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Transition-metal-free aerobic C–O bond formation *via* C–N bond cleavage†

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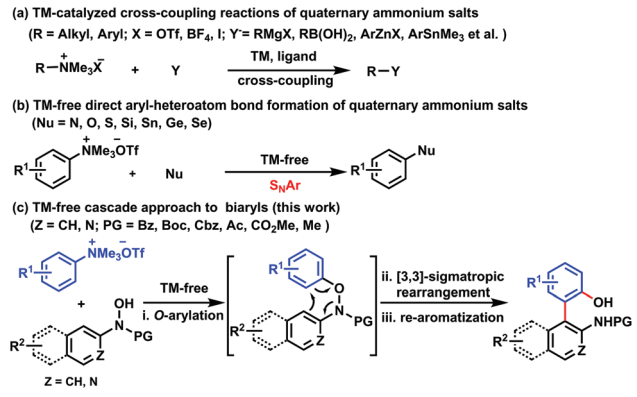
Herein, we disclosed a transition metal-free cascade protocol for the construction of 2-hydroxy-2′-amino-1,1′-biaryls that are difficult to prepare by employing conventional methods. The nucleophilic substitution of arylhydroxylamines to arylammonium salts at room temperature generates transient *N*,*O*-diarylhydroxylamines that could rapidly undergo a tandem process, including a [3,3]-sigmatropic rearrangement and rearomatization to afford NOBIN analogues.

Introduction

Amino groups are common structural motifs in many natural products, and are also found in numerous pharmaceuticals, organic dyestuff and synthetic molecules.[1] It is not surprising that numerous strategies have been developed for the preparation of amines, in particular anilines.[2] A number of amines are commercially available at a relatively low price. However, while so much attention has been focused on the C–N bond formation, it is comparatively hard to transform amino groups to other functional groups, due to the chemical inertness of the carbon–nitrogen bond.[3] Therefore, it is reasonable to conclude that the high-efficiency C–N bond conversion method, which is propitious to late-stage functionalization, would greatly facilitate the application of amine compounds as building blocks.[4] In order to overcome the difficulty of direct C–N bond cleavage, the pre-activation of anilines, for instance, converting anilines into the corresponding quaternary ammonium salts, is a promising strategy.

Quaternary ammonium salts, which can be easily prepared from various anilines (NH_2, NHMe, or NMe_2), was firstly used for Ni-catalyzed Kumada cross-coupling reaction with Grignard reagent by Wenkert *et al.* in 1980s.[5] Afterwards, their potential application was further explored by MacMillan,[6] Wang,[7] Watson[8] and others[9] for a series of TM-catalyzed C–C bond formation reactions with different organometallic reagents, for example organoboron reagent,[6,8,10] organozinc reagent,[7] and organostannyl reagent[11] (Scheme 1a). Moreover, quaternary ammonium salts have also been widely applied to numerous TM-catalyzed C–H activation[12] and C–B bond formation reactions.[13] These reports indicate that quaternary ammonium salts can serve as versatile electrophiles through C–N bond cleavage in the presence of TM catalysts and as a complementary alternative to organic halides. TM-free C–N bond fluorination of quaternary ammonium salts through a nucleophilic aromatic substitution (S_NAr) mechanism was firstly reported in 1982[14] and this method is currently applied to ^{18}F-labeling of bioactive molecules. Recently, Zhang, Wang and Uchiyama *et al.* developed diverse aryl-heteroatom bond formation reactions of arylammonium salts *via* a S_NAr process in the absence of a transition metal[15] (Scheme 1b). In these studies, aryltrimethylammonium salts serve as electrophiles to react with various heteroatom nucleophiles, including N, O, S, Si, Sn, Ge, and Se, under mild conditions.

Inspired by these elegant work, we speculated that arylhydroxylamines may react with quaternary ammonium salts



Scheme 1 Synthetic applications of quaternary ammonium salts.

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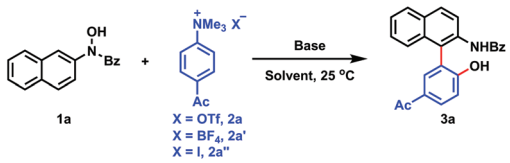
through a S_NAr pathway/C–N bond cleavage to generate a *N*,*O*-diarylhydroxylamine intermediate,[16] which could undergo a cascade [3,3]-sigmatropic rearrangement and rearomatization to form NOBIN-type (2-amino-2′-hydroxy-1,1′-binaphthyl) products (Scheme 1c).

Results and discussion

We began our investigation by conducting the reaction of *N*-hydroxy-*N*-(naphthalene-2-yl)-benzamide **1a** and 4-acetyl-*N*,*N*,*N*-trimethylbenzenaminium trifluoromethanesulfonate **2a** in the presence of various organic bases in DMF at room temperature under air. We found that the expected biaryl product **3a** was obtained in 34% yield in the presence of *t*BuOK while *t*BuONa and NaHDMS were ineffective (Table 1, entries 1–3). The screening of solvents revealed that the polar solvent DMSO was more efficient than other less polar solvents (DCE, THF, toluene and 1,4-dioxane), which is in accordance with other reported S_NAr reactions[15,16b] (Table 1, entries 4–8). When we increased the amount of aryltrimethylammonium salt **2a** from 1.2 to 1.5 equivalents, the yield of the target product was slightly decreased (Table 1, entry 9). To our delight, the corresponding biaryl product **3a** was obtained in 80% yield when we employed 2.0 equivalents of *t*BuOK rather than 1.5 equivalents (Table 1, entry 10). Other frequently used inorganic bases, including K_3PO_4, KOH, NaOH, Na_2CO_3 and K_2CO_3, were also examined and the results showed that *t*BuOK is the best option (Table 1, entries 11–15). It is worth noting that the inert atmosphere does not affect the efficiency of this cascade transformation (Table 1, entry 16). In addition, other quaternary ammonium salts **2a′** and **2a″** with different anions rather than $^-$OTf were also investigated and they were found to be less effective than **2a** (Table 1, entries 17 and 18). Finally, we found that 1.5 equivalents of aryltrimethylammonium salt **2a**, and 2.0 equivalents of *t*BuOK in DMSO at room temperature were the optimal reaction conditions (Table 1, entry 10).

Table 1 Optimization of reaction conditions[a]

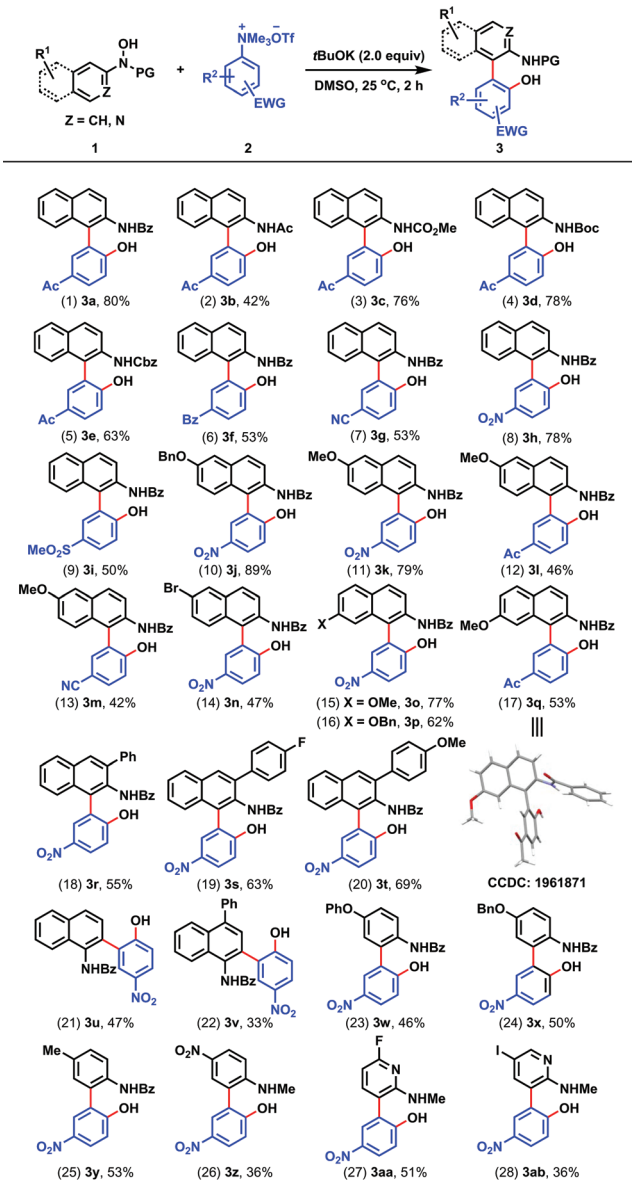


Entry	Base	Solvent	Yield[b] (%)
1	*t*BuOK	DMF	34
2	*t*BuONa	DMF	Trace
3	NaHMDS	DMF	N.P.
4	*t*BuOK	DMSO	51
5	*t*BuOK	DCE	Trace
6	*t*BuOK	THF	27
7	*t*BuOK	Toluene	26
8	*t*BuOK	1,4-Dioxane	24
9[c]	*t*BuOK	DMSO	36
10[d]	***t*BuOK**	**DMSO**	**80**
11[d]	K_3PO_4	DMSO	N.P.
12[d]	KOH	DMSO	25
13[d]	NaOH	DMSO	Trace
14[d]	Na_2CO_3	DMSO	N.P.
15[d]	K_2CO_3	DMSO	Trace
16[d,e]	*t*BuOK	DMSO	75
17[f]	*t*BuOK	DMSO	30
18[g]	*t*BuOK	DMSO	15

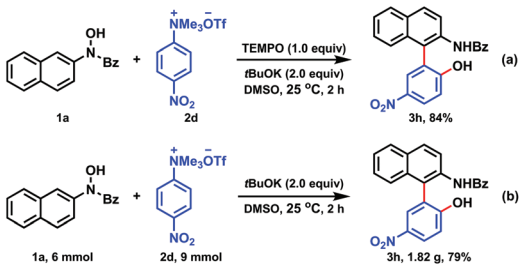
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (1.2 equiv.), base (1.5 equiv.), solvent (2 mL) under air at 25 °C for 2 h. [b] Yields of the isolated products. [c] 1.5 equivalents of **2a** were employed. [d] 1.5 equivalents of **2a** and 2.0 equivalents of base were employed. [e] Under N_2. [f] 1.5 equivalents of **2a′** and 2.0 equivalents of base were employed. [g] 1.5 equivalents of **2a″** and 2.0 equivalents of base were employed. Bz = benzoyl, Ac = acetyl, N.P. = no product.

We next investigated the scope and limitation of this reaction. In most cases, this cascade protocol proceeded smoothly to generate NOBIN analogues in moderate to good yields and excellent regioselectivities under the optimized reaction conditions (Scheme 2). We first investigated various protecting groups on the nitrogen atom of the arylhydroxylamine and the benzoyl group was found to be the best choice to afford a good yield of the expected biaryl product (Scheme 2, entries 1–5). The reaction of arylhydroxylamine **1a** and aryltrimethylammonium salts with diverse substituents on the phenyl ring revealed that strong electron-withdrawing groups, such as Bz, CN, NO_2, and SO_2Me, afforded the expected products in moderate to good yields (Scheme 2, entries 6–9). Nevertheless, the reactions of **1a** and aryltrimethylammonium salts with *para*-substituted weak electron-withdrawing groups (F, Cl, Br, CO_2Et *etc.*) or electron-donating groups (Me) or electron-neutral ammonium salts (phenyl, naphthyl) usually showed weak reactivity or complex reaction mixtures were obtained (for more details, see the ESI†).

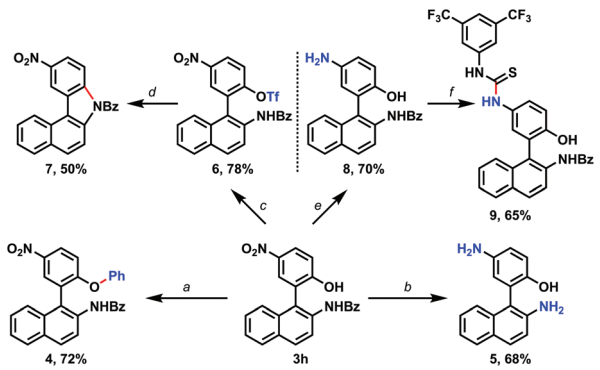
Subsequently, we turned our attention to explore the substrate scope of arylhydroxylamines in this tandem transformation (Scheme 2, entries 10–28). The variation of different substituents at the 6-, 7-, 3-position of 2-naphthalenylhydroxylamines was then evaluated. Both electron-donating groups and electron-withdrawing groups were well tolerated in this tandem reaction to afford the corresponding NOBIN-type biaryl products in moderate to good yields (Scheme 2, entries 10–20). 1-Naphthalenylhydroxylamines were amenable to this transformation as well (Scheme 2, entries 21 and 22). To our delight, this cascade protocol was also suitable to substituted phenylhydroxylamines albeit with relatively lower yields than the corresponding naphthylhydroxylamines under standard reaction conditions (Scheme 2, entries 23–26). Notably, phenylhydroxylamine with a strong electron-withdrawing group (NO_2) is applicable to this transformation when the protecting group was switched to an electron-donating group (Me) (Scheme 2, entry 26). We delightfully found that heteroarylhydroxylamines, such as *N*-(6-fluoropyridin-2-yl)-*N*-methylhydroxylamine **1t** and *N*-(5-iodopyridin-2-yl)-*N*-methylhydroxylamine **1u**, can also be introduced into this cascade reaction to afford heterobiaryl products in moderate yields (Scheme 2, entries 27 and 28). The structure of **3q** was explicitly confirmed by the single crystal X-ray diffraction study (Scheme 2, entry 17).



Scheme 2 Substrate scope. Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), *t*BuOK (0.6 mmol), DMSO (3 mL) under air at 25 °C for 2 hours. Yields of isolated products are given. Bn = benzyl.



Scheme 3 Large scale reaction and control experiments. TEMPO = 2,2,6,6-Tetramethylpiperidine 1-oxyl.



Scheme 4 Synthetic transformations of biaryl products. (a) $Cu(OAc)_2$, phenylboronic acid, Et_3N, 30 °C, 16 h. (b) Hydrazine hydrate, 150 °C, 8 h. (c) Tf_2O, pyridine, CH_2Cl_2, 0 °C, 12 h. (d) $Pd(OAc)_2$, Cs_2CO_3, toluene, reflux, 16 h. (e) $SnCl_2$, iPrOH, 100 °C, 8 h. (f) Isothiocyanate, THF, 30 °C, 12 h.

In order to gain deeper insight into the mechanism of this cascade reaction, a control experiment was conducted in the presence of a radical scavenger, such as TEMPO, and it was found that the reaction still proceeded smoothly to generate the corresponding biary product in 84% yield (Scheme 3a). This result suggested that a radical pathway can be excluded and a nucleophilic aromatic substitution mechanism is more likely in this cascade reaction.

Finally, the usefulness and practicality of this cascade protocol were exemplified by scale-up synthesis and the synthetic transformations of these biaryl products (Schemes 3b and 4). This method is synthetically practical since it is readily scalable and grams of the NOBIN-type product can be prepared in good yield under mild conditions (Scheme 3b). As shown in Scheme 4, the biaryl product **3h** can be further *O*-arylated with arylboronic acid through a Chan–Lam reaction (Scheme 4a).[17] Biaryl diamine **5** can be generated in good yield *via* the simultaneous reduction of the nitro group and deprotection of amine in one pot while hydrazine hydrate was employed (Scheme 4b).[18] Palladium-catalyzed intramolecular aminantion/cyclization of compound **6**, which is prepared from **3h** in good yield,[19] affords benzocarbazole 7 in moderate yield (Scheme 4c and d).[20] Reduction of **3h** with $SnCl_2$ gave arylaniline **8** in 70% yield,[21] which can be further converted into the corresponding thiourea in 65% yield in the presence of isothiocyanate (Scheme 4e and f).[22]

Conclusions

In conclusion, we have presented a general, operationally simple, cascade S_NAr-[3,3] rearrangement–rearomatization approach to achieve the efficient construction of NOBIN-type biaryls, which are difficult to synthesize by employing conventional methods, from (hetero)arylhydroxylamines and aryltrimethylammonium salts in the presence of a base under mild conditions. A broad range of functional groups can be well tolerated and this method provides an efficient strategy to produce structurally diverse NOBIN analogues. The transform-

ation of biaryl products presented great potential to synthesize novel atropoisomeric biaryl compounds and heterocycles. Further extension of the potential applications of biaryl products and studies of related transformation are currently undergoing in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 (*a*) H. Gao, Z. Zhou, D.-H. Kwon, J. Coombs, S. Jones, N. E. Behnke, D. H. Ess and L. Kürti, Rapid heteroatom transfer to arylmetals utilizing multifunctional reagent scaffolds, *Nat. Chem.*, 2017, **9**, 681–688; (*b*) J. Liu, X. Qiu, X. Huang, X. Luo, C. Zhang, J. Wei, J. Pan, Y. Liang, Y. Zhu, Q. Qin, S. Song and N. Jiao, From alkylarenes to anilines via site-directed carbon–carbon amination, *Nat. Chem.*, 2019, **11**, 71–77; (*c*) Z. Rappoport, *The Chemistry of Anilines, Parts 1–2*, John Wiley & Sons, 2007.

2 (*a*) F. Monnier and M. Taillefer, Catalytic C-C, C-N, and C-O Ullmann-Type Coupling Reactions, *Angew. Chem., Int. Ed.*, 2009, **48**, 6954–6971; (*b*) S. Bhunia, G. G. Pawar, S. V. Kumar, Y. Jiang and D. Ma, Selected Copper-Based Reactions for C–N, C–O, C–S, and C–C Bond Formation, *Angew. Chem., Int. Ed.*, 2017, **56**, 16136–16179.

3 (*a*) T. Koreeda, T. Kochi and F. Kakiuchi, Cleavage of C-N Bonds in Aniline Derivatives on a Ruthenium Center and Its Relevance to Catalytic C-C Bond Formation, *J. Am. Chem. Soc.*, 2009, **131**, 7238–7239; (*b*) M. Tobisu, K. Nakamura and N. Chatani, Nickel-Catalyzed Reductive and Borylative Cleavage of Aromatic Carbon-Nitrogen Bonds in N-Aryl Amides and Carbamates, *J. Am. Chem. Soc.*, 2014, **136**, 5587–5590; (*c*) X. Cong, F. Fan, P. Ma, M. Luo, H. Chen and X. Zeng, Low-Valent, High-Spin Chromium-Catalyzed Cleavage of Aromatic Carbon-Nitrogen Bonds at Room Temperature: A Combined Experimental and Theoretical Study, *J. Am. Chem. Soc.*, 2017, **139**, 15182–15190; (*d*) A. Hernan-Gomez, A. R. Kennedy and E. Hevia, C-N Bond activation and ring opening of a saturated N-heterocyclic carbene by lateral alkali-metal-mediated metalation, *Angew. Chem., Int. Ed.*, 2017, **56**, 6632–6635.

4 K. Ouyang, W. Hao, W.-X. Zhang and Z. Xi, Transition-Metal-Catalyzed Cleavage of C-N Single Bonds, *Chem. Rev.*, 2015, **115**, 12045–12090.

5 E. Wenkert, A. L. Han and C. J. Jenny, Nickel-induced conversion of carbon-nitrogen into carbon-carbon bonds. One-step transformations of aryl quaternary ammonium salts into alkylarenes and biaryls, *J. Chem. Soc., Chem. Commun.*, 1988, 975–976.

6 S. B. Blakey and D. W. C. MacMillan, The First Suzuki Cross-Couplings of Aryltrimethylammonium Salts, *J. Am. Chem. Soc.*, 2003, **125**, 6046–6047.

7 (*a*) L.-G. Xie and Z.-X. Wang, Nickel-Catalyzed Cross-Coupling of Aryltrimethylammonium Iodides with Organozinc Reagents, *Angew. Chem., Int. Ed.*, 2011, **50**, 4901–4904; (*b*) X.-Q. Zhang and Z.-X. Wang, Cross-Coupling of Aryltrimethylammonium Iodides with Arylzinc Reagents Catalyzed by Amido Pincer Nickel Complexes, *J. Org. Chem.*, 2012, **77**, 3658–3663; (*c*) X. Yang and Z.-X. Wang, Mono- and Dinuclear Pincer Nickel Catalyzed Activation and Transformation of C-Cl, C-N, and C-O Bonds, *Organometallics*, 2014, **33**, 5863–5873.

8 P. Maity, D. M. Shacklady-McAtee, G. P. A. Yap, E. R. Sirianni and M. P. Watson, Nickel-Catalyzed Cross Couplings of Benzylic Ammonium Salts and Boronic Acids: Stereospecific Formation of Diarylethanes via C-N Bond Activation, *J. Am. Chem. Soc.*, 2013, **135**, 280–285.

9 (*a*) J. T. Reeves, D. R. Fandrick, Z. Tan, J. J. Song, H. Lee, N. K. Yee and C. H. Senanayake, Room Temperature Palladium-Catalyzed Cross Coupling of Aryltrimethylammonium Triflates with Aryl Grignard Reagents, *Org. Lett.*, 2010, **12**, 4388–4391; (*b*) W.-J. Guo and Z.-X. Wang, Iron-catalyzed cross-coupling of aryltrimethylammonium triflates and alkyl Grignard reagents, *Tetrahedron*, 2013, **69**, 9580–9585; (*c*) T. Moragas, M. Gaydou and R. Martin, Nickel-Catalyzed Carboxylation of Benzylic C-N Bonds with CO_2, *Angew. Chem., Int. Ed.*, 2016, **55**, 5053–5057; (*d*) M. Guisán-Ceinos, V. Martín-Heras and M. Tortosa, Regio- and Stereospecific Copper-Catalyzed Substitution Reaction of Propargylic Ammonium Salts with Aryl Grignard Reagents, *J. Am. Chem. Soc.*, 2017, **139**, 8448–8451; (*e*) H. Ogawa, Z.-K. Yang, H. Minami, K. Kojima, T. Saito, C. Wang and M. Uchiyama, Revisitation of Organoaluminum Reagents Affords a Versatile Protocol for C–X (X = N, O, F) Bond-Cleavage Cross-Coupling: A Systematic Study, *ACS Catal.*, 2017, **7**, 3988–3994; (*f*) L.-L. Liao, G.-M. Cao, J.-H. Ye, G.-Q. Sun, W.-J. Zhou, Y.-Y. Gui, S.-S. Yan, G. Shen and D.-G. Yu, Visible-Light-Driven External-Reductant-Free Cross-Electrophile Couplings of Tetraalkyl Ammonium Salts, *J. Am. Chem. Soc.*, 2018, **140**, 17338–17342; (*g*) Z.-K. Yang, N.-X. Xu, R. Takita, A. Muranaka, C. Wang and M. Uchiyama, Cross-coupling polycondensation via C–O or C–N bond cleavage, *Nat. Commun.*, 2018, **9**, 1587; (*h*) G. Li, Y. Chen and J. Xia, Progress on Transition-Metal-Catalyzed Cross-Coupling Reactions of Ammonium Salts via C-N Bond Cleavage, *Chin. J. Org. Chem.*, 2018, **38**, 1949–1962; (*i*) R.-D. He,

C.-L. Li, Q.-Q. Pan, P. Guo, X.-Y. Liu and X.-Z. Shu, Reductive Coupling between C–N and C–O Electrophiles, *J. Am. Chem. Soc.*, 2019, **141**, 12481–12486; (*j*) D.-T. Yang, M. Zhu, Z. J. Schiffer, K. Williams, X. Song, X. Liu and K. Manthiram, Direct Electrochemical Carboxylation of Benzylic C–N Bonds with Carbon Dioxide, *ACS Catal.*, 2019, **9**, 4699–4705; (*k*) M. Miao, L.-L. Liao, G.-M. Cao, W.-J. Zhou and D.-G. Yu, Visible-light-mediated external-reductant-free reductive cross coupling of benzylammonium salts with (hetero)aryl nitriles, *Sci. China: Chem.*, 2019, **62**, 1519–1524; (*l*) Z.-X. Wang and B. Yang, Chemical transformations of quaternary ammonium salts via C-N bond cleavage, *Org. Biomol. Chem.*, 2020, **18**, 1057–1072.

10 (*a*) K. R. Buszek and N. Brown, N-Vinylpyridinium and -ammonium tetrafluoroborate salts: new electrophilic coupling partners for Pd(0)-catalyzed Suzuki cross-coupling reactions, *Org. Lett.*, 2007, **9**, 707–710; (*b*) G. De la Herran, A. Segura and A. G. Csakye, Benzylic Substitution of Gramines with Boronic Acids and Rhodium or Iridium Catalysts, *Org. Lett.*, 2007, **9**, 961–964.

11 D.-Y. Wang, M. Kawahata, Z.-K. Yang, K. Miyamoto, S. Komagawa, K. Yamaguchi, C. Wang and M. Uchiyama, Stille coupling via C–N bond cleavage, *Nat. Commun.*, 2016, **7**, 12937.

12 (*a*) F. Zhu, J.-L. Tao and Z.-X. Wang, Palladium-Catalyzed C-H Arylation of (Benzo)oxazoles or (Benzo)thiazoles with Aryltrimethylammonium Triflates, *Org. Lett.*, 2015, **17**, 4926–4929; (*b*) S. Yu, S. Liu, Y. Lan, B. Wan and X. Li, Rhodium-Catalyzed C-H Activation of Phenacyl Ammonium Salts Assisted by an Oxidizing C-N Bond: A Combination of Experimental and Theoretical Studies, *J. Am. Chem. Soc.*, 2015, **137**, 1623–1631; (*c*) T. Uemura, M. Yamaguchi and N. Chatani, Phenyltrimethylammonium Salts as Methylation Reagents in the Nickel-Catalyzed Methylation of C-H Bonds, *Angew. Chem., Int. Ed.*, 2016, **55**, 3162–3165; (*d*) F. J. R. Klauck, M. J. James and F. Glorius, Deaminative Strategy for the Visible-Light-Mediated Generation of Alkyl Radicals, *Angew. Chem., Int. Ed.*, 2017, **56**, 12336–12339; (*e*) M. Spettel, R. Pollice and M. Schnuerch, Quaternary Ammonium Salts as Alkylating Reagents in C-H Activation Chemistry, *Org. Lett.*, 2017, **19**, 4287–4290.

13 (*a*) H. Zhang, S. Hagihara and K. Itami, Making Dimethylamino a Transformable Directing Group by Nickel-Catalyzed C-N Borylation, *Chem. – Eur. J.*, 2015, **21**, 16796–16800; (*b*) J. Hu, H. Sun, W. Cai, X. Pu, Y. Zhang and Z. Shi, Nickel-catalyzed borylation of aryl- and benzyltrimethylammonium salts via C-N bond cleavage, *J. Org. Chem.*, 2016, **81**, 14–24; (*c*) C. H. Basch, K. M. Cobb and M. P. Watson, Nickel-catalyzed borylation of benzylic ammonium salts: stereospecific synthesis of enantioenriched benzylic boronates, *Org. Lett.*, 2016, **18**, 136–139; (*d*) A. M. Mfuh, J. D. Doyle, B. Chhetri, H. D. Arman and O. V. Larionov, Scalable, Metal- and Additive-Free, Photoinduced Borylation of Haloarenes and Quaternary Arylammonium Salts, *J. Am. Chem. Soc.*, 2016, **138**, 2985–2988; (*e*) S. Jin, H. T. Dang, G. C. Haug, R. He, V. D. Nguyen, V. T. Nguyen, H. D. Arman, K. S. Schanze and O. V. Larionov, Visible Light-Induced Borylation of C-O, C-N, and C-X Bonds, *J. Am. Chem. Soc.*, 2020, **142**, 1603–1613.

14 T. Irie, K. Fukushi, O. Inoue, T. Yamasaki, T. Ido and T. Nozaki, Preparation of fluorine-18-labeled 6-fluoro-9-benzylpurine and 2-fluoro-9-benzylpurine as a potential brain scanning agent, *Int. J. Appl. Radiat. Isot.*, 1982, **33**, 633–636.

15 (*a*) D.-Y. Wang, Z.-K. Yang, C. Wang, A. Zhang and M. Uchiyama, From Anilines to Aryl Ethers: A Facile, Efficient, and Versatile Synthetic Method Employing Mild Conditions, *Angew. Chem., Int. Ed.*, 2018, **57**, 3641–3645; (*b*) D.-Y. Wang, X. Wen, C.-D. Xiong, J.-N. Zhao, C.-Y. Ding, Q. Meng, H. Zhou, C. Wang, M. Uchiyama, X.-J. Lu and A. Zhang, Non-transition Metal-Mediated Diverse Aryl-Heteroatom Bond Formation of Arylammonium Salts, *iScience*, 2019, **15**, 307–315.

16 (*a*) H. Gao, D. H. Ess, M. Yousufuddin and L. Kurti, Transition-Metal-Free Direct Arylation: Synthesis of Halogenated 2-Amino-2′-hydroxy-1,1′-biaryls and Mechanism by DFT Calculations, *J. Am. Chem. Soc.*, 2013, **135**, 7086–7089; (*b*) L. Guo, F. Liu, L. Wang, H. Yuan, L. Feng, L. Kürti and H. Gao, Cascade Approach to Highly Functionalized Biaryls by a Nucleophilic Aromatic Substitution with Arylhydroxylamines, *Org. Lett.*, 2019, **21**, 2894–2898.

17 (*a*) D. M. T. Chan, K. L. Monaco, R.-P. Wang and M. P. Winters, New N- and O-arylation with phenylboronic acids and cupric acetate, *Tetrahedron Lett.*, 1998, **39**, 2933–2936; (*b*) P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters, D. M. T. Chan and A. Combs, New aryl/heteroaryl C-N bond cross-coupling reactions via arylboronic acid/cupric acetate arylation, *Tetrahedron Lett.*, 1998, **39**, 2941–2944.

18 X. Yang, G. Shan and Y. Rao, Synthesis of 2-Aminophenols and Heterocycles by Ru-Catalyzed C-H Mono- and Dihydroxylation, *Org. Lett.*, 2013, **15**, 2334–2337.

19 P. Tolstoy, S. X. Y. Lee, C. Sparr and S. V. Ley, Synthesis of Enantiomerically Enriched 3-Amino-2-oxindoles through a Palladium-Mediated Asymmetric Intramolecular Arylation of α-Ketimino Amides, *Org. Lett.*, 2012, **14**, 4810–4813.

20 T. Watanabe, S. Oishi, N. Fujii and H. Ohno, Palladium-Catalyzed Direct Synthesis of Carbazoles via One-Pot N-Arylation and Oxidative Biaryl Coupling: Synthesis and Mechanistic Study, *J. Org. Chem.*, 2009, **74**, 4720–4726.

21 (*a*) M. Jasiński, J. S. Gerding, A. Jankowiak, K. Gębicki, J. Romański, K. Jastrzębska, A. Sivaramamoorthy, K. Mason, D. H. Evans, M. Celeda and P. Kaszyński, Functional Group Transformations in Derivatives of 6-Oxoverdazyl, *J. Org. Chem.*, 2013, **78**, 7445–7454; (*b*) S. Yang, M. Chen and P. Tang, Visible-Light Photoredox-Catalyzed and Copper-Promoted Trifluoromethoxylation of Arenediazonium Tetrafluoroborates, *Angew. Chem., Int. Ed.*, 2019, **58**, 7840–7844.

22 K. Xu, W. Li, S. Zhu and T. Zhu, Atroposelective Arene Formation by Carbene-Catalyzed Formal [4 + 2] Cycloaddition, *Angew. Chem., Int. Ed.*, 2019, **58**, 17625–17630.