Synthetic Methods

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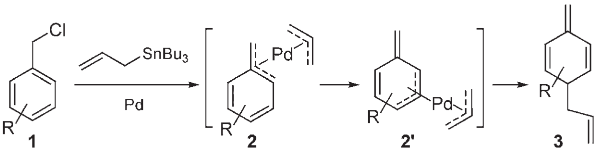
Carbocycle Synthesis through Facile and Efficient Palladium-Catalyzed Allylative De-aromatization of Naphthalene and Phenanthrene Allyl Chlorides**

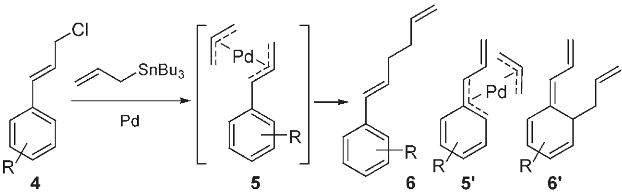
Shirong Lu, Zhanwei Xu, Ming Bao, and Yoshinori Yamamoto**

De-aromatization reactions of arenes have attracted considerable attention because they provide a simple way to synthesize functionalized alicyclic compounds, which can be used as intermediates for the preparation of natural products and bioactive compounds.[1] Over the past four decades, many methods, including oxidation,[2] reduction,[3] photocycloaddition,[4] [2,3] σ-rearrangement,[5] electrophilic addition,[6] nucleophilic addition,[7] and other approaches[8] have been developed for breaking up the conjugated π system. The complexation of aromatic system to transition metals leads to the activation of arenes and thus facilitates the electrophilic addition of [M(η^2-arene)] (M = Os, Re, Mo, and W) complexes and the nucleophilic addition of [M(η^6-arene)] (M = Cr, Mn, and Ru) complexes.

We recently reported the facile palladium-catalyzed allylative de-aromatization reaction of benzylic chlorides **1** with allyltributytin.[9] This process appears to involve the formation and isomerization of the η^3-allyl-η^3-benzylpalladium intermediate **2** to give **2′**, which led to **3**, where an allyl group is linked *para* to the exocyclic methylene group [Eq. (1)]. Our interest in extending the scope of this de-aromatization reaction led us to examine the cinnamyl chloride **4**. We assumed that, if the bis(η^3-allyl)palladium intermediate **5**, generated from the cinnamyl chlorides and allyltributyltin in the presence of a palladium catalyst, could undergo rearrangement to give the η^3-benzylpalladium intermediate **5′**, and **6′** (or its *para* isomer) would be produced. However, only the Stille cross-coupling product **6** was obtained [Eq. (2)].[10] Thus, extension of the de-aromatization to the cinnamyl chlorides **4** was not feasible.



(1)



(2)

Herein, we report the facile and efficient allylative de-aromatization of naphthalene and phenanthrene derivatives bearing an allyl chloride unit (Tables 1 and 2). These reactions did not form the corresponding Stille cross-coupling products, but pleasingly gave the *ortho* allylated product **8**; this regioselectivity is in marked contrast to the *para* selectivity of the de-aromatization of benzylic chlorides. This result introduces the possibility of synthesizing six-membered ring systems with three or four fused rings from naphthalenes or phenanthrenes, respectively.

The allylative de-aromatization reactions of naphthalene derivatives **7a–i** with allyltributylstannane were performed in the presence of [$Pd_2(dba)_3$] (5 mol%) and PPh_3 (20 mol%; Table 1). The simple substrates **7a** and **7h** underwent the de-aromatization reaction smoothly to afford **8a** and **8h** in high yields (84% and 78%, respectively; Table 1, entries 1 and 8). Neither the electron-donating group nor the electron-withdrawing group on the aromatic ring exerted a strong influence on the reaction (except in terms of the reaction times). The yields of **8b–g** and **8i** were in the range of 74 to 89% (Table 1, entries 2–7 and 9); a longer reaction time was needed for **7b** than for **7a** and **7c–i**. The lower reactivity of **7b** is perhaps due to steric hindrance from the β methyl group. The de-aromatization reactions of **7e** and **7f** were accelerated by the electron-withdrawing groups (Br or PhCOO, respectively) at the *para* position, and were completed in shorter reaction times compared with **7a–d** and **7g–i**). Products **8a** and **8c–i** were sensitive to acid, but were comparatively more stable than **3** derived from benzylic chlorides. Product **8b** with a quaternary carbon center was very robust, and could be purified by standard column chromatography on silica gel.

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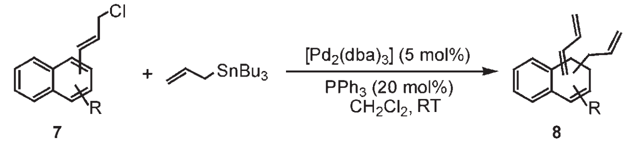
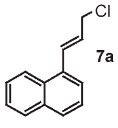
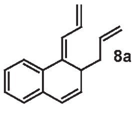
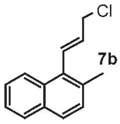
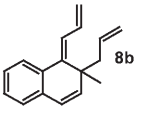
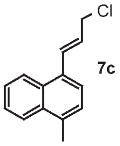
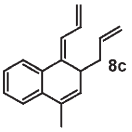
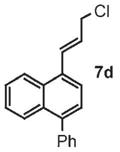
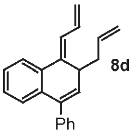
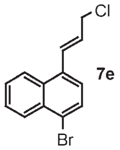
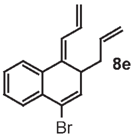
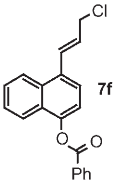
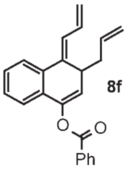
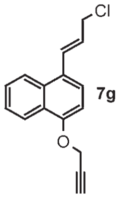
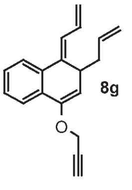
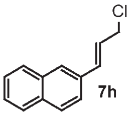
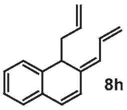
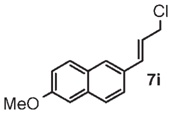
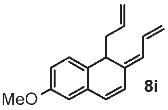
Table 1: Palladium-catalyzed de-aromatization reaction of naphthalene derivatives **7a–i** with allyltributylstannane.[a]



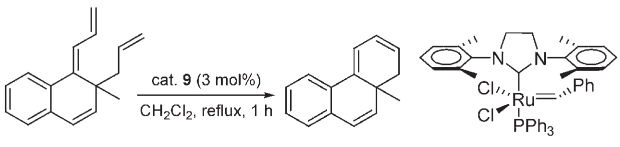
7 **8**

Entry	Substrate	t [h]	Product	Yield [%][b]
1	 **7a**	12	 **8a**	84
2	 **7b**	24	 **8b**	82
3	 **7c**	12	 **8c**	82
4	 **7d**	14	 **8d**	87
5	 **7e**	2	 **8e**	89
6	 **7f**	6	 **8f**	87
7	 **7g**	14	 **8g**	80
8	 **7h**	18	 **8h**	78
9	 **7i**	12	 **8i**	74

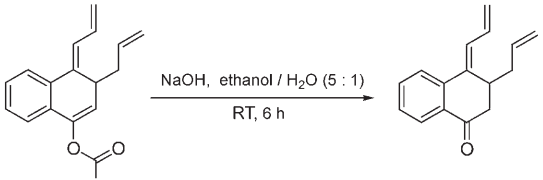
[a] A solution of naphthalene derivative **7** (0.5 mmol), allyltributylstannane (0.5 mmol), $[Pd_2(dba)_3]$ (5 mol%), and Ph_3P (20 mol%) in dichloromethane (3 mL) was stirred at room temperature under N_2 for the period indicated. The reaction progress was monitored by TLC. [b] Yields of isolated product. dba = *trans,trans*-dibenzylideneacetone.

Each of the new products was characterized through NMR[11] and IR spectroscopy as well as HRMS.

It occurred to us that the two terminal olefinic groups of **8** might undergo a metathesis reaction to construct a new alicyclic ring. Indeed, when **8b** was treated with the ruthenium-carbene catalyst **9**,[12] the cyclized product **10** was isolated in 62% yield [Eq. (3)]. This result further confirmed that the configuration of the 1,3-butadiene moiety of **8b** was identical to that presented in Table 1. The de-aromatization products were very stable under basic conditions, thus suggesting that **8f** could be hydrolyzed in an NaOH solution to produce a cyclic ketone derivative without the formation of any isomerization product. In fact, the desired product **11** was isolated in 77% yield [Eq. (4)]; it seemed that the functionalized product **11** might be useful for further manipulation.

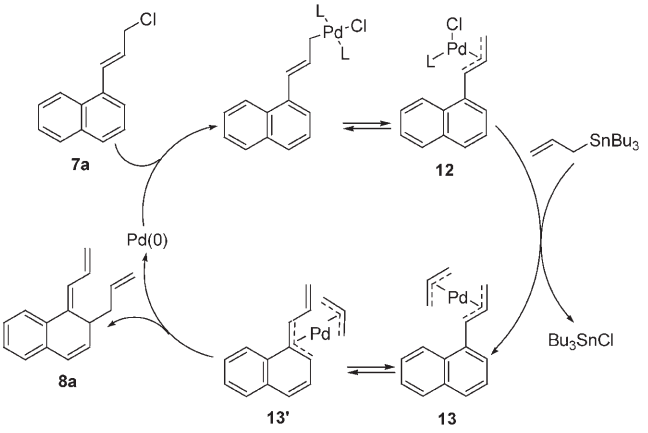


8b **10** 62% **9** (3)



8f Ph **11** 77% (4)

A plausible mechanism for the allylative de-aromatization reaction is shown in Scheme 1. The oxidative addition of **7a** to a Pd^0 species would produce the η^3-allylpalladium chloride intermediate **12**, which would react with allyltributylstannane to generate a bis(η^3-allyl)palladium intermediate **13** upon ligand exchange. Isomerization of **13** would occur to give a bis(η^3-allyl)palladium intermediate **13′**, which could undergo

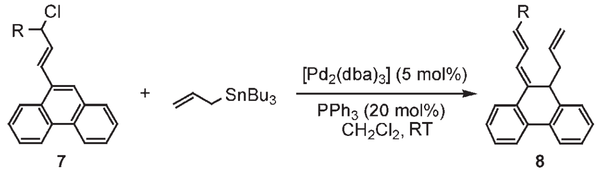


Scheme 1. Proposed mechanism for the de-aromatization reaction.

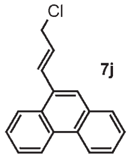
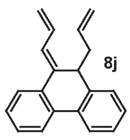
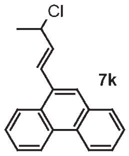
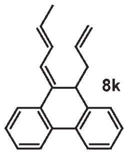
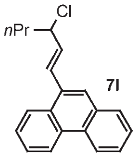
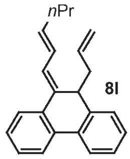
reductive elimination to form the de-aromatization product **8a** and regenerate the Pd^0 catalyst.

The successful extension of the allylative de-aromatization to the naphthalene derivatives **7a–i** encouraged us to examine the phenanthrene derivatives **7j–l**, and the results are summarized in Table 2. The simple substrate **7j** gave the corresponding product **8j** in 87% yield (Table 2, entry 1). Even **7k**, with a $C(sp^3)$-H β-hydrogen atom, underwent the reaction smoothly and afforded **8k** as the only product in 84% yield (Table 2, entry 2).[13] The substrate **7l**, bearing an *n*Pr group α to the chlorine atom, also provided the de-aromatization product **8l** in 86% yield, without the formation of any β-hydride elimination product (Table 2, entry 3). The products **8j–l** are very stable, and each was purified by standard column chromatography on silica gel. No re-aromatized compounds were observed.

Table 2: Palladium-catalyzed de-aromatization reaction of phenanthrene derivatives **7j–l** with allyltributylstannane.[a]



7 8

Entry	Substrate	*t* [h]	Product	Yield [%][b]
1	 **7j**	12	 **8j**	87
2	 **7k**	9	 **8k**	84
3	 **7l**	21	 **8l**	86

[a] A solution of phenanthrene derivative **7** (0.5 mmol), allyltributylstannane (0.5 mmol), $[Pd_2(dba)_3]$ (5 mol%), and Ph_3P (20 mol%) in dichloromethane (3 mL) was stirred at room temperature under N_2 for the period indicated. The reaction progress was monitored by TLC. [b] Yields of isolated product.

Even though the de-aromatization of the benzene derivatives **4** bearing allyl chloride was not successful, that of the naphthalene and phenanthrene derivatives **7** proceeded readily and efficiently. Perhaps, this difference is due to lower resonance energies of the aromatic rings of **7** compared to those of **4**.[14] The facile and efficient construction of **8** and their rather unexpected stability allows the synthesis of extended fused and functionalized ring systems from naphthalenes and phenanthrenes.

Experimental Section

General procedure for the allylative de-aromatization reaction: Allyltributylstannane (165.6 mg, 0.5 mmol) and **7a** (101.3 mg, 0.5 mmol) were added to a solution of $[Pd_2(dba)_3]$ (22.8 mg, 0.025 mmol) and PPh_3 (26.2 mg, 0.1 mmol) in dichloromethane (3 mL) at room temperature, and the reaction mixture was stirred for 12 h under N_2. After the allyltributylstannane was consumed (as evident by TLC), the solvent was removed under reduced pressure. The residue was filtered through a short column of basic alumina to remove palladium by-products and eluted with pentane to give **8a** in 84% yield (87.5 mg) as a colorless liquid.

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Keywords: de-aromatization · naphthalenes · palladium · phenanthrenes · synthetic methods

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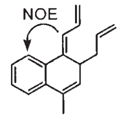
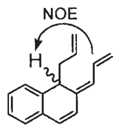


8c



8h

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[14] DFT computation of intermediates and products are now under investigation, and a detailed mechanistic discussion will appear in due course.