C–H Activation

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Modular Assembly of Spirocarbocyclic Scaffolds through Pd^0-Catalyzed Intermolecular Dearomatizing [2+2+1] Annulation of Bromonaphthols with Aryl Iodides and Alkynes

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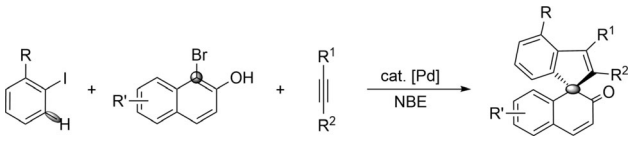
Abstract: *A novel palladium(0)-catalyzed dearomatizing [2+2+1] spiroannulation of 1-bromo-2-naphthols with aryl iodides and alkynes was developed for the rapid assembly of spiro[indene-1,1′-naphthalen]-2′-ones. This three-component cascade reaction was realized through consecutive Catellani-type C–H activation, unsymmetrical biaryl coupling, alkyne migratory insertion, and arene dearomatization. The potential utility of our method is illustrated by the one-step construction of the polycyclic skeletons of dalesconols A and B from alkyne-tethered aryl iodides and 1-bromo-2-naphthol.*

Spirocyclic frameworks are commonly occurring structural motifs in many bioactive compounds[1] and have been used as core building blocks for a wide range of functional materials[2] and chiral ligands.[3] Transition-metal-catalyzed dearomatization of aromatic systems, which offers unusual strategic disconnections, have proven to be a powerful tool for accessing a variety of challenging but synthetically valuable spirocyclic molecules.[4] Pioneering examples of transition-metal-catalyzed dearomative spirocyclizations were realized by the groups of Hamada,[5] You,[6] Buchwald,[7] and Feringa[8] through an intramolecular design by using tethered phenol,[5,6b,7a] naphthol,[5,6f–g,7a,8] indole,[5b,6a,c] or pyrrole[6d–e] derivatives to avoid the unwanted heteroatom alkylation/arylation or Friedel–Crafts-type reaction pathway. However, further advancement of this intramolecular strategy for building other diversified spirocylces has been dramatically limited, in part due to the need for high-cost substrates that often require multistep synthesis. In this context, substantial efforts have been focused on the development of more atom- and step-economical intermolecular processes. Very recently, we,[9] and the groups of Gulías and Mascareñas,[10] Lam,[11] and You[12] have independently demonstrated Ru^{II}- and Rh^{III}-catalyzed dearomatizing [3+2] spiroannulations of phenol-derived biaryls with alkynes through a C–H bond activation approach. Soon afterwards, a non-oxidative version was enabled by Pd^0 catalysis.[13] Moreover, the potent strategy of palladium-catalyzed two-component dearomative cyclization[14] allowed the direct use of phenol diazonium salts, halophenols, halonaphthalenes, naphthols, and *N*-aryl ureas as one-carbon synthons to react with two equivalents of alkynes, thereby leading to various spirocarbocylces. Meanwhile, the pursuit of Pd^0-catalyzed dearomative spirocyclizations of indole derivatives with a second reactant has also seen significant progress.[15] Despite these elegant achievements on two-component processes, the discovery of related annulations with three distinct starting materials to assemble complex spirocyclic frameworks still remains a formidable challenge.[16] Herein we disclose a Pd^0-catalyzed dearomatizing [2+2+1] spiroannulation of readily available bromonaphthols with aryl iodides and alkynes for the one-step direct assembly of spiro[indene-1,1′-naphthalen]-2′-ones (Scheme 1).



Scheme 1. Three-component dearomatizing [2+2+1] spiroannulation. NBE = norbonene.

This work stems from palladium/norbornene (NBE) chemistry, which was originally discovered by Catellani et al.[17] Seminal works[18] by Catellani and Lautens revealed that a myriad of biaryl-containing carbocyclic and heterocyclic compounds (**III**) could be obtained through palladium-catalyzed *ortho*-arylation of an aryl iodide (**I**) with a bifunctional aromatic reagent (**II**) followed by intramolecular ring closure with NBE as a transient mediator (Scheme 2). These processes are initiated by NBE-assisted C–H palladation to form five-membered palladacycle **A**, which then reacts with haloarene **II** to generate biarylpalladium species **B**. Subsequent elimination of NBE through β-carbon elimination then occurs to give the key intermediate **C**. In connection with our persistent interest in the development of cooperative C–H activation/dearomatization reactions,[9,14d] we wondered whether the in situ formed intermediate **C** could be intercepted with alkyne **IV** through a dearomative pathway to produce spirocyclic compound **V** (path a). However, additional challenges arise from the fact that: 1) the utilization of aromatic motif **II**, which is prone to undergo dearomatization, dramatically increases the risk for the direct cyclization of intermediate **B** to provide NBE-containing spirocarbocylce **VI** (path b),[16,19] and 2) the two-component annulation of two

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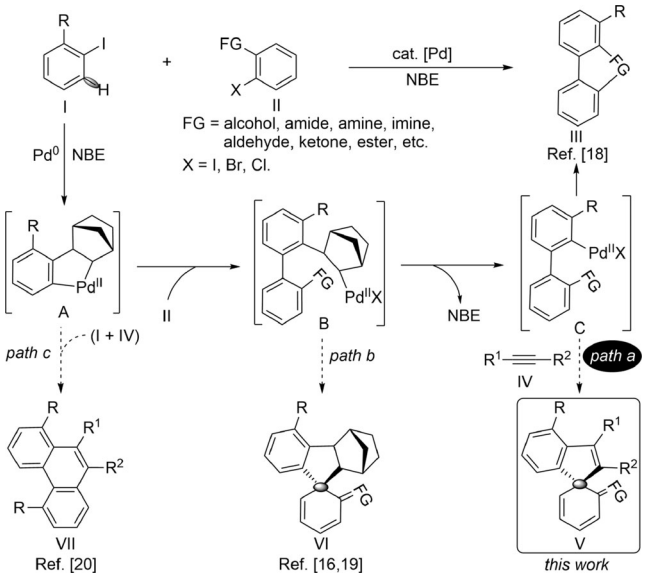
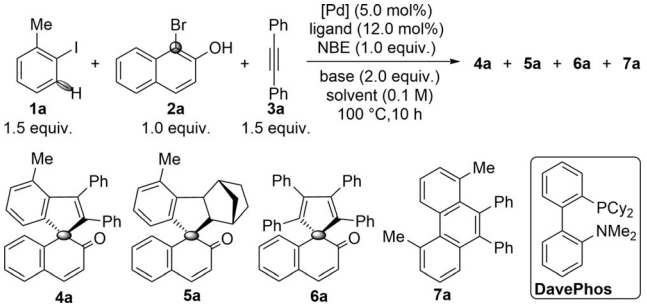


Scheme 2. Reaction design for the palladium/norbornene catalysis.

equivalents of **I** with alkyne **V** might form phenathrene product **VII** (path c).[20] Therefore, the key for the envisioned reaction is to find suitable conditions to effectively prevent the unwanted side reactions.

To address the aforementioned challenge, we commenced our studies with 1-bromo-2-naphthol (**2a**), which possesses a higher potential to undergo dearomatization,[8,21] as the bifunctional reactant **II** for the designed three-component reaction (Table 1). At the outset, a reaction mixture of **1a**, **2a**, and **3a** in DMF was heated at 100 °C in the presence of 5.0 mol % $Pd(OAc)_2$, 12.0 mol % PPh_3, 1.0 equivalent of NBE, and 2.0 equivalent of K_2CO_3, but neither the dearomatizing products (**V** and **VI**) nor dibenzofuran (**III**)[22] were observed under these typical Catellani-reaction conditions,[23] and only side product **7a**[20] was obtained through the annulation of **1a** with **3a** (entry 1). Upon optimization on the base, the envisioned **4a**[13a] was indeed obtained, albeit with low yields (entries 2–3). Despite this encouraging outcome with the use of Cs_2CO_3, the desired transformation suffered from the concomitant generation of byproducts **5a**, **6a**,[14a,b] and **7a**. Other common solvents and palladium precursors for Catellani-type reactions were tested, but none of them showed a positive effect (entries 4–7). Further results revealed that various phosphine ligands were effective, and the troublesome issue of the formation of unwanted **5a** and **7a** could be addressed (entries 8–17). When BINAP was employed, product **4a** was isolated in 41 % yield, with only 2 % of the NBE-containing byproduct **5a** (entry 10). This observation indicated that the evolution from intermediate **B** to **C** through β-carbon elimination could be facilitated with the more rigid ligand. However, the use of bisphosphine ligands did not inhibit the formation of **7a** (entries 8–10), thus implying that the cross-coupling of **1a** with **2a** was not rendered fast enough to suppress the unwanted homocoupling of **1a**. Although several monophosphine ligands failed to improve the reaction (entries 11–13), Buchwald-type ligands gave a dramatic enhancement in both reactivity and

Table 1: Optimization of the reaction conditions.



Entry	[Pd]	Ligand	Base	Solvent	Yield [%][a]			
					4a	**5a**	**6a**	**7a**[b]
1	$Pd(OAc)_2$	PPh_3	K_2CO_3	DMF	0	0	0	36
2	$Pd(OAc)_2$	PPh_3	K_3PO_4	DMF	11	24	2	22
3	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DMF	46	27	7	25
4	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	MeCN	21	15	0	18
5	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DME	33	11	6	2
6	$PdCl_2$	PPh_3	Cs_2CO_3	DMF	18	5	0	25
7	$[Pd(allyl)Cl]_2$	PPh_3	Cs_2CO_3	DMF	35	34	0	13
8	$Pd(OAc)_2$	DPPP[c]	Cs_2CO_3	DMF	23	13	2	46
9	$Pd(OAc)_2$	DPPF[c]	Cs_2CO_3	DMF	32	22	4	20
10	$Pd(OAc)_2$	BINAP[c]	Cs_2CO_3	DMF	41	2	3	30
11	$Pd(OAc)_2$	TFP	Cs_2CO_3	DMF	39	30	0	22
12	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	DMF	41	20	2	12
13	$Pd(OAc)_2$	$P(o\text{-Tol})_3$	Cs_2CO_3	DMF	9	7	1	4
14	$Pd(OAc)_2$	XPhos	Cs_2CO_3	DMF	60	16	3	10
15	$Pd(OAc)_2$	*t*-BuXPhos	Cs_2CO_3	DMF	48	9	0	16
16	$Pd(OAc)_2$	JohnPhos	Cs_2CO_3	DMF	79	8	0	8
17	$Pd(OAc)_2$	DavePhos	Cs_2CO_3	DMF	84	2	0	3
18[d]	$Pd(OAc)_2$	DavePhos	Cs_2CO_3	DMF	–	17	–	–
19[e]	$Pd(OAc)_2$	DavePhos	Cs_2CO_3	DMF	–	–	32	–
20[f]	$Pd(OAc)_2$	DavePhos	Cs_2CO_3	DMF	–	–	–	31

[a] Yield of isolated product. [b] Yield was based on the amount of **2a**. [c] 6.0 mol %. [d] **3a** was not added. [e] **1a** was not added. [f] **2a** was not added. DMF = *N*,*N*-dimethylformamide, DME = dimethyl ether, DPPP = 1,3-bis(diphenylphosphino)propane, DPPF = 1,1′-bis(diphenylphosphino)ferrocene, BINAP = 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl.

selectivity (entries 14–17). As a result, the electron-rich DavePhos, which has been employed by the Liu group for the selective *ortho* C–H trifluoroethylation of aryl iodies under Pd/NBE catalysis,[24] turned out to be the optimal ligand, affording **4a** in 84 % yield, with negligible amounts of byproducts **5a**–**7a** (entry 17). Finally, three control reactions were conducted with different combinations of two of the three substrates, and the expected products **5a**, **6a**, and **7a** were isolated in 17 %, 32 %, and 31 % yield, respectively (entries 18–20). Therefore, the successful execution of the title reaction was realized by avoiding at least three competitive side reactions.

With the optimized conditions established, the scope with respect to the aryl iodides was first examined. The results indicated that various functional groups are tolerated, and the reactions of aryl iodides **1b**–**p** with **2a** and **3a** underwent the envisioned [2+2+1] spiroannulations efficiently to deliver the dearomatized products **4b**–**p** in 46–82 % yields (Table 2). For example, functionalization of the 3- and 4-positions of **1a** with methyl (**1b**,**e**), chloro (**1c**), nitro (**1d**), or ester (**1f**) groups was

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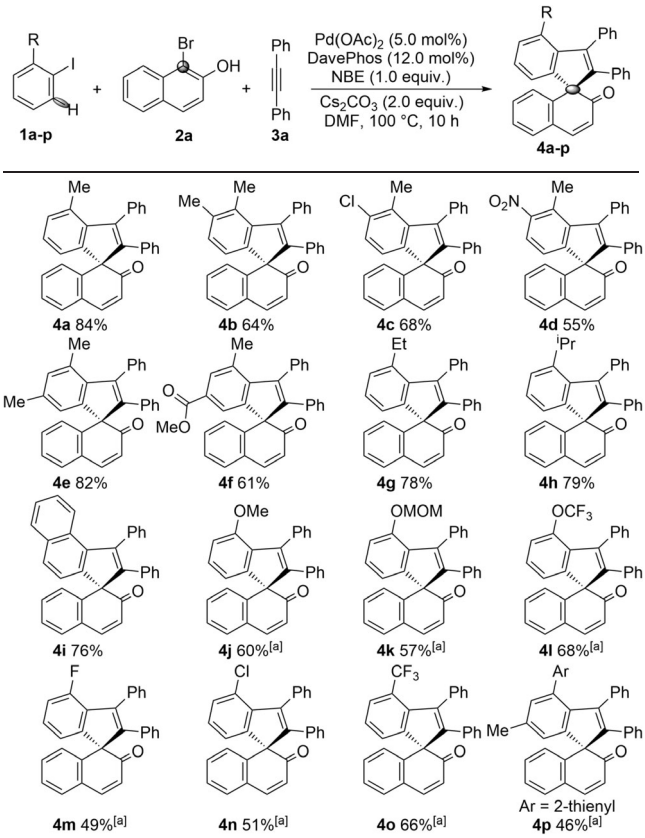
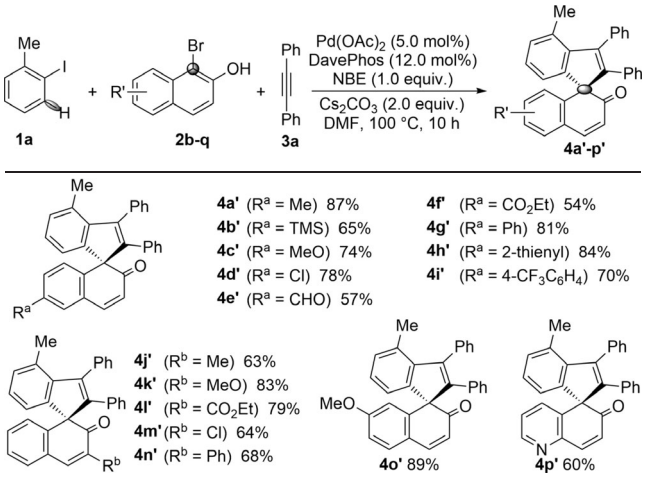
Table 2: Scope with respect to the aryl iodides.



[a] Reactions were conducted in DME at 120 °C.

Table 3: Scope with respect to the 1-bromo-2-naphthols.

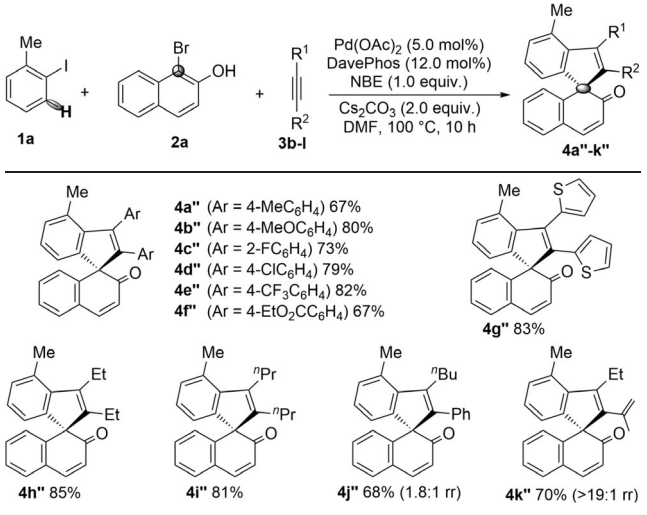


well tolerated. The methyl substituent could be varied with a bulkier ethyl or isopropyl group to afford compounds **4g–h** in good yields (78 % and 79 %). Moreover, a high yield (76 %) of **4i** was obtained with naphthalene-derived substrate (**1i**). When the methyl group of **1a** was substituted with other substituents, such as methoxy (**1j**), methoxymethoxy (**1k**), trifluoromethoxy (**1l**), fluoro (**1m**), chloro (**1n**), trifluoromethyl (**1o**), or 2-thienyl (**1p**) groups, the corresponding reactions had to be run in DME at a higher temperature (120 °C), which gave spirocyclic molecules **4j–p** in 46–68 % yields. Notably, this method features the direct use of three commercially available substrates, thereby avoiding multistep substrate preparation and enabling the synthesis of many highly functionalized spirocylic compounds that were extremely difficult or inaccessible by the prior method with halogenated biaryls and alkynes.[13a] In sharp contrast to the previously reported two-component reactions that rely on a highly regioselective C–H functionalization approach,[9–12] this new process served as a reliable complementary strategy for exclusive formation of the opposite regioisomer.

Next, we continued to explore the generality of this new three-component reaction by using a variety of functionalized 1-bromo-2-naphthols (**2b–q**) to react with **1a** and **3a**, and the experimental data are shown in Table 3. Gratifyingly, the corresponding reactions proceeded smoothly to give the desired spirocyclic products **4a′-p′** in 54–89 % yields. Besides aliphatic (**2b**,**k**) and aromatic (**2h–j**,**o**) groups, the 3-, 6-, and 7-positions of bromonaphthols could be substituted with electron-donating groups (EDGs) such as a methoxy group (**2d**,**l**,**p**), or electron-withdrawing groups (EWGs) such as chloro (**2e**,**n**), formyl (**2f**), and ester (**2g**,**m**) groups. The electron-rich 1-bromo-2-naphthols generally showed better performance for the title transformation. The potentially labile aryl chloride remained intact in the process, and the structure of **4m′** was confirmed by X-ray crystallography.[25] A TMS-substituted substrate (**2c**) was found to be compatible as well. It is noteworthy that heterocyclic 5-bromoquinolin-6-ol (**2q**) behaved quite well in the dearomatizing [2+2+1] spiroannulation with **1a** and **3a**, leading to the anticipated compound **4p′** in 60 % yield. However, it should be mentioned that *o*-bromophenols were not applicable under the current reaction conditions.

Having examined the reaction scope of aryl iodides and bromonaphthols, we eventually turned our focus to evaluating the performance of alkynes (Table 4). Overall, a broad range of symmetrical alkynes containing various aromatic groups were tolerated in the three-component [2+2+1] annulation

Table 4: Scope with respect to the alkynes.



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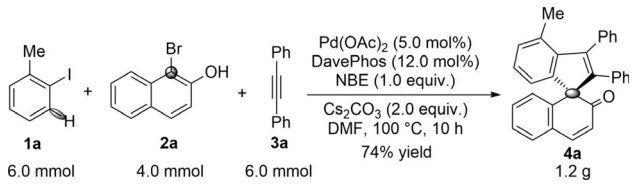
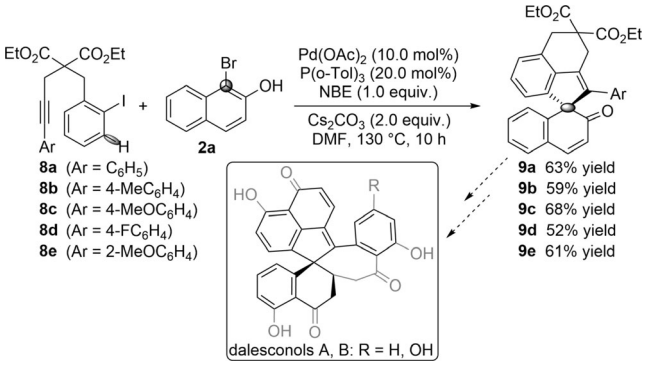
reaction, affording products **4a″–g″** in 67%-83% yields. Diaryl alkynes substituted with methyl (**3b**), methoxy (**3c**), fluoro (**3d**), chloro (**3e**), trifluoromethyl (**3f**), or ester (**3g**) groups were well accommodated. Additionally, the alkyne **3h**, which bears a heterocyclic 2-thienyl group, efficiently underwent the [2+2+1] annulation with **1a** and **2a**, leading to **4g″** in 83% yield. To our delight, dialkylacetylenes (**3i,j**), which were not tolerated in the Pd/NBE-catalyzed [2+2+2] annulation of aryl iodides with alkynes for the synthesis of phenanthrenes,[20] were found to be suitable for this new process, providing the desired products **4h″** and **4i″** in high yields (85% and 81%), without the potential allenic byproduct being formed through β-hydride elimination. Moreover, the catalytic run with alkyl/aryl mixed alkynes **3k** proceeded smoothly to give product **4j″** in 68% yields but with poor regioselectivity (1.8:1 *rr*). In contrast, the reaction with unsymmetrical alkyne **3l** led to the formation of **4k″** as a single regioisomer, with **3l** being installed in such a manner that the alkene group is close to the spirocyclic carbon center, and its structure was confirmed by X-ray crystallography.[25]

In order to further demonstrate the practicality of this three-component domino process, a scale-up experiment (4.0 mmol) was carried out under the standard reaction conditions. As depicted in Scheme 3, gram-scale preparation of product **4a** (1.2 g) was successfully achieved in 74% yield.



Scheme 3. Gram-scale preparation of **4a**.

To highlight the potential utility of this new synthetic method, preliminary studies were performed to construct the structural cores of the immunosuppressive polyketides dalesconols A and B[1a] by using alkyne-tethered aryl iodides **8a–e** to react with **2a** (Scheme 4). After further optimization, the two-component reactions, which were heated in DMF at 130 °C for 10 hours, showed excellent performance when using 10.0 mol% of $Pd(OAc)_2$, 20.0 mol% of $P(o\text{-}Tol)_3$, 1.0 equivalent of NBE, and 2.0 equivalents of Cs_2CO_3, affording the desired products **9a–e** in 52–68% yields. The structure of **9a** was unambiguously assigned by X-ray crystallography.[25] Remarkably, the main polycyclic skeleton of dalesconols A and B could be rapidly assembled from two readily available starting materials in a single step through the formation of three C–C bonds. Moreover, the pendant phenyl group could be substituted with different functional groups, offering a great opportunity to furnish the final ring for the whole skeleton of these two molecules.



Scheme 4. Preliminary studies on the synthetic application of our dearomatizing [2+2+1] spiroannulation.

In summary, we have developed an unprecedented Pd^0-catalyzed NBE-mediated dearomatizing [2+2+1] spiroannulation of bromonaphthols with aryl iodides and alkynes, which provides a variety of spirocyclic molecules in good yields. With NBE as a transient mediator, this three-component domino process is likely realized through a sequence of C–H activation, biaryl coupling, alkyne migratory insertion, and naphthol dearomatization. Notably, this method represents a rare example of transition-metal-catalyzed processes for the rapid assembly of spirocarbocycles in an intermolecular fashion starting from three very simple substrates. Efforts to expand the reaction scope and detailed mechanistic studies are underway.

Acknowledgements

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Conflict of interest

The authors declare no conflict of interest.

Keywords: C–H activation · dearomatization · homogeneous catalysis · palladium · spiroannulation

[1] Selected examples: a) Y. Zhang, H. Ge, W. Zhao, H. Dong, Q. Xu, S. Li, J. Li, J. Zhang, Y. Song, R. Tan, *Angew. Chem. Int. Ed.* **2008**, *47*, 5823; *Angew. Chem.* **2008**, *120*, 5907; b) A. Arnone, A. Bava, G. Fronza, L. Malpezzi, G. Nasini, *J. Nat. Prod.* **2010**, *73*, 1049; c) H. Zhang, S. L. Shyaula, J. Li, J. Yue, *J. Nat. Prod.* **2015**, *78*, 2761.

[2] A review: a) T. P. I. Saragi, T. Spehr, A. Siebert, T. Fuhrmann-Lieker, J. Salbeck, *Chem. Rev.* **2007**, *107*, 1011; For selected examples, see: b) D. Vak, J. Jo, J. Ghim, C. Chun, B. Lim, A. J. Heeger, D. Kim, *Macromolecules* **2006**, *39*, 6433; c) J. Kim, C. Lee, J. G. Jang, M. Gong, *Dyes Pigm.* **2012**, *94*, 304.

[3] Reviews: a) J. Xie, Q. Zhou, *Acc. Chem. Res.* **2008**, *41*, 581; b) K. Ding, Z. Han, Z. Wang, *Chem. Asian J.* **2009**, *4*, 32.

[4] Reviews: a) S. P. Roche, J. Porco, Jr., *Angew. Chem. Int. Ed.* **2011**, *50*, 4068; *Angew. Chem.* **2011**, *123*, 4154; b) C. Zhuo, W. Zhang, S. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 12662; *Angew. Chem.* **2012**, *124*, 12834; c) W.-T. Wu, L. Zhang, S.-L. You, *Chem.*

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These are not the final page numbers!

Soc. Rev. **2016**, *45*, 1570; d) M. J. James, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Chem. Eur. J.* **2016**, *22*, 2856; e) T. Nemoto, Y. Hamada, *Synlett* **2016**, 2301; f) H. Wang, X. Luan, *Org. Biomol. Chem.* **2016**, *14*, 9451.

[5] a) T. Nemoto, Y. Ishige, M. Yoshida, Y. Kohno, M. Kanematsu, Y. Hamada, *Org. Lett.* **2010**, *12*, 5020; b) T. Nemoto, Z. Zhao, T. Yokosaka, Y. Suzuki, R. Wu, Y. Hamada, *Angew. Chem. Int. Ed.* **2013**, *52*, 2217; *Angew. Chem.* **2013**, *125*, 2273; c) T. Nemoto, N. Matsuo, Y. Hamada, *Adv. Synth. Catal.* **2014**, *356*, 2417.

[6] a) Q.-F. Wu, H. He, W.-B. Liu, S.-L. You, *J. Am. Chem. Soc.* **2010**, *132*, 11418; b) Q.-F. Wu, W.-B. Liu, C.-X. Zhuo, Z.-Q. Rong, K.-Y. Ye, S.-L. You, *Angew. Chem. Int. Ed.* **2011**, *50*, 4455; *Angew. Chem.* **2011**, *123*, 4547; c) K.-J. Wu, L.-X. Dai, S.-L. You, *Org. Lett.* **2012**, *14*, 3772; d) C.-X. Zhuo, W.-B. Liu, Q.-F. Wu, S.-L. You, *Chem. Sci.* **2012**, *3*, 205; e) K.-J. Wu, L.-X. Dai, S.-L. You, *Chem. Commun.* **2013**, *49*, 8620; f) W.-T. Wu, R.-Q. Xu, L. Zhang, S.-L. You, *Chem. Sci.* **2016**, *7*, 3427; g) Q. Cheng, Y. Wang, S.-L. You, *Angew. Chem. Int. Ed.* **2016**, *55*, 3496; *Angew. Chem.* **2016**, *128*, 3557.

[7] a) S. Rousseaux, J. García-Fortanet, M. A. Del Aguila Sanchez, S. L. Buchwald, *J. Am. Chem. Soc.* **2011**, *133*, 9282; For the pioneering examples on the dearomatization of anilines, see: b) J. García-Fortanet, F. Kessler, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 6676; c) R. B. Bedford, C. P. Butts, M. F. Haddow, R. Osborne, R. F. Sankey, *Chem. Commun.* **2009**, 4832.

[8] A. Rudolph, P. H. Bos, A. Meetsma, A. Minnaard, B. L. Feringa, *Angew. Chem. Int. Ed.* **2011**, *50*, 5834; *Angew. Chem.* **2011**, *123*, 5956.

[9] a) J. Nan, Z. Zuo, L. Luo, L. Bai, H. Zheng, Y. Yuan, J. Liu, X. Luan, Y. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 17306; b) Z. Zuo, X. Yang, J. Liu, J. Nan, L. Bai, Y. Wang, X. Luan, *J. Org. Chem.* **2015**, *80*, 3349.

[10] A. Seoane, N. Casanova, N. Quiñones, J. L. Mascareñas, M. Gulías, *J. Am. Chem. Soc.* **2014**, *136*, 7607.

[11] S. Kujawa, D. Best, D. J. Burns, H. W. Lam, *Chem. Eur. J.* **2014**, *20*, 8599.

[12] J. Zheng, S.-B. Wang, C. Zheng, S.-L. You, *J. Am. Chem. Soc.* **2015**, *137*, 4880.

[13] a) H. Zheng, L. Bai, J. Liu, J. Nan, Z. Zuo, L. Yang, Y. Wang, X. Luan, *Chem. Commun.* **2015**, *51*, 3061; b) L. Yang, H. Zheng, L. Luo, J. Nan, J. Liu, Y. Wang, X. Luan, *J. Am. Chem. Soc.* **2015**, *137*, 4876; c) L. Luo, H. Zheng, J. Liu, H. Wang, Y. Wang, X. Luan, *Org. Lett.* **2016**, *18*, 2082.

[14] a) B. Schmidt, R. Berger, A. Kelling, U. Schilde, *Chem. Eur. J.* **2011**, *17*, 7032; b) L. Bai, Y. Yuan, J. Liu, J. Wu, L. Han, H. Wang, Y. Wang, X. Luan, *Angew. Chem. Int. Ed.* **2016**, *55*, 6946; *Angew. Chem.* **2016**, *128*, 7060; c) Y. Dou, L. Yang, L. Zhang, P. Zhang, H. Li, G. Yang, *RSC Adv.* **2016**, *6*, 100632; d) S. Gu, L. Luo, J. Liu, L. Bai, H. Zheng, Y. Wang, X. Luan, *Org. Lett.* **2014**, *16*, 6132; e) P. Jiang, Y. Xu, F. Sun, X. Liu, F. Li, R. Yu, Y. Li, Q. Wang, *Org. Lett.* **2016**, *18*, 1426.

[15] a) T. D. Montgomery, A. E. Nibbs, Y. Zhu, V. H. Rawal, *Org. Lett.* **2014**, *16*, 3480; b) R.-D. Gao, C. Liu, L.-X. Dai, W. Zhang, S.-L. You, *Org. Lett.* **2014**, *16*, 3919; c) X. Wu, Y. Shen, W. Chen, S. Chen, P. Xu, Y. Liang, *Chem. Commun.* **2015**, *51*, 16798.

[16] Only known example: M. Larraufie, G. Maestri, A. Beaume, É. Derat, C. Ollivier, L. Fensterbank, C. Courillon, E. Lacôte, M. Catellani, M. Malacria, *Angew. Chem. Int. Ed.* **2011**, *50*, 12253; *Angew. Chem.* **2011**, *123*, 12461.

[17] M. Catellani, F. Frignani, A. Rangoni, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 119; *Angew. Chem.* **1997**, *109*, 142.

[18] Reviews: a) M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res.* **2008**, *41*, 1512; b) A. Martins, B. Mariampillai, M. Lautens, *Top. Curr. Chem.* **2010**, *292*, 1; c) J. Ye, M. Lautens, *Nat. Chem.* **2015**, *7*, 863; d) N. Della Ca', M. Fontana, E. Motti, M. Catellani, *Acc. Chem. Res.* **2016**, *49*, 1389.

[19] M. Catellani, F. Cugini, G. Bocelli, *J. Organomet. Chem.* **1999**, *584*, 63.

[20] M. Catellani, E. Motti, S. Baratta, *Org. Lett.* **2001**, *3*, 3611.

[21] a) T. Oguma, T. Katsuki, *J. Am. Chem. Soc.* **2012**, *134*, 20017; b) C.-X. Zhuo, S.-L. You, *Angew. Chem. Int. Ed.* **2013**, *52*, 10056; *Angew. Chem.* **2013**, *125*, 10240.

[22] E. Motti, N. Della Ca', D. Xu, S. Armani, B. M. Aresta, M. Catellani, *Tetrahedron* **2013**, *69*, 4421.

[23] Most of Catellani reactions were realized by using two equivalents of monophosphine ligands versus the amount of palladium precursor.

[24] H. Zhang, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 10174; *Angew. Chem.* **2014**, *126*, 10338.

[25] CCDC 1521363 (**4m′**), 1521366 (**4k″**) and 1521365 (**9a**) contain the supplementary crystallographic data for this paper. These data are provided free of charge from The Cambridge Crystallographic Data Centre.

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Communications

C–H Activation

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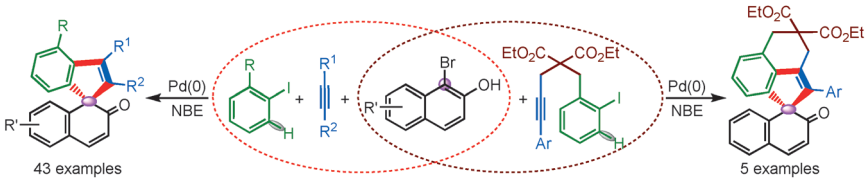
Modular Assembly of Spirocarbocyclic Scaffolds through Pd^0-Catalyzed Intermolecular Dearomatizing [2+2+1] Annulation of Bromonaphthols with Aryl Iodides and Alkynes



Spiro staircase: A novel palladium(0)-catalyzed dearomatizing [2+2+1] spiroannulation of 1-bromo-2-naphthols with aryl iodides and alkynes was developed for the rapid assembly of spiro[indene-1,1′-naphthalen]-2′-ones. This three-component cascade reaction was realized through consecutive Catellani-type C–H activation, unsymmetrical biaryl coupling, alkyne migratory insertion, and arene dearomatization steps.

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