Novel η^3-Allylpalladium−Pyridinylpyrazole Complex: Synthesis, Reactivity, and Catalytic Activity for Cyclopropanation of Ketene Silyl Acetal with Allylic Acetates

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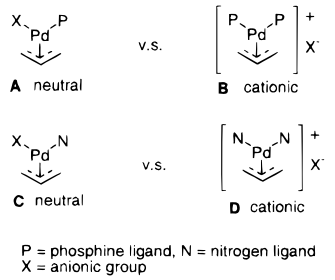
Received June 29, 1998

Abstract: Novel cationic η^3-allylpalladium−pyridinylpyrazole complexes **1a** and **1b** were synthesized from 3-alkyl-5-(2-pyridinyl)pyrazole and η^3-allylpalladium chloride dimer in the presence of $AgBF_4$. Cationic complexes **1a** and **1b** were converted into neutral complexes **2a** and **2b** under basic conditions. These complexes were characterized by ^1H, ^{13}C, and ^{15}N NMR studies. Neutral complexes **2a** and **2b** have high catalytic activity for cyclopropanation of ketene silyl acetals with allylic acetates. Comparison of the cationic and neutral complexes and the reaction mechanism of cyclopropanation were discussed.

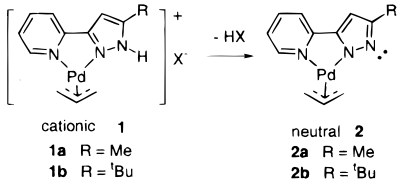
Introduction

Palladium complexes are well-known to exhibit good performance in various catalytic organic reactions.[1] In these reactions, ligands attached to palladium play an important role. Ligands affect metals electronically and sterically by complexation. The resulting complexes can control the reactivity of substrates and selectivity of products. In nucleophilic substitution reactions of allylic compounds via η^3-allylpalladium complexes, especially, differences in the nature and reactivity between neutral monophosphine η^3-allylpalladium complex **A** and cationic bisphosphine complexes **B** have been fully discussed.[2] In contrast to the phosphine palladium complexes, there are few detailed studies of η^3-allylpalladium complexes coordinated with nitrogen ligands (**C** and **D** in Scheme 1) because neutral mononitrogen η^3-allylpalladium complexes may be unstable and the isolation is difficult.[3] Therefore, it is a challenging task to synthesize stable cationic and neutral η^3-allylpalladium complexes having nitrogen ligands, and to compare the properties of these complexes. Pyrazoles are known as both monodentate and exobidentate ligands, and their nitrogen atoms coordinate with the metal center as both anionic and donor groups.[4] Pyrazole having a 2-pyridinyl group[5] that we focus on here could be a good candidate for production of both cationic and neutral η^3-allylpalladium complexes (**1** and **2** in Scheme 2). Further, we observed that the neutral complex **2** prepared from **1** worked as an effective catalyst for cyclopropanation of ketene silyl acetals with allylic acetates. The palladium-catalyzed cyclopropanation by nucleophilic attack to the central carbon on the η^3-allylpalladium intermediate followed by reductive elimination of palladacyclobutane is very rare[6]

Scheme 1



Scheme 2



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(1) (a) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: Chichester, 1995. (b) *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 435; Vol. 4, p 585; Vol. 4, p 833.

(2) (a) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. (b) Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1975**, *97*, 2534. (c) Oshima, M.; Shimizu, I.; Yamamoto, A.; Ozawa, F. *Organometallics* **1991**, *10*, 1221. (d) Åkermark, B.; Krakenberger, B.; Hansson, S.; Vitagliano, A. *Organometallics* **1987**, *6*, 620.

(3) Although syntheses of many cationic bisnitrogen η^3-allylpalladium complexes were reported, there are few reports on neutral η^3-allylpalladium complexes. Huttel, R.; Rau, B. *J. Organomet. Chem.* **1977**, *139*, 89.

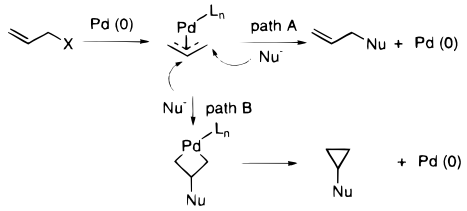
(4) (a) Minghetti, G.; Banditelli, G.; Bonati, F. *J. Chem. Soc., Dalton Trans.* **1979**, 1851. (b) Bushnell, G. W.; Dixon, K. R.; Eadie, D. T.; Stobart, S. R. *Inorg. Chem.* **1981**, *20*, 1545.

(5) (a) Sugiyarto, K. H.; Goodwin, H. A. *Aust. J. Chem.* **1988**, *41*, 1645. (b) Jones, P. J.; Jeffery, J. C.; McCleverty, J. A.; Ward, M. D. *Polyhedron* **1997**, *16*, 1567. (c) Amoroso, A. J.; Jeffery, J. C.; Jones, P. L.; McCleverty, J. A.; Thornton, P.; Ward, M. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1443.

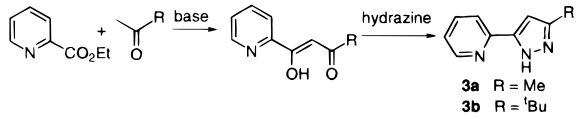
(6) (a) Hegedus, L. S.; Darlington, W. H.; Russell, C. E. *J. Org. Chem.* **1980**, *45*, 5193. (b) Carfagna, C.; Mariani, L.; Musco, A.; Sallese, G. *J. Org. Chem.* **1991**, *56*, 3924. (c) Hoffmann, H. M. R.; Otte, A. R.; Wilde, A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 234. (d) Carfagna, C.; Galarini, R.; Musco, A.; Santi, R. *J. Mol. Catal.* **1992**, *72*, 19. (e) Wilde, A.; Otte, A. R.; Hoffmann, H. M. R. *J. Chem. Soc., Chem. Commun.* **1993**, 615. (f) Formica, M.; Musco, A.; Pontellini, R.; Linn, K.; Mealli, C. *J. Organomet. Chem.* **1993**, *448*, C6. (g) Hoffmann, H. M. R.; Otte, A. R.; Wilde, A.; Menzer, S.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1280. (h) Otte, A. R.; Wilde, A.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 100.

S0002-7863(98)02269-0 CCC: $15.00
Published on Web 09/25/1998

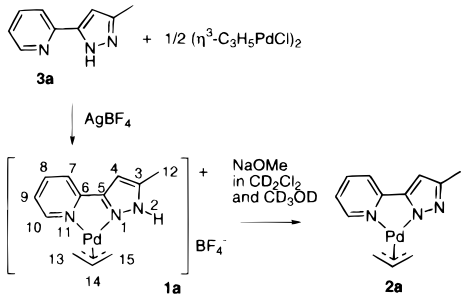
Scheme 3



Scheme 4



Scheme 5



(path B in Scheme 3) although palladium-catalyzed allylation is well-known[1] (path A in Scheme 3). In this paper, we report the synthesis and reactivity of novel cationic and neutral palladium−pyridinylpyrazole complexes **1a**, **1b**, **2a**, and **2b**. Catalytic cyclopropanation of ketene silyl acetals with **2** and its reaction mechanism are also reported.

Results

A. Synthesis and Properties of Palladium Complexes. Pyridinylpyrazole ligands **3a** (MePPH)[7] and **3b** (tBuPPH) were easily obtained by Claisen condensation of ethyl pyridinecarboxylate with methyl ketones and subsequent formation of the pyrazole ring with hydrazine (Scheme 4). Reaction of **3a** and η^3-allylpalladium chloride dimer in the presence of $AgBF_4$ in dichloromethane gave air-stable complex **1a** in 89% yield as a white powder (Scheme 5). Rotation of the allyl moiety in **1a** was observed by decoupling study in ^{1}H NMR at room temperature.[8] A hydrogen on nitrogen at the 2-position was observed at 14.25 ppm as a broad signal in DMSO-d_6. The acidic hydrogen was easily abstracted by a base to give a deprotonated complex (**X**); treatment of **1a** with sodium methoxide produced neutral η^3-allylpalladium complex **2a** in a 1:1 mixture of CD_2Cl_2 and CD_3OD. Data of **1a** and **2a** in ^{1}H, ^{13}C, and ^{15}N NMR are shown in Table 1. Major signals moved to upfield by conversion from cationic **1a** into neutral **2a** except for N(1), N(2), C(3), C(6), and C(12). On the contrary, there was pronounced downfield shift of the N(2) nitrogen in ^{15}N NMR because of deprotonation.

Deprotonated complex **X**[9] indicated different ^{1}H NMR spectra in various solvents. Although **X** showed mainly a simple spectrum derived from a monomer form in $CDCl_3$ or a mixture of CD_2Cl_2 and CD_3OD, complicated signals were observed in DMSO-d_6 or DMF-d_7. From the NMR spectra, a mixture of the monomer form and other structures seemed to exist in DMSO or DMF. FAB mass spectrum of **X** indicated the existence of a dimer complex.[10]

A bulky group on the 3-position of pyrazole prevented production of a dimer. We synthesized η^3-allylpalladium complex **1b** from 3-*tert*-butyl-5-(2-pyridinyl)pyrazole (**3b**) and η^3-allylpalladium chloride dimer using a similar procedure to that of **1a**. The proton NMR spectrum of the deprotonated complex prepared from **1b** showed monomer complex **2b** even in DMSO-d_6 [(b) in Figure 1]. The FAB mass spectrum of **2b** also indicated peaks derived mainly from the monomer complex.

Table 1. NMR Data of **1a** and **2a** in CD_2Cl_2:CD_3OD (1:1)[a]

	chem shifts in ppm (coupling constant in Hz)	
	1a	**2a**
N1	219.7	236.3
N2	189.9	288.3
N11	225.3	218.7
C3	145.3	150.7
C4	103.9	101.9
C5	153.4	152.4
C6	151.8	155.4
C7	122.7	120.4
C8	141.4	140.2
C9	126.5	122.8
C10	154.4	153.6
C12	11.0	13.4
C14	118.5	116.7
C13, C15	58.7, 63.7	56.2, 60.8
H4	6.79 (s)	6.42 (s)
H7	7.98 (ddd, 7.8, 1.5, 1.0)	7.64 (br.dd, 7.8, 1.5)
H8	8.13 (dd, 7.8, 7.8, 1.5)	7.88 (ddd, 7.8, 7.8, 1.5)
H9	7.54 (ddd, 7.8, 5.4, 1.5)	7.18 (ddd, 7.8, 5.4, 1.5)
H10	8.70 (ddd, 5.4, 1.5, 1.0)	8.52 (br.dd, 5.4, 1.5)
H12	2.46 (s)	2.31 (s)
H14	5.86 (tt, 12.7, 7.3)	5.68 (tt, 12.7, 6.8)
H13, H15 syn	4.52 (br.), 4.37 (br.)	4.31, 3.96 (dd, 6.8, 1.5)
H13, H15 anti	3.52 (br.), 3.30 (br.)	3.23, 3.11 (d, 12.7)

[a] ^{1}H NMR (600 MHz):^{13}C NMR (150 MHz):^{15}N NMR spectra were obtained by the ^{1}H−^{15}N PEG-HMBC method (ref NH_4NO_3 in DMSO-d_6 at 0 ppm).

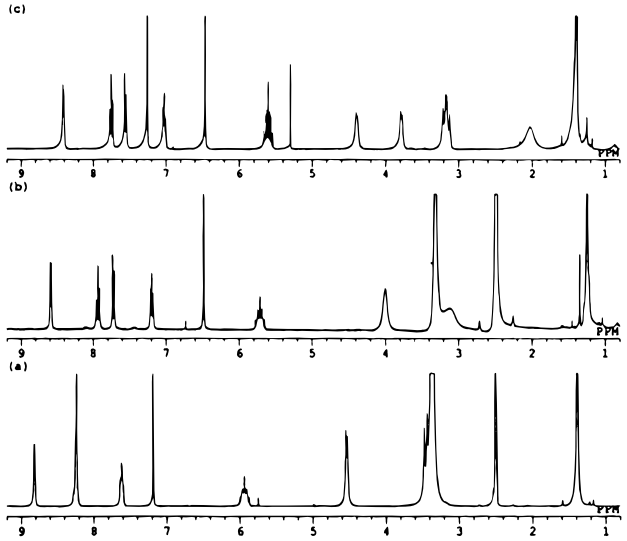


Figure 1. ^{1}H NMR spectra of palladium complexes: (a) **1b** in DMSO-d_6 (300 MHz), (b) **2b** in DMSO-d_6 (300 MHz), and (c) **2b** in $CDCl_3$ (300 MHz).

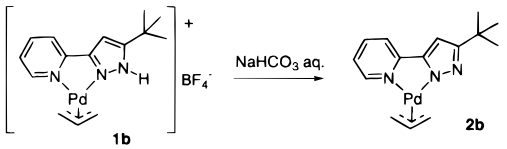
(7) Ferles, M.; Kafka, S.; Šilhánková, A.; Šputová, M. *Collect. Czech. Chem. Commun.* **1981**, *46*, 1167.

(8) Because each anti proton was exchanged by rotation of the allyl moiety at room temperature, the signal of one proton disappeared by a decoupling study on another proton. A similar phenomenon was observed in the case of a decoupling study on syn protons.

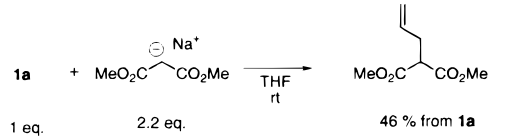
(9) See Experimental Section.

(10) Pyrazoles can usually coordinate as exobidentate ligands to give a bimetallic complex. Trofimenko, S. *Chem. Rev.* **1972**, *72*, 497.

Scheme 6



Scheme 7



Scheme 8

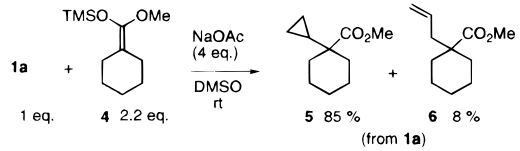
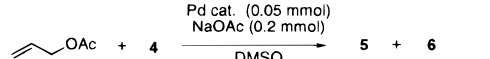
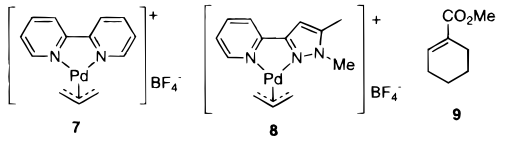


Table 2. Catalytic Cyclopropanation of Ketene Silyl Acetal



Run	Pd cat.	Products[a] 5	6
1	**1a**	87 % (83 %[b])	7 %
2[c]	**7**	3 %	trace
3[c]	**8**	5%	trace

(a) Yields were determined by GLC and NMR (500 MHz) with n-decane as an internal standard. (b) Isolated yield (c) Allyl acetate was completely consumed.

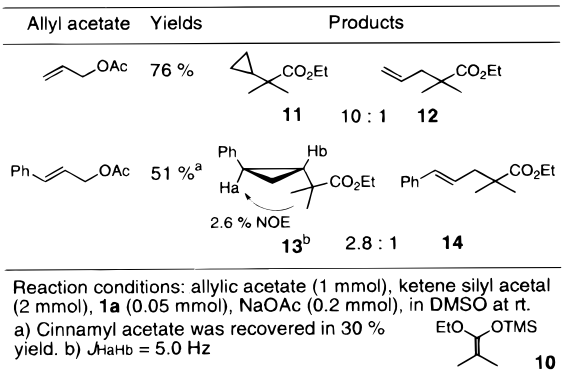


B. Reactivity. Complex **1a** reacted with nucleophiles to give allylated products and cyclopropane compounds. Reaction of **1a** with the sodium enolate of dimethyl malonate in THF at room temperature gave dimethyl allylmalonate in 46% yield (Scheme 7). On the other hand, reaction of **1a** with ketene silyl acetal **4** in the presence of NaOAc in DMSO at room temperature gave cyclopropane **5** and allylated compound **6** in 85% and 8% yields, respectively (Scheme 8).

Further, complex **1a** catalyzed cyclopropanation of ketene silyl acetal **4** with allyl acetate. Reaction of allyl acetate (1 mmol) and ketene silyl acetal **4** (2 mmol) with **1a** (0.05 mmol) and sodium acetate (0.2 mmol) in DMSO (4 mL) gave cyclopropane **5** and allylated ester **6** in 87% and 7% yields, respectively (Run 1 in Table 2). As described in the Discussion section, the present cyclopropanations proceeded via neutral complex **2a**. To compare other cationic palladium−bisnitrogen complexes which could not transform into neutral complexes, we examined cationic complexes **7** and **8** (Runs 2 and 3 in Table 2). Although allyl acetate disappeared after 24 h in the case of **7** and **8**, the yields of **5** and **6** were very low. When **7** or **8** was used as a catalyst, α,β-unsaturated ester **9** was obtained in about 60% yield based on ketene silyl acetal **4**.

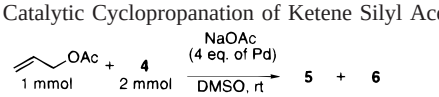
Results of reactions of another ketene silyl acetal with allylic acetates are shown in Table 3. Cyclopropane compounds were obtained only in the case of the ketene silyl acetal of 2-methylpropionate **10**. When ketene silyl acetals of *tert*-butyl acetate and ethyl propionate were used instead of **10**, no cyclopropane was obtained. Reaction of substituted allyl acetate with **10** proceeded stereoselectively to give **13**.

Table 3. Reaction of Allylic Acetates with Ketene Silyl Acetal **10**



Reaction conditions: allylic acetate (1 mmol), ketene silyl acetal (2 mmol), **1a** (0.05 mmol), NaOAc (0.2 mmol), in DMSO at rt. a) Cinnamyl acetate was recovered in 30 % yield. b) J_{HaHb} = 5.0 Hz

Table 4. Catalytic Cyclopropanation of Ketene Silyl Acetal



Run	Pd cat. (mmol)	Time	Yields[a] 5 + 6	Ratio (5 : 6)	TON[b]
1	**1a** (0.05)	0.5 h	94 %	(12.4 : 1)	18.8
2	**1a** (0.01)	36 h	14 %[c]	almost **5**	14
3	**1b** (0.05)	0.5 h	85 %	(2.9 : 1)	17
4	**1b** (0.01)	24 h	88 %	(2.4 : 1)	88

(a) Yields were determined by GLC and NMR with n-decane as an internal standard. (b) the turnover number (c) Allyl acetate was recovered in 41 % yield.

We changed the amounts of **1a** and **1b** to examine the turnover number (TON) of the palladium catalysts in the reaction of allyl acetate and **4**. Although the reaction was almost completed with 5 mol % of **1a** in 0.5 h, in the case of using 1 mol % of **1a** the reaction terminated, giving only 14% yield of **5** (Runs 1 and 2 in Table 4). Although use of **1b** lowered selectivity of **5**, the turnover number was heightened to 88 times (Runs 3 and 4 in Table 4).

Discussion

A. Comparison of Cationic and Neutral Complexes. ^{13}C NMR shifts of the allyl moiety are a good indication to understand the properties and reactivity of η^3-allyl complexes.[2d] In the case of neutral η^3-allylpalladium complex having a phosphine and an anionic ligand (**A** in Scheme 1), two terminal ^{13}C NMR shifts appear in different positions, and the difference is usually large (>16 ppm). However, the difference in two terminal ^{13}C NMR shifts of neutral complex **2a** is only 4.6 ppm and is close in the case of cationic complex **1a** (5.0 ppm). This result means that the two terminal carbons do not lean to one side electronically, and the pyridinylpyrazole ligand behaves like a bisnitrogen ligand, not an anionic group such as halogen or cyanide.

Cationic complex **1a** is soluble in DMSO and DMF, but almost insoluble in $CHCl_3$, CH_2Cl_2, MeOH, acetone, and H_2O. Interestingly, **1a** is soluble in a mixture of CH_2Cl_2 and MeOH.[11] On the other hand, neutral complex **2a** is very soluble in various organic solvents, such as $CHCl_3$, CH_2Cl_2, MeOH, acetone, DMSO, and DMF. The solubility is advantageous in terms of the broad choice of solvents.

(11) At the present time, the reason the combination of CH_2Cl_2 and MeOH is effective to solve **1a** is not clear.

It is apparent in Table 2 that there is a great difference between **1a**, which is a precursor for neutral complex **2a**, and cationic complexes **7** and **8**, which cannot be converted into neutral form. When **7** and **8** were used as catalysts, a considerable amount of **9** was obtained. Tsuji et al. reported[12] that **9** was obtained in the reaction of **4** with allyl carbonate and palladium acetate without phosphine in benzonitrile. They explained formation of **9** by attack of enolate on palladium and subsequent β-elimination. Thus, formation of **9** in the case of **7** and **8** means that ligand dissociation and attack of enolate on palladium occurred. On the contrary, because **2a** generated from **1a** prevents ligand dissociation even in DMSO, cyclopropanation proceeded smoothly.

B. Cyclopropanation. Formation of cyclopropane from allylic acetate and ketene silyl acetal is considered to take place by regioselective nucleophilic attack to the central carbon of the allyl moiety on palladium and subsequent reductive elimination of palladacyclobutane[13] (path B in Scheme 3). Completion of cyclopropanation is dependent on the kind of nucleophile and ligand. Generally, when phosphine is used as a ligand, allylated products are obtained mainly. On the contrary, in the case of nonphosphine ligands cyclopropanes are obtained.[6] Nucleophiles for the cyclopropanation are limited to less stabilized carbon nucleophiles ($pK_a = 20-30$). When the allyl moiety has a good leaving group on the center carbon, soft nucleophiles also react with the η^3-allylpalladium complex. However, only disubstituted propene, not cyclopropane, is obtained.[13c,d,e]

In the catalytic cyclopropanation, regeneration of an active palladium species that can react with allylic compounds to produce η^3-allylpalladium is also important. Musco and coworkers succeeded in selective cyclopropanation of ketene silyl acetals with allyl bromide using a palladium−TMEDA catalyst.[6f] In their catalytic system, however, use of reactive allyl bromide and a stoichiometric amount of thulium acetate[14] was essential. Therefore, it is desirable that allylic acetate is used instead of allyl bromide and thulium acetate. Complex **1a** can react with allyl acetate to give cyclopropanes. This is the first example of selective cyclopropanation with use of allyl acetate directly.

Two major mechanisms, the Pd(0)/Pd(II) cycle [(1) in Scheme 9] and the Pd(II)/Pd(IV) cycle [(2) in Scheme 9], are considered in the present catalytic cyclopropanation. The Pd(II)/Pd(IV) cycle was proposed in Musco's reports.[6f] Actually, a dimethylpalladium complex having a bisnitrogen ligand reacts with additional allyl bromide to give a four-valent palladium species, whose reductive elimination proceeds to give η^3-allylpalladium species and ethane.[15] In our case, however, no additional allyl acetate was necessary to produce cyclopropane (Scheme 8). This result means that reductive elimination of palladacyclobutane directly occurred. Therefore, the catalytic cycle of **2a** must be the Pd(0)/Pd(II) cycle. A plausible mechanism is shown in Figure 2. Cationic complex **1a** is converted into neutral complex **2a** under basic conditions, and nucleophilic attack occurs on the central carbon of the η^3-allyl moiety to produce palladacyclobutane. The palladacyclobutane gives cyclopropane **5** and an active Pd(0) species, which react with allyl acetate to generate **2a** and sodium acetate again. We consider that DMSO plays an important role because no reaction proceeded in other solvents, even in DMF. DMSO may accelerate the reaction in the oxidative addition and reductive elimination steps. Therefore, the difference in catalytic ability among complexes **2a**, **7**, and **8** may arise from their stability and that of their derivatives[16] in DMSO.

The turnover number of **1a** was lower than that of complex **1b**, and complex **2a** can easily form dimeric structures in DMSO whereas **2b** mainly exists as a monomer form. These two facts seem to suggest dimers of **2a** were unreactive. Formation of

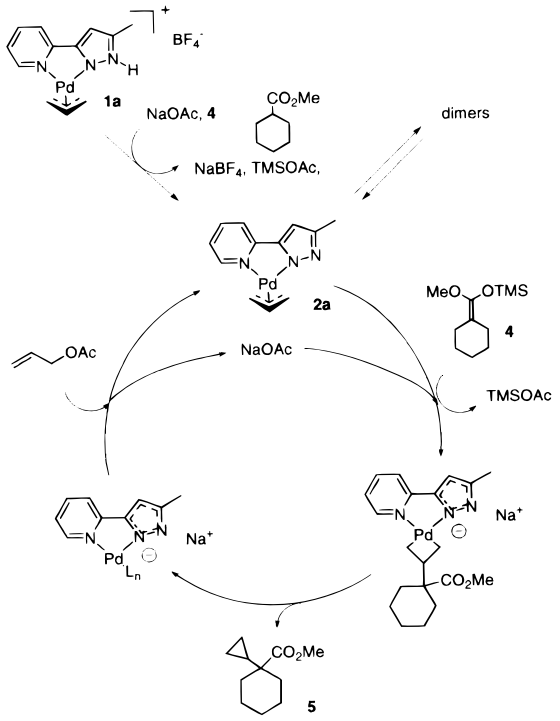
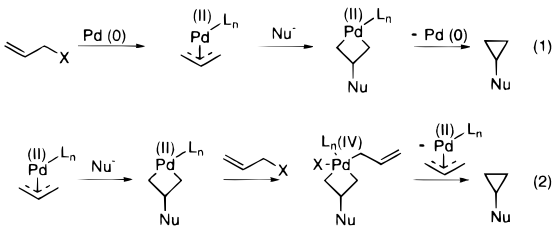


Figure 2.

Scheme 9. Pd(0)/Pd(II) Cycle (eq 1) and Pd(II)/Pd(IV) Cycle (eq 2)



(12) Tsuji, J.; Takahashi, K.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1984**, *42*, 4783.

(13) Center carbon attack of a nucleophile against an allyl ligand to produce metalacyclobutanes was observed in various metals; however, there are few examples of the reductive elimination of metalacyclobutanes to produce cyclopropanes. Center carbon attack: Pd and Pt: (a) Carfagna, C.; Galarini, R.; Musco, A.; Santi, R. *Organometallics* **1991**, *10*, 3956. (b) Carfagna, C.; Galarini, R.; Linn, K.; López, J. A.; Mealli, C.; Musco, A. *Organometallics* **1993**, *12*, 3019. (c) Ohe, K.; Matsuda, H.; Morimoto, T.; Ogoshi, S.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 4125. (d) Aranyos, A.; Szabó, K. J.; Castaño, A. M.; Bäckvall, J.-E. *Organometallics* **1997**, *16*, 1058. (e) Organ, M. G.; Miller, M. *Tetrahedron Lett.* **1997**, *47*, 8181. Other metals: (f) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1984**, *106*, 7272. (g) McGhee, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 3388. (h) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7346. (i) Ephritikhine, M.; Green, M. L. H.; MacKenzie, R. E. *J. Chem. Soc., Chem. Commun.* **1976**, 619. (j) Ephritikhine, M.; Francis, B. R.; Green, M. L. H.; MacKenzie, R. E.; Smith, M. J. *J. Chem. Soc., Dalton Trans.* **1977**, 1131. Reductive elimination of metalacyclobutane: (k) Benyunes, S. A.; Brandt, L.; Green, M.; Parkins, A. W. *Organometallics* **1991**, *10*, 57. (l) Wakefield, J. B.; Stryker, J. M. *J. Am. Chem. Soc.* **1991**, *113*, 7057. (m) Tjaden, E. B.; Stryker, J. M. *Organometallics* **1992**, *11*, 16. (n) Tjaden, E. B.; Stryker, J. M. *J. Am. Chem. Soc.* **1993**, *115*, 2083. (o) Schwiebert, K. E.; Stryker, J. M. *Organometallics* **1993**, *12*, 600.

(14) Thulium acetate is very toxic. Musco reported that no reaction took place with use of allyl acetate instead of allyl bromide and thulium acetate.

(15) (a) Byers, P. K.; Canty, A. J.; Traill, P. R.; Watson, A. A. *J. Organomet. Chem.* **1990**, *390*, 399. (b) de Graaf, W.; Boersma, J.; van Koten, G. *Organometallics* **1990**, *9*, 1479.

(16) The derivatives include the palladacyclobutane and palladium(0) species in Figure 2.

dimers depends on a substituent group on the pyrazole ring, the solvent, and concentration. The exact structures of the dimers are not clear at the present time. At least, more than three kinds of methyl groups on the pyrazole ring were observed in ^{13}C NMR in DMF-d_7. Structures and ratios of dimers varied in the time-course, and this is the reason for the difficulty in determining the structures.

Conclusion

We have developed stable η^3-allylpalladium cationic and neutral bisnitrogen ligand complexes **1a**, **1b**, **2a**, and **2b**. The neutral complexes **2a** and **2b** generated from **1a** and **1b** have high catalytic activity for cyclopropanation of ketene silyl acetals with allylic acetates. Other cationic complexes which cannot be converted into neutral form are ineffective for the cyclopropanation. It is considered that the catalytic ability of the neutral complexes **2a** and **2b** depends on the stability of their derivatives in DMSO.

Experimental Section

General Procedure. Methylene chloride, ethanol, and methanol were dried over activated molecular sieves 4A or 3A prior to use. Dehydrated ether and THF were purchased from Kanto Chemical Co., Inc. Commercially available DMSO (special grade) was used without purification or dryness. NMR spectra were obtained from JEOL α-600, JEOL GSX-500, and JEOL AL-300. ^{1}H NMR chemical shift are reported in ppm from tetramethylsilane (0 ppm) in $CDCl_3$ and a mixture of CD_2Cl_2 and CD_3OD, and residual DMSO (3.35 ppm) in DMSO-d_6. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (0 ppm) in a mixture of CD_2Cl_2 and CD_3OD, and residual $CDCl_3$ (77.0 ppm) or DMSO (39.5 ppm). ^{15}N NMR spectra were obtained by the ^{1}H−^{15}N PEG-HMBC method, and chemical shifts are reported in ppm from NH_4NO_3 (0 ppm) in DMSO-d_6. Melting points were determined on a Yanaco MP-500 melting point apparatus and were not corrected. Analytical gas chromatography was performed on a Hewlett-Packard 5890 with J&W Scientific DB-5 (15 m × 0.25 mm). Mass spectral analyses were performed on a JEOL JMS-HX100. Microanalyses were performed by the Division of Chemical Analysis in RIKEN. Flash chromatographies were performed by using Merck silica gel 60 (230−400 mesh).

2-H-3-Methyl-5-(2-pyridynyl)pyrazole (MePPH, 3a).[7] To a suspension of NaH (60 wt % in mineral oil, 5.2 g, 130 mmol) in THF (50 mL) at 0 °C was added acetone (9.54 mL, 130 mmol). The mixture was stirred at room temperature for 20 min, and then allowed to heat to 60 °C. Ethyl 2-pyridinecarboxylate (16.5 g, 100 mmol) in THF (50 mL) was slowly added to the mixture. After the mixture was stirred at 70 °C for 20 min, dilute HCl solution was added to the mixture until pH 8−9 at 0 °C. The mixture was extracted with diethyl ether (10 mL X 4), and the combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give yellow oil (17.9 g). To a refluxing solution of the above oil (17.9 g) in EtOH (180 mL) was added dropwise for 10 min, hydrazine monohydrate (9.7 mL, 200 mmol) in EtOH (20 mL). After the mixture was refluxed for 1.5 h, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2, and the solution was washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residual solid was washed with ether on a filter paper and dried under reduced pressure to give white solid **3a** (11.3 g, 71%): ^{1}H NMR (500 MHz, CD_3OD) δ 8.55 (br d, 1H, J = 5.0 Hz), 7.84 (br d, 1H, J = 8.2 Hz), 7.78 (dt, 1H, J = 1.4, 7.8 Hz), 7.28−7.24 (m, 1H), 6.62 (s, 1H), 2.36 (s, 3H).

2-H-3-*tert*-Butyl-5-(2-pyridynyl)pyrazole (tBuPPH, 3b) was prepared in 65% yield (1.18 g) from ethyl 2-pyridinecarboxylate (1.65 g, 10 mmol), 3,3-dimethyl-2-butanone (1.1 g, 11 mmol), and hydrazine monohydrate (9.7 mL, 200 mmol) by using a similar procedure to that of **3a**. **3b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, 1H, J = 4.6 Hz), 7.81 (br d, 1H), 7.72 (dt, 1H, J = 1.3, 7.3 Hz), 7.20 (dd, 1H, J = 4.6, 7.2 Hz), 6.67 (s, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 136.7, 122.5, 119.9, 99.7, 31.6, 30.4; mp 106 °C. Anal. Calcd for $C_{12}H_{15}N_3$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.48; H, 7.56; N, 20.64.

[(η^3-C_3H_5)Pd(MePPH)]$^+BF_4^-$ (1a). Dichloromethane (40 mL) was added at 0 °C to a brown two-necked round-bottom flask containing $AgBF_4$ (216 mg, 1.11 mmol) and (η^3-C_3H_5)PdCl dimer (203 mg, 0.555 mmol). Ligand **3a** (177 mg, 1.11 mmol) was added to the mixture. After the mixture was stirred at room temperature for 1.5 h, methanol (40 mL) was added to the mixture. A white precipitate was filtered off with Celite and membrane filter (Millipore, LCR25-LH), and the filtrate was concentrated to give white solid. The white solid was washed with CH_2Cl_2 on a filter paper and dried under reduced pressure to give **1a** (387 mg, 89%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.25 (H2, br), 8.81 (H10, d, J = 5.4 Hz), 8.24 (H8, dd, J = 7.8, 7.8 Hz), 8.19 (H7, d, J = 7.8 Hz), 7.62 (H9, dd, J = 7.8, 5.4 Hz), 7.06 (H4, s), 5.93 (H14, tt, J = 11.7, 6.4 Hz), 4.47 (H13syn and H15syn, 2H, d, J = 6.4 Hz), 3.43 (H13anti and H15anti, 2H, d, J = 11.7 Hz), 2.40 (H12, 3H, s); ^{1}H NMR, ^{13}C NMR, and ^{15}N NMR in CD_2Cl_2−CD_3OD (1:1), see Table 1; mp >285 °C dec. Anal. Calcd for $C_{12}H_{14}N_3BF_4Pd$: C, 36.63; H, 3.59; N, 10.68. Found: C, 36.73; H, 3.56; N, 10.64.

[(η^3-C_3H_5)Pd(tBuPPH)]$^+BF_4^-$ (1b) (480 mg, 97%) was prepared from **3b** (229 mg, 1.14 mmol) by using a similar procedure to that of **1a**. **1b**: ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.95 (br, 1H), 8.83 (d, 1H, J = 5.1 Hz), 8.28−8.22 (m, 2H), 7.62 (ddd, 1H, J = 2.2, 5.1, 6.6 Hz), 7.19 (s, 1H), 5.93 (dt, 1H, J = 6.5, 12.4 Hz), 4.54 (d, 1H, J = 6.5 Hz), 3.46 (d, 1H, J = 12.4 Hz), 1.38 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.8, 154.0, 151.4, 150.1, 141.0, 126.0, 122.1, 117.9, 101.1, 62.1 (2C), 31.3, 29.6; mp >140 °C dec. Anal. Calcd for $C_{15}H_{20}N_3BF_4Pd$: C, 41.37; H, 4.63; N, 9.65. Found: C, 41.17; H, 4.59; N, 9.54.

(η^3-C_3H_5)Pd(MePP) (2a). To a mixture of **1a** (4.1 mg) and sodium methoxide (5.2 mg, excess) were added dichloromethane-d_2 (0.25 mL) and methanol-d_4 (0.25 mL) at room temperature, and the mixture was stirred under sonication for 5 min. After the precipitate was filtered off, the solution containing **2a** was obtained: ^{1}H NMR, ^{13}C NMR, and ^{15}N NMR in CD_2Cl_2−CD_3OD (1:1), see Table 1; HRMS (FAB) calcd for $C_{12}H_{13}N_3Pd$ 306.0228, found 306.0229.

Preparation of X from 1a. Suspension of **1a** (18.5 mg) in CH_2Cl_2 (5 mL) was washed with saturated aqueous $NaHCO_3$ in a separatory funnel. An organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to give **X** (16.0 mg) as pale yellow oil. Data for ^{1}H and ^{13}C NMR in DMF-d_7 and FAB mass spectra of **X** are available in the Supporting Information.

(η^3-C_3H_5)Pd(tBuPP) (2b). White solid **2b** (24 mg) was prepared from **1b** (49.3 mg) by using a similar procedure to that of **X**. **2b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (br d, 1H, J = 5.3 Hz), 7.75 (dt, 1H, J = 1.3, 7.9 Hz), 7.56 (br d, 1H, J = 7.9 Hz), 7.03 (br t, 1H, J = 6.0 Hz), 6.46 (s, 1H), 5.60 (tt, 1H, J = 7.0, 12.5 Hz), 4.39 (br d, 1H, J = 7.0 Hz), 3.79 (br d, 1H, J = 7.0 Hz), 3.17 (br t, 2H, J = 12.5 Hz), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 155.2, 152.4, 150.9, 138.9, 121.1, 119.5, 115.6, 98.4, 59.4, 56.5, 32.2, 31.1; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.59 (br d, 1H, J = 5.3 Hz), 7.94 (br t, 1H, J = 7.7 Hz), 7.72 (br d, 1H, J = 8.3 Hz), 7.20 (br t, 1H, J = 6.2 Hz), 6.49 (s, 1H), 5.72 (tt, 1H, J = 9.2, 9.9 Hz), 4.00 (br, 2H), 3.13 (br, 2H), 1.25 (s, 9H); mp >150 °C dec; HRMS (FAB) calcd for $C_{15}H_{19}N_3Pd$ 348.0698, found 348.0698.

2, 3-Dimethyl-5-(2-pyridynyl)pyrazole (Me_2PP). A mixture of 1,3-dimethyl-5-(2-pyridynyl)pyrazole and 2,3-dimethyl-5-(2-pyridynyl)-pyrazole (**Me_2PP**) was obtained from ethyl 2-pyridinecarboxylate, acetone, and methylhydrazine according to the procedure for **3a**. These products were isolated by flash chromatography (25% EtOAc in hexane). 2,3-Dimethyl-5-(2-pyridynyl)pyrazole (**Me_2PP**, 29%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62−8.58 (m, 1H), 7.85 (br d, 1H, J = 8.2 Hz), 7.69−7.63 (m, 1H), 7.17−7.11 (m, 1H), 6.62 (s, 1H), 3.83 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 152.1, 149.7, 149.0, 139.6, 136.1, 121.8, 119.4, 103.6, 36.2, 11.2; mp 97−99 °C dec. Anal. Calcd for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26. Found: C, 69.24; H, 6.45; N, 23.83. 1,3-Dimethyl-5-(2-pyridynyl)pyrazole) (27%, colorless oil, less polar product than **Me_2PP**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (br d, 1H, J = 4.6 Hz), 7.69−7.65 (m, 1H), 7.49 (br d, 1H, J = 8.2 Hz), 7.19−7.15 (m, 1H), 6.34 (s, 1H), 4.14 (s, 3H), 2.29

(s, 3H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 149.6,148.6, 146.6, 141.5, 136.2, 122.2, 121.8, 105.6, 38.7, 13.2.

[(η^3-C_3H_5)Pd(Me_2PP)]$^+BF_4^-$ (8) was prepared in 53% yield from **Me_2PP** by using a similar procedure to that of **1a**. **8**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.79 (br d, 1H, J = 5.1 Hz), 8.23 (br t, 1H, J = 7.6 Hz), 8.17 (br d, 1H, J = 7.8 Hz), 7.60 (br t, 1H, J = 6.2 Hz), 7.10 (s, 1H), 5.94 (tt, 1H, J = 7.0, 12.6 Hz), 4.59 (d, 2H, J = 7.0 Hz), 3.86 (s, 3H), 3.54 (d, 2H, J = 12.6 Hz), 2.42 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 153.9, 150.1, 149.8, 144.4, 141.1, 125.9, 121.9, 117.9, 104.8, 62.5, 37.6, 11.6; mp >170 °C dec. Anal. Calcd for $C_{13}H_{16}N_3BF_4Pd$: C, 38.32; H, 3.96; N, 10.31. Found: C, 38.25; H, 3.91; N, 10.25.

Stoichiometric Reaction. (a) Allylation of Dimethyl Malonate. To a suspension of **1a** (20 mg, 0.0508 mmol) in THF (2 mL) was added sodium enolate of dimethyl malonate [generated from dimethyl malonate (15 mg, 0.112 mmol) and NaH (60 wt % in mineral oil, 4.9 mg, 0.122 mmol) in THF (1 mL) at 0 °C]. After the mixture was stirred for 1 h, precipitate was removed through Celite, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography to give dimethyl allylmalonate (4.0 mg, 46%).

(b) Cyclopropanation of Ketene Silyl Acetal. To a mixture of **1a** (31.5 mg, 0.080 mmol) and NaOAc (26.2 mg, 0.32 mmol) in DMSO (5 mL) was added ketene silyl acetal **4** (35 μL, ca. 0.16 mmol) at room temperature. After the mixture was stirred for 0.5 h, ether and dilute HCl solution were added to the mixture, and the mixture was stirred for 10 min. The mixture was extracted with ether, and the combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. Decane (9.4 mg) was added as an internal standard to the residue, and yields and the ratio of a mixture of **5** and **6** were obtained (see in Scheme 8).

Catalytic Reaction. All the catalytic reactions were carried out under argon. The appropriate allyl acetate (1 mmol) and ketene silyl acetal (2 mmol) were added to a solution containing cationic palladium catalyst (0.05 or 0.01 mmol) and NaOAc (0.2 or 0.04 mmol, 4 equiv of palladium) in DMSO. The reaction mixture was stirred at room temperature, and progress of the reaction was monitored by GLC or TLC analysis. Diethyl ether and diluted HCl solution were added to the reaction mixture, and the mixture was extracted with ether. The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated in vacuo. From the residue, a mixture of cyclopropane derivatives and allylated compounds was obtained by distillation (Kugelrohr apparatus) and flash chromatography. Yields and ratios were determined by GLC and NMR with *n*-decane as a internal standard. Pure cyclopropane derivatives were obtained after dihydroxylation with OsO_4 and purification by flash chromatography.

5:[6a] ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.71 (s, 3H), 2.62−1.94 (m, 2H), 1.68−1.53 (m. 3H), 1.37−1.03 (m, 5H), 0.94−0.81 (m, 1H), 0.31 (d, 4H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 176.3, 51.3, 46.4, 32.6, 25.8, 23.6, 20.8, 0.71.

11:[6d] (volatile) ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.08 (q, 2H), 1.21 (t, 3H), 1.01 (s, 3H), 1.00 (m, 1H), 0.35−0.22 (m, 4H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 177.9, 60.2, 41.1, 22.9, 19.5, 14.5, 0.70; MS, *m*/*z* (rel intensity) 156 (M^+, 3.3), 141 (17.5), 128 (6.6), 113 (9.9), 110 (10.4), 100 (24.8), 83 (100), 67 (11.6), 55 (99.3).

13: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, 2H), 7.18 (t, 1H), 7.13 (d, 2H), 4.17 (m, 2H), 1.99 (s, 3H), 1.93 (ddd, 1H, J = 5.0, 5.7, 9.2 Hz), 1.39 (ddd, 1H, J = 5.0, 5.7, 8.7 Hz), 1.26 (t, 3H, J = 7.1 Hz), 1.20 (s, 3H), 1.01 (ddd, 1H, J = 5.5, 5.7, 8.7 Hz), 0.90 (ddd, 1H, J = 5.5, 5.7, 9.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 143.0, 128.2, 126.1, 125.4, 60.4, 41.5, 31.1, 23.2 (2C), 19.1, 14.2, 11.3. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.69. Found: C, 77.27; H, 8.85.

14 could not be isolated from a mixture of **13** and **14**. **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.05 (m, 5H), 6.35 (d, 1H, J = 15.3 Hz), 6.11 (dt, 1H, J = 6.8, 15.3 Hz), 4.10−4.04 (m, 2H), 2.39 (d, 2H, J = 6.8 Hz), 1.19 (t, 3H, J = 7.1 Hz), 1.18 (s, 6H); MS, *m*/*z* (rel intensity) 232 (M^+, 31.6), 159 (18.4), 117 (100), 91 (12.3).

Reaction with Complexes 7 and 8. The reactions with complexes **7** and **8** were carried out according to the procedure described above. The unsaturated ester **9**[12] was obtained in 60% (in the case of **7**) and 58% (in the case of **8**) yields, respectively, based on ketene silyl acetal **4**.

Acknowledgment. A.S. gratefully acknowledges the financial support by the Special Postdoctoral Researchers Program. We thank Dr. Hiroyuki Koshino for measurement of NMR spectra and Ms. Kumiko Harata for operation of FAB mass spectra.

Supporting Information Available: NMR data of **X** in DMF-d_7, mass spectra of **X** and **2b** (3 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA982269C