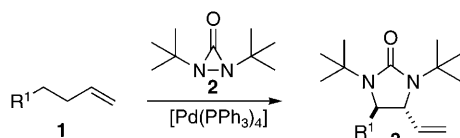


# A Palladium-Catalyzed Dehydrogenative Diamination of Terminal Olefins\*\*

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Metal-mediated and -catalyzed diamination of olefins provides an effective approach to vicinal diamines, which are very important functional moieties contained in various biologically active compounds and are widely used as chiral-control elements in asymmetric synthesis.<sup>[1–6]</sup> Recently, we reported that various dienes and trienes can be regio- and stereoselectively diaminated using di-*tert*-butyldiaziridinone (**2**)<sup>[7]</sup> as the nitrogen source and palladium(0)<sup>[8]</sup> or copper(I)<sup>[9]</sup> as the catalyst. When readily available terminal olefins were treated with **2** and [Pd(PPh<sub>3</sub>)<sub>4</sub>], the diamination occurred regio- and diastereoselectively at the allylic and homoallylic carbon centers to form **3** (Scheme 1). This reaction is likely to proceed via a diene species which is formed in situ.<sup>[10]</sup> However, when *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide



Scheme 1. Previous work.

(**4**)<sup>[11,12]</sup> is used as the nitrogen source along with the Pd catalyst, then terminal olefins are regioselectively diaminated at the terminal carbon position to form **5** via a different reaction mechanism to that already reported (Scheme 2). Herein, we report our preliminary results on this subject.

When terminal olefins such as 1-nonene (**1a**) were treated with 5 mol % [Pd(PPh<sub>3</sub>)<sub>4</sub>] and **4**, no allylic or homoallylic

diamination products similar to **3** were detected. Instead terminal diamination product **5** was formed with a 34 % conversion. The diamination process was further improved by using 10 mol % Pd catalyst which was prepared from [Pd<sub>2</sub>(dba)<sub>3</sub>] and tri-2-furylphosphine at a higher reaction temperature. For example, treatment of **1a** with [Pd<sub>2</sub>(dba)<sub>3</sub>] (0.05 equiv), tri-2-furylphosphine (0.3 equiv), and **4** (2.0 equiv) at 75 °C for 10 h gave terminal diamination product **5a** in 68 % yield (Table 1, entry 1). This diamination process can be extended to a variety of terminal olefins (Table 1, entries 2–11; the X-ray structure of **5f** is shown in Figure 1). In all cases, the diamination products **5** were formed as major products along with small amounts of unidentified isomers. One possible isomer could result from the migration of the double bond in **5**. In one case a substantial amount of this type of isomer was observed (**5d'**; Table 1, entry 4).

When a mixture of 1,3-pentadiene (**6**) and **1a** was subjected to the diamination reaction conditions, compounds

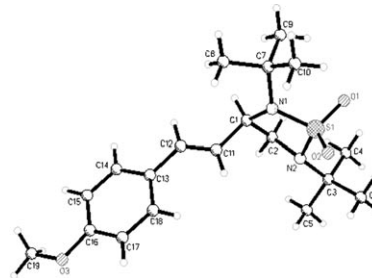
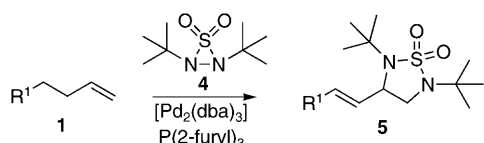


Figure 1. The X-ray structure of compound **5f**.

**7** and **5a** were formed, respectively (Scheme 3). Diene **6** underwent diamination predominately at the internal double bond,<sup>[13]</sup> whereas for terminal olefin **1a** diamination occurred at the terminal carbon position. These results indicate that the diamination reaction is unlikely to proceed via a diene species which is generated in situ, as is the case when **2** was used as the nitrogen source (Scheme 1).

While the elucidation of a precise reaction mechanism awaits further study, a plausible catalytic cycle is shown in Scheme 4. Firstly, Pd<sup>0</sup> inserts into the N–N bond of **4** to form the four-membered-Pd<sup>II</sup> species **8**, which then forms complex **9** with olefin **1**. Removal of an allylic hydrogen from **9** forms the [( $\pi$ -allyl)Pd] complex **10**,<sup>[14,15]</sup> which gives allyl sulfamide **11** and regenerates the Pd<sup>0</sup> catalyst after reductive elimination.<sup>[16]</sup> Subsequently, **11** complexes with **8** to form **12**, which then undergoes a palladium(II)-catalyzed cyclization to form **13**.<sup>[17]</sup> Finally, **13** undergoes a  $\beta$ -hydride elimination and



Scheme 2. This work.

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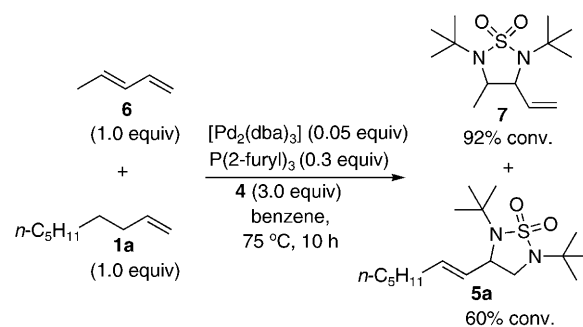
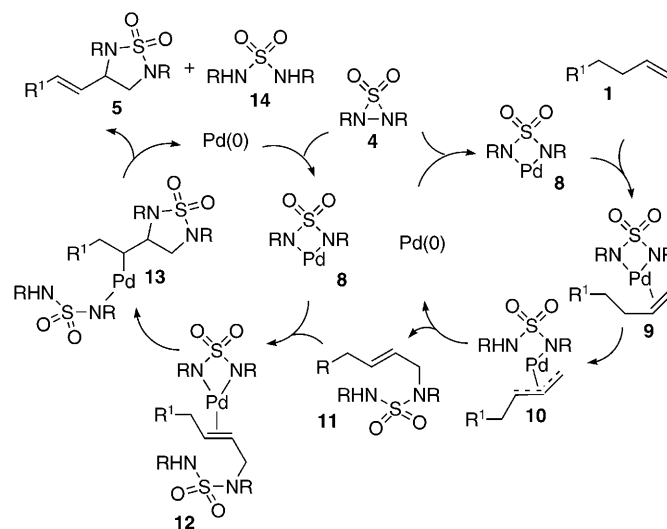
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**Table 1:** Catalytic dehydrogenative diamination<sup>[a]</sup>

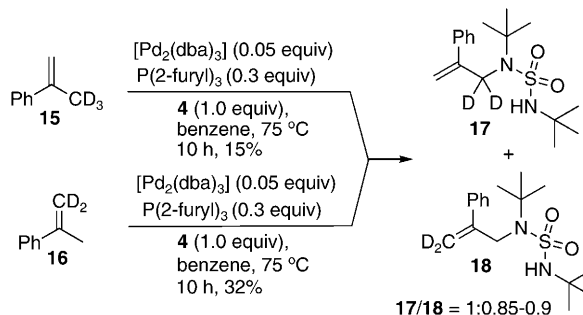
| Entry             | Substrate (1) | Product (5) | Yield [%] <sup>[b]</sup> |
|-------------------|---------------|-------------|--------------------------|
| 1                 |               |             | 68                       |
| 2                 |               |             | 47                       |
| 3                 |               |             | 74                       |
| 4                 |               |             | 77 <sup>[c]</sup>        |
|                   |               |             |                          |
| 5 <sup>[d]</sup>  |               |             | 45                       |
| 6                 |               |             | 62                       |
| 7                 |               |             | 61                       |
| 8                 |               |             | 61                       |
| 9 <sup>[e]</sup>  |               |             | 42                       |
| 10 <sup>[f]</sup> |               |             | 40                       |
| 11 <sup>[e]</sup> |               |             | 66 <sup>[g]</sup>        |

[a] All reactions were carried out with olefin (1.0 mmol), [Pd<sub>2</sub>(dba)<sub>3</sub>] (0.050 mmol), tri-2-furylphosphine (0.30 mmol), and **4** (2.0 mmol) in benzene (0.25 mL) at 75 °C under argon for 10 h, unless otherwise stated. dba = *trans,trans*-dibenzylideneacetone. [b] Yield of isolated product. [c] **5d/5d'** 2:1; reported yield is a combined yield. [d] The reaction was carried out at 75 °C for 22 h. [e] The reaction was carried out at 65 °C for 6 h. [f] The reaction was carried out at 50 °C for 20 h. [g] 7% yield of the 1Z,3E isomer was also isolated. Bn = benzyl, Boc = *tert*-butoxycarbonyl.

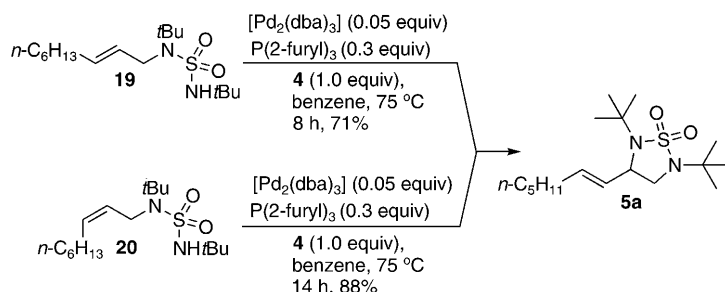
reductive elimination to form the product **5** and sulfamide **14** with regeneration of the Pd<sup>0</sup> catalyst. For aryl-substituted 1-butenes (Table 1, entries 5 and 6), some amounts of diene were also formed from β-hydride elimination of [(π-allyl)Pd] complex **10**,<sup>[18,19]</sup> and this outcome is consistent with the


**Scheme 3.**

**Scheme 4.** A proposed catalytic cycle for the diamination process. R = *tert*-butyl.

proposed mechanism. To further probe the allylic amination process, deuterium-labeled styrene derivatives **15** and **16** were subjected to the reaction conditions. Although these two substrates were found to be less reactive owing to steric effect, some allylic amination products were isolated and the deuterium label was almost equally distributed at terminal and allylic positions of the olefin in both cases (Scheme 5). This result suggests that the initial allylic amination of complex **10** is a viable process (Scheme 4).


**Scheme 5.** Allylic amination of deuterium-labeled styrene derivatives.

Clear identification and isolation of allyl sulfamide **11** from the crude reaction mixtures proved to be difficult. However, in the case of 1-nonene (Table 1, entry 1), trace amounts of **11** could be detected in the reaction mixture by  $^1\text{H}$  NMR and GC–MS analysis. Thus, allyl sulfamides **19** and **20** were prepared and subjected to the reaction conditions (Scheme 6). These sulfamides indeed cyclized to form **5a** in



**Scheme 6.** Cyclization of sulfamides.

good yield. However, no cyclization was observed without using **4**. These results are in agreement with the mechanism described in Scheme 4. The exact mechanism for the palladium(II)-catalyzed cyclization of **11** into **5** awaits further study.

In summary, a variety of terminal olefins have been dehydrogenatively diaminated at the terminal carbon positions using *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**4**) as the nitrogen source and Pd as the catalyst, to give the diamination products in high regioselectivity. The diamination is likely to proceed through a palladium(II)-catalyzed allylic amination and subsequent cyclization. This diamination is mechanistically distinct from the process when di-*tert*-butyldiaziridinone (**2**) was used as the nitrogen source, thus resulting in different regioselectivity. Further effort will be devoted to understanding the reaction mechanism, searching for an even more effective catalytic process, expansion of the substrate scope, and development of an asymmetric methodology.

## Experimental Section

Preparation of *N,N*-di-*tert*-butylthiadiaziridine 1,1-dioxide (**4**).<sup>[11]</sup> Over a period of 30 min, *N,N*-di-*tert*-butyl sulfamide (10.0 g, 48.0 mmol) was added to a suspension of sodium hydride (60%; 2.0 g, 50.0 mmol) in hexanes (400 mL). The resulting slurry was stirred at reflux under argon for 2 h. Upon cooling to  $-30^\circ\text{C}$ , *tert*-butyl hypochlorite (5.43 g, 50.0 mmol) was added dropwise to the slurry while exposure to direct light was avoided. The reaction mixture was stirred in the dark at  $-30^\circ\text{C}$  for 3 h and then at  $0^\circ\text{C}$  for 1 h before cold diethyl ether (200 mL) was added. The organic layers were washed with water (100 mL), dried over  $\text{MgSO}_4$ , filtered, concentrated, and distilled under reduced pressure ( $95^\circ\text{C}$ , 8 mmHg) to give **4** as a colorless oil, which solidified at room temperature (8.5 g, 86%).

A typical procedure for dehydrogenative diamination (Table 1, entry 1): A Pyrex glass tube was charged with  $[\text{Pd}_2(\text{dba})_3]$  (0.046 g, 0.050 mmol) and tri-2-furylphosphine (0.070 g, 0.30 mmol), and then filled and evacuated with argon three times before benzene (0.25 mL) was added. The mixture was stirred at  $75^\circ\text{C}$  for 15 min before **1a**

(0.126 g, 1.0 mmol) and **4** (0.413 g, 2.0 mmol) were added successively and the reaction mixture stirred at  $75^\circ\text{C}$  for 10 h. Purification of the crude reaction mixture by flash chromatography on silica gel [eluent: toluene (to remove the dba) then petroleum ether/EtOAc (40:1  $\rightarrow$  30:1)] gave **5a** as a colorless oil (0.225 g, 68%).

A typical procedure for allylic amination of deuterated styrene derivatives (Scheme 5): As outlined above, but using the following reagents:  $[\text{Pd}_2(\text{dba})_3]$  (0.023 g, 0.025 mmol), tri-2-furylphosphine (0.035 g, 0.15 mmol), benzene (0.125 mL), **16** (0.060 g, 0.50 mmol), **4** (0.103 g, 0.50 mmol). Purification by flash chromatography on silica gel [eluent: toluene then petroleum ether/EtOAc (30:1)] gave a mixture of **17** and **18** as a white solid (0.052 g, 32%).

A typical procedure for the cyclization of allyl sulfamides (Scheme 6): As outlined above, but using the following reagents:  $[\text{Pd}_2(\text{dba})_3]$  (0.018 g, 0.020 mmol), tri-2-furylphosphine (0.028 g, 0.12 mmol), benzene (0.1 mL), **20** (0.133 g, 0.40 mmol), **4** (0.083 g, 0.40 mmol). The reaction time was 14 h. Purification by flash chromatography on silica gel [eluent: toluene then petroleum ether/EtOAc (30:1  $\rightarrow$  20:1)] gave **5a** as a colorless oil (0.116 g, 88%).

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