CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Title: Pd-Catalyzed Annulation of 1-Halo-8-arylnaphthalenes and Alkynes Leading to Heptagon-Embedded Aromatic Systems

Authors: Jianming Yan, Md. Shafiqur Rahman, and Naohiko Yoshikai

To be cited as: *Chem. Eur. J.* 10.1002/chem.201805746

Link to VoR: http://dx.doi.org/10.1002/chem.201805746

Supported by
ACES

WILEY-VCH

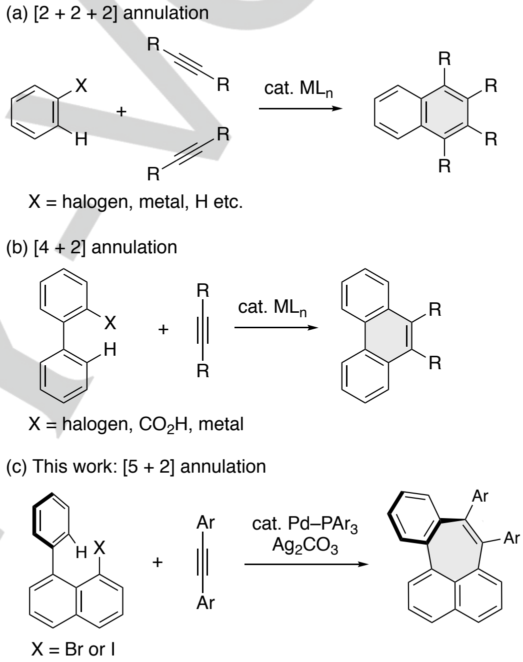
Pd-Catalyzed Annulation of 1-Halo-8-arylnaphthalenes and Alkynes Leading to Heptagon-Embedded Aromatic Systems**

Jianming Yan[+], Md. Shafiqur Rahman[+], Naohiko Yoshikai*

Abstract: A palladium-catalyzed heptagon-forming annulation reaction between 1-halo-8-arylnaphthalene and diarylacetylene is reported. The reaction is promoted using a catalytic system comprised of $Pd(OAc)_2$, moderately electron-deficient triarylphosphine $P(4\text{-}ClC_6H_4)_3$, and Ag_2CO_3 to afford benzo[4,5]cyclohepta[1,2,3-*de*]naphthalene derivatives in moderate to good yields, in preference to fluoranthene as a competing byproduct. Twofold annulation can also be achieved to access a novel heptagon-embedded polycyclic aromatic hydrocarbon compound.

Polycyclic aromatic hydrocarbons (PAHs) are among quintessential structural elements in functional molecules for optoelectronic applications, and therefore the development of efficient methods for the construction of PAHs from readily available starting materials represents an important subject in synthetic chemistry.[1] In this context, transition metal-catalyzed annulation reactions of aromatic substrates with alkynes have been extensively explored as means to achieve extension of the π-system,[2] among which those involving C–H activation have attracted significant attention due to the greater availability of the starting materials. Thus, [2 + 2 + 2] annulation reactions of a monofunctionalized benzene derivative with two molecules of alkyne have been developed for the synthesis of naphthalene, anthracene, and related acenes (Scheme 1a).[3] Meanwhile, [4 + 2] annulation reactions of a 2-functionalized biaryl with an alkyne have been achieved to enable expedient synthesis of phenanthrene-type hexagonal polyaromatic compounds (Scheme 1b).[4,5]

Recently, PAHs that contain a seven-membered ring comprised of all sp^2-carbon atoms have gained increasing attention for their warped structures that could lead to unique optoelectronic properties.[6,7] However, the synthesis of such heptagon-embedded PAHs usually requires multiple steps, and direct construction of heptagons from simple and readily available fragments has been rare. Recently, Lin, Kwong, and coworkers disclosed a Pd-catalyzed three-component annulation reaction of aryl iodide, 8-bromo-1-naphthoic acid, and norbornadiene to afford a heptagon-containing benzo[4,5]cyclohepta[1,2,3-*de*]naphthalene derivative, in which naphthalene and benzene rings are linked by a *cis*-ethenyl (C_2H_2) bridge.[8] Except this report, annulative approaches to heptagons have been elusive.[9] Herein, we disclose a palladium-catalyzed heptagon-forming annulation reaction between 1-halo-8-arylnaphthalene and diarylacetylene. The reaction affords benzo[4,5]cyclohepta[1,2,3-*de*]naphthalenes bearing a variety of aryl groups on the 7- and 8-positions, and thus complements the scope of Lin/Kwong's annulation.



Scheme 1. Transition metal-catalyzed alkyne annulations for π-extension.

The present study commenced with a screening of reaction conditions for the annulation of 1-bromo-8-phenylnaphthalene (**1a**) and diphenylacetylene (**2a**) (Table 1). The reaction in the presence of $Pd(OAc)_2$ (10 mol%) and Ag_2CO_3 (1 equiv) in dichloroethane at 80 °C afforded, after 18 h, the desired heptagon product **3aa** in a low yield of 18% (entry 1). The addition of triphenylphosphine (30 mol%) decreased the yield of **3aa** while affording a trace amount of fluoranthene **4** (entry 2).[10] The use of less electron-donating triphenylarsine promoted full conversion of **1a** and improved the yield of **3aa** to 59%, albeit with increased amount (20%) of **4** (entry 3). At the reaction time of 1.5 h, the yields of **3aa** and **4** reached 29% and 21%, respectively, indicating that the formation of **4** stopped at the early stage. Moderately electron-deficient triarylphosphines such as $P(4\text{-}ClC_6H_4)_3$, $P(3\text{-}ClC_6H_4)_3$, and $C(4\text{-}FC_6H_4)_3$ were found to promote the annulation to afford **3aa** in up to 78% yield, while suppressing the fluoranthene formation (entries 4–6). Note that the reaction using $P(4\text{-}ClC_6H_4)_3$ reached full conversion at 1.5 h (entry 4). The annulation reaction became sluggish with more electron-deficient phosphines such as $P(4\text{-}CF_3C_6H_4)_3$ and

---

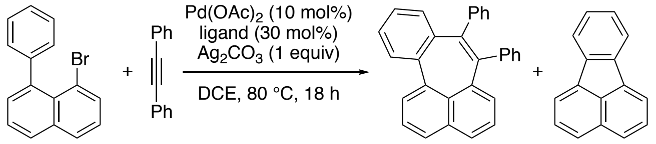
[*] Dr. J. Yan[+], M. S. Rahman[+], Prof. N. Yoshikai
Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences
Nanyang Technological University
Singapore 637371, Singapore
E-mail: nyoshikai@ntu.edu.sg

[+] These authors equally contributed to the work.

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

$P(C_6F_5)_3$ (entries 7 and 8), and no annulation was observed with electron-rich $P(4\text{-}MeOC_6H_4)_3$ (entry 9). Other monophosphines such as tri(2-furyl)phosphine and SPhos did not improve the reaction (entries 10 and 11). The reaction using AgOAc instead of Ag_2CO_3 afforded **3aa** in a slightly lower but comparable yield (entry 12), while removal of Ag_2CO_3 resulted in sluggish conversion (entry 13).

Table 1. Optimization of reaction conditions.[a]



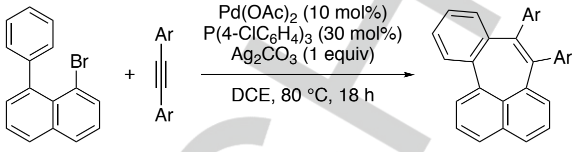
1a **2a** **3aa** **4**

Entry	Ligand[b]	Conv of **1a** [%][b]	**3aa** [%][b]	**4** [%][b]
1	None	45	18	0
2	PPh_3	58	8	3
3	$AsPh_3$	100 (60)	59 (29)	20 (21)
4	$P(4\text{-}ClC_6H_4)_3$	100 (100)	78 (75)	3 (4)
5	$P(3\text{-}ClC_6H_4)_3$	100	77	3
6	$P(4\text{-}FC_6H_4)_3$	100	65	0
7	$P(4\text{-}CF_3C_6H_4)_3$	55	37	4
8	$P(C_6F_5)_3$	29	15	0
9	$P(4\text{-}MeOC_6H_4)_3$	20	0	1
10	P(2-furyl)$_3$	85	38	2
11	SPhos	83	10	3
12[c]	$P(4\text{-}ClC_6H_4)_3$	100	72	4
13[d]	$P(4\text{-}ClC_6H_4)_3$	40	30	0

[a] The reaction was performed using 0.1 mmol of **1a** and 0.2 mmol of **2a**. [b] Determined by GC using *n*-tridecane as an internal standard. The conversion and yield in the parentheses were determined at the reaction time of 1.5 h. [c] AgOAc was used instead of Ag_2CO_3. [d] The reaction was performed in the absence of Ag_2CO_3.

Having established the optimal catalytic system, various diarylacetylenes were subjected to the annulation reaction with **1a** (Table 2). Besides **2a** (entry 1), diarylacetylenes bearing electron-donating groups such as methoxy, methyl, and silyl groups or electron-withdrawing groups such as halogen and trifluoromethyl groups at the *para* positions participated in the reaction to afford the corresponding products **3ab**–**3ag** in moderate to good yields (entries 2–7). Diarylacetylenes bearing *meta*-substituents also afforded the desired products **3ah** and **3ai** in moderate yields (entries 8 and 9). Di(2-methoxyphenyl)acetylene smoothly participated in the reaction to afford **3aj** in 77% yield (entry 10), while di(1-naphthyl)acetylene reacted rather sluggishly (< 5% GC yield) presumably due to steric hindrance. Di(2-thienyl)acetylene was also amenable to the annulation, affording the product **3ak** in good yield (entry 11). Unfortunately, other types of alkynes such as 5-decyne, 1-phenyl-1-butyne, and diethyl acetylenedicarboxylate failed to undergo the annulation with **1a** under the present conditions.

Table 2. Annulation of **1a** with various diaryl alkynes.[a]



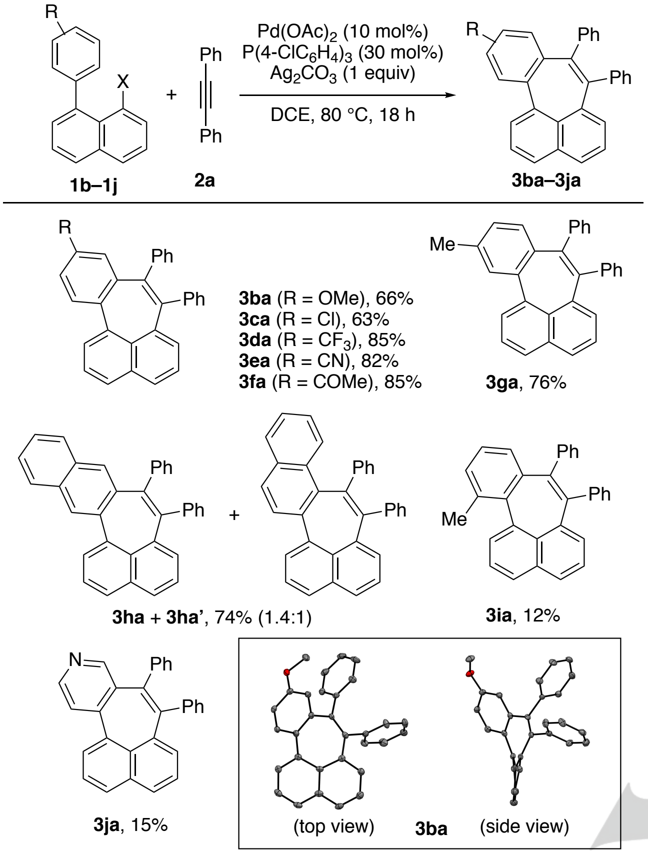
1a **2a–2k** **3aa–3ak**

Entry	Ar	Product	Yield [%]
1	Ph	**3aa**	79
2	$4\text{-}MeOC_6H_4$	**3ab**	75 (68)[b]
3	$4\text{-}MeC_6H_4$	**3ac**	63
4	$4\text{-}Me_3SiC_6H_4$	**3ad**	58
5	$4\text{-}ClC_6H_4$	**3ae**	53
6	$4\text{-}FC_6H_4$	**3af**	60
7	$4\text{-}F_3CC_6H_4$	**3ag**	55
8	$3,4\text{-}(MeO)_2C_6H_3$	**3ah**	57[c]
9	$3\text{-}MeC_6H_4$	**3ai**	67
10	$2\text{-}MeOC_6H_4$	**3aj**	77
11	2-thienyl	**3ak**	70

[a] Unless otherwise noted, the reaction was performed using 0.1 mmol of **1a** and 0.2 mmol of **2** according to the conditions in Table 1, entry 4. [b] The yield of a 0.5 mmol-scale reaction is shown in the parentheses. [c] The reaction was performed on a 0.6 mmol scale.

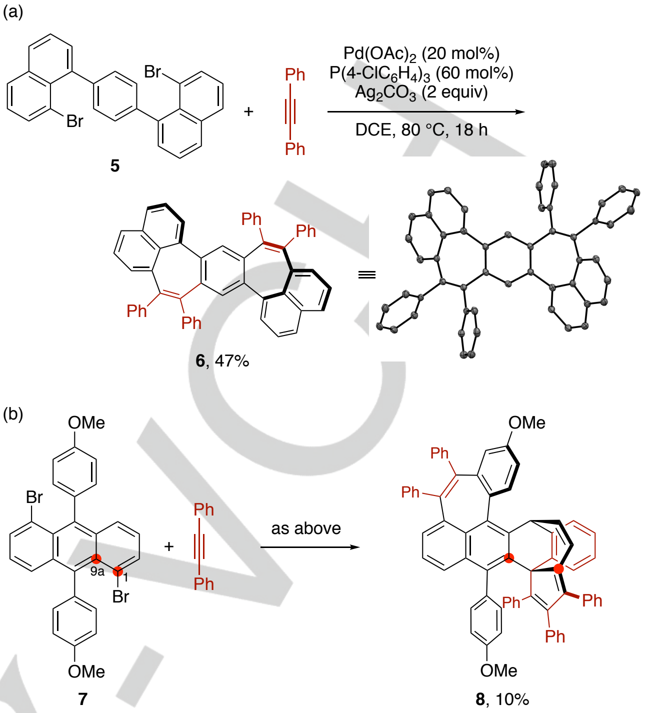
Next, a variety of 1-halo-8-arylnaphthalenes were tested for the annulation with **2a** (Scheme 2). The substrate bearing 4-methoxyphenyl and iodo groups (**1b**) smoothly underwent the annulation to afford the desired product **3ba** in 66% yield. The nonplanar structure of **3ba** was unambiguously confirmed by X-ray crystallographic analysis (see the box in Scheme 2).[11] Likewise, naphthalene substrates bearing different *para*-substituted phenyl groups (**1c**–**1f**) furnished the desired annulation products **3ca**–**3fa** in moderate to good yields. The substrate bearing a *meta*-tolyl group (**1g**) underwent exclusive annulation on the less hindered aryl C–H bond, thus affording **3ga** as the single regioisomer. By contrast, the substrate bearing a 2-naphthyl group (**1h**) afforded a mixture of the regioisomeric products **3ha** and **3ha'** with low regioselectivity, which would reflect the difficulty in controlling the regioselectivity of naphthalene C–H palladation.[12] The *ortho*-tolyl-substituted substrate reacted rather sluggishly (see **3ia**), presumably due to steric clash between the methyl group and the naphthyl ring. The reaction tolerated the substrate bearing 4-pyridyl group, albeit with low reaction efficiency (see **3ja**).

Table 3. Annulation of various 1-aryl-8-halonaphthalenes with **2a**.[a]



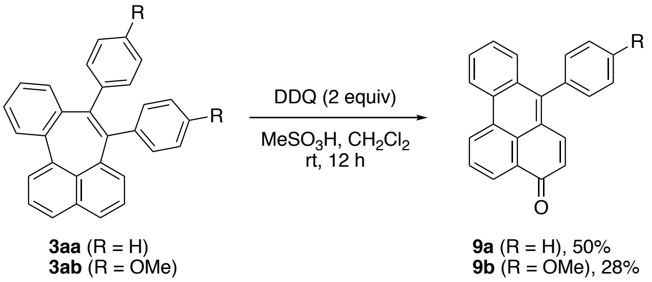
Scheme 2. Pd-catalyzed annulation of various 1-halo-8-arylnaphthalenes (**1b**–**1j**) with diphenylacetylene (**2a**). X = Br except for **1b** (X = I). The products **3ha** and **3ha'** were obtained as a mixture, and their ratio was determined by ^{1}H NMR (see the Supporting Information for more detail).

The present catalytic system proved also effective for twofold annulation between a teraryl substrate **5** bearing two 1-bromonaphthyl moieties and **2a**, which afforded the double heptagon product **6** in a respectable yield of 47% (Scheme 3a). X-ray crystallographic analysis of **6** revealed its highly nonplanar and C_i-symmetric structure and the lack of significant π-π stacking in the crystal packing.[11] By contrast, we could not detect a twofold annulation product in the reaction between 1,5-dibromo-9,10-diarylanthracene **7** and **2a**. The reaction gave multiple products, among which only an unusual 1:3 coupling product **8** could be isolated and unambiguously characterized by X-ray analysis (Scheme 4b).[11] Thus, one of the two reaction sites of **7** underwent the expected heptagon formation, while the other site reacted with two molecules of diphenylacetylene to give rise to the peculiar bridged polycyclic moiety through cleavage of the C^1–C^{9a} bond of the anthracene moiety.



Scheme 3. Attempts on twofold annulation.

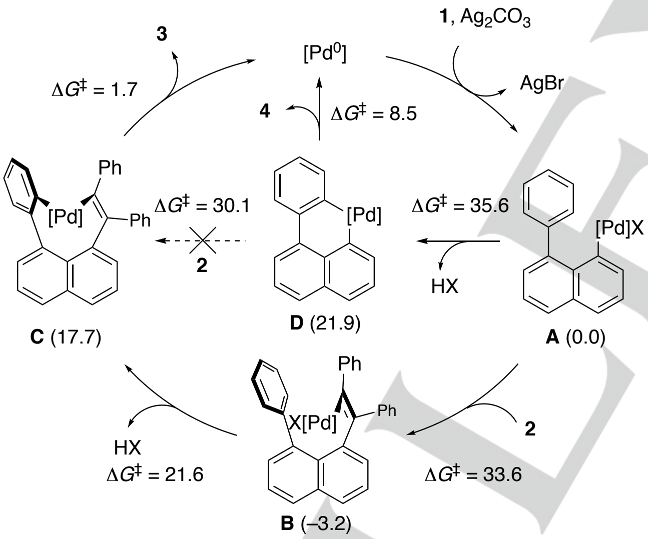
Exposure of the heptagon products **3aa** and **3ab** to DDQ/methanesulfonic acid, which is among typical conditions for the Scholl reaction,[13] did not cause expected dehydrogenative C–C coupling between the aryl substituents or between the aryl substituent and the benzo[4,5]cyclohepta[1,2,3-*de*]naphthalene core. Instead, oxidative fragmentation and ring contraction took place to afford 4*H*-benzo[*de*]anthracen-4-one derivatives **9a** and **9b** in moderate yields.[11,14] Further exploration of transformations of the present heptagon compounds is under way.



Scheme 4. Dehydrogenative cyclization leading to an extended conjugated system.

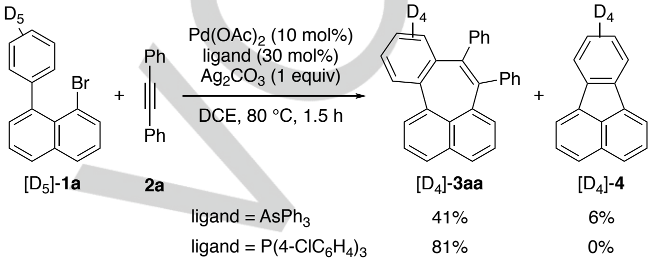
UV-vis absorption spectra of selected mono-heptagon compounds in CH_2Cl_2 featured the longest wavelength absorption maximum (λ_{max}) around 350–360 nm, showing moderate impact of the peripheral substituents on λ_{max} (see Figures S7 and S8). None of them showed visible fluorescence in dilute solution presumably due to nonradiative decay of the excited state through facile rotation of the aryl–aryl bonds. On the other hand, the bis-heptagon compound **6** showed λ_{max} of 284, 320, and 380 nm and moderate fluorescence at 558 nm (Φ = 0.38) (Figure S9). All the heptagon compounds are more distinctly emissive in the solid state, with λ_{em} of 489, 496, and 508 nm for **3ab**, **3fa**, and **6**, respectively (Figure S10). The aggregation-induced emission (AIE)[15] behavior of **3ab** was also observed using THF/water mixture samples (Figure S11). These fluorescence behaviors would be ascribed to the nonplanar geometry that prevents π-π stacking as well as the aryl–aryl bonds that freely rotate in solution but are rotationally restricted in the aggregated state.

Proposed reaction pathways of the present annulation reaction are shown in Scheme 5. Oxidative addition of the C–Br bond of **1** to Pd^0, followed by halide abstraction by Ag_2CO_3,[3a] would generate a naphthylpalladium species **A** (X = carbonate). Insertion of the alkyne **2** into **A** and subsequent intramolecular C–H palladation of the alkenylpalladium species **B**, presumably via the concerted metallation-deprotonation mechanism, would lead to an eight-membered palladacycle **C**. Finally, reductive elimination of **C** would furnish the heptagon product **3** while regenerating Pd^0. The species **A** could also undergo intramolecular C–H palladation to give a six-membered palladacycle **D**. Reductive elimination of **D** would afford fluoranthene **4**, while **D** might also undergo alkyne insertion into either of the Pd–C bonds, leading to **C** or its isomer.



Scheme 5. Proposed reaction pathways for the Pd-catalyzed annulation. Relative free energies (in parentheses) and activation energies (kcal mol^{-1}) were calculated for a model system with [Pd] = $PdP(4\text{-}ClC_6H_4)_3$ and X = OAc.

The feasibility of the key steps in the above catalytic cycle was probed by DFT calculations starting from a model 8-phenylnaphthylpalladium complex **A** bearing $P(4\text{-}ClC_6H_4)_3$ and acetate ligands (see the Supporting Information for detail). Insertion of diphenylacetylene into **A** required an activation energy ($\Delta G^‡$) of 33.6 kcal mol^{-1}, which was slightly lower than that of intramolecular C–H palladation of **A** (35.6 kcal mol^{-1}). The alkyne insertion was exergonic by 3.2 kcal mol^{-1}, and the subsequent C–H palladation of **B** and reductive elimination of **C** occurred with lower barriers. The formation of **D** was endergonic by 21.9 kcal mol^{-1}. While reductive elimination of **D** was feasible ($\Delta G^‡$ = 8.5 kcal mol^{-1}), alkyne insertion into **D** required an exceedingly higher barrier ($\Delta G^‡$ = 30.1 kcal mol^{-1}). Thus, **D** is unlikely to be responsible for the product **3**, and the selectivity between **3** and **4** would be determined by the competition between alkyne insertion and C–H palladation pathways of **A**. In agreement with this implication, the reaction of pentadeuterated substrate [D$_5$]-**1a** with **2a** using $AsPh_3$ or $P(4\text{-}ClC_6H_4)_3$ resulted in a markedly diminished yield of **4** (Scheme 6), as compared with the reaction of parent **1a** (Table 1, entries 3 and 4).



Scheme 6. Reaction of pentadeuterated substrate [D$_5$]-**1a**.

In summary, we have developed a palladium-catalyzed annulation reaction between 1-halo-8-arylnaphthalenes and diarylacetylenes. The reaction represents a rare example of direct heptagon formation from simple aromatic precursors, enabling facile preparation of PAHs with warped geometries. Further extension of the scope of heptagon-forming annulation and its application to the synthesis of novel heptagon-embedded PAHs are underway.

Acknowledgements

This work was funded by the Ministry of Education (Singapore) and Nanyang Technological University (RG 114/15 and MOE2016-T2-2-043). We thank Drs. Yongxin Li and Rakesh Ganguly (Nanyang Technological University) for assistance with X-ray crystallographic analysis, and Prof. Qichun Zhang and Dr. Changjiang Yao (Nanyang Technological University) for assistance with measurement of solid state fluorescence.

Keywords: polycyclic aromatic hydrocarbons • alkyne • C–H activation • palladium • annulation

[1] For selected reviews, see: a) J. E. Anthony, *Angew. Chem. Int. Ed.* **2008**, *47*, 452-483; b) X. Feng, W. Pisula, K. Müllen, *Pure Appl. Chem.* **2009**, *81*, 2203-2224; c) L. Chen, Y. Hernandez, X. Feng, K. Mullen, *Angew. Chem. Int. Ed.* **2012**, *51*, 7640-7654; d) A. Narita, X. Feng, K. Müllen, *Chem. Rec.* **2015**, *15*, 295-309; e) Y. Segawa, H. Ito, K. Itami, *Nat. Rev. Mater.* **2016**, *1*, 15002.

[2] H. Ito, K. Ozaki, K. Itami, *Angew. Chem. Int. Ed.* **2017**, *56*, 11144-11164.

[3] a) S. Kawasaki, T. Satoh, M. Miura, M. Nomura, *J. Org. Chem.* **2003**, *68*, 6836-6838; b) K. Ueura, T. Satoh, M. Miura, *J. Org. Chem.* **2007**, *72*, 5362-5367; c) T. Uto, M. Shimizu, K. Ueura, H. Tsurugi, T. Satoh, M.

Miura, *J. Org. Chem.* **2008**, *73*, 298-300; d) T. Fukutani, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 2867-2874; e) L. Adak, N. Yoshikai, *Tetrahedron* **2012**, *68*, 5167-5171; f) L. Ilies, A. Matsumoto, M. Kobayashi, N. Yoshikai, E. Nakamura, *Synlett* **2012**, 2381-2384; g) A. Bej, A. Chakraborty, A. Sarkar, *RSC Adv.* **2013**, *3*, 15812-15819; h) K. Komeyama, T. Kashihara, K. Takaki, *Tetrahedron Lett* **2013**, *54*, 5659-5662; i) M. V. Pham, N. Cramer, *Angew. Chem. Int. Ed.* **2014**, *53*, 3484-3487.

[4] a) G. Wu, A. L. Rheingold, S. J. Geib, R. F. Heck, *Organometallics* **1987**, *6*, 1941-1946; b) R. C. Larock, M. J. Doty, Q. Tian, J. M. Zenner, *J. Org. Chem.* **1997**, *62*, 7536-7537; c) C. Wang, S. Rakshit, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 14006-14008; d) A. Matsumoto, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2011**, *133*, 6557-6559; e) T. Nagata, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2014**, *79*, 8960-8967; f) T. Nagata, T. Satoh, Y. Nishii, M. Miura, *Synlett* **2016**, *27*, 1707-1710; g) J. Yan, N. Yoshikai, *Org. Lett.* **2017**, *19*, 6630-6633.

[5] For [4 + 2] annulation reactions using 2,2'-difunctionalized biaryls, see: a) Y. Wu, F. Wu, D. Zhu, B. Luo, H. Wang, Y. Hu, S. Wen, P. Huang, *Org. Biomol. Chem.* **2015**, *13*, 10386-10391; b) Y. Shoji, N. Tanaka, S. Muranaka, N. Shigeno, H. Sugiyama, K. Takenouchi, F. Hajjaj, T. Fukushima, *Nat. Commun.* **2016**, *7*, 12074; c) K. Ozaki, K. Murai, W. Matsuoka, K. Kawasumi, H. Ito, K. Itami, *Angew. Chem. Int. Ed.* **2017**, *56*, 1361-1364; d) K. Kanno, Y. Liu, A. Iesato, K. Nakajima, T. Takahashi, *Org. Lett.* **2005**, *7*, 5453-5456.

[6] a) K. Kawasumi, Q. Y. Zhang, Y. Segawa, L. T. Scott, K. Itami, *Nat Chem* **2013**, *5*, 739-744; b) K. Kato, Y. Segawa, L. T. Scott, K. Itami, *Chem. Asian J.* **2015**, *10*, 1635-1639; c) K. Kawai, K. Kato, L. Peng, Y. Segawa, L. T. Scott, K. Itami, *Org. Lett.* **2018**, *20*, 1932-1935.

[7] a) K. Y. Cheung, X. Xu, Q. Miao, *J. Am. Chem. Soc.* **2015**, *137*, 3910-3914; b) X. Gu, H. Li, B. Shan, Z. Liu, Q. Miao, *Org. Lett.* **2017**, *19*, 2246-2249; c) S. H. Pun, C. K. Chan, J. Luo, Z. Liu, Q. Miao, *Angew. Chem. Int. Ed.* **2018**, *57*, 1581-1586.

[8] W. C. Fu, Z. Wang, W. T. K. Chan, Z. Lin, F. Y. Kwong, *Angew. Chem. Int. Ed.* **2017**, *56*, 7166-7170.

[9] N. Chernyak, D. Tilly, Z. Li, V. Gevorgyan, *Chem. Commun.* **2010**, *46*, 150-152.

[10] a) M. Smet, J. Van Dijk, W. Dehaen, *Synlett* **1999**, 495-497; b) M. Bown, C. J. Dunn, C. M. Forsyth, P. Kemppinen, T. B. Singh, M. A. Skidmore, K. N. Winzenberg, *Aust. J. Chem.* **2012**, *65*, 145-152; c) J. E. Rice, Z.-W. Cai, *J. Org. Chem.* **1993**, *58*, 1415-1424; d) M. Yamaguchi, M. Higuchi, K. Tazawa, K. Manabe, *J. Org. Chem.* **2016**, *81*, 3967-3974.

[11] CCDC 1831779 (**3ba**), 1831782 (**6**), 1871891 (**8**), and 1871892 (**9b**) contain crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936-946.

[13] M. Grzybowski, K. Skonieczny, H. Butenschon, D. T. Gryko, *Angew. Chem. Int. Ed.* **2013**, *52*, 9900-9930.

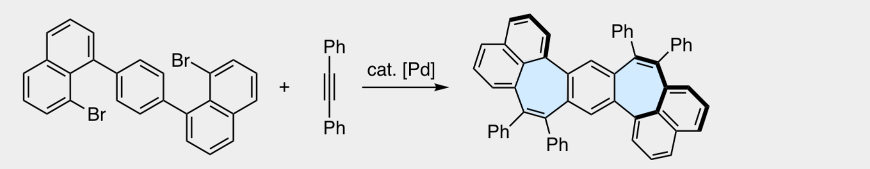
[14] See Scheme S1 for a possible reaction pathway.

[15] J. Mei, N. L. C. Leung, R. T. K. Kwok, J. W. Y. Lam, B. Z. Tang, *Chem. Rev.* **2015**, *115*, 11718-11940.

Entry for the Table of Contents (Please choose one layout)

Layout 2:

COMMUNICATION



*Jianming Yan, Md. Shafiqur Rahman, Naohiko Yoshikai**

Page No. – Page No.

Pd-Catalyzed Annulation of 1-Halo-8-arylnaphthalenes and Alkynes Leading to Heptagon-Embedded Aromatic Systems

A palladium-catalyzed annulation reaction between 1-halo-8-arylnaphthalene and diarylalkyne is reported. Using a moderately electron-poor triarylphosphine, the reaction takes place in preference to fluoranthene formation, affording benzo[4,5]cyclohepta[1,2,3-*de*]naphthalene derivatives in moderate to good yields. Twofold annulation is also achieved to access a novel heptagon-embedded polycyclic aromatic hydrocarbon.