# Facile Allylative Dearomatization Catalyzed by Palladium

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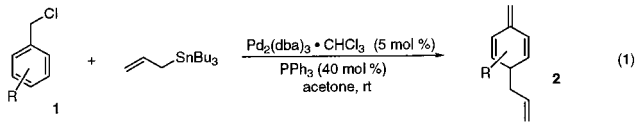
In general it is believed that dearomatization of benzene is not an easy task, since such a process breaks the resonance stabilization of the benzene ring. Accordingly, the substitution of the C−H of benzene is more common in comparison with the addition to the C═C unsaturated bond of benzene. Although the Birch reduction is one of the easiest ways to break the aromaticity of benzene, it is a *hydrogenatio*n reaction.[1] Certain structural requirements have to be fulfilled for *alkylative* dearomatization of the benzene ring: (1) Strong electron-withdrawing groups (EWG) are bonded directly to the benzene ring, and thus such benzene derivatives become rather electron deficient, facilitating the addition of carbon nucleophiles that lead to dearomatization.[2] (2) Instead of EWG, certain metal complexes coordinated to the aromatic ring also act as an electron-withdrawing group and nucleophilic attack to benzene causes alkylative dearomatization.[3] (3) Intramolecular attack of certain carbon nucleophiles to the benzene ring also gives dearomatization products,[4] but this type of reaction is applicable only to a limited range of substrates. (4) Finally, the conversion of phenols to quinones takes place very readily upon oxidation, but the resulting quinones still hold a certain level of aromaticity. On the other hand, there are few examples in which phenols were converted to dearomatized cyclohexenone derivatives.[5]

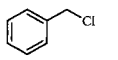
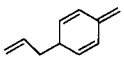
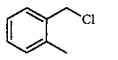
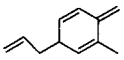
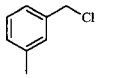
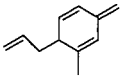
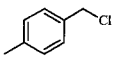
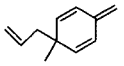
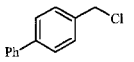
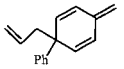
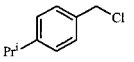
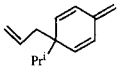
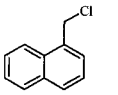
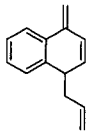
We have found that the reaction of benzylic chlorides **1** with allyltributylstannane in the presence of Pd catalyst in acetone at room temperature gives the allylative dearomatization products **2** in high yields (eq 1). The results are summarized in Table 1.




(1)

The dearmatization products **2a**−**g** were obtained in the range of 71−85% yields. No other products were obtained at all. A methyl substituent at the meta, ortho, or para position of the aromatic ring did not exert strong influence upon the dearomatization reaction, except for the reaction times (entries 2−4 vs 1); slightly longer reaction times were needed for **1b**−**d** in comparison with **1a**. Even if a bulky substituent was located at the para position of the aromatic ring, the allylative dearomatization proceeded very smoothly (entries 5 and 6). The naphthyl derivative **1g** reacted much faster than the benzene derivatives **1a**−**f**, giving **2g** in high yield (entry 7). It was rather surprising for us that the dearomatization products **2a**−**g** were isolated without being accompanied by the isomerized benzene derivatives **3a**−**g**, since it is known that allyl groups migrate rapidly at either room temperature or below from C-4 to the exocyclic methylene group of cross-conjugated methylenecyclohexadienes **4**.[6] Contrary to the previous observation of pentamethyl-substituted methylene cyclohexadiene,[6] **2a**−**g** were quite stable at room temperature; **2g** dissolved in $CDCl_3$ remained unchanged even after 3 days at room temperature in a NMR tube; **2d**−**f** in $CDCl_3$ were essentially unchanged for 1 day under the same conditions mentioned above and in the refrigerator they did not change at all even after 1 week. **2a** in $CDCl_3$ at room temperature underwent isomerization very slowly; after 1 day the ratio of **2a** to **3a** (R = H) became 20 to 1, and 2 days later, it became 10:1. However, it did not undergo isomerization at all in the refrigerator even after 1 week. The difference between the stability of the products obtained through our method and that through the previous one[6] is most probably due to the reaction conditions of the synthetic procedures: they used acidic and basic reagents and therefore even after a careful workup procedure the medium containing products would not be entirely neutral, whereas our method could be carried out under essentially neutral conditions. Transfer of a proton from C-4 to the exocyclic methylene carbon took place more readily than the

**Table 1.** Dearomatization Reaction of Benzylic Chlorides **1a**−**1g** with Allyltributylstannane[a]

| entry | substrate | | time (h) | product | | isolated yield (%) |
|---|---|---|---|---|---|---|
| 1 |  | **1a** | 24 |  | **2a** | 80 |
| 2 |  | **1b** | 32 |  | **2b** | 82 |
| 3 |  | **1c** | 35 |  | **2c** | 80 |
| 4 |  | **1d** | 37 |  | **2d** | 76 |
| 5 |  | **1e** | 60 |  | **2e** | 71 |
| 6 |  | **1f** | 34 |  | **2f** | 79 |
| 7 |  | **1g** | 11 |  | **2g** | 85 |

[a] A mixture of benzylic chloride (0.5 mmol), allyltributylstannane (0.5 mmol), $Pd_2(dba)_3$•$CHCl_3$ (5 mol %), and $Ph_3P$ (40 mol %) in acetone (3 mL) was stirred at room temperature under Ar for the period indicated in the table. The reaction progress was monitored by TLC.

(1) For the Birch reduction followed by alkylation, see: Schultz, A. G. *Chem. Commun*. **1999**, 1263.

(2) Most of the previous examples are concerning the dearomatization of naphthalene derivatives, since it is much more easy in comparison with that of benzene itself (see entry 7, Table 1). (a) Barner, B. A.; Meyers, A. I. *J. Am. Chem. Soc*. **1984**, *106*, 1865. (b) Tomioka, K.; Shindo, M.; Koga, K. *Tetrahedron Lett*. **1990**, *31*, 1739. (c) Plunian, B.; Mortier, J.; Vaultier, M. *J. Org. Chem*. **1996**, *61*, 5206. (d) Maruoka, K.; Ito, M.; Yamamoto, H. *J. Am. Chem. Soc*. **1995**, *117*, 9091. (e) Bartoli, G.; Bosco, M.; Baccolini, G. *J. Org. Chem*. **1980**, *45*, 2649. (f) Stoyanovich, F. M.; Karpenko, R. G.; Gol'dfarb, Y. L. *Tetrahedron* **1971**, *27*, 433.

(3) For a review, see: Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. *Chem. Rev*. **2000**, *100*, 2917. In the case of arene osmium complexes, the metal acts as a donor group, activating the arene toward electrophilic addition reactions.

(4) (a) Ahmed. A.; Clayden, J.; Rowley, M. *Chem. Commun*. **1998**, 297. (b) Ahmed, A.; Clayden, J.; Rowley, M. *Synlett* **1999**, 1954. (c) Ahmed, A.; Clayden, J.; Yasin, S. A. *Chem. Commun*. **1999**, 231. (d) Negishi, E.; Merrill, R. E. *J. Chem. Soc., Chem. Commun*. **1974**, 860. (e) Hauser, C. R.; Eenam, D. N. V. *J. Am. Chem. Soc*. **1957**, *79*, 5512. (f) Shirai, N.; Sumiya, F.; Sato, Y.; Hori, M. *J. Org. Chem*. **1989**, *54*, 836. (g) Hayashi, Y.; Oda, R. *Tetrahedron Lett*. **1968**, *51*, 5381. (h) Berger, R.; Ziller, J. W.; Vranken, D. L. V. *J. Am. Chem. Soc*. **1998**, *120*, 841. (i) Bolton, R. E.; Moody, C. J.; Rees, C. W. *J. Chem. Soc., Perkin Trans 1* **1989**, 2136. (j) Boivin, J.; Yousfi, M.; Zard, S. Z. *Tetrahedron Lett*. **1997**, *38*, 5985.

(5) (a) Woodward, R. B. *J. Am. Chem. Soc*. **1940**, *62*, 1208. (b) Adler, E.; Brasen, S.; Miyake, H. *Acta Chem. Scand*. **1971**, *25*, 2055. (c) Corey, E. J.; Dittami, J. P. *J. Am. Chem. Soc*. **1985**, *107*, 256. (d) Krohn, K.; Brüggmann, K.; Döring, D.; Jones, P. G. *Chem. Ber*. **1992**, *125*, 2439.

(6) Miller, B.; Lai, K. H. *J. Am. Chem. Soc*. **1972**, *94*, 3472.

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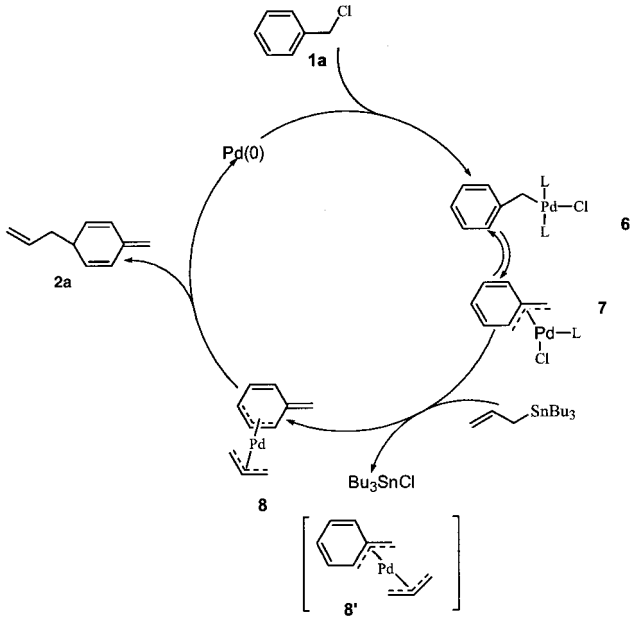
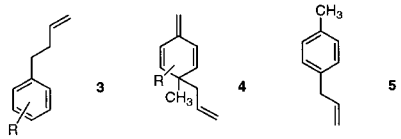
**Scheme 1**




transfer of the allyl group.[7] For example, if purification of the reaction product of **1a** (entry 1) was carried out via standard silica gel column chromatography, the isomerized benzene derivative **5** was obtained along with **2a**. Accordingly, we used a basic alumina column for purification purposes.

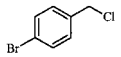
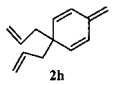
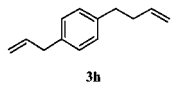
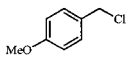
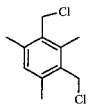
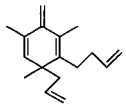
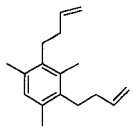
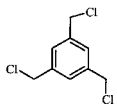
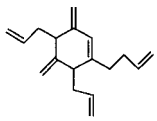
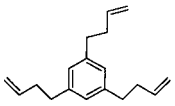



The synthesis of **2a** from **1a** is representative. To a mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (26 mg, 0.025 mmol) and $PPh_3$ (52.5 mg, 0.2 mmol) in acetone (3 mL) at room temperature were added benzyl chloride **2a** (66.3 mg, 0.5 mmol) and allyltributylstannane (165.6 mg, 0.5 mmol), and then the mixture was stirred for 24 h under an Ar atmosphere. The reaction progress was monitored by TLC. Allyltributylstannane disappeared after 24 h. The solvent was removed under reduced pressure. The product was filtered through a short basic alumina column with pentane to remove palladium residue and then was purified with a basic alumina column with pentane as eluent, giving **2a** in 80% yield (52.8 mg).

A plausible mechanism for the allylative dearomatization reaction is shown in Scheme 1. Benzyl chloride **1a** reacts with Pd(0) to produce the Pd(II) intermediate **6**, which would be in equilibrium with the corresponding $\pi$-allyl intermediate **7** under the reaction conditions with acetone as solvent. Allyltributylstannane would react with **7** to produce a bis-$\pi$-allylpalladium intermediate **8**[8] upon ligand exchange. A regioisomeric bis-$\pi$-allyl intermediate **8′** is also conceivable, but for a certain reason complex **8** would be more stable (or more reactive) than **8′**, giving **2a** upon reductive coupling and regenerating Pd(0) catalyst. In addition, the commercially available $PhCH_2PdCl(PPh_3)_2$ complex reacted with allyltributylstannane in acetone at room temperature to give **2a** in 84% yield (stoichiometric reaction).

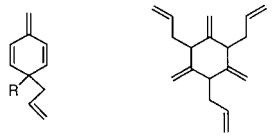
To determine the scope of this interesting dearomatization reaction, we carried out the reaction of the functional group substituted and/or multi-substituted benzyl chloride derivatives

**Table 2.** Dearomatization Reaction of Benzyl Chloride Derivatives **1h**−**1k** with Allyltributylstannane[a]

| entry | substrate | time (h) | product | | yield (%) |
|---|---|---|---|---|---|
| 1 |  **1h** | 35 |  **2h** 83 |  **3h** 17 | 82 |
| 2 |  **1i** | 43 | **2h** 89 | **3h** 11 | 85 |
| 3 |  **1j** | 76 |  **2j** 25 |  **3j** 75 | 83 |
| 4 |  **1k** | 69 |  **2k** 75 |  **3k** 25 | 87 |

[a] In entries 1−3, 2 equiv of allyltributylstannane were used. In entry 4, 3 equiv of allyltributylstannane were used. Products **2** and **3** were separated by GPC with $CHCl_3$ as an eluent.

and the results are summarized in Table 2. *p*-Bromobenzyl chloride **1h** gave a 83:17 mixture of **2h** and **3h** in 82% isolated yield (entry 1). Similarly, *p*-methoxybenzyl chloride **1i** afforded an 89:11 mixture of **2h** and **3h** in 85% yield (entry 2). The double allylation took place in these cases perhaps because the mono-allylated product **9** still possessed another allylic unit which may undergo the second allylation reaction. The allyl-transferred isomer **3h** was formed as a minor product. Here also, **2h** is fairly stable at room temperature. In entry 3, the ordinary allylation product **3j** was obtained predominantly, suggesting that if the steric congestion on the aromatic ring is too severe, the ordinary allylic−benzylic coupling[9] (or allylic migration) would be preferentially obtained. Instead of **10**, **2k** was obtained from **1k**.




In conclusion, we have found a new method for allylative dearomatization with palladium catalyst. Contrary to the observation made previously, these dearomatized products are, in general, stable at room temperature for a prolonged period of time. The present finding provides a wider appreciation that allylative dearomatization is easy under the palladium-catalyzed conditions.

**Supporting Information Available:** Characterization data for new compounds **2** and **3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA003718N

(7) Benkeser, R. A.; Johnston, T. E.; Tong, W. H. *J. Org. Chem*. **1968**, *33*, 2203.

(8) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc*. **1996**, *118*, 6641.

(9) The palladium-catalyzed Stille coupling between organostannanes ($R^1-SnR_3$) and organic halides ($R^2-X$) gives the coupling products $R^1-R^2$: Stille, J. K. *Angew. Chem., Int. Ed. Engl*. **1986**, *25*, 508. It is very curious that the coupling between allylstannanes and benzyl chloride has not been investigated, to the best of our knowledge, in the Stille coupling reaction.