DOI: 10.1002/adsc.201601296
Advanced Synthesis & Catalysis

Rhodium(III)-Catalyzed Cascade Redox-Neutral C–H Functionalization and Aromatization: Synthesis of Unsymmetrical *ortho*-Biphenols

Zhiyong Hu[a] and Guixia Liu[a,*]

[a] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 345 Lingling Road, Shanghai 200032, People's Republic of China
E-mail: guixia@sioc.ac.cn

Received: November 24, 2016; Revised: February 25, 2017; Published online: ■■ ■■, 0000

Supporting information for this article can be found under http://dx.doi.org/10.1002/adsc.201601296.

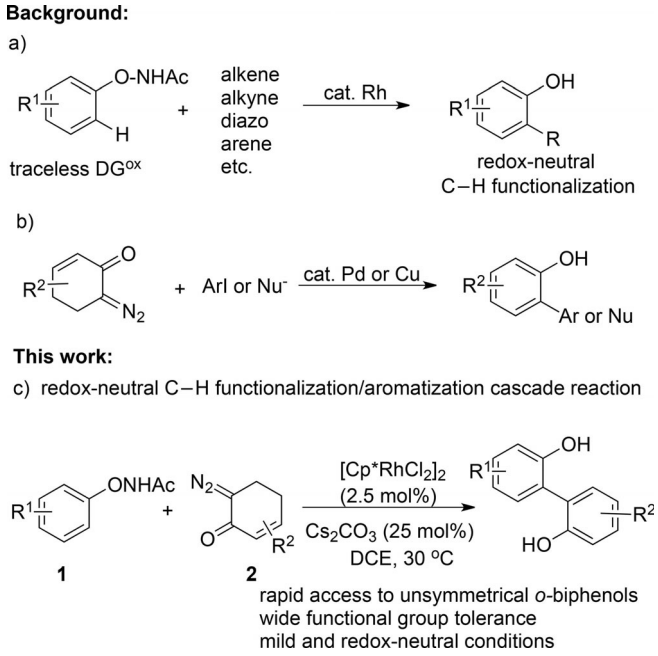
Abstract: An efficient rhodium(III)-catalyzed coupling reaction of *N*-aryloxyacetamides with 6-diazo-2-cyclohexenones through a cascade redox-neutral C–H functionalization and aromatization has been developed. This novel and scalable transformation provides a straightforward way to construct unsymmetrical *ortho*-biphenols with broad substrate scope under mild and redox-neutral conditions. The synthetic utility of this approach is demonstrated in the late-stage functionalization of bioactive compounds and the synthesis of an optically active *ortho*-biphenol.

Keywords: *ortho*-biphenols; C–H functionalization; diazo compounds; redox-neutral conditions; rhodium

ortho-Biphenols (2,2′-dihydroxy-1,1′-biaryls) are important structures featured in numerous natural and synthetic substances with a wide array of interesting biological properties.[1] Furthermore, their derivatives are useful ligands or catalysts in catalysis.[2] Therefore, the development of practical protocols to access structurally diverse *ortho*-biphenols is highly significant. Although the oxidative phenolic coupling offers a direct approach to *ortho*-biphenols,[3] the synthesis of unsymmetrical *ortho*-biphenols remains elusive[4] due to homocoupling and poor regioselectivity. Unsymmetrical *ortho*-biphenols can be constructed by indirect oxidative coupling of two phenols, in which one coupling partner is oxidized to the quinone derivative and then couples with the other phenol under organocatalysis.[5] In addition, studies on the synthesis of non-C_2-symmetical *ortho*-biphenols *via* transition metal-catalyzed C–X/C–M cross-coupling[6] or intramolecular C–H/C–X coupling have also been reported.[7] However, these approaches require selective *ortho*-halogenation of phenols and multistep synthesis, thus limiting their efficiency.

Transition metal-catalyzed C–H functionalization provides a straightforward route to construct complex organic frameworks from readily accessible substrates.[8] Recently, the redox-neutral strategy employing an oxidizing directing group[9] has been emerged in the field of C–H functionalization. This strategy avoids the use of stoichiometric amounts of an external metal oxidant and allows for a step-economical and waste-reducing transformation under mild conditions.[10] In our own efforts,[11] we developed a traceless oxidizing directing group ONHAc for the redox-neutral C–H functionalization of ArONHAc towards an efficient synthesis of *ortho*-functionalized phenols (Scheme 1a).[11,12] We envisioned that this powerful strategy could be explored for the synthesis of unsymmetrical *ortho*-biphenols.

α-Diazocyclohexenones are versatile molecules having both diazo and α,β-unsaturated carbonyl groups. They have been used as phenolic precursors in transition metal-catalyzed aromatization cascade reactions.[13] Inspired by these elegant works, we conceive α-diazocyclohexenones as an alternative arylating agent for the synthesis of unsymmetrical *o*-biphenols. While most approaches for the construction of *ortho*-biphenols are concentrated on the direct coupling of two phenolic units, few have been shown to introduce the *ortho*-phenolic group from non-aromatic precursors. Herein, we disclose a rhodium-catalyzed cascade reaction involving redox-neutral C–H functionalization and aromatization from *N*-aryloxyacetamides and 6-diazo-2-cyclohexenones (Scheme 1c). This process delivers unsymmetrical *ortho*-biphenols with diverse substitutions, some of which are difficultly accessed by traditional methods. The reaction proceeds under mild and redox-neutral conditions, and is readily scalable.



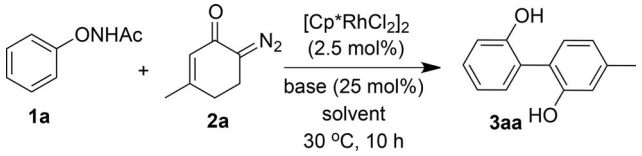
Scheme 1. Our strategy for the synthesis of unsymmetrical *ortho*-biphenols.

Our initial experiments were carried out with *N*-phenoxyacetamide (**1a**) and 6-diazo-3-methylcyclohex-2-enone (**2a**) as the model substrates to evaluate the feasibility of the proposed cascade strategy. To our delight, when the reaction was performed with the commonly used $[RhCp^*Cl_2]_2$/CsOAc catalytic system in dichloroethane at 30 °C, the desired 2,2′-biphenol **3aa** was obtained in a yield of 83% (Table 1, entry 1). Screening of bases (entries 2–6) demonstrated that Cs_2CO_3 was the most effective, affording the desired product in 88% yield (entry 4). Other bases, such as NaOAc, KOAc, K_2CO_3 and K_3PO_4, also delivered the desired product, albeit in relatively lower yields. Changing the solvent from dichloroethane to MeCN, THF, acetone and chloromethane did not cause any improvement (entries 7–10). It is noteworthy that the reaction tolerates a lower catalyst loading. The reaction proceeded smoothly even with 1.25 mol% of catalyst giving the product in 80% yield (entry 11). Fine-tuning the amounts of Cs_2CO_3 and the ratios of both substrates[14] did not further improve the yield (for a more detailed optimization study, see the Supporting Information). Notably, this transformation could run smoothly even in the absence of a base (entry 12), which may indicate that C–H activation of *N*-phenoxyacetamide could occur without the assistance of a base. Nonetheless, control experiments showed that no reaction happened in the absence of a rhodium catalyst.

The versatility of the rhodium(III)-catalyzed redox-neutral C–H functionalization/aromatization cascade process was probed under the optimized reaction conditions (Scheme 2). When diazo compound **2a** was used as the coupling partner, a diverse array of *N*-aryloxyacetamides **1** could participate in the reaction smoothly, providing the corresponding unsymmetrical 2,2′-biphenols in moderate to high yields. Substrates bearing *para*, *meta* and *ortho* substituents were compatible with the reaction conditions (**3aa**–**3fa**). For *meta*-trifluoromethyl substrate, C–H functionalization took place at the less hindered position selectively furnishing a single isomer (**3fa**). In contrast, the *meta*-methoxy-substituted substrate gave a mixture of two regioisomers (**3ga** and **3ga′**), probably because the methoxy group could play the role of a secondary directing group leading to the formation of **3ga′**. Notably, the hindered di-*meta*-substituted aromatic compounds (**1h** and **1i**) delivered the desired products (**3ha** and **3ia**) in high yields. Halogen-substituted *N*-phenoxyacetamides, including the *para*-bromo-substituted one, underwent the cascade reaction in high yields (**3ja**–**3la**) without any dehalogenation products. Besides the commonly encountered functional groups, strong electron-withdrawing functional groups, such as ester and nitro groups, were also tolerated (**3ma** and **3na**). Furthermore, *N*-naphthoxyacetamide was found to be a suitable substrate for this transformation, thus allowing the synthesis of the desired product **3oa** in high yield (90%).

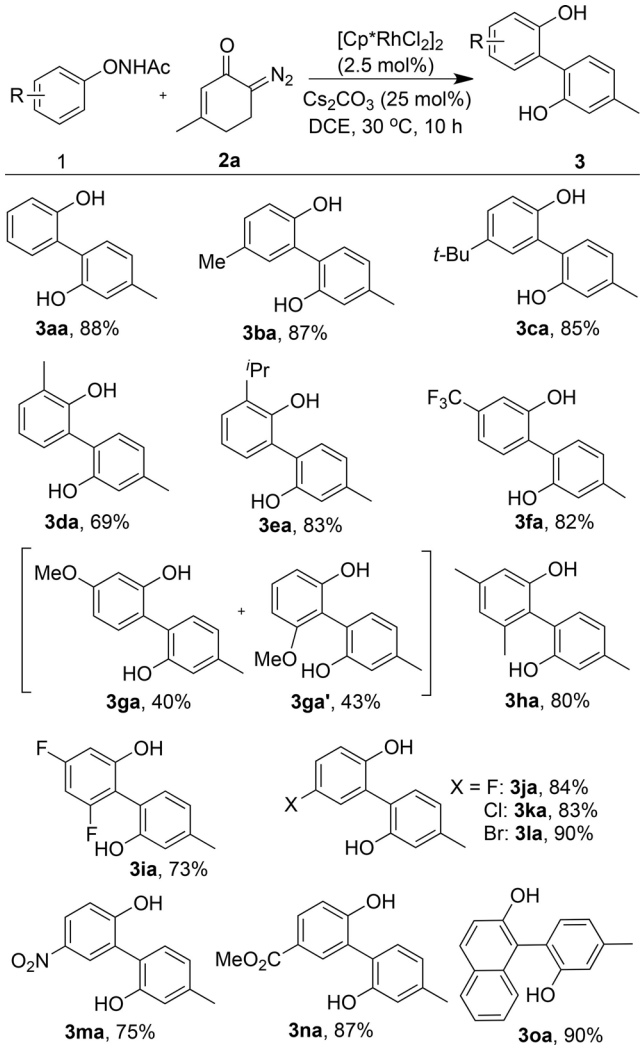
We then examined differently decorated 6-diazo-2-cyclohexenones with the protocol (Scheme 3). Various 6-diazo-2-cyclohexenones efficiently coupled with **1a**

Table 1. Optimization of the reaction conditions for the model reaction.

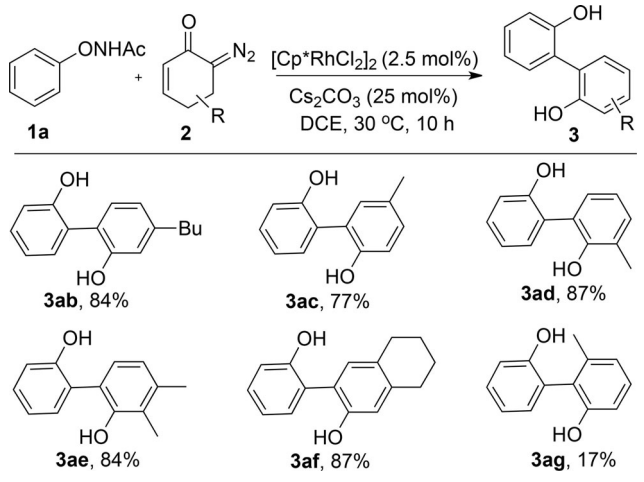


Entry[a]	Base	Solvent	Yield [%][b]
1	CsOAc	$ClCH_2CH_2Cl$	83
2	NaOAc	$ClCH_2CH_2Cl$	60
3	KOAc	$ClCH_2CH_2Cl$	60
4	Cs_2CO_3	$ClCH_2CH_2Cl$	88
5	K_2CO_3	$ClCH_2CH_2Cl$	76
6	K_3PO_4	$ClCH_2CH_2Cl$	73
7	Cs_2CO_3	MeCN	25
8	Cs_2CO_3	THF	50
9	Cs_2CO_3	CH_2Cl_2	80
10	Cs_2CO_3	acetone	58
11[c]	Cs_2CO_3	$ClCH_2CH_2Cl$	80
12	–	$ClCH_2CH_2Cl$	73

[a] *Reaction conditions:* **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.4 mmol, 2.0 equiv.), $[Cp^*RhCl_2]_2$ (2.5 mol%) and base (25 mol%) in solvent (0.1 M).
[b] Isolated yields.
[c] 1.25 mol% of $[Cp^*RhCl_2]_2$ were used.



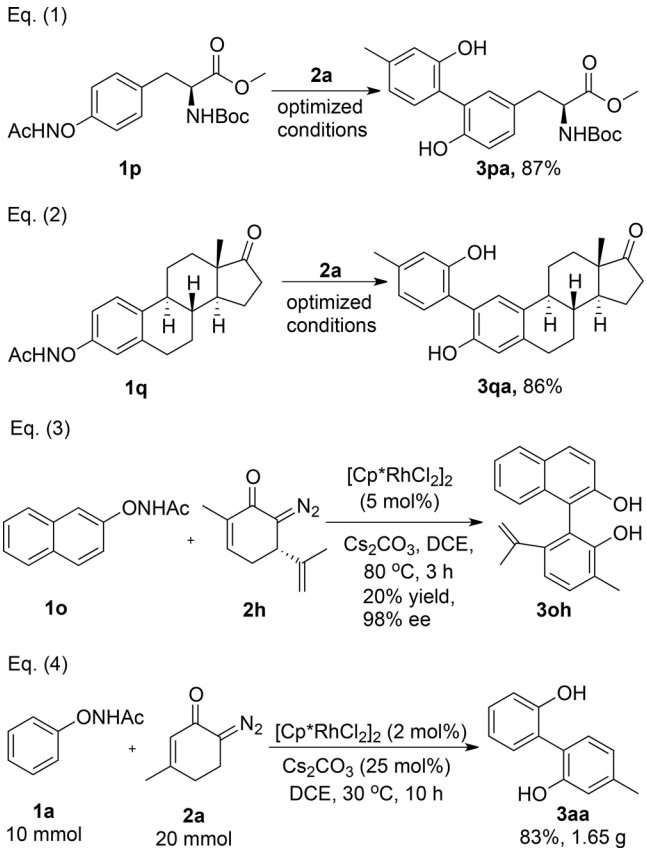
Scheme 2. Scope of the *N*-aryloxyacetamides **1**.



Scheme 3. Scope of 6-diazo-2-cyclohexenones **2**.

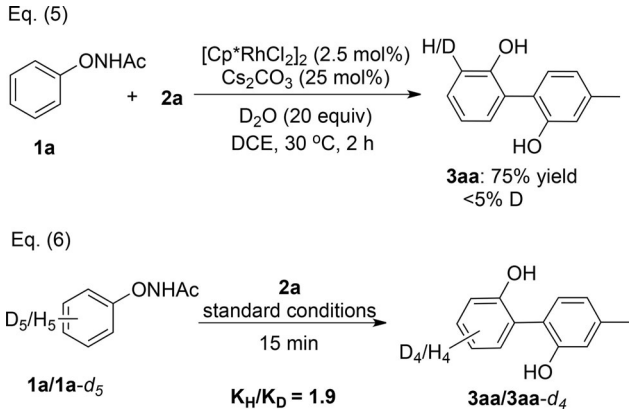
to deliver the expected *ortho*-biphenols. We observed that the reactivity of the diazo compounds was influenced by the position of the substituents. While most diazo substrates could give the corresponding products in high yields (**3aa**–**3af**), the substrate bearing a substituent adjacent to the diazo group reacted rather sluggishly (**3ag**, 17%).

The broad substrate scope and mild reaction conditions prompted us to apply the present method in the late-stage functionalization of complex bioactive compounds. Remarkably, the derivatives of L-tyrosine and estrone (**1p** and **1q**) underwent the coupling with **2a** smoothly to afford the desired 2,2′-biphenol scaffolds, which are difficult to be accessed by the traditional synthetic methods [Eqs. (1) and (2)]. Furthermore, we also tested whether our approach could be used to synthesize optical active *ortho*-biphenols from chiral 5-substituted 6-diazo-2-cyclohexenone *via* central-to-axial chirality transfer. The reaction of optical active diazo **2h** with **1o** provided the desired *orhto*-biphenol with high *ee* value (98%) albeit in a poor yield [20% yield, Eq. (3)], along with a complex mixture of side products. Finally, a relatively large-scale reaction was conducted. With 2 mol% of Rh catalyst under the standard conditions, the desired *ortho*-biphenol could be produced conveniently on a gram scale without any obvious decrease in yield [Eq. (4)].

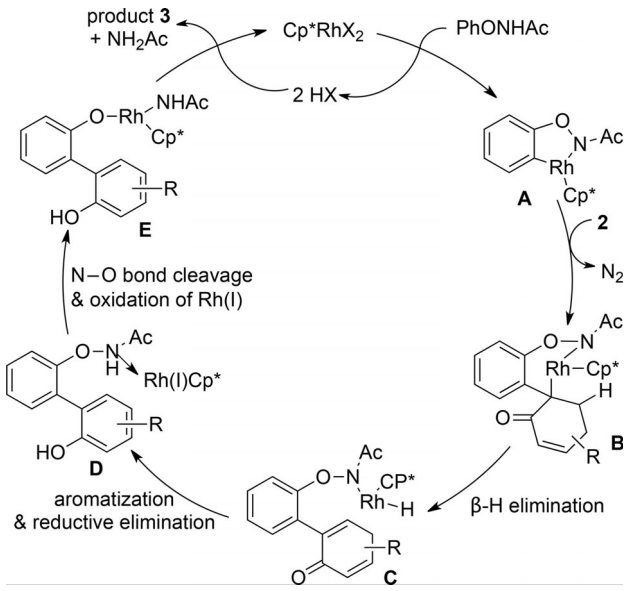


To gain some insights into the reaction mechanism, deuterium-labelling experiments were conducted. When the reaction between **1a** and **2a** was performed

in the presence of D_2O, **3aa** was obtained in a good yield and no deuterium incorporation was observed [Eq. (5)]. Next, the kinetic isotope effect was studied in competition experiments and a KIE of 1.9 was determined [Eq. (6)]. Based on these results, we propose that the C–H activation might be irreversible under the reaction conditions and the C–H bond cleavage process might not be involved in the rate-determining step.



A plausible mechanism for this redox-neutral C–H functionalization/aromatization cascade process is proposed (Scheme 4). The reaction is presumably initiated by a facile directed C–H activation to afford the intermediate **A**. According to the literature,[12a,c] the rhodacyclic intermediate **A** may react with the diazo compound **2** through metal carbene formation and migratory insertion to produce the intermediate **B** accompanied by the release of N_2.[15–17] Subsequent β-H elimination produces the intermediate **C**,[18] which undergoes aromatization and reductive elimination to furnish one *o*-phenolic group and generate the Rh(I) species (intermediate **D**). Intramolecular oxidative addition of the N–O bond to Rh(I) would give the intermediate **E**, which upon protonlysis will deliver the product **3** and regenerate the Rh(III) catalyst. For 5-substituted diazo substrates (**2g** and **2h**), the steric congestion around the diazo group may result in the low reactivity.[13a,e] It is also possible that the substituent adjacent to the diazo group may partially generate the *trans*-H intermediate **B**, which impedes the subsequent β-H elimination and results in the observed low yields.



Scheme 4. Proposed mechanism.

In conclusion, we have developed a rhodium-catalyzed cascade C–H functionalization/aromatization coupling of *N*-aryloxyacetamides with 6-diazo-2-cyclohexenones under mild and redox-neutral conditions. This process provides an efficient way for the synthesis of unsymmetrical *ortho*-biphenols with broad substrate scope. Moreover, this practical transformation could be used in the late-stage functionalization of bioactive compounds and the synthesis of an optical active *ortho*-biphenol. Further investigations on the synthetic application of this reaction are in progress.

Experimental Section

General Procedure

Without any particular precaution to exclude oxygen or moisture, *N*-aryloxyacetamide **1** (0.3 mmol, 1 equiv.), diazo compound **2** (0.6 mmol, 2 equiv.), $[Cp^*RhCl_2]_2$ (2.5 mol%, 4.8 mg) and Cs_2CO_3 (24.5 mg, 0.075 mmol, 25 mol%) were weighed into a 10-mL vial equipped with a stirring bar. Then DCE (3 mL, 0.1 M) was added. The reaction mixture was stirred at 30 °C for 10 h. Afterwards, the reaction mixture was diluted with EtOAc and transferred to a round-bottom flask. Silica gel was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel.

Acknowledgements

We thank the National Basic Research Program of China (2015CB856600), the National Natural Science Foundation of China (21202184, 21232006, 21572255), and the Chinese Academy of Science for financial support.

References

[1] a) M. C. Kozlowski, B. J. Morgan, E. C. Linton, *Chem. Soc. Rev.* **2009**, *38*, 3193; b) S. Quideau, K. S. Feldman, *Chem. Rev.* **1996**, *96*, 475; c) G. Bringmann, T. Gulder, T. A. M. Gulder, M. Breuning, *Chem. Rev.* **2011**, *111*,

563; d) K.-S. Masters, S. Bräse, *Chem. Rev.* **2012**, *112*, 3717.

[2] a) Q.-L. Zhou, *Privileged Chiral Ligands and Catalysts*, Wiley-VCH, Weinheim, **2011**; b) R. Franke, D. Selent, A. Börner, *Chem. Rev.* **2012**, *112*, 5675; c) Z. Su, W. Li, J. Wang, C. Hu, X. Feng, *Chem. Eur. J.* **2013**, *19*, 17827; d) H.-W. Zhao, Z.-H. Sheng, W. Meng, Y.-Y. Yue, H.-L. Li, X.-Q. Song, Z. Yang, *Synlett* **2013**, *24*, 2743; e) J. L. Freeman, Q. Zhao, Y. Zhang, J. Wang, C. M. Lawson, G. M. Gray, *Dalton Trans.* **2013**, *42*, 14281; f) C. Miao, G. Khalil, A. Chaumont, P. Mobian, M. Henry, *Dalton Trans.* **2016**, *45*, 7998.

[3] a) W. I. Taylor, A. R. Battersby, *Oxidative Coupling of Phenols*, Marcel Dekker, New York, **1967**; b) T. Pal, A. Pal, *Curr. Sci.* **1996**, *71*, 106; c) G. Lessene, K. S. Feldman, in: *Modern Arene Chemistry*, (Ed.: D. Astruc), Wiley-VCH, Weinheim, **2002**, Chapter 14.

[4] For a review, see: a) P. Kočovský, S. Vyskočil, M. Smrčina, *Chem. Rev.* **2003**, *103*, 3213. For some examples of oxidative cross-coupling of phenols or naphthols, see: b) K. Yamamoto, H. Yumioka, Y. Okamoto, H. Chikamatsu, *J. Chem. Soc. Chem. Commun.* **1987**, 168; c) M. Smrčina, Š. Vyskočil, B. Máca, M. Polášek, T. A. Claxton, A. P. Abbott, P. Kočovský, *J. Org. Chem.* **1994**, *59*, 2156; d) Y. E. Lee, T. Cao, C. Torruellas, M. C. Kozlowski, *J. Am. Chem. Soc.* **2014**, *136*, 6782; e) B. Elsler, D. Schollmeyer, K. M. Dyballa, R. Franke, S. R. Waldvogel, *Angew. Chem.* **2014**, *126*, 5311; *Angew. Chem. Int. Ed.* **2014**, *53*, 5210; f) N. Y. More, M. Jeganmohan, *Org. Lett.* **2015**, *17*, 3042; g) A. Libman, H. Shalit, Y. Vainer, S. Narute, S. Kozuch, D. Pappo, *J. Am. Chem. Soc.* **2015**, *137*, 11453; h) A. Wiebe, D. Schollmeyer, K. M. Dyballa, R. Franke, S. R. Waldvogel, *Angew. Chem.* **2016**, *128*, 11979; *Angew. Chem. Int. Ed.* **2016**, *55*, 11801.

[5] a) Y.-H. Chen, D.-J. Cheng, J. Zhang, Y. Wang, X.-Y. Liu, B. Tan, *J. Am. Chem. Soc.* **2015**, *137*, 15062; b) H. Cao, Q.-L. Xu, C. Keene, M. Yousufuddin, D. H. Ess, L. Kürti, *Angew. Chem.* **2016**, *128*, 576; *Angew. Chem. Int. Ed.* **2016**, *55*, 566; c) J.-Z. Wang, J. Zhou, C. Xu, H. Sun, L. Kürti, Q.-L. Xu, *J. Am. Chem. Soc.* **2016**, *138*, 5202.

[6] B. Schmidt, M. Riemer, M. Karras, *J. Org. Chem.* **2013**, *78*, 8680.

[7] a) C. Huang, V. Gevorgyan, *J. Am. Chem. Soc.* **2009**, *131*, 10844; b) C. Huang, V. Gevorgyan, *Org. Lett.* **2010**, *12*, 2442; c) K.-S. Masters, S. Bräse, *Angew. Chem.* **2013**, *125*, 899; *Angew. Chem. Int. Ed.* **2013**, *52*, 866; d) K.-S. Masters, A. Bihlmeier, W. Klopper, S. Bräse, *Chem. Eur. J.* **2013**, *19*, 17827.

[8] For some recent reviews on transition metal-catalyzed C–H functionalization, see: a) G. Rouquet, N. Chatani, *Angew. Chem.* **2013**, *125*, 11942; *Angew. Chem. Int. Ed.* **2013**, *52*, 11726; b) B. Li, P. H. Dixneuf, *Chem. Soc. Rev.* **2013**, *42*, 5744; c) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369; d) L. Ackermann, *Acc. Chem. Res.* **2014**, *47*, 281; e) X.-S. Zhang, K. Chen, Z.-J. Shi, *Chem. Sci.* **2014**, *5*, 2146; f) A. Ros, R. Fernández, J. M. Lassaletta, *Chem. Soc. Rev.* **2014**, *43*, 3229; g) G. Shi, Y. Zhang, *Adv. Synth. Catal.* **2014**, *356*, 1419; h) N. Kuhl, N. Schröder, F. Glorius, *Adv. Synth. Catal.* **2014**, *356*, 1443; i) X.-X. Guo, D.-W. Gu, Z. Wu, W. Zhang, *Chem. Rev.* **2015**, *115*, 1622.

[9] For reviews, see: a) F. W. Patureau, F. Glorius, *Angew. Chem.* **2011**, *123*, 2021; *Angew. Chem. Int. Ed.* **2011**, *50*, 1977; b) H. Huang, X. Ji, W. Wu, H. Jiang, *Chem. Soc. Rev.* **2015**, *44*, 1155; c) J. Mo, L. Wang, Y. Liu, X. Cui, *Synthesis* **2015**, *47*, 439; d) Z. Hu, X. Tong, G. Liu, *Chin. J. Org. Chem.* **2015**, *35*, 539.

[10] a) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740; b) T. Gensch, M. N. Hopkinson, F. Glorius, J. Wencel-Delord, *Chem. Soc. Rev.* **2016**, *45*, 2900.

[11] a) G. Liu, Y. Shen, Z. Zhou, X. Lu, *Angew. Chem.* **2013**, *125*, 6149; *Angew. Chem. Int. Ed.* **2013**, *52*, 6033; b) Y. Shen, G. Liu, Z. Zhou, X. Lu, *Org. Lett.* **2013**, *15*, 3366; c) Z. Zhou, G. Liu, Y. Shen, X. Lu, *Org. Chem. Front.* **2014**, *1*, 1161; d) Z. Zhou, G. Liu, Y. Chen, X. Lu, *Org. Lett.* **2015**, *17*, 5874; e) Z. Hu, X. Tong, G. Liu, *Org. Lett.* **2016**, *18*, 1702; f) Z. Zhou, G. Liu, Y. Chen, X. Lu, *Adv. Synth. Catal.* **2015**, *357*, 2944.

[12] a) F. Hu, Y. Xia, F. Ye, Z. Liu, C. Ma, Y. Zhang, J. Wang, *Angew. Chem.* **2014**, *126*, 1388; *Angew. Chem. Int. Ed.* **2014**, *53*, 1364; b) H. Zhang, K. Wang, B. Wang, H. Yi, F. Hu, C. Li, Y. Zhang, J. Wang, *Angew. Chem.* **2014**, *126*, 13450; *Angew. Chem. Int. Ed.* **2014**, *53*, 13234; c) J. Zhou, J. Shi, X. Liu, J. Jia, H. Song, H. E. Xu, W. Yi, *Chem. Commun.* **2015**, *51*, 5868; d) S. Prakash, K. Muralirajan, C.-H. Cheng, *Chem. Commun.* **2015**, *51*, 13362; e) J. Zhou, J. Shi, Z. Qi, X. Li, H. E. Xu, W. Yi, *ACS Catal.* **2015**, *5*, 6999; f) B. Li, J. Lan, D. Wu, J. You, *Angew. Chem.* **2015**, *127*, 14214; *Angew. Chem. Int. Ed.* **2015**, *54*, 14008; g) A. Lerchen, T. Knecht, C. G. Daniliuc, F. Glorius, *Angew. Chem.* **2016**, *128*, 15391; *Angew. Chem. Int. Ed.* **2016**, *55*, 15166.

[13] a) K. Yang, J. Zhang, Y. Li, B. Cheng, L. Zhao, H. Zhai, *Org. Lett.* **2013**, *15*, 808; b) D. Ding, X. Lv, J. Li, L. Qiu, G. Xu, J. Sun, *Org. Biomol. Chem.* **2014**, *12*, 4084; c) D. Ding, X. Lv, J. Li, G. Xu, B. Ma, J. Sun, *Chem. Asian J.* **2014**, *9*, 1539; d) N. Yasui, C. G. Mayne, J. A. Katzenellenbogen, *Org. Lett.* **2015**, *17*, 5540; e) H. Zhao, K. Yang, H. Zheng, R. Ding, F. Yin, N. Wang, Y. Li, B. Cheng, H. Wang, H. Zhai, *Org. Lett.* **2015**, *17*, 5744.

[14] Fine-tuning the ratio of both substrates indicated that 2 equiv. of diazo compound gave the best result, presumably due to the decomposition of the diazo compound under the reaction conditions.

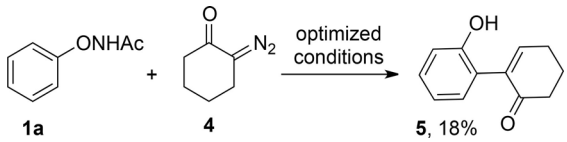
[15] For a review on transition metal-catalyzed cross-coupling reactions using the diazo compounds, see: Z. Liu, J. Wang, *J. Org. Chem.* **2013**, *78*, 10024.

[16] For some early examples of rhodium(III) catalyzed C–H functionalization with diazo compounds, see: a) W.-W. Chan, S.-F. Lo, Z. Zhou, W.-Y. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 13565; b) T. K. Hyster, K. E. Ruhl, T. Rovis, *J. Am. Chem. Soc.* **2013**, *135*, 5364; c) Z. Shi, D. C. Koester, M. Boultadakis-Arapinis, F. Glorius, *J. Am. Chem. Soc.* **2013**, *135*, 12204.

[17] For some examples of redox-neutral C–H functionalization using diazo compounds, see: a) S. Cui, Y. Zhang, D. Wang, Q. Wu, *Chem. Sci.* **2013**, *4*, 3912; b) Y. Zhang, J. Zheng, S. Cui, *J. Org. Chem.* **2014**, *79*, 6490; c) B.

Zhou, Z. Chen, Y. Yang, W. Ai, H. Tang, Y. Wu, W. Zhu, Y. Li, *Angew. Chem.* **2015**, *127*, 12289; *Angew. Chem. Int. Ed.* **2015**, *54*, 12121; d) Y. Yang, X. Wang, Y. Li, B. Zhou, *Angew. Chem.* **2015**, *127*, 15620; *Angew. Chem. Int. Ed.* **2015**, *54*, 15400; e) R. B. Dateer, S. Chang, *Org. Lett.* **2016**, *18*, 68.

[18] To trap the possible intermediate, α-diazocyclohexanone, **4** was subjected to the optimized reaction conditions. The isolation of hexenone product **5** indicates that β-H elimination occurred before aromatization, which indicates the formation of intermediate **C**.



Rhodium(III)-Catalyzed Cascade Redox-Neutral C–H Functionalization and Aromatization: Synthesis of Unsymmetrical *ortho*-Biphenols

Adv. Synth. Catal. **2017**, *359*, 1 – 7

Zhiyong Hu, Guixia Liu*