15** (eq 3) or with isocyanates **9**, whereas the [8+2] adducts were produced predominantly or in significant yields in a noncoordinative solvent (CH_2Cl_2): (ii) in the reaction with the activated alkenes **3c** and **3l**, bearing an electron-donating group at the para-position of the benzene ring, the [8+2] adducts **18c** and **18l** were produced as minor products, whereas those adducts **18m**−**q** were obtained as major products in the reaction with the activated alkenes **3m**−**q** bearing an electron-withdrawing group at the para position. The difference in these reactivities is explained later in Scheme 4, based on the structure of the intermediate (η^1,η^3-octadienediyl)palladium complex.



17b

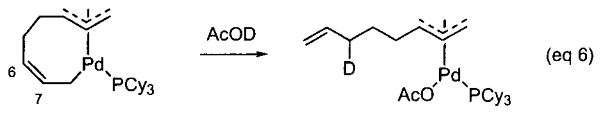


17c: n = 3

The reaction of **17b** with **3a** proceeded smoothly in the presence of $Pd(PPh_3)_4$ catalyst (10 mol %) in THF under reflux to give the [9+2] cycloaddition (endo−endo mode cycloaddition) products **19a** (*n* = 2) and **23a** (*n* = 2) in 19% and 41% yields, respectively, and the [5+2] and [7+2] cycloaddition (exo−exo or exo−endo mode cycloaddition) products were not obtained (entry 11). The $Pd_2dba_3{\cdot}CHCl_3/4P(OPh)_3$ (5 mol %) catalyst system was also effective for the [9+2] cycloaddition, in which the product distribution and the combined yield of **19a** and **22a** were influenced by the reaction temperature. When the reaction was carried out in the presence of $Pd_2dba_3{\cdot}CHCl_3/4P(OPh)_3$ catalyst at 0 °C, the product **22a** was obtained in 35% yield along with a trace amount of **19a** (entry 12). The reaction at room temperature gave **22a** in 58% yield together with 6% yield of **19a**, and the yield of **19a** increased to 17% by carrying out the reaction under reflux (entries 13 and 14). The structures of **19a** and **22a** were also determined by X-ray analysis as shown in Figures 2 and 3 in the Supporting Information. The stereochemistry of the C4−C5 double bond of **19a** was cis and that of the C9−C10 double bond was trans (Figure 2), and the stereochemistry of both double bonds at C4−C5 and C9−C10 of **22a** was trans (Figure 3). The other 4-substituted benzylidenemalononitriles, **3c**, **3l**, and **3p**, underwent the [9+2] cycloaddition reaction with **17b** in the presence of a palladium(0) catalyst, giving the corresponding 1,1-dicyano-4-*trans*-9-*trans*-undecadienes, **22c**, **22l**, and **22p**, respectively, in 41−47% yields along with the stereoisomeric 1,1-dicyano-4-*cis*-9-*trans*-undecadienes, **19c**, **19l**, and **19p**, in 14−24% yields (entries 15−17). It should be noted that the reactions of **17b** gave the [9+2] cycloadducts selectively, and none of the [7+2] and [5+2] adducts were obtained.

Encouraged by the above results, we further examined the [10+2] cycloaddition reaction. However, the reaction of **17c** with **3a** in the presence of $Pd(PPh_3)_4$ catalyst (10 mol %) gave small amounts of the 12-membered carbocycles, **20a** and **23a** (entry 18). The use of the $Pd_2dba_3\cdot CHCl_3/4P(OPh)_3$ (5 mol %) catalyst system gave even worse results: only trace amounts of **20a** and **23a** were obtained (entry 19).

[4+2] vs [8+2] (or [4+2] vs [9+2]) Cycloaddition of Bis-π-allylpalladium Intermediates. **(1) Addition of C═Z.** It is known that the telomerization of 1,3-butadiene with aldehydes, imines, and isocyanates proceeds regioselectively to afford the corresponding [4+2] cycloaddition products.[11−15] Tsuji[13b] and Wilke[17] proposed that this reaction proceeded via a bis-π-allylpalladium intermediate generated from the butadiene dimerization process as shown in eq 3. Jolly and co-workers[16] studied the intermediates in the palladium-catalyzed reactions of 1,3-dienes and found that the reaction of (η^1,η^3-octadienediyl)palladium−phosphine complex **26** with AcOD gave η^3-allylic palladium acetate−phosphine complex **27** in which deuterium was labeled exclusively at the C6 position (eq 6). This indicates that in the case of η^1,η^3-octadienediylpalladium complexes electrophilic attack takes place at the C-6 position: for example, a heteroatom of **15** (or of a coordinative solvent) would coordinate to the palladium of **14**, producing the η^1,η^3-octadienediyl complex that would react with the carbon electrophiles (**15**) at the C-6 position as shown in **28** (Scheme 4). The C−C bond formation would give **29**, which, upon reductive elimination of Pd(0), may produce either **16** or its eight-membered regioisomer. The reductive coupling at the C-3 position of **29** is more preferable due to thermodynamic stability of the six-membered heterocycles **16**. Similar argument can be made for the reaction of **17a** with **9** (eq 4). Consequently, in the reaction with C═Z electrophiles, the [4+2]adducts are obtained exclusively.

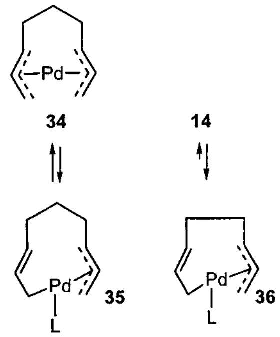


(eq 6)

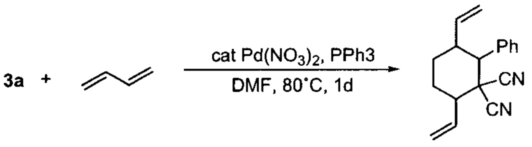
26 **27**

(2) Addition of Activated Alkenes. As started above, [4+2]-addition was predominant in THF and DMF whereas [8+2] addition became predominant (in the case of **3m**−**q**) in CH_2Cl_2. THF and DMF would coordinate to palladium of the bis-π-allylpalladium **14**, generated from **17a**, to produce an η^1,η^3-octadienediyl complex, or such solvents might enhance the coordination of PPh_3 to Pd of **14**. Then, the nucleophilic addition of the η^1-allylic palladium to the activated alkene **3a** would take place as shown via **30**, leading to **31**, which upon reductive coupling would produce the [4+2]adducts **24a** and **25a**. In the reaction of **3a**,**c**,**l** in CH_2Cl_2, a pathway through the alkene-Pd coordination in **32** (or **33**) would compete with the ordinary nucleophilic addition pathway via **30**, giving a mixture of the [8+2] and [4+2] adducts. In the case of **3m**−**q** having an electron-withdrawing group at the para position of the benzene ring, the coordination of the electron-deficient alkene to Pd(II) would become much stronger favoring a pathway via **32**. Accordingly, the [8+2] adducts are obtained predominantly over [4+2] adducts.

Scheme 5



To further confirm the above postulate, we carried out the reaction of excess amounts of 1,3-butadiene with **3a** in the presence of $Pd(NO_3)_2$ (2.5 mol %) and PPh_3 (8 mol %) in DMF at 80 °C for 1 d (eq 7), the same reaction conditions as those used in the reaction of 1,3-butadiene with imines.[13] A 1:1 mixture of **24a** and **25a** was produced in good yield, but no [8+2] adducts were obtained most probably due to DMF solvent. We also examined the same reaction in CH_2Cl_2, instead of DMF, but the reaction was quite sluggish and after 9 d at 80 °C a messy product mixture was obtained. Accordingly, the 10-membered carbocycles **18** can be obtained by the [8+2] cycloaddition reaction with **17a**, and cannot be obtained by the usual butadiene-dimerization pathway.



(eq 7)

24a, 25a

In the reaction of **17b**, the [9+2] adducts were produced and the other adducts through [5+2] or [7+2] cycloaddition were not obtained. In contrast to the reaction of **17a**, the solvent effect in the reaction of **17b** was very small: the reaction of **3a** with **17b** in CH_2Cl_2 at room temperature in the presence of $Pd_2dba_3\cdot CHCl_3/4P(OPh)_3$ gave the [9+2] adducts (**19a** and **22a**) in approximately similar yield with similar stereoisomer ratio. The reason only [9+2] addition takes place in **17b** and why solvent effect is not observed are not clear at present. We assume that the bis-π-allylpalladium intermediate **34** derived from **17b** may be more stable than **14** derived from **17a**, and thus the cycloaddition of **17b** may proceed through **34** whereas that of **30** via **36** (Scheme 5).

Conclusion

Intermolecular amphiphilic bis-allylation of activated alkenes and imines with bis-π-allylpalladium, derived from allyltributylstannane-allyl chloride-palladium catalyst, gives the corresponding 1,2-bisallylated alkanes and amines in good to high

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[17] Wilke, G.; Bogdanovic; Hardt, P.; Heimbach, P.; Keim, W.; Kröner, M.; Oberkirch, W.; Tanaka, K.; Steinrücke. D.-C. E.; Walter, D.; Zimmermann, D.-C. H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 151.

yields. Intramolecular version of the bis-allylation using activated alkenes enables to synthesize 10- and 11-membered carbocycles in good to high yields. Those carbocycles are not able to be obtained through the conventional butadiene dimerization method or through related methodologies.

Experimental Section

Intermolecular Amphiphilic bis-Allylation of Activated Olefins. The reaction of phenylethylidenemalononitrile **3a**, allyltributylstannane **4**, and allyl chloride **5a** is representative. To a solution of **3a** (77 mg, 0.5 mmol), **4** (119 mg, 0.6 mmol), and $PdCl_2(PPh_3)_2$ (10 mg, 3 mol %) in THF (5 mL) was added **5a** (49 mL, 0.6 mmol) at room temperature under Ar atmosphere and the mixture was stirred for 13 h. The reaction was quenched with water, and the reaction mixture was extracted with ether and concentrated. The resulting residue was dissolved in ethyl acetate and a saturated solution of KF was added. The mixture was stirred for 5 h, and then extracted with ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by column chromatography on silica gel with hexane/ethyl acetate (10:1) as eluent gave allyl-(1-phenyl-3-butenyl)malononitrile **6a** in 91% yield.

Intermolecular Amphiphilic bis-Allylation of Imines and Isocyanates. The reaction of the imine **9a**, allyltributylstannane **4**, and allyl chloride **5a** is representative.

To a solution of **9a** (84 mg, 0.51 mmol) and $Pd2dba_3{\bullet}CHCl_3$ (25 mg, 0.024 mmol) in DMF (2 mL) were added **4** (90 μL, 0.61 mmol) and **5a** (50 μL, 0.61 mmol) at room temperature under Ar atmosphere and the mixture was stirred for 4 d. Palladium residue was removed by short column chromatography on silica gel with ether. Purification by column chromatography on silica gel with hexane/ethyl acetate (10:1) as eluent gave 4-aza-4-methyl-5-(4-nitrophenyl)-1,7-octadiene **10a** in 81% yield (102 mg, 0.414 mmol).

[4+2] Cycloaddition of 17a to Isocyanates 9 g−h. The reaction of *p*-toluenesulfonyl isocyanate **9g** with 8-chloro-2,6-octadienyl- tributylstannane **17a** is representative. To a solution of **9a** (32 mg, 0.21 mmol) and $Pd(PPh_3)_4$ (21 mg, 0.02 mmol) in dry CH_2Cl_2 (1 mL) was added **17a** (110 mg, 0.25 mmol) at 40 °C under Ar atmosphere and the mixture was stirred for 2 d. The catalyst residue was removed by short column chromatography on silica gel with ether. Purification by column chromatography on silica gel with hexane/ethyl acetate (3:1) as eluent gave **16g** in 50% yield (32 mg, 0.11 mmol).

[8+2] Cycloaddition of 17a to Activated Olefins. The reaction of 4-methoxycarbonylbenzilidenemalononitrile **3p** with **17a** is representative. To a solution of **3p** (41 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (21 mg, 0.02 mmol) in dry CH_2Cl_2 (2 mL) was added **17a** (120 mg, 0.28 mmol) at 40 °C under Ar atmosphere and the mixture was stirred for 2 d. The catalyst residue was removed by short column chromatography on silica gel with ether. Purification by column chromatography on silica gel with hexane/ethyl acetate (3:1) as eluent gave **18p** (47 mg, 0.15 mmol, 68% yield), **24p** (4.7 mg, 0.015 mmol, 7% yield), and **25p** (6.0 mg, 0.019 mmol, 9%yield).

[9+2] Cycloaddition of 17b to Activated Olefins. The reaction of benzilidenmalononitrile **3a** with **17b** is representative. To a solution of **3a** (46 mg, 0.30 mmol), $Pd_2dba_3CHCl_3$ (16 mg, 0.015 mmol), and $P(OPh)_3$ (31 mg, 0.06 mmol) in dry THF (2 mL) was added **17b** (160 mg, 0.36 mmol) under reflux under Ar atmosphere and the mixture was stirred for 2 d. The catalyst residue was removed by short column chromatography on silica gel with ether. Purification by column chromatography on silica gel with hexane/ethyl acetate (10:1) as eluent gave **19a** (35 mg, 0.16 mmol, 54% yield) and **22a** (11 mg, 0.051 mmol, 17% yield).

[10+2] Cycloaddition of 17c to Activated Olefins. To a solution of **3a** (31 mg, 0.20 mmol) and $Pd(PPh_3)_4$ (22 mg, 0.02 mmol) in dry THF (2 mL) was added **17c** (110 mg, 0.24 mmol) under reflux under Ar atmosphere and the mixture was stirred for 2 d. The catalyst residue was removed by short column chromatography on silica gel with ether. Purification by column chromatography on silica gel with hexane/ethyl acetate (15:1) as eluent gave **20a** (7.0 mg, 0.024 mmol, 13% yield) and **23a** (1.8 mg, 0.006 mmol, 2% yield).

Supporting Information Available: Characterization data for new compounds **6**, **10**, **16**, **17**, **18−20**, and **22−25** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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