Pd-Catalyzed Dearomative Three-Component Reaction of Bromoarenes with Diazo Compounds and Allylborates

Masaaki Komatsuda, Hiroki Kato, Kei Muto,* and Junichiro Yamaguchi*

Department of Applied Chemistry, Waseda University, 3-4-1, Ohkubo, Shinjuku, Tokyo, 169-8555, Japan

ABSTRACT: A catalytic dearomative three-component reaction of bromoarenes with TMS-diazomethane and allyl borate was developed. The key of this assembling reaction is the use of a diazo compound to generate a Pd-π-benzyl intermediate through a Pd-carbenoid species. This method allowed for a dearomative functionalization using arenes as limiting reagents. Heteroaryl bromides were also applicable to give dearomatized structures under the reaction conditions.

Dearomatization is a powerful method to construct structurally complex alicyclic scaffolds from simple and abundant aromatic molecules. Examples of Birch reduction and metal-catalyzed hydrogenation of arenes have found wide use in organic synthesis.[1] Meanwhile, dearomative functionalization, which combines the molecular assembling with dearomatization, is recently attracting much attention.[2] Several dearomative functionalizations of arenes have been reported, mainly using electronically biased arenes such as phenols,[3] indoles,[4] and azines.[5] In contrast, more general but electronically unbiased arenes such as benzenes are still underdeveloped substrates.[6] Existing methods for benzenes often require the use of stoichiometric amounts of metal reagents as well as excess amounts of substrates. Recently, catalytic dearomative functionalizations using arenes as limiting agents have been emerging. For example, the reactions using nitrobenzenes[7] as well as phenyl malonates [8] were achieved by Trost and You, respectively.

As another catalytic method, the dearomative functionalization of electronically non-biased arenes through a π-benzyl complex[9] generated by benzylic bond cleavages is known. In this context, Yamamoto and our group have developed dearomative allylation of benzyl chlorides and phosphates (Figure 1A). [10,11] These methods hold several benefits: arenes can be used as the limiting reagent, and the reactions can be conducted with catalytic amounts of palladium. The key for these reactions is the generation of a palladium π-benzyl complex as a catalytic intermediate. With this intermediate, allyl nucleophiles undergo transmetalation, followed by remote C–C bond forming reductive elimination to afford dearomatized products.[12,13] However, this dearomatization strategy has so far necessitated benzylic bond cleavage, forming an exocyclic olefin in the product.

We targeted the use of haloarenes as the starting material for the dearomative reaction because they are abundant and also easy to prepare. In order to achieve dearomatization, we focused on the Pd-catalyzed reaction of haloarenes with diazo compounds developed by Van Vranken, Wang and Barluenga.[14] These reactions are thought to proceed through a palladium carbenoid, which is known to allow for migratory insertion to generate a benzyl-palladium intermediate. We hypothesized that if allyl nucleophiles react with the benzyl complex, we could use haloarenes entry as ubiquitous starting materials for dearomative functionalization, initiated by aromatic C–halogen bond cleavage (Figure 1B). To achieve this reaction, the control of the reaction sequence (of diazo compound addition and then allyl nucleophiles addition) is required. We herein report a Pd-catalyzed dearomative C–C bond formation of bromoarenes.

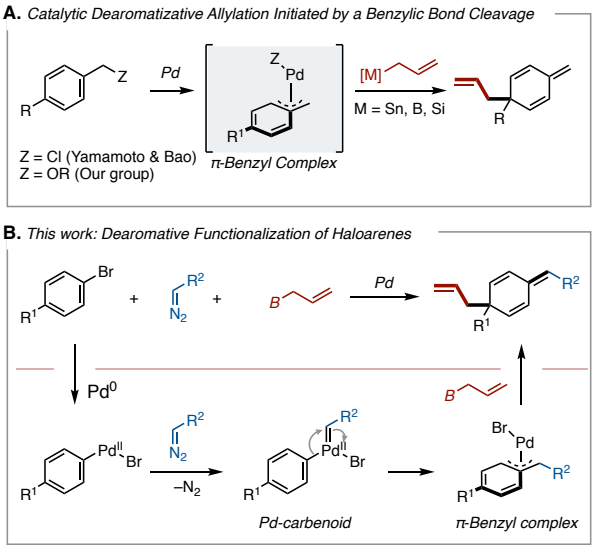
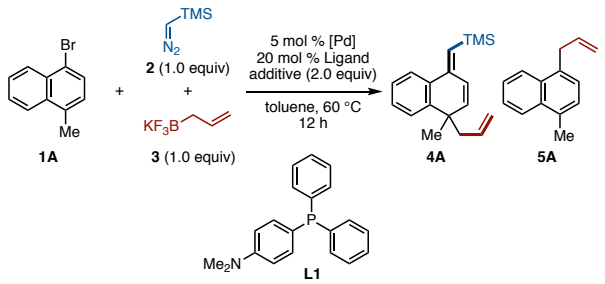


Figure 1. Dearomative functionalization initiated by a bond cleavage.

We initiated the study by screening conditions using bromonaphthalene **1A** with TMS-diazomethane (**2**) and allyl borates **3** (Table 1). An initial attempt using PPh_3 as a ligand delivered the desired product **4A** in low yield along with Suzuki–Miyaura coupling product **5A** (Table 1, entry 1). Encouraged by this result, we modified the ligand. To our delight, the use of electron-donating triarylphosphines as well as a trialkylphosphine improved both the reaction yield and reaction selectivity (Table 1, entries 2–4). The sterically demanding monophosphines and bidentate phosphines dropped the yield of **4A** but generated **5A** as a major product (Table 1, entries 5–7). Increasing the reaction temperature and using 1,4-dioxane gave a better result (Table 1, entry 8). $Pd_2(dba)_3$ was a better catalyst precursor than $Pd(OAc)_2$ (Table 1, entry 9). Because further improvement was difficult by changing parameters,[15] we then tested the effect of additives. Among several inorganic and organic bases, we found that potassium fluoride had a positive effect, producing **4A** in good yield (Table 1, entry 10).[16] Although sodium fluoride was also effective, cesium fluoride resulted in a poor product yield (Table 1, entries 11 and 12). Finally, we identified the optimized conditions: $Pd_2(dba)_3$, **L1**, and KF in 1,4-dioxane at 70 °C for 12 h. It is noteworthy that the reaction conditions give the desired product using equimolar amounts of bromoarenes **1**, TMS-diazomethane (**2**), and allyl borate **3**.

Table 1. Conditions screening



entry	[Pd]	ligand	additive	**4A**/%[a]	**5A**/%[a]
1	$Pd(OAc)_2$	PPh_3	-	18	16
2	$Pd(OAc)_2$	P(*p*-anis)$_3$	-	30	2
3	$Pd(OAc)_2$	**L1**	-	35	0
4	$Pd(OAc)_2$	P^{n}Bu$_3$	-	25	0
5	$Pd(OAc)_2$	Xphos	-	2	17
6	$Pd(OAc)_2$	dppf[b]	-	5	15
7	$Pd(OAc)_2$	DPEphos[b]	-	2	21
8[c,d]	$Pd(OAc)_2$	**L1**	-	46	0
9[c,d]	$Pd_2(dba)_3$	**L1**	-	48	0
10[c,d]	$Pd_2(dba)_3$	**L1**	KF	81	0
11[c,d]	$Pd_2(dba)_3$	**L1**	NaF	65	0
12[c,d]	$Pd_2(dba)_3$	**L1**	CsF	7	0

Conditions; **1A** (0.20 mmol), **2A** (0.20 mmol), **3a** (0.20 mmol), [Pd] (5 mol %), ligand (20 mol %), additive (2.0 equiv), solvent (1 mL), 60 °C, 12 h. [a] NMR yield [b] 10 mol % of ligand [c] 70 °C [d] 1,4-dioxane instead of toluene

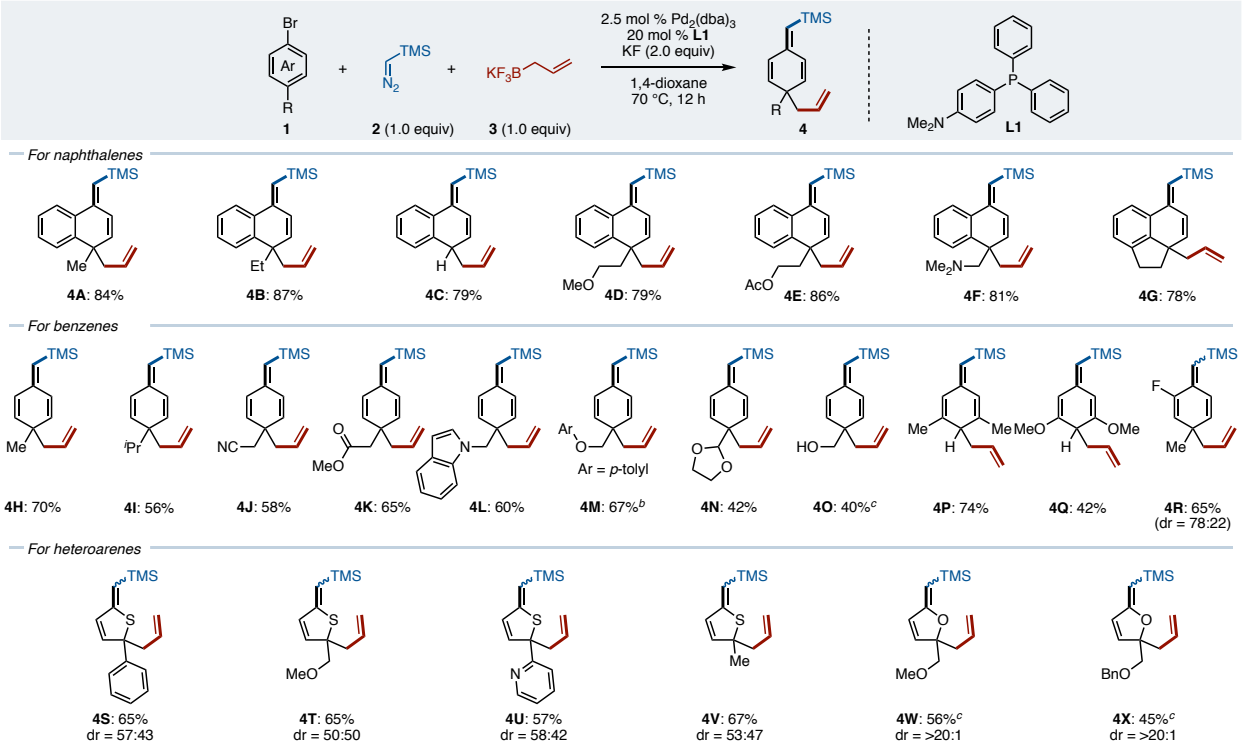
With the optimized conditions in hand, the substrate scope of the reaction was examined (Scheme 1). Owing to the instability of some of the products, ^{1}H NMR yield are shown in Scheme 1.[15] Both quaternary and tertiary carbons could be constructed on naphthyl bromides (**4A**–**4C**). Several functional groups such as ether (**4D**), acetate (**4E**), amines (**4F**) were tolerated in the reaction. An acenaphthene core was also smoothly dearomatized to afford the corresponding product **4G** in good yield. Because of the higher aromatic stability of benzenes compared with naphthalenes, benzenes have been recognized as challenging substrates for the dearomative functionalizations. Previously, our dearomative reaction of benzyl phosphates was also suffered from this limitation.[11] However, pleasingly, the present methodology was exceptional, as a variety of bromobenzenes were applicable. C4-alkylated bromobenzenes could be converted to the corresponding products in moderate to good yields (**4H**, **4I**), however, bulky substituents at the C4 position resulted in low yields. We also observed good functional group tolerance for bromobenzene, as nitrile (**4J**), ester (**4K**), indoles (**4L**) and acetal (**4N**) were compatible. Even a hydroxy group was tolerated to form **4O** in 40% yield. *meta*-Disubstituted molecules could also be transformed to alicyclic compounds (**4P**, **4Q**) in moderate to good yields.[17] The reaction of 2-fluoro bromotoluene generated dearomatized compound **4R** in good yield in a 78:22 diastereoisomeric ratio.

Delightfully, it was found that this method was applicable to five-membered heteroaryl bromides as well. For thiophene bromides, the products were generated as a mixture of diastereoisomers in an approximate 1:1 ratio (**4S**–**4V**). A pyridine-bearing bromothiophene **1U** could also be dearomatized smoothly. Moreover, furans were found to be amenable to the reaction conditions to form dihydrofuran cores in good yield with good diastereoselectivity (**4W** and **4X**). It is noteworthy that these heterocyclic products were more stable compared to dearomatized compounds derived from benzenes.

In order to showcase the utility of the Pd-catalyzed method, we conducted a one-pot reaction[18] starting from simple arenes (Scheme 2A). NBS bromination of thiophene **6** quantitatively proceeded to give **1S** with exclusive regioselectivity. After removing the solvent, the dearomative reaction successfully provided heterocycle **4S** in 55% yield in over two steps. Furthermore, we succeeded in demonstrating the viability of the method by functionalizing a drug-molecule (Scheme 2B). To this end, brominated ticlopidine[19] **7** was subjected to the present reaction to generate the corresponding dearomatized compound **8** in 49% isolated yield , albeit with low diastereoselectivity. This ticlopidine derivative **7** possesses highly reactive functional groups such as a tertiary amine and aryl chloride, but they did not influence the reaction efficiency. With these results, we expect that the further applications of the

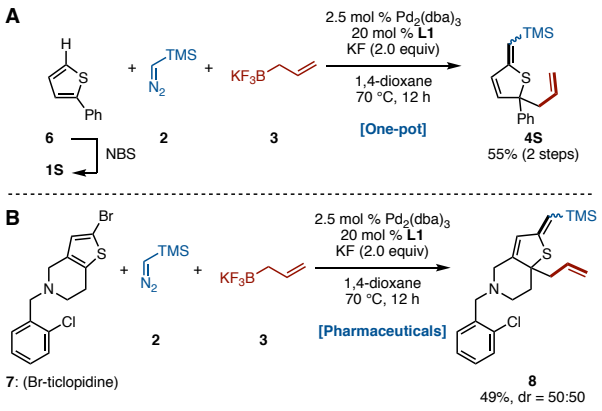
method to access otherwise novel chemical space would accelerate drug discovery.

Scheme 1. Substrate scope[a]



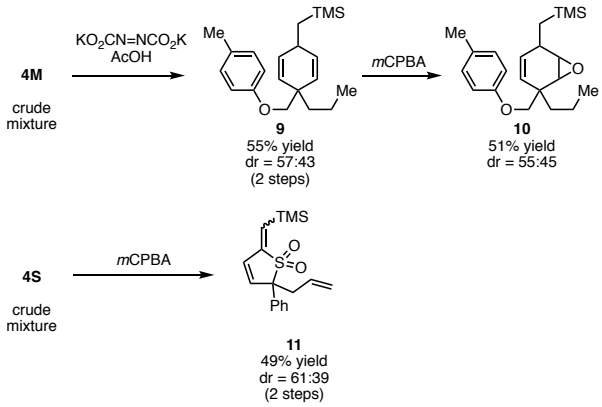
Conditions; **1** (0.40 mmol), **2** (1.0 equiv), **3** (1.0 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %), **L1** (20 mol %), KF (2.0 equiv), 1,4-dioxane (2 mL), 70 °C, 12 h. [a] ^1H NMR yields are shown because of the instability of products during purification process. [b] 5 mol % of $Pd(OAc)_2$ was used instead of $Pd_2(dba)_3{\cdot}CHCl_3$. [c] **2** (1.3 equiv), **3** (1.3 equiv).

Scheme 2. (A) A one-pot operation and (B) the reaction of a pharmaceutical substrate



After this catalytic dearomatization method, we could perform further functionalizations of the cyclic core (Scheme 3). For example, a crude mixture of **4M** was directly subjected to the diimide reduction conditions to give 1,4-cyclohexadiene **9** in good yield in over two steps. In this reaction, the allyl moiety was also reduced to propyl. The obtained compound **9** was further converted by *m*CPBA to furnish epoxide **10** in 28% yield, along with another diastereoisomer in 23% yield. Furthermore, oxidation of sulfur containing heterocycle **4S** generated the corresponding alkenyl sulfone **11** in 49% yield (2 steps).

Scheme 3. Derivatization of products



In summary, we have developed a dearomative three-component reaction of bromoarenes. This method could be

applied to a variety of aromatic systems ranging from simple benzenes to five-membered heteroarenes. Of note, the protocol is catalytic, and aromatic substrates can be used as a limiting reagent. This allows the derivatization of drug molecules by late-stage structural modifications. Further studies to expand the generality of this dearomative functionalization utilizing other diazo compounds as well as nucleophilic participants are ongoing in our laboratory.

ASSOCIATED CONTENT

Experimental procedures and spectroscopic data for compounds including ^{1}H-, ^{13}C NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

*keimuto@aoni.waseda.jp
*junyamaguchi@waseda.jp

ORCID

Masaaki Komatsuda: 0000-0001-5886-837X
Hiroki Kato: 0000-0002-0086-2191
Kei Muto: 0000-0001-8301-4384
Junichiro Yamaguchi: 0000-0002-3896-5882

Notes

No competing financial interests have been declared.

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REFERENCES

(1) (a) Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. Transition-metal-mediated dearomatization reactions. *Chem. Rev.* **2000**, *100*, 2917. (b) Roche, S. P.; Porco, J. A. *Angew. Chem., Int. Ed.* Dearomatization Strategies in the Synthesis of Complex Natural Products. **2011**, *50*, 4068. (c)Zhuo, C.-X.; Zhang, W.; You, S.-L. Catalytic Asymmetric Dearomatization Reactions. *Angew. Chem., Int. Ed.* **2012**, *51*, 12662. (d) Wu, W.-T.; Zhang, L.; You, S.-L. Catalytic asymmetric dearomatization (CADA) reactions of phenol and aniline derivatives. *Chem. Soc. Rev.* **2016**, *45*, 1570. (e) Zheng, C. You, S.-L. Catalytic Asymmetric Dearomatization by Transition-Metal Catalysis: A Method for Transformations of Aromatic Compounds. *Chem* **2016**, *1*, 830. (f) Liang, X.-W.; Zheng, C.; You, S.-L. Dearomatization through Halofunctionalization Reactions. *Chem. Eur. J.* **2016**, *22*, 11918.

(2) For a review, see: (a) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. Asymmetric Hydrogenation of Heteroarenes and Arenes. *Chem. Rev.* **2011**, *112*, 2557. Selected recent examples on catalytic hydrogenation of arenes, see: (b) Wiesenfeldt, M. P.; Nairoukh, Z.; Li, W.; Glorius, F. Hydrogenation of fluoroarenes: Direct access to all-*cis*-(multi)fluorinated cycloalkanes. *Science* **2017**, *357*, 908. (c) Wiesenfeldt, M. P.; Knecht, T.; Schlepphorst, C.; Glorius, F. Silylarene Hydrogenation: A Strategic Approach that Enables Direct Access to Versatile Silylated Saturated Carbo- and Heterocycles. *Angew. Chem., Int. Ed.* **2018**, 57, 8297. (d) Nairoukh, Z.; Wollenburg, M.; Schlepphorst, C.; Bergander, K.; Glorius, F. The formation of all-*cis*-(multi)fluorinated piperidines by a dearomatization-hydrogenation process. *Nat. Chem.* **2019**, *11*, 264. (e) Wollenburg, M.; Moock, D.; Glorius, F. Hydrogenation of Borylated Arenes. *Angew. Chem., Int. Ed.* **2019**, early view (DOI: 10.1002/anie.201810714).

(3) (a) Wu, W.-T.; Zhang, L.; You, S.-L. Catalytic asymmetric dearomatization (CADA) reactions of phenol and aniline derivatives. *Chem. Soc. Rev.* **2016**, *45*, 1570. (b) Uyanik, M.; Mutsuga, T.; Ishihara, K. 4,5-Dimethyl-2-Iodoxybenzenesulfonic Acid Catalyzed Site-Selective Oxidation of 2-Substituted Phenols to 1,2-Quinols. *Angew. Chem., Int. Ed.* **2017**, *56*, 3956.

(4) For a review, see: (a) Ding, Q.; Zhou, X.; Fan, R. Recent advances in dearomatization of heteroaromatic compounds. *Org. Biomol. Chem.* **2014**, *12*, 4807. For selected recent examples, see: (b) Wang, Y.; Zheng, C.; You, S.-L. Iridium-Catalyzed Asymmetric Allylic Dearomatization by a Desymmetrization Strategy. *Angew. Chem., Int. Ed.* **2017**, *56*, 15093. (c) Xia, Z.-L.; Zheng, C.; Wang, S.-G.; You, S.-L. Catalytic Asymmetric Dearomatization of Indolyl Dihydropyridines through an Enamine Isomerization/Spirocyclization/Transfer Hydrogenation Sequence. *Angew. Chem., Int. Ed.* **2018**, *57*, 2653.

(5) For recent representative examples, see: (a) Kubota, K.; Watanabe, Y.; Hayama, K.; Ito, H. Enantioselective Synthesis of Chiral Piperidines via the Stepwise Dearomatization/Borylation of Pyridines. *J. Am. Chem. Soc.* **2016**, *138*, 4338. (b) Bertuzzi, G.; Sinisi, A.; Caruana, L.; Mazzanti, A.; Fochi, M.; Bernardi, L. Catalytic Enantioselective Addition of Indoles to Activated *N*-Benzylpyridinium Salts: Nucleophilic Dearomatization of Pyridines with Unusual C-4 Regioselectivity. *ACS Catal.* **2016**, *6*, 6473. (c) Gribble, M. W., Jr.; Guo, S.; Buchwald, S. L. Asymmetric Cu-Catalyzed 1,4-Dearomatization of Pyridines and Pyridazines without Preactivation of the Heterocycle or Nucleophile. *J. Am. Chem. Soc.* **2018**, *140*, 5057. (d) Yang, Z.-P.; Jiang, R.; Zheng, C.; You, S.-L. Iridium-Catalyzed Intramolecular Asymmetric Allylic Alkylation of Hydroxyquinolines: Simultaneous Weakening of the Aromaticity of Two Consecutive Aromatic Rings. *J. Am. Chem. Soc.* **2018**, *140*, 3114.

(6) (a) Hudlický, T. Recent chemoenzymatic total syntheses of natural and unnatural products: codeine, balanol, pancratistatin, and oseltamivir. *Pure Appl. Chem.* **2010**, *82*, 1785. (b) Wertjes, W. C.; Southgate, E H.; Sarlah, D. Recent advances in chemical dearomatization of nonactivated arenes. *Chem. Soc. Rev.* **2018**, *47*, 7996. (c) Duchek, J.; Adams, D. R.; Hudlicky, T. Chemoenzymatic Synthesis of Inositols, Conduritols, and Cyclitol Analogues. *Chem. Rev.* **2011**, *111*, 4223. (d) Southgate, E. H.; Pospech, J.; Fu, J.; Holycross, D. R.; Sarlah, D. Dearomative dihydroxylation with arenophiles. *Nat. Chem.* **2016**, *8*, 922. (e) Okumura, M.; Nakamata Huynh, S. M.; Pospech, J.; Sarlah, D. Arenophile-Mediated Dearomative Reduction. *Angew. Chem., Int. Ed.* **2016**, *55*, 15910. (f) Okumura, M.; Shved, A. S.; Sarlah, D. Palladium-Catalyzed Dearomative syn-1,4-Carboamination. *J. Am. Chem. Soc.* **2017**, *139*, 17787. (g) Hernandez, L. W.; Klöckner, U.; Pospech, J.; Hauss, L.; Sarlah, D. Nickel-Catalyzed Dearomative *trans*-1,2-Carboamination. *J. Am. Chem. Soc.* **2018**, *140*, 4503. (h) Hamrock, S. J.; Sheridan, R. S. Para photoaddition of N-methyltriazolinedione to benzene. Synthesis of energy-rich azo compounds comprising benzene + nitrogen. *J. Am. Chem. Soc.* **1989**, *111*, 9247. (i) Fujita, M.; Matsushima, H.; Sugimura, T.; Tai, A.; Okuyama, T. Asymmetric Addition of an Electrophile to Naphthalenes Promoted and Stereodirected by Alcohol. *J. Am. Chem. Soc.* **2001**, *123*, 2946.

(7) Trost, B. M.; Ehmke, V.; O'Keefe, B. M.; Bringley, D. A. Palladium-Catalyzed Dearomative Trimethylenemethane Cycloaddition Reactions. *J. Am. Chem. Soc.* **2014**, *136*, 8213.

(8) Yang, Z.-P.; Jiang, R.; Wu, Q.-F.; Huang, L.; Zheng, C.; You, S.-L. Iridium-Catalyzed Intramolecular Asymmetric Allylic Dearomatization of Benzene Derivatives. *Angew. Chem., Int. Ed.* **2018**, *57*, 16190.

(9) Trost, B. M.; Czabaniuk, L. C. Structure and Reactivity of Late Transition Metal η^3-Benzyl Complexes. *Angew. Chem., Int. Ed.* **2014**, *53*, 2826.

(10) (a) Bao, M.; Nakamura, H.; Yamamoto, Y. Facile Allylative Dearomatization Catalyzed by Palladium. *J. Am. Chem. Soc.*, **2001**, *123*, 759. (b) Peng, B.; Feng, X.; Zhang, X.; Ji, L.; Bao, M. Regioselective control using a catalyst switch in the reaction of diarylmethyl chlorides with allyltributylstannane. *Tetrahedron* **2010**, *66*, 6013. (c) Peng, B.; Zhang, S.; Yu, X.; Feng, X.; Bao, M. Nucleophilic Dearomatization of Chloromethyl Naphthalene Derivatives via η^3-Benzylpalladium Intermediates: A New Strategy for Catalytic Dearomatization. *Org. Lett.* **2011**, *13*, 5402. (d) Zhang, S.; Cai, J.;

Yamamoto, Y.; Bao, M. Palladium-Catalyzed sp^2–sp^3 Coupling of Chloromethylarenes with Allyltrimethoxysilane: Synthesis of Allyl Arenes. *J. Org. Chem.* **2017**, *82*, 5974. (e) Zhang, S.; Ullah, A.; Yamamoto, Y.; Bao, M. Palladium-Catalyzed Regioselective Allylation of Chloromethyl(hetero)arenes with Allyl Pinacolborate. *Adv. Synth. Catal.* **2017**, *359*, 2723. (f) Zhang, S.; Yu, X.; Feng, X.; Yamamoto, Y.; Bao, M. Palladium-catalyzed regioselective allylation of five-membered heteroarenes with allyltributylstannane. *Chem. Commun.* **2015**, *51*, 3842.

(11) Komatsuda, M.; Muto, K.; Yamaguchi, J. Pd-Catalyzed Dearomative Allylation of Benzyl Phosphates. *Org. Lett.* **2018**, *20*, 4354.

(12) Ariafard, A.; Lin, Z. DFT Studies on the Mechanism of Allylative Dearomatization Catalyzed by Palladium. *J. Am. Chem. Soc.* **2006**, *128*, 13010.

(13) For related 3,3'-reductive eliminations of bis-π-allyl palladium species, see: (a) Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. Intramolecular Coupling of Allyl Carboxylates with Allyl Stannanes and Allyl Silanes: A New Type of Reductive Elimination Reaction?. *Chem. Eur. J.* **2002**, *8*, 3620. (b) García-Iglesias, M.; Buñuel, E.; Cárdenas, D. J. Cationic (η^1-Allyl)-palladium Complexes as Feasible Intermediates in Catalyzed Reactions. *Organometallics* **2006**, *25*, 3611. (c) Sieber, J. D.; Liu, S.; Morken, J. P. Catalytic Conjugate Addition of Allyl Groups to Styryl-Activated Enones. *J. Am. Chem. Soc.* **2007**, *129*, 2214. (d) Keith, J. A.; Behenna, D. C.; Sherden, N.; Mohr, J. T.; Ma, S.; Marinescu, S. C.; Nielsen, R. J.; Oxgaard, J.; Stoltz, B. M.; Goddard, W. A. The Reaction Mechanism of the Enantioselective Tsuji Allylation: Inner-Sphere and Outer-Sphere Pathways, Internal Rearrangements, and Asymmetric C–C Bond Formation. *J. Am. Chem. Soc.* **2012**, *134*, 19050.

(14) For reviews, see: (a) Xia, Y.; Qiu, D.; Wang, J. Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810. (b) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981. (c) Xia, Y.; Zhang, Y.; Wang, J. Catalytic Cascade Reactions Involving Metal Carbene Migratory Insertion. *ACS Catal.* **2013**, *3*, 2586. (d) Xiao, Q.; Zhang, Y.; Wang, J. Diazo Compounds and *N*-Tosylhydrazones: Novel Cross-Coupling Partners in Transition-Metal-Catalyzed Reactions. *Acc. Chem. Res.* **2012**, *46*, 236. For selected examples, see: (e) Greenman, K. L.; Carter, D. S.; Van Vranken, D. L. Palladium-catalyzed insertion reactions of trimethylsilyldiazomethane. *Tetrahedron* **2001**, *57*, 5219. (f) Greenman, K. L.; Van Vranken, D. L. Palladium-catalyzed carbene insertion into benzyl bromides. *Tetrahedron* **2005**, *61*, 6438. (g) Chen, S.; Wang, J. Palladium-catalyzed reaction of allyl halides with α-diazocarbonyl compounds. *Chem. Commun.* **2008**, 4198. (h) Kudirka, R.; Van Vranken, D. L. Cyclization Reactions Involving Palladium-Catalyzed Carbene Insertion into Aryl Halides. *J. Org. Chem.* **2008**, *73*, 3585. (i) Yu, W.-Y.; Tsoi, Y.-T.; Zhou, Z.; Chan, A. S. C. Palladium-Catalyzed Cross Coupling Reaction of Benzyl Bromides with Diazoesters for Stereoselective Synthesis of (*E*)-α,β-Diarylacrylates. *Org. Lett.* **2009**, *11*, 469. (j) Kudirka, R.; Devine, S. K. J.; Adams, C. S.; Van Vranken, D. L. Palladium-Catalyzed Insertion of α-Diazoesters into Vinyl Halides To Generate α,β-Unsaturated γ-Amino Esters. *Angew. Chem., Int. Ed.* **2009**, *48*, 3677. (k) Peng, C.; Yan, G.; Wang, Y.; Jiang, Y.; Zhang, Y.; Wang, J. Palladium-Catalyzed Coupling Reaction of α-Diazocarbonyl Compounds with Aromatic Boronic Acids or Halides. *Synthesis* **2010**, *2010*, 4154. (l) Zhou, L.; Ye, F.; Zhang, Y.; Wang, J. Pd-Catalyzed Three-Component Coupling of N-Tosylhydrazone, Terminal Alkyne, and Aryl Halide. *J. Am. Chem. Soc.* **2010**, *132*, 13590. (m) Chen, Z.-S.; Duan, X.-H.; Zhou, P.-X.; Ali, S.; Luo, J.-Y.; Liang, Y.-M. Palladium-Catalyzed Divergent Reactions of α-Diazocarbonyl Compounds with Allylic Esters: Construction of Quaternary Carbon Centers. *Angew. Chem., Int. Ed.* **2011**, *51*, 1370. (n) Xu, S.; Chen, R.; Fu, Z.; Zhou, Q.; Zhang, Y.; Wang, J. Palladium-Catalyzed Formal [4 + 1] Annulation via Metal Carbene Migratory Insertion and C(sp^2)–H Bond Functionalization. *ACS Catal.* **2017**, *7*, 1993.

(15) For details, see Supporting Information.

(16) Although the exact effect is still not unclear yet, ligand exchanging of Pd–Br species to Pd–F to accelerate transmetalation of allyl borate was supposed to be one of the factors of the improvement.

(17) These two products were detected by crude NMR, however, it was found that they smoothly rearomatized. For details, see Supporting Information.

(18) Hayashi, Y. Pot economy and one-pot synthesis. *Chem. Sci.* **2016**, *7*, 866.

(19) Maffrand, J.-P. The story of clopidogrel and its predecessor, ticlopidine: Could these major antiplatelet and antithrombotic drugs be discovered and developed today?. *Comptes Rendus Chimie* **2012**, *15*, 737.