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Synthetic and Mechanistic Studies on Pd(0)-Catalyzed Diamination of Conjugated Dienes

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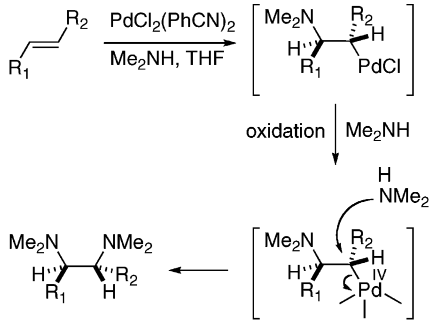
Abstract: Various dienes and a triene can be regioselectively diaminated at the internal double bond with good yields and high diastereoselectivity using di-*tert*-butyldiaziridinone (**5**) as the nitrogen source and $Pd(PPh_3)_4$ (1−10 mol %) as the catalyst. Kinetic studies with ^1H NMR spectroscopy show that the diamination is first-order in total Pd catalyst and inverse first-order in PPh_3. For reactive dienes, such as 1-methoxybutadiene (**6g**) and alkyl 1,3-butadienes (**6a**, **6j**), the diamination is first-order in di-*tert*-butyldiaziridinone (**5**) and zero-order in the olefin. For olefins with relatively low reactivity, such as (*E*)-1-phenylbutadiene (**6b**) and (3*E*,5*E*)-1,3,5-decatriene (**6i**), similar diamination rates were observed when 3.5 equiv of olefins were used. $Pd(PPh_3)_2$ is likely to be the active species for the insertion of Pd(0) into the N−N bond of di-*tert*-butyldiaziridinone (**5**) to form a four-membered Pd(II) complex (**A**), which can be detected by NMR spectroscopy. The olefin complex (**B**), formed from intermediate **A** via ligand exchange between the olefin substrate and the PPh_3, undergoes migratory insertion and reductive elimination to give the diamination product and regenerate the Pd(0) catalyst.

Introduction

Vicinal diamines are very important functional moieties that are present in various biologically active compounds, chemical materials, and chiral catalysts.[1] Diamination of olefins presents an attractive strategy to introduce vicinal nitrogen atoms. Various metal-free,[1,2] metal-mediated,[1,3,4] or metal-catalyzed[5,6] processes have been developed. Palladium has been one of the most important metals explored for the diamination process. In a pioneering study, Bäckvall reported stereospecific diamination of olefins via *trans*-aminopalladation, oxidation of Pd(II) to possible Pd(IV) with oxidants such as *m*CPBA, and subsequent nucleophilic displacement of Pd by an amine (Scheme 1).[7] In 2005, Lloyd-Jones, Booker-Milburn, and co-workers reported a Pd(II)-catalyzed intermolecular diamination of conjugated dienes with ureas (Scheme 2).[8] The diamination occurred regioselectively at the less-substituted double bond of dienes. The reaction is likely to proceed via a Pd(II)-promoted aza-Wacker-type process (*trans*-aminopalladation)[9] to form a π-allyl Pd complex, followed by the displacement of Pd with N. The resulting Pd(0) is oxidized by O_2 or benzoquinone to regenerate the Pd(II) catalyst. In 2005, Muñiz and co-workers reported a Pd(II)-catalyzed intramolecular diamination of olefins tethered

Scheme 1



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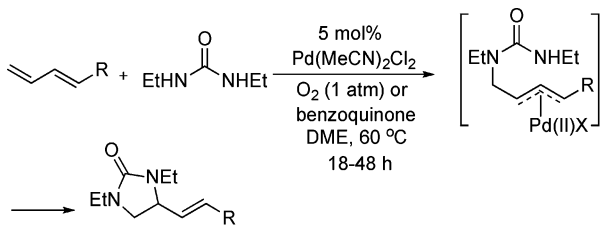
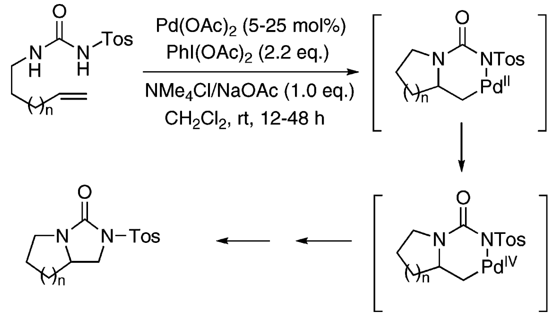
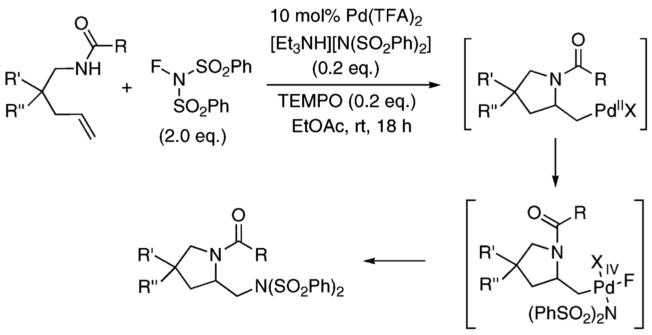
Scheme 2



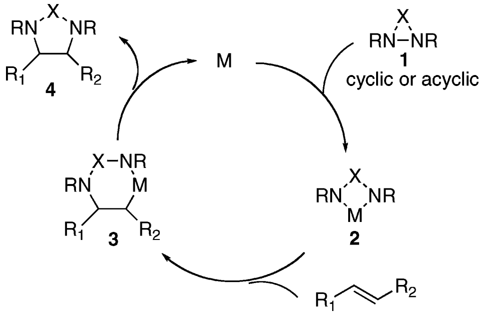
Scheme 3



Scheme 4



Scheme 5



with ureas (Scheme 3).[10] The reaction was proposed to proceed via aminopalladation to form a Pd(II) intermediate, which is oxidized to Pd(IV) species, followed by the replacement of the C−Pd(IV) bond with a C−N bond to give the diamination product and regenerate the Pd(II) catalyst.[10c,11−13] Very recently, Michael and co-workers reported the diamination of olefins tethered with amide groups using *N*-fluorobenzenesulfonimide as electrophilic nitrogen source (Scheme 4).[14] The diamination is proposed to proceed via a Pd(II)-promoted aminopalladation, oxidative addition of *N*-fluorobenzenesulfonimide to the Pd(II) species, and subsequent reductive elimination.

As part of our general interest in the oxidation of olefins,[15] we have explored a possible diamination of olefins via the activation of a N−N bond (Scheme 5). It was hoped that a suitable metal catalyst could oxidatively insert into the N−N bond of dinitrogen compound **1** (cyclic or acylic) to form diamido species **2**, which would then undergo migratory insertion into a double bond to form **3**,[16] followed by reductive elimination to give diamination product **4**. Our studies started with the investigation of the feasibility of diaziridines and related analogues as nitrogen source and various metals as catalyst. It was found that conjugated dienes can be effectively diaminated at the internal double bond with di-*tert*-butyldiaziridinone (**5**)[17,18] as nitrogen source and Pd(PPh$_3$)$_4$ as catalyst (Scheme 6).[19] In subsequent studies, the reaction parameters such as ligand and solvent have been examined to improve the reaction process. The catalyst loading can be reduced to 1−2 mol % from the original 10 mol % (Scheme 6).[17b] The reaction mechanism has also been investigated via NMR spectroscopy and kinetic studies, providing a better understanding of the reaction

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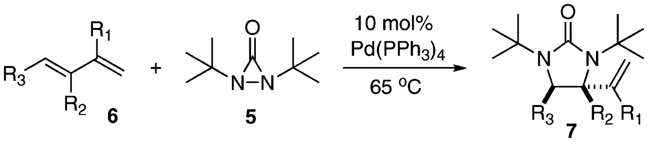
Scheme 6

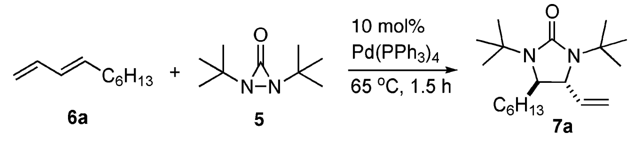


process.[20-22] Herein, we wish to report our detailed studies on this subject.[23-26]

Results and Discussion

1. Reaction Condition Studies. Several solvents were screened for the diamination using (*E*)-1,3-decadiene (**6a**) as substrate, 10 mol % $Pd(PPh_3)_4$ as catalyst, and di-*tert*-butyldiaziridinone (**5**) as nitrogen source at 65 °C. As shown in Table 1, a number of solvents[27] are suitable for the diamination except $CDCl_3$ and CH_3CN. Since $Pd(PPh_3)_4$ was found to be less soluble in solvents such as hexanes or toluene, benzene was then typically used for the diamination study.

Table 1. Solvent Study on the $Pd(PPh_3)_4$-Catalyzed Diamination[a]



entry	solvent	conv. (%)[b]
1	$CDCl_3$	0
2	C_6D_6	100
3	toluene	100
4	THF	100
5	hexanes	100
6	DCM	100
7	CH_3CN	0

[a] All reactions were carried out with olefin **6a** (0.20 mmol), di-*tert*-butyldiaziridinone (**5**) (0.24 mmol), $Pd(PPh_3)_4$ (0.020 mmol) at 65 °C in dry solvent (0.60 mL) with stirring under argon for 1.5 h. [b] Conversion was determined by crude ^1H NMR spectroscopy based on the olefin.

Table 2. Ligand Study on the Pd(0)-Catalyzed Diamination[a]

entry	ligand	conv. (%)[b]	entry	ligand	conv. (%)[b]
1	PPh_3	100	11	PPh_2Me	0
2	P(4-tolyl)$_3$	100	12	PMe_2Ph	0
3	$P(4\text{-}MeOC_6H_4)_3$	100	13	P(*n*-Bu)$_3$	0
4	$P(4\text{-}CF_3C_6H_4)_3$	91	14	P(*c*-hexyl)$_3$	10
5	P(3-tolyl)$_3$	100	15[c]	dppe	0
6	P(2-furyl)$_3$	92	16[c]	dppb	0
7	P(2-tolyl)$_3$	15	17	$P(OMe)_3$	0
8	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$	3	18	$P(OEt)_3$	4
9	$P[2,6\text{-}(MeO)_2C_6H_3]_3$	0	19	$P(OPh)_3$	18
10	$P(2,4,6\text{-}Me_3C_6H_2)_3$	0			

[a] All reactions were carried out with olefin (**6a**) (0.20 mmol), di-*tert*-butyldiaziridinone (**5**) (0.25 mmol), and Pd catalyst (0.020 mmol) [prepared *in situ* from $Pd(OAc)_2$ (0.020 mmol), phosphorus ligand (0.080 mmol), *n*-butyllithium (0.040 mmol, 0.025 mL, 1.6 M in hexanes) at room temperature] in benzene-d_6 (0.20 mL) at 65 °C under argon for 2 h unless otherwise stated. [b] Conversion was determined by crude ^1H NMR spectroscopy based on olefin. [c] Phosphorus ligand (0.040 mmol).

A series of phosphorus ligands were examined for the diamination of (*E*)-1,3-decadiene (**6a**) at 65 °C in dry benzene-d_6 using 10 mol % Pd complex as catalyst. Catalysts were prepared *in situ* by treating $Pd(OAc)_2$ with *n*-BuLi and phosphorus ligands at room temperature.[28] Studies showed that monodentate triarylphosphines with exception of bulkier ones, were effective ligands for the diamination (Table 2, entries 1−6 vs entries 7−10). However, phosphines containing one or more alkyl groups, bidentate phosphine ligands, and phosphites were found to be poor ligands for this diamination (Table 2, entries 11−19). Overall, PPh_3 became the ligand of choice for the diamination due to its effectiveness and low cost.

The previously reported diamination procedure requires 10 mol % $Pd(PPh_3)_4$.[19] Only 20% conversion was obtained for (*E*)-

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(27) All the solvents were dried according to standard drying procedures. It was found that moisture in the solvent could lead to the decomposition of di-*tert*-butyldiaziridinone (**5**) and deactivation of the Pd catalyst.

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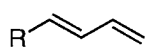
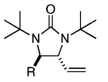
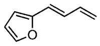
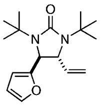
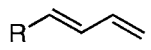
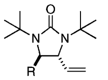
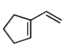
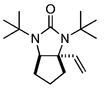
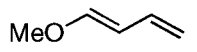
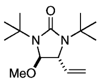
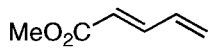
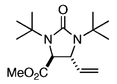
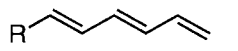
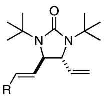
Table 3. Diamination of Conjugated Dienes and a Triene with $Pd(PPh_3)_4$

Entry	Substrate (**6**)	Product (**7**)	Method[a]	Yield (%)[b]
1	 **6b**, R = Ph		A B	90 92
2	**6c**, R = *p*-MeOPh		A B	94 95
3	 **6d**		A B	78 80
4	 **6e**, R = *n*-C_5H_{11}		A	91
5	**6a**, R = *n*-C_6H_{13}		B	86
6	 **6f**		A B	72 82
7[c]	 **6g**		A B	95 91(81[d])
8	 **6h**		A	62
9	 **6i**, R = *n*-C_5H_{11}		A B	81 79

[a] Method A (ref 19): All reactions were carried out with di-*tert*-butyldiaziridinone (**5**) (0.20 mmol), olefin (*E* isomer, 0.24 mmol), and $Pd(PPh_3)_4$ (0.02 mmol) in benzene-d_6 (0.6 mL) in an NMR tube at 65 °C under argon for 0.25−5 h unless otherwise stated. For entry 3, diene (*E*/*Z* = 1/1, *E* isomer: 0.24 mmol). For more examples, see ref 19. Method B: All reactions were carried out with olefin (0.80 mmol), di-*tert*-butyldiaziridinone (**5**) (0.90 mmol, slow addition at a rate of 0.3 mmol/h), $Pd(PPh_3)_4$ (0.016 mmol) at 65 °C under solvent-free conditions and argon for 4 h unless otherwise stated. For entry 2, benzene-d_6 (0.10 mL) was used to dissolve diene. [b] Isolated yield based on **5** for Method A and based on olefin for Method B. [c] Containing <10% *Z* isomer, diamination product **7g** is acid sensitive and was purified on less acidic silica gel (Iatrobeads 6RS-8060, Mitsubishi Kagaku Iatron, Inc. Japan). [d] $Pd(PPh_3)_4$ (1 mol %, 0.008 mmol) was used.

1-phenylbutadiene (**6b**) when the catalyst loading was reduced to 5 mol %. It was surmised that the relatively high concentration of di-*tert*-butyldiaziridinone (**5**) in the reaction system might cause the deactivation of the Pd catalyst, and that slow addition of **5** could lower its concentration and might be beneficial for this diamination. It was indeed the case. As shown in Table 3, the catalyst could be reduced to 2 mol % (even to 1 mol % as illustrated in entry 7)[17b] when di-*tert*-butyldiaziridinone (**5**) was added slowly via syringe pump (Method B). Various dienes and a triene can be efficiently diaminated at 65 °C to give diamination products with good to excellent yields (79−95%) in high regio- and diastereoselectivity. Essentially only one regio- and stereoisomer was obtained. Other regio- and stereoisomers were barely detectable by ^1H NMR spectroscopy of the crude reaction mixture if there was any. The yields obtained with 2 mol % $Pd(PPh_3)_4$ (Method B) are comparable to the ones obtained with the previous conditions (Method A) in most cases. However, electron-deficient diene **6h**, was not an effective substrate for Method B (Table 3, entry 8).

2. Monitoring the Diamination Reaction by ^1H, ^{13}C, and ^{31}P NMR Spectroscopy. In an effort to gain a better understanding of the diamination, the reaction was monitored by ^1H NMR spectroscopy. As shown in Figure 1, a new singlet peak at 1.59 ppm appeared when di-*tert*-butyldiaziridinone (**5**) was treated with $Pd(PPh_3)_4$ in dry benzene-d_6 at 40 °C. This singlet peak (1.59 ppm) is corresponding to the signal of the *tert*-butyl groups of intermediate **A** [the signal of the *tert*-butyl groups of di-*tert*-butyldiaziridinone (**5**) appeared as a singlet at 1.05 ppm (Figure 1)]. After 85 min at 40 °C, all the di-*tert*-butyldiaziridinone (**5**) was consumed, and the singlet peak at 1.59 ppm reached its highest point. At that point, (*E*)-1-phenylbutadiene (**6b**) was added, the signals of the *tert*-butyl groups of diamination product **7b** appeared immediately as two singlet peaks at 1.32 and 1.36 ppm and gradually increased while the singlet peak at 1.59 ppm gradually decreased. The diamination was practically complete 40 min after the addition of diene substrate **6b**. As shown in Figure 2, more electron-rich 1-methoxybutadiene (**6g**) was much more reactive toward this diamination. The reaction between intermediate **A** and the diene was finished in less than one minute. These results indicate a two-step mechanism for the $Pd(PPh_3)_4$-catalyzed diamination. Di-*tert*-butyldiaziridinone (**5**) first reacts with $Pd(PPh_3)_4$ to form an active intermediate with a singlet peak at 1.59 ppm (corresponding to the signal of its *tert*-butyl groups), which subsequently reacts with the olefin substrate to give the diamination product. The singlet peak at 1.59 ppm is consistent with the symmetry of four-membered Pd(II) species **A**, whose structure is also supported by its ^{13}C NMR spectrum (177.3 ppm for C═O, 58.1 ppm for $\underline{C}Me_3$, and 33.6 ppm for Me, see Supporting Information).

The reaction between $Pd(PPh_3)_4$ and di-*tert*-butyldiaziridinone (**5**) (Scheme 7) was also monitored *in situ* by ^{31}P NMR spectroscopy. The reaction was carried out in benzene-d_6 at 40 °C in an NMR tube, and ^{31}P NMR spectra were collected at room temperature for higher quality spectra. As shown in Figure 3, a new singlet at 19.8 ppm appeared and increased gradually as more di-*tert*-butyldiaziridinone (**5**) was consumed. A broad singlet between −4.3 pm and 17.1 ppm appeared as an averaged spectrum of $Pd(PPh_3)_m$ and PPh_3 as a result of rapid ligand exchange between $Pd(PPh_3)_m$ and free PPh_3 [PPh_3 at −4.3 ppm, $Pd(PPh_3)_4$ at 17.1 ppm)].[29] As the reaction proceeded, and more free PPh_3 was released, the broad singlet moved upfield in the direction of PPh_3, and its intensity decreased gradually. After 85 min, di-*tert*-butyldiaziridinone (**5**) was completely consumed as judged by ^1H NMR spectroscopy, and the new singlet at 19.8 ppm in the ^{31}P NMR spectrum reached the highest intensity. The integration ratio of the singlet at 19.8 ppm to the broad singlet at 7.2 ppm is 1:1.65 as shown in Figure 3, which is smaller than the theoretical value (1:1). A possible reason is that the partial decomposition of di-*tert*-butyldiaziridinone (**5**) under the reaction conditions led to incomplete conversion of $Pd(PPh_3)_4$ to intermediate **A** when **5** was consumed. At that point, additional PPh_3 or $Pd(PPh_3)_4$ was added to the reaction mixture to monitor any changes of the signals. It was observed that the broad ^{31}P NMR singlet moved further upfield in the direction of PPh_3 upon addition of PPh_3 and moved downfield in the direction of $Pd(PPh_3)_4$ upon addition of $Pd(PPh_3)_4$. The signal intensity increased in similar magnitude in both of the cases as expected. The singlet at 19.8 ppm is consistent with

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(29) (a) Tolman, C. A.; Seidel, W. C.; Gerlach, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 2669. (b) Mann, B. E.; Musco, A. *J. Chem. Soc., Dalton Trans.* **1975**, 1673.

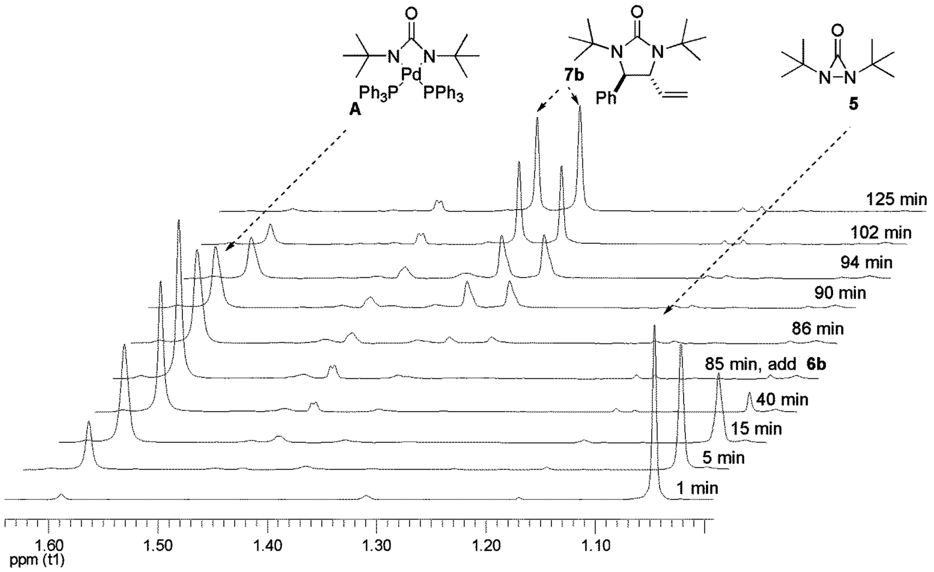


Figure 1. Monitoring of the reaction of $Pd(PPh_3)_4$ with di-*tert*-butyldiaziridinone (**5**) and the subsequent diamination of (*E*)-1-phenylbutadiene (**6b**) by ^1H NMR spectroscopy. $Pd(PPh_3)_4$ (0.030 mmol) reacted with di-*tert*-butyldiaziridinone (**5**) (0.020 mmol) in dry benzene-d_6 (0.6 mL) in an NMR tube under argon atmosphere at 40 °C for 85 min, followed by the addition of (*E*)-1-phenylbutadiene (**6b**) (0.040 mmol). The NMR spectra were recorded at 40 °C.

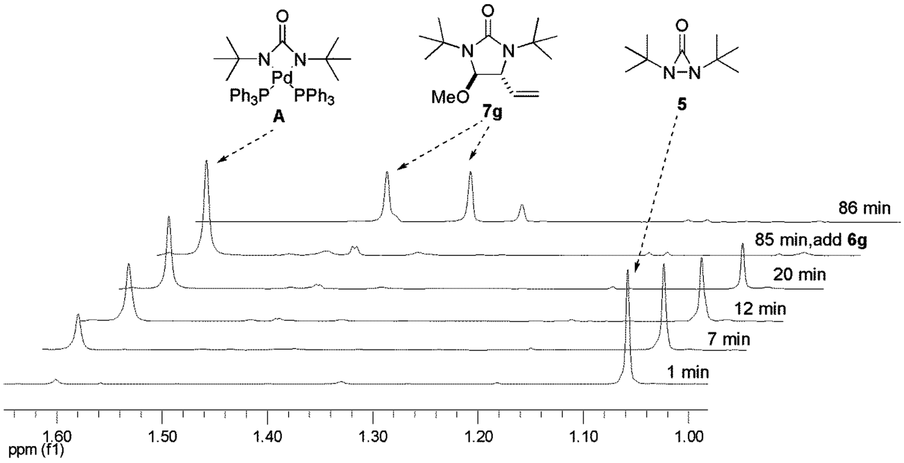
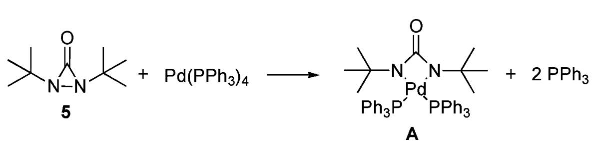


Figure 2. Monitoring of the reaction of $Pd(PPh_3)_4$ with di-*tert*-butyldiaziridinone (**5**) and the subsequent diamination of (*E*)-1-methoxybutadiene (**6g**) by ^1H NMR spectroscopy. $Pd(PPh_3)_4$ (0.030 mmol) reacted with di-*tert*-butyldiaziridinone (**5**) (0.02 mmol) in dry benzene-d_6 (0.6 mL) in an NMR tube under argon atmosphere at 40 °C for 85 min, followed by the addition of (*E*)-1-methoxybutadiene (**6g**) (*E*:*Z* = 15.7:1, *E* isomer: 0.040 mmol). The NMR spectra were recorded at 40 °C.

Scheme 7



the PPh_3 signal of symmetric four-membered Pd(II) intermediate **A**, generated from $Pd(PPh_3)_4$ and di-*tert*-butyldiaziridinone (**5**).

3. Kinetic Model for the Diamination. Based on the above NMR spectroscopy studies, a detailed catalytic cycle for the $Pd(PPh_3)_4$-catalyzed diamination is proposed in Scheme 8. The 14e species $Pd(PPh_3)_2$, generated from $Pd(PPh_3)_4$ by loss of two PPh_3 ligands,[29,30] inserts into the N−N bond of di-*tert*-butyldiaziridinone (**5**), giving four-membered Pd(II) species **A**.[31,32] Olefin-complex **B,** resulting from intermediate **A** via the ligand exchange between olefin **6** and the PPh_3, then undergoes migratory insertion to form π-allyl Pd intermediate **C**,[33−35]

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(30) (a) Fauvarque, J.-F.; Pflüger, F.; Troupel, M. *J. Organomet. Chem.* **1981**, *208*, 419. (b) Amatore, C.; Pflüger, F. *Organometallics* **1990**, *9*, 2276.

(31) For leading references on metal insertion into N−N bonds, see: (a) Erker, G.; Froemberg, W.; Krueger, C.; Raabe, E. *J. Am. Chem. Soc.* **1988**, *110*, 2400. (b) Kitamura, M.; Yanagisawa, H.; Yamane, M.; Narasaka, K. *Heterocycles* **2005**, *65*, 273. (c) Hoover, J. M.; DiPasquale, A.; Mayer, J. M.; Michael, F. E. *Organometallics* **2007**, *26*, 3297. (d) Hoover, J. M.; Freudenthal, J.; Michael, F. E.; Mayer, J. M. *Organometallics* **2008**, *27*, 2238.

(32) The insertion of Ni and Pd to the N−N bond of diaziridinone has been reported, see: Komatsu, M.; Tamabuchi, S.; Minakata, S.; Ohshiro, Y. *Heterocycles* **1999**, *50*, 67. However, to the best of our knowledge, the reaction of the resulting complex with an olefin has not been reported.

(33) For a recent leading review on π-allyl Pd chemistry, see: Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813.

(34) For a recent book on Pd, see: Tsuji, J. *Palladium Reagents and Catalysts: New Perspective for the 21st Century*: John Wiley & Sons Ltd: New York, 2004.

(35) The precise understanding for the first C−N formation and the origin of the observed high regioselectivity awaits further studies.

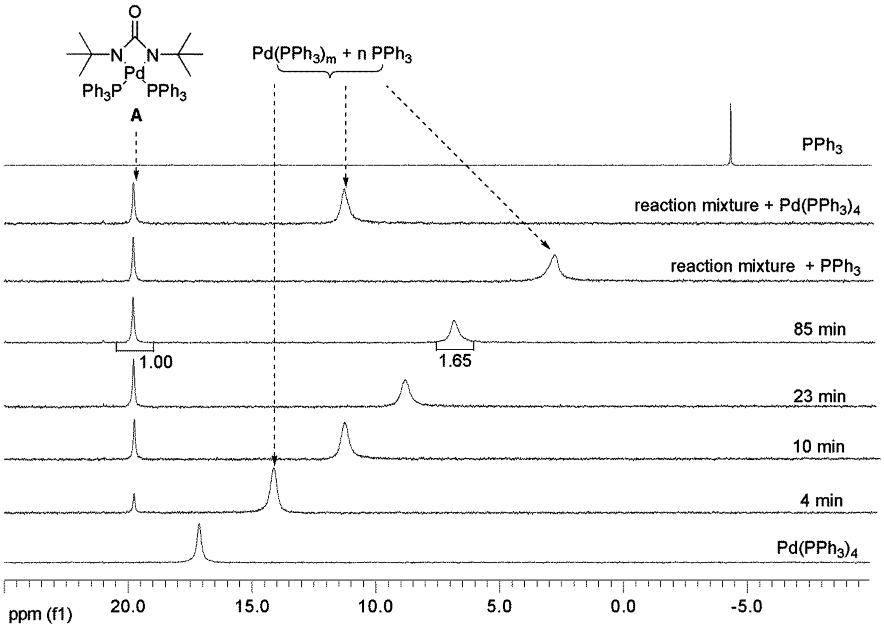
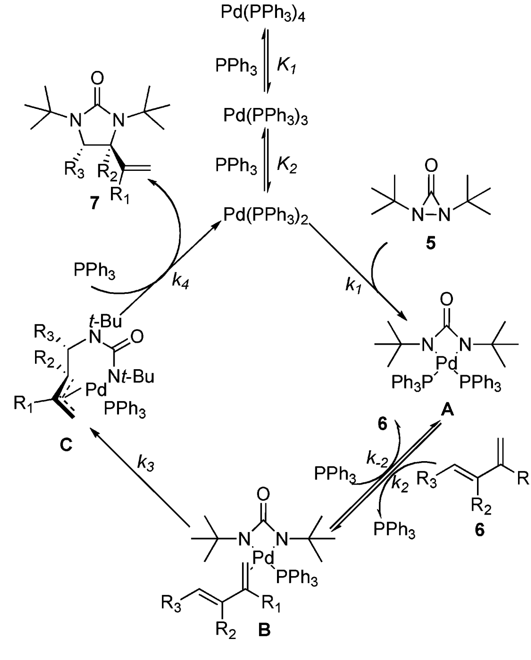
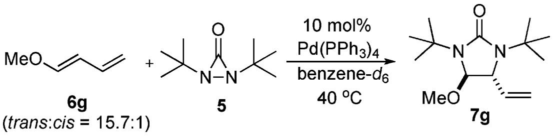


Figure 3. Monitoring of the reaction between di-*tert*-butyldiaziridinone (**5**) (0.030 mmol) and $Pd(PPh_3)_4$ (0.030 mmol) by ^{31}P NMR spectroscopy. The reaction was carried out at 40 °C, and ^{31}P NMR spectra were collected at room temperature (for higher quality spectra). "reaction mixture + PPh_3": additional PPh_3 (0.040 mmol) was added to the reaction mixture after 85 min. "reaction mixture + $Pd(PPh_3)_4$": additional $Pd(PPh_3)_4$ (0.010 mmol) was added to the reaction mixture after 85 min in a separate experiment.

Scheme 8. Proposed Catalytic Cycle for Pd(0)-Catalyzed Diamination of Olefin



Scheme 9



followed by reductive elimination to give diamination product **7**[36] and regenerate the active catalyst $Pd(PPh_3)_2$.

Ligand exchange between the $Pd(PPh_3)_m$ and free PPh_3 in solution is very fast even at room temperature.[29] Therefore, it is reasonable to assume that there are two fast pre-equilibria among $Pd(PPh_3)_4$, $Pd(PPh_3)_3$, and $Pd(PPh_3)_2$.[30] According to the literature, $Pd(PPh_3)_4$ in solution mainly exists as $Pd(PPh_3)_3$.[29,30] Using steady-state approximation, the reaction rate for the diamination can be expressed as eq 1, which indicates that the diamination is first-order in total $Pd(PPh_3)_4$ and inverse first-order in PPh_3 (for derivation of eq 1, see Supporting Information). If the Pd(0) insertion into the N−N bond of di-*tert*-butyldiaziridinone (**5**) is the rate-determining step, the reaction rate can be expressed with $[Pd(PPh_3)_2]$ and [**5**] (eq 2). Based on the quick pre-equilibria among $Pd(PPh_3)_2$, $Pd(PPh_3)_3$, and $Pd(PPh_3)_4$, $[Pd(PPh_3)_2]$ can be expressed with $[Pd(PPh_3)_4]_0$ and $[PPh_3]$. Therefore, the reaction rate can be further expressed with $[Pd(PPh_3)_4]_0$, $[PPh_3]$, and [**5**] (eq 2) (for detailed derivation, see Supporting Information), indicating first-order in total $Pd(PPh_3)_4$ and di-*tert*-butyldiaziridinone (**5**) respectively, zero-order in olefin **6**, and inverse first-order in PPh_3.

$$\text{rate} = \frac{K_2k_1k_2k_3}{k_2k_3[\mathbf{6}] + K_2k_1k_{-2}[\mathbf{5}]} \cdot \frac{[\mathrm{Pd(PPh_3)_4}]_0[\mathbf{5}][\mathbf{6}]}{[\mathrm{PPh_3}]} \tag{1}$$

$$\text{rate} = k_1[\mathrm{Pd(PPh_3)_2}][\mathbf{5}] = \frac{K_2k_1[\mathrm{Pd(PPh_3)_4}]_0[\mathbf{5}]}{[\mathrm{PPh_3}]} = k_{\mathrm{obs}}[\mathbf{5}] \tag{2}$$

4. Kinetic Studies for the $Pd(PPh_3)_4$-Catalyzed Diamination with 1-Methoxybutadiene (6g). Using ^1H NMR spectroscopy, kinetics studies of the diamination were carried out in benzene-d_6 with 10 mol % $Pd(PPh_3)_4$ as catalyst using $Si(SiMe_3)_4$ as internal standard (Scheme 9). The diamination was run at 40 °C so that the reaction was slow enough to allow the data collection. 1-Methoxybutadiene (**6g**) was chosen as substrate for the kinetic experiment to avoid any interference with the *tert*-butyl signals of di-*tert*-butyldiaziridinone (**5**) and the diamination product (**7g**) in the 1.0−2.0 ppm region. The

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(36) It appears that the cyclization for the five-membered ring is kinetically favored with no seven-membered ureas being observed.

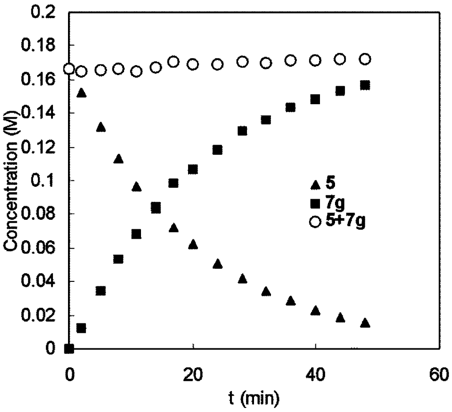


Figure 4. Plots of concentrations of di-*tert*-butyldiaziridinone (**5**), diamination product (**7g**), and their sum (**5** + **7g**) against the reaction time (min) for the diamination of 1-methoxybutadiene (**6g**) (*E*:*Z* = 15.7:1, *E* isomer: 0.24 mmol) with **5** (0.20 mmol) and $Pd(PPh_3)_4$ (0.020 mmol) in dry benzene-d_6 (1.2 mL) at 40 °C in an NMR tube.

concentrations of **5** and diamination product **7g** were determined by integration of the signals corresponding to the respective *tert*-butyl groups. As judged by ^1H NMR spectroscopy, this diamination was very clean and no side-reaction was observed under the reaction conditions.

(a) Reaction Order in Di-*tert*-Butyldiaziridinone (5) for the Diaminations. The diamination of 1-methoxybutadiene (**6g**) was monitored by ^1H NMR spectroscopy at 40 °C. The concentrations of di-*tert*-butyldiaziridinone (**5**) and diamination product (**7g**) at different reaction times were obtained via integration of the signals corresponding to the respective *tert*-butyl groups. The plots of the concentrations of **5** and **7g** against the reaction time are shown in Figure 4. No induction period was observed for this reaction, suggesting that the active catalyst species $Pd(PPh_3)_2$ is generated very quickly, then enters the catalytic cycle. The sum of the concentrations of **5** and **7g** remained almost constant over the reaction time (Figure 4), indicating that di-*tert*-butyldiaziridinone (**5**) was quantitatively converted to diamination product **7g**. The ^{31}P NMR spectrum of the reaction mixture is similar to that of $Pd(PPh_3)_4$, and no reaction intermediates were observed from the ^1H NMR spectrum, indicating that the concentrations of Pd intermediates in the catalytic cycle were very low during the reaction. A plot of $\ln([\mathbf{5}]_0/[\mathbf{5}])$ against the reaction time gives a straight line with a slope, $k_{obs} = 8.2 \times 10^{-4}\ s^{-1}$ (Figure 5), indicating first-order kinetics in di-*tert*-butyldiaziridinone (**5**) for the diamination of 1-methoxybutadiene (**6g**).

(b) Effect of 1-Methoxybutadiene (6g) Concentration. Diaminations with different amounts of **6g** were investigated with 10 mol % $Pd(PPh_3)_4$ at 40 °C. As shown in Figure 6, these diaminations have similar reaction rates, indicating zero-order kinetics in olefin **6g**. All these results show that the diamination is first-order in di-*tert*-butyldiaziridinone (**5**) and zero-order in diene **6g** as expressed in eq 2, which indicates that the Pd(0) insertion into the N—N bond of di-*tert*-butyldiaziridinone (**5**) is the rate-determining step for the diamination of 1-methoxybutadiene (**6g**).

(c) Effect of PPh₃ Concentration. According to eq 2, the observed rate constant of the diamination (k_{obs}) would be inversely proportional to $[PPh_3]$. The diaminations were carried out at 40 °C with 10 mol % $Pd(PPh_3)_4$ and varying amounts of PPh_3. Since $Pd(PPh_3)_3$ is the main Pd species in the solution of $Pd(PPh_3)_4$,[29,30] the concentration of free PPh_3 in the reaction mixture should approximately equal to the sum of the initial $[Pd(PPh_3)_4]$ and $[PPh_3]$ added.[30a] The plot of $1/k_{obs}$ against the concentration of PPh_3 was found to be a straight line as shown in Figure 7, indicating the diamination is inverse first-order in PPh_3 ligand and also validating the approximation of the value of $[PPh_3]_{free}$. This result is consistent with eq 2, which further supports the reaction mechanism proposed in Scheme 8.

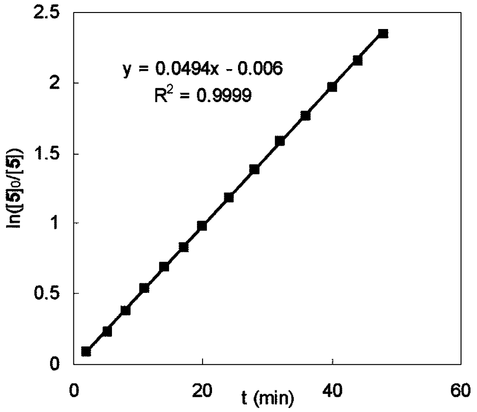


Figure 5. Plot of $\ln([\mathbf{5}]_0/[\mathbf{5}])$ against the reaction time for the diamination of 1-methoxybutadiene (**6 g**) (*E*:*Z* = 15.7:1, *E* isomer: 0.24 mmol) with **5** (0.20 mmol) and $Pd(PPh_3)_4$ (0.020 mmol) in dry benzene-d_6 (1.2 mL) in an NMR tube at 40 °C. $[\mathbf{5}]_0$ stands for the initial concentration of **5** in M and $[\mathbf{5}]$ stands for the concentration of **5** in M at a particular reaction time.

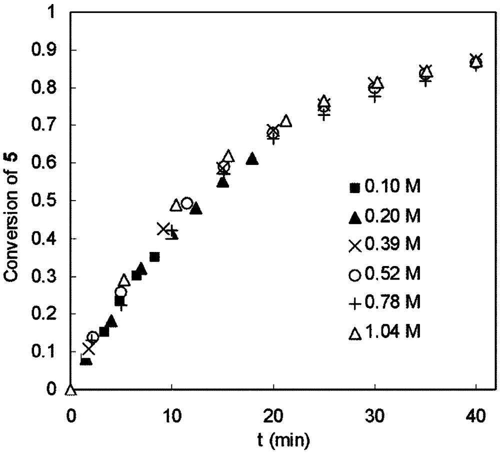


Figure 6. Plots of the conversion of di-*tert*-butyldiaziridinone (**5**) against the reaction time (min) for the diamination of 1-methoxybutadiene (**6g**) with different initial olefin concentrations. The diaminations were carried out with **6g** (*E*:*Z* = 15.7:1, *E* isomer: 0.12 mmol, 0.24 mmol, 0.47 mmol, 0.62 mmol, 0.94 mmol, or 1.25 mmol), di-*tert*-butyldiaziridinone (**5**) (0.40 mmol), and $Pd(PPh_3)_4$ (0.040 mmol) in dry benzene-d_6 (1.2 mL) in an NMR tube at 40 °C.

(d) Effect of Total Pd Concentration. Equation 2 indicates that the diamination should be first-order in the total Pd catalyst. In order to investigate the influence of Pd catalyst, the diamination of 1-methoxybutadiene (**6g**) was investigated with different amounts of $Pd(PPh_3)_4$ and fixed concentration of free PPh_3. The plot of k_{obs} against $[Pd(PPh_3)_4]_0$ was found to be a straight line as shown in Figure 8, indicating the diamination is first-order in total Pd catalyst as expressed in eq 2.

5. Effect of Olefin Structure. Thus far, studies have been mainly focused on the diamination of 1-methoxybutadiene (**6g**), which is zero-order in **6g** under the diamination conditions. Several other dienes and a triene were also examined, and the results are shown in Figure 9. Alkyl diene **6a** has a diamination rate similar to that of **6g**. The diamination was found to also be

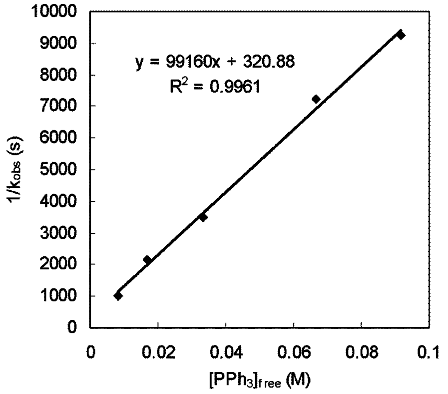


Figure 7. Plot of $1/k_{obs}$ against the concentration of free PPh_3 for the diamination of 1-methoxybutadiene (**6g**) (E:Z = 15.7:1, E isomer: 0.12 mmol) with di-*tert*-butyldiaziridinone (**5**) (0.10 mmol), $Pd(PPh_3)_4$ (0.010 mmol), and added PPh_3 (0, 0.010, 0.030, 0.070, and 0.10 mmol, respectively) in dry benzene-d_6 (1.2 mL) in an NMR tube at 40 °C. The value of $[PPh_3]_{free}$ is corresponding to $[PPh_3]_{added}$ + $[Pd(PPh_3)_4]_0$.

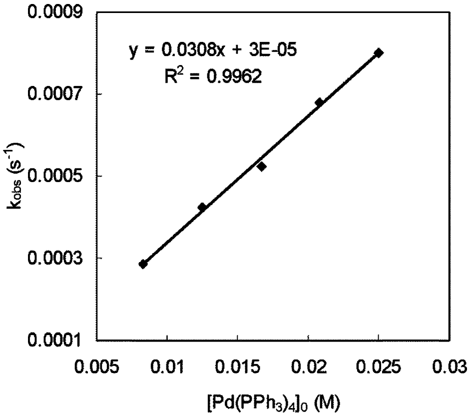


Figure 8. Plot of k_{obs} against $[Pd(PPh_3)_4]_0$ for the diamination of 1-methoxybutadiene (**6g**) (E:Z = 15.7:1, E isomer: 0.12 mmol) with di-*tert*-butyldiaziridinone (**5**) (0.10 mmol), various amounts of $Pd(PPh_3)_4$ (0.010−0.030 mmol), and fixed amount of free PPh_3 (0.040 mmol) in dry benzene-d_6 (1.2 mL) in an NMR tube at 40 °C. Additional PPh_3 (0.030−0.010 mmol) was added to maintain the amount of PPh_3 (0.040 mmol) in each reaction [PPh_3 (added) = 0.040 mmol − $Pd(PPh_3)_4$ (added)].

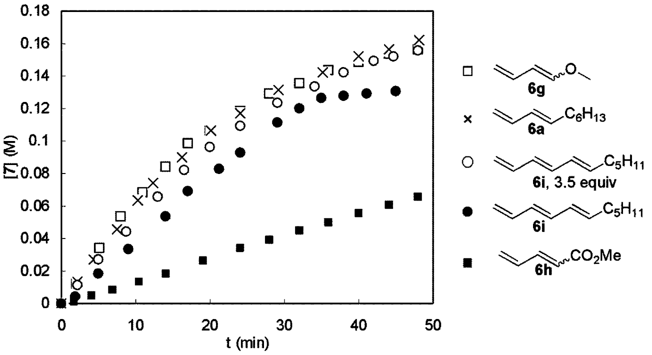
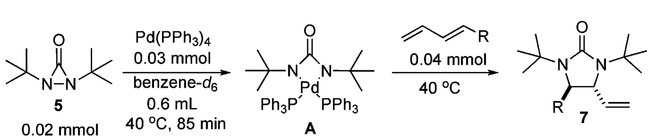


Figure 9. Plots of [**7**] against the reaction time for the diaminations of different dienes or triene with di-*tert*-butyldiaziridinone (**5**) (0.20 mmol), $Pd(PPh_3)_4$ (0.020 mmol) in dry benzene-d_6 (1.2 mL) in an NMR tube at 40 °C. For 1-methoxybutadiene (**6g**): E:Z = 15.7:1, E isomer: 0.24 mmol; for (E)-1,3-decadiene (**6a**): 0.24 mmol; for (3E,5E)-undeca-1,3,5-triene (**6i**): 3.5 equiv (0.70 mmol), 1.2 equiv (0.24 mmol); for methyl 1,3-butadiene-1-carboxylate (**6h**): E:Z = 8.3:1, E isomer: 0.24 mmol.

first-order in **5**. The diamination of triene **6i** was found to be a little slower but with some unidentified side reaction(s) under the same reaction conditions. The reaction was no longer first order in di-*tert*-butyldiaziridinone (**5**) possibly due to the side reaction(s) and/or lower substrate reactivity. When more substrate was used (3.5 equiv), the diamination rate of **6i** was similar to that of **6g**. Significantly slower diamination was observed for electron-deficient olefin **6h**.

Scheme 10



6. Studies on the Reaction of Olefins with Pd(II) Intermediate A. To investigate the olefin reactivity toward intermediate **A** (Scheme 8), the diaminations of various olefins were carried out with preformed Pd(II) species **A** by treating di-*tert*-butyldiaziridinone (**5**) with $Pd(PPh_3)_4$ (1.5 equiv) in dry benzene-d_6 in an NMR tube at 40 °C under argon atmosphere for 85 min (Scheme 10). The reaction was monitored by ^{1}H NMR spectroscopy at 40 °C upon addition of olefins (2.0 equiv). As shown in Figure 10, the reaction was influenced significantly by the electronic and steric properties of the olefin. Electron-rich olefins were more reactive toward complex **A**. 1-Methoxybutadiene (**6g**) was the most reactive for the diamination and the reaction was finished in several seconds at 40 °C. Alkyl dienes such as **6j** and **6a** were more reactive than aryl dienes such as **6b** and aliphatic triene **6i**.

In the aforementioned kinetic studies with 1-methoxybutadiene (**6g**), little information was obtained about the details for the reaction between the four-membered Pd(II) species **A** and olefins because the rate-determining step was the insertion of Pd(0) into the N−N bond of di-*tert*-butyldiaziridinone (**5**) and the C−N bond formation occurred after the rate-determining step. In order to get some insight into C−N bond formation, an olefin with relatively low activity was needed for the kinetic studies so that the rate of C−N bond formation is slower than or competitive to the rate of the insertion of Pd into the N−N bond of **5**. (3E,5E)-Undeca-1,3,5-triene (**6i**) showed a relatively low activity in the reaction with intermediate **A** (Figure 10). Intermediate **A** could be detected by ^{1}H NMR spectroscopy

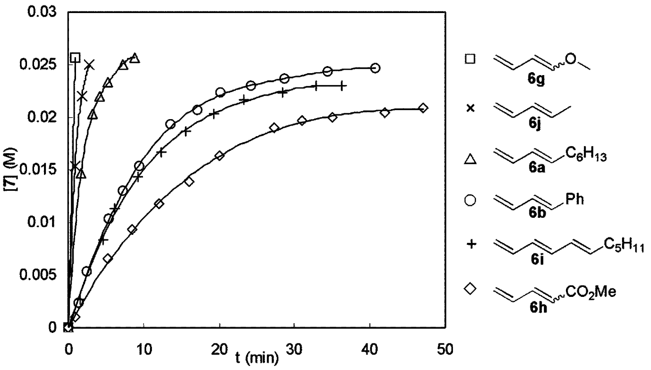


Figure 10. Plots of [**7**] against the reaction time for the reactions between Pd(II) intermediate **A** and different dienes or triene (**6**) (E isomer: 0.040 mmol) in dry benzene-d_6 (0.6 mL) at 40 °C in an NMR tube. For 1-methoxybutadiene (**6g**): E:Z = 15.7:1, E isomer: 0.040 mmol; for (E)-1,3-pentadiene (**6j**): 0.040 mmol; for (E)-1,3-decadiene (**6a**): 0.040 mmol; for (E)-1-phenylbutadiene (**6b**): 0.040 mmol; for (3E,5E)-undeca-1,3,5-triene (**6i**): 0.040 mmol; for methyl 1,3-butadiene-1-carboxylate (**6h**): E:Z = 8.3:1, E isomer: 0.040 mmol. Compound **A** was prepared by reacting di-*tert*-butyldiaziridinone (**5**) (0.020 mmol) with $Pd(PPh_3)_4$ (0.030 mmol) in dry benzene-d_6 (0.6 mL) at 40 °C in an NMR tube for 85 min.

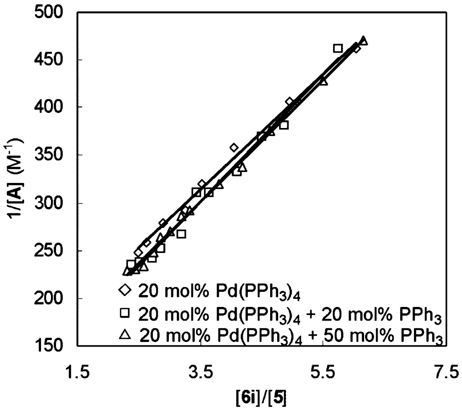


Figure 11. Plots of 1/[**A**] against [**6i**]/[**5**] for the diaminations of (3*E*,5*E*)-undeca-1,3,5-triene (**6i**) (0.20 mmol) with di-*tert*-butyldiaziridinone (**5**) (0.10 mmol), $\mathrm{Pd(PPh_3)_4}$ (0.020 mmol), and different amounts of $\mathrm{PPh_3}$ added (0 mmol; 0.020 mmol; 0.050 mmol) in dry benzene-d_6 (1.2 mL) at 40 °C in an NMR tube.

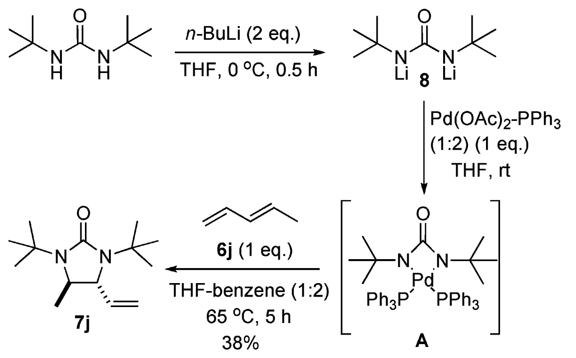
during the reaction when **6i** was subjected to the catalytic diamination conditions, which provides an opportunity to get some insight into the C−N bond formation. Using pre-equilibrium and steady-state approximations, the concentration of intermediate **A** for the diamination is expressed in eq 3 (see Supporting Information). The corresponding reciprocal of eq 3 is shown as eq 4, which indicates that the plot of 1/[**A**] against [**6**]/[**5**] should be a straight line and $\mathrm{PPh_3}$ would have little impact on the slope. Diamination of **6i** was carried out with 20 mol % $\mathrm{Pd(PPh_3)_4}$ and varying amounts of $\mathrm{PPh_3}$ added in an NMR tube at 40 °C. The data of [**A**], [**5**], and [**6i**] were collected for the plot after the reaction reached steady state (∼20% conversion of **5**). As shown in Figure 11, the plot of 1/[**A**] against [**6i**]/[**5**] gives three almost overlapped straight lines with different amounts of $\mathrm{PPh_3}$ present in the reaction, illustrating that $\mathrm{PPh_3}$ has little impact on [**A**] as expected based on eq 4. These results support that the reaction between intermediate **A** and the olefin proceeds via the pathway proposed in Scheme 8. One $\mathrm{PPh_3}$ ligand in intermediate **A** is substituted by olefin **6** via ligand exchange to form olefin complex **B** before the C−N formation. This proposed pathway is consistent with the observation that no diamination was observed with bidentate phosphorus ligands (Table 2, entries 15 and 16). According to the proposed pathway, one ligand is still attached to the Pd during the C−N bonds formation, providing opportunities for asymmetric induction with a chiral ligand. High enantioselectivity has indeed been achieved for this diamination with a BINOL-tetramethylpiperidine based phosphorus amidite ligand.[23a]

$$[\mathbf{A}] = \frac{K_2k_1k_{-2}[\mathbf{5}]}{K_2k_1k_{-2}[\mathbf{5}] + k_2k_3[\mathbf{6}]}[\mathrm{Pd(PPh_3)_4}]_0 \tag{3}$$

$$\frac{1}{[\mathbf{A}]} = \frac{k_2k_3}{K_2k_1k_{-2}[\mathrm{Pd(PPh_3)_4}]_0}\cdot\frac{[\mathbf{6}]}{[\mathbf{5}]} + \frac{1}{[\mathrm{Pd(PPh_3)_4}]_0} \tag{4}$$

7. Diamination with Urea. The above studies show that the four-membered Pd(II) species **A** resulting from the Pd(0) insertion into the N−N bond of di-*tert*-butyldiaziridinone **5** is an active intermediate for the diamination of dienes. It has been reported that some four-membered Pd(II) species can be generated by reacting $\mathrm{PdX_2}$ with dilithium salts of ureas,[37] which prompted us to investigate if such a process could be used for diamination. The dilithium salt **8** generated from di-*tert*-butylurea and *n*-BuLi was treated with a mixture of $\mathrm{Pd(OAc)_2}$-$\mathrm{PPh_3}$ (1:2) and diene **6j** (Scheme 11). At the end of the reaction, the palladium complex was removed by filtration, and diamination product **7j** was isolated by flash chromatography on silica gel in 38% yield. The diamination occurred regioselectively at the internal double bond, suggesting that the reaction proceeded via four-membered Pd(II) intermediate **A**. The regioselectivity obtained in this case is different from the Pd(II)-catalyzed terminal diamination of diene with urea as previously reported by Lloyd-Jones, Booker-Milburn, and co-workers,[8] illustrating that the current diamination proceeds via a completely different reaction mechanism. While the reaction efficiency needs to be improved and a catalytic process needs to be developed, the diamination process using a urea salt described in Scheme 11 is very encouraging, which could open up a new approach to the diamination. Further study on this subject is in progress.

Scheme 11



Conclusions

Various conjugated dienes and a triene can be efficiently diaminated with high yields and high regio- and diastereoselectivity using $\mathrm{Pd(PPh_3)_4}$ as catalyst and di-*tert*-butyldiaziridinone (**5**) as nitrogen source. The catalyst loading was reduced to 1−2 mol % by slowly adding di-*tert*-butyldiaziridinone (**5**) under solvent-free conditions. A detailed catalytic pathway has been proposed based on the NMR spectroscopy and kinetic studies (Scheme 8). The Pd(0) [likely $\mathrm{Pd(PPh_3)_2}$] first inserts into the N−N bond of di-*tert*-butyldiaziridinone (**5**) to form a symmetric four-membered Pd(II) intermediate (**A**), which can be detected by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy. This four-membered Pd(II) intermediate forms an olefin complex (**B**) via ligand exchange between the olefin substrate and the $\mathrm{PPh_3}$. The resulting Pd-diene complex (**B**) undergoes migratory insertion into the internal double bond to form a π-allyl Pd intermediate (**C**), which gives the diamination product and regenerates the Pd(0) catalyst after reductive elimination. For reactive substrates such as 1-methoxybutadiene (**6g**) and alkyl dienes, kinetic studies show that the diamination is first-order in di-*tert*-butyldiaziridinone (**5**) and the Pd(0) catalyst, zero-order in the olefin substrate, and inverse first-order in $\mathrm{PPh_3}$, which is consistent with the fact that the Pd(0) insertion into the N−N bond of di-*tert*-butyldiaziridinone (**5**) is the rate-determining step. Further studies show that the four-membered Pd(II) complex generated from $\mathrm{Pd(OAc)_2}$ and dilithium salts of di-*tert*-butylurea can also regioselectively diaminate the internal double bond of a diene although the reaction efficiency needs to be improved. This result further validates the four-membered Pd(II) intermediate in the proposed catalytic pathway and opens up new opportunities for diamination using urea salts. The studies presented in this work provide a better understanding of the Pd(0)-catalyzed diamination process and will facilitate further development of more effective diamination systems.

Acknowledgment. We are grateful to the generous financial support from the General Medical Sciences of the National Institutes of Health (GM083944-02).

Supporting Information Available: The procedures for diamination, NMR spectroscopy studies, and kinetic studies along with the kinetic analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

JA909459H

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(37) For a leading reference, see: Paul, F.; Fischer, J.; Ochsenbein, P.; Osborn, J. A. C. R. *Chimie* **2002**, *5*, 267.