Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2021, **19**, 4593

Assembly of polycyclic N-heterocycles *via* copper-catalyzed cycloamination of indolylquinones and aromatic amines†

Yu Dong, *[a] Ting Mei,[a] Ji-Xian Ye,[a] Xiang-Long Chen,[a] Hui Jiang,[a] Bo Chang,[a] Zhi-Fan Wang, [a] Zhi-Chuan Shi,[b] Zhong-Hui Li*[a] and Bing He*[a]

Received 6th April 2021,
Accepted 1st May 2021

DOI: 10.1039/d1ob00666e

rsc.li/obc

The copper-catalyzed cycloamination of indolylquinones and various (hetero)aromatic amines under ligand-free conditions for the synthesis of polycyclic N-heterocycles has been developed. This method allows facile access to polycyclic N-heterocycles with the tolerance of chloride, bromide, amino, thio, *etc*. groups in moderate to high yields (60–89%).

Introduction

The nitrogen-containing heterocycle nucleus is an important structural scaffold frequently found in drugs, functional materials and natural products.[1] Among nitrogen-containing heterocycles, polycyclic N-heterocycles are widespread in nature and exhibit several interesting biological activities.[2] The representative compounds include the quinone-fused polycyclic N-heterocycles pixantrone (experimental antineoplastic drug with fewer toxic effects on cardiac tissue)[3] and ascididemin (possessing prominent cytotoxic properties)[4] and the indole-fused carbazole rebeccamycin (topoisomerase I inhibitor),[5] and the naphtho[*a*]carbazole (a potential candidate for cancer treatment)[6] (Fig. 1). On the other hand, polycyclic N-heterocycles exhibit interesting properties for application as fluorescent probes[7] and optoelectronic materials.[8]

Pentacyclic complexes bearing a quinone skeleton have been used for metal ion recognition and have also been proven to be suitable receptors for the colorimetric sensing of certain anions.[9] Owing to their various applications, numerous methods for the synthesis of annellated polycyclic complexes bearing a quinone skeleton have been developed. The representative approaches usually include the classical Friedel–Crafts reactions,[10] Lewis acid catalyzed intramolecular cyclization with a Lewis acid as a catalyst,[11] introduction of the 9,10-carbonyl functions by the oxidation of the corresponding hydrocarbon,[12] transition-metal-catalyzed oxidative cyclization,[13] and thermal or Lewis acid catalyzed Diels–Alder reaction followed by aromatization.[14] Despite their merits, many existing synthetic approaches have several shortcomings. However, some of them rely heavily on the use of expensive transition metal catalysts, and cannot avoid harsh conditions, multistep synthesis, poor yield of the proposed product and the preparation of the prerequisite functional groups.

Transition-metal-catalyzed C–H amination is a step-economical and straightforward synthetic methodology to form aromatic C–N bonds.[15] In particular, transition-metal catalyzed cross-dehydrogenative coupling (CDC) amination is highly desirable owing to aromatic amines being utilized as reactants.[16] Recently, we discovered that polycyclic N-heterocyclic complexes are synthesized by cobalt-catalyzed cycloamination reaction between indolylquinones and aromatic amines and

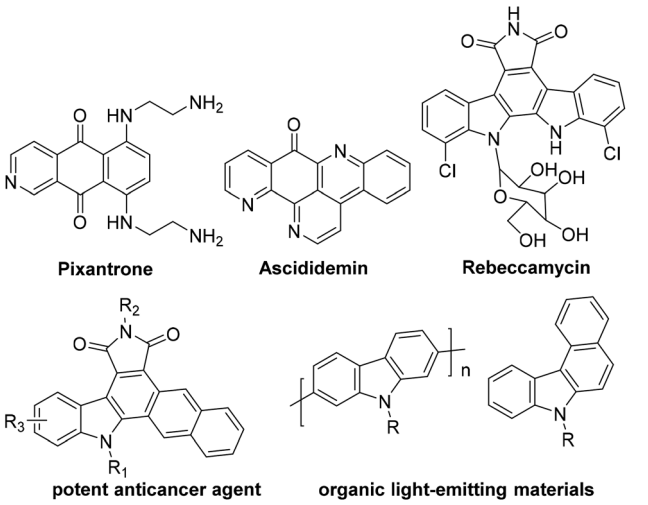
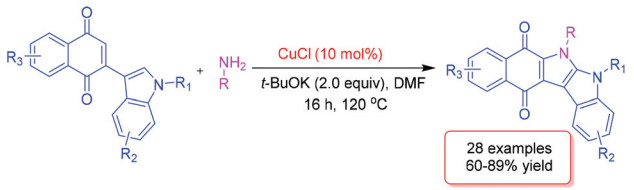


Fig. 1 A representative polycyclic N-heterocyclic complex.

[a]*College of Chemistry and Life Science, Sichuan Provincial Key Laboratory for Structural Optimization and Application of Functional Molecules, Chengdu Normal University, Chengdu, 611130, P. R. China. E-mail: ssdy1990@126.com*
[b]*Southwest Minzu University, Chengdu 610041, P. R. China*

†Electronic supplementary information (ESI) available. See DOI: 10.1039/d1ob00666e



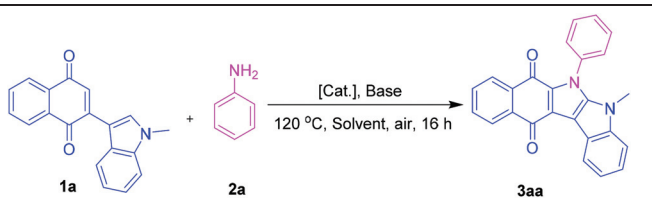
Scheme 1 Copper-catalyzed cycloamination for the synthesis of polycyclic N-heterocycles.

t-BuOK mediated oxidative coupling amination of 1,4-naphthoquinone and related 3-indolylnaphthoquinones with amines.[17] Further studies revealed that commercially available CuCl is very efficient for Cu-catalyzed cycloamination reaction between indolylquinones and aromatic amines (Scheme 1). It is noteworthy that unactivated indolylquinones and simple aromatic amines were employed as the starting materials with good functional group tolerance. Herein, we wish to disclose our results.

Results and discussion

We selected the reaction of readily available indolylnaphthoquinone (**1a**) and aniline (**2a**) as the model reaction for optimizing the CDC aromatic amination conditions (see Table 1, as well as Tables S1–S5 in the ESI†). To our delight, under the reaction of CuCl (10 mol%), *t*-BuOK (2.0 equiv.), and DMF (2 mL), at 120 °C, for 16 h (Table 1, entry 1), the desired product **3aa** was obtained in 87% isolated yield. Other metal salts including CuBr, CuI, $CuBr_2$, $Cu(OAc)_2$, $CuSO_4{\cdot}5H_2O$, $CuCl_2{\cdot}2H_2O$ and $Cu(OTf)_2$ did not provide better results for the cycloamination (entries 2–6, see the ESI†). Subsequently, the variation of *t*-BuOK to *t*-BuONa, KOH, CH_3ONa, K_2CO_3, Et_3N, or DMAP did not show any improvement (entries 7–9, see the ESI†). The reaction performed under air atmosphere in the absence of a catalyst or a base afforded very low yield of the products or no product (entries 14 or 15), which showed that the catalyst or base played a pivotal role in obtaining the desired product. The use of DMF as a solvent was crucial, as the reaction gave poor results in other solvents such as DMAC, NMP, DMSO, CH_3NO_2, DCE or CH_3CN (Table 1, entries 10–13, see the ESI†). It should be noted that increasing or decreasing the reaction temperature gave slightly inferior results, indicating that the transformation was sensitive to temperature (see the ESI†).

Table 1 Optimization of the reaction conditions[a]



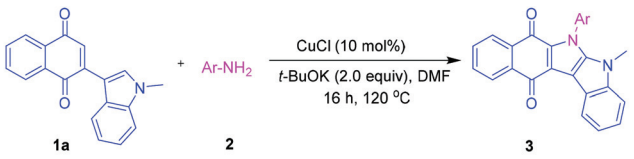
Entry	[Cat.]	Base	Solvent	Yield[b]
1	CuCl	*t*-BuOK	DMF	87
2	CuBr	*t*-BuOK	DMF	43
3	CuI	*t*-BuOK	DMF	61
4	$CuBr_2$	*t*-BuOK	DMF	49
5	$Cu(OAc)_2$	*t*-BuOK	DMF	42
6	$Cu(OTf)_2$	*t*-BuOK	DMF	45
7	CuCl	*t*-BuONa	DMF	60
8	CuCl	KOH	DMF	51
9	CuCl	DMAP	DMF	NR
10	CuCl	*t*-BuOK	DMAC	52
11	CuCl	*t*-BuOK	DMSO	31
12	CuCl	*t*-BuOK	CH_3NO_2	NR
13	CuCl	*t*-BuOK	NMP	NR
14	No	*t*-BuOK	DMF	15
15	CuCl	No	DMF	NR

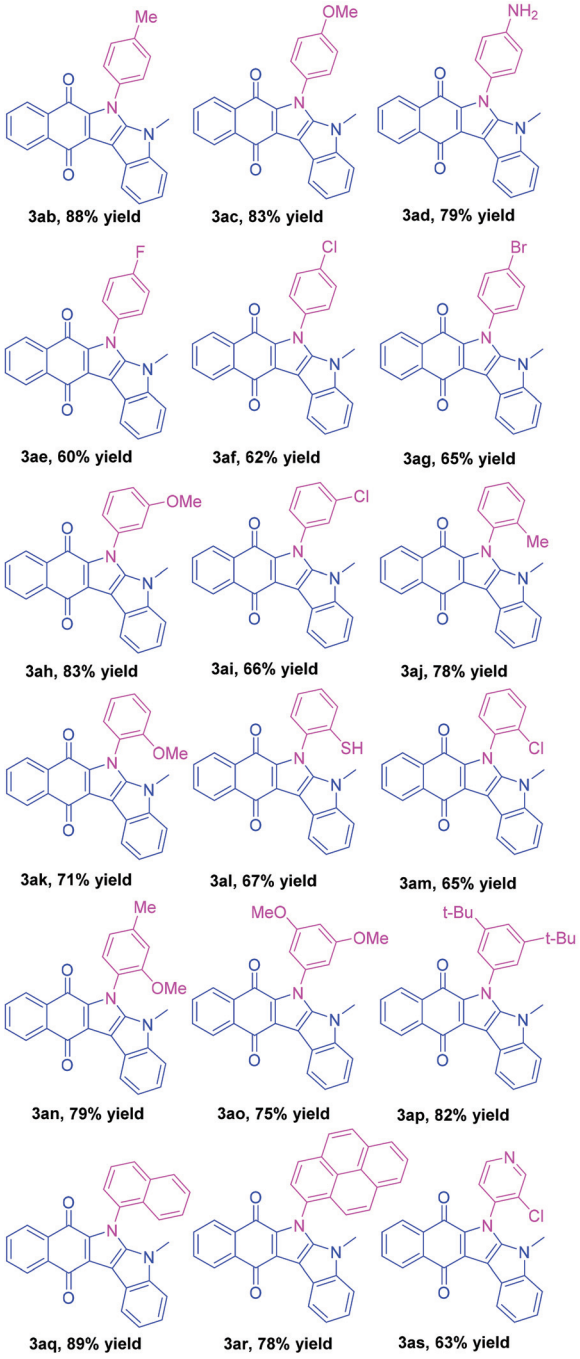
[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.6 mmol, 2.0 equiv.), [cat.] (10 mol%), base (0.6 mmol, 2.0 equiv.), solvent (2.0 mL), 16 h, air, 120 °C. [b] Isolated yield. DMF = *N*,*N*-dimethylformamide; DMAC = *N*,*N*-dimethylacetamide; NMP = *N*-methylpyrrolidone; DMSO = dimethyl sulfoxide; DMAP = 4-dimethylaminopyridine; N.R. = no reaction.

With the optimized reaction conditions in hand, subsequently, the scope of the anilines was investigated (Table 2). A variety of substituted anilines were compatible with the Cu-catalyzed cycloamination, regardless of the electronic properties of the substrates (**3ab–3ai**). It is noteworthy that the valuable groups (NH_2, SH, F, Cl, and Br) could be readily tolerated, which provides an opportunity for further elaboration. Although *ortho*-monosubstituted aromatic amines are sterically hindered even for cyclization, the *ortho*-substituted anilines underwent reactions successfully to give the corresponding aminated products (**3aj–3am**). For disubstituted anilines, the reaction was also found to proceed smoothly (**3an–3ap**). In particular, naphthylamine and aminopyrene were amenable under our reaction conditions and provided the expected cyclization products **3aq** and **3ar**. Even heteroanilines are well tolerated in this reaction. The use of aminopyridine provides moderate yields of the desired product (**3as**). The strongly coordinating groups (pyridine), which were employed as reagents for direct C–H functionalization, were fully tolerated with high chemoselectivity and regioselectivity. Unfortunately, no desired product can be obtained when aliphatic amines are used.

Next, a series of substituted indolylnaphthoquinones was tested for the cycloamination sequence (Table 3). As summarized in Table 3, the reaction was compatible with a variety of indole moieties (**1a–1i**) bearing electron-donating and electron-withdrawing substituents to produce the desired polycyclic N-heterocyclic products (**3aa–3ia**) in moderate to good yields (62–87%). Notably, the gram-scale synthesis afforded 1.50 g of **3ba** in 83% yield. To our delight, the reaction also showed good compatibility with a wide range of valuable functional groups such as fluoro (**3ha**), chloro (**3fa**), and bromo (**3ga**) groups. Tolerance to the halogen atoms was noteworthy since they have been frequently used for further modifications. *N*-Methylindoles and *N*-benzylindole naphthoquinone can smoothly react to give the corresponding products in good yields (**3aa** and **3ba**). Unfortunately, no desired product can be obtained when **1c** is used as the substrate. Moreover, we were

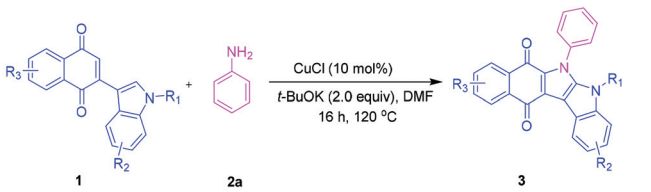
Table 2 Scope for anilines[a]

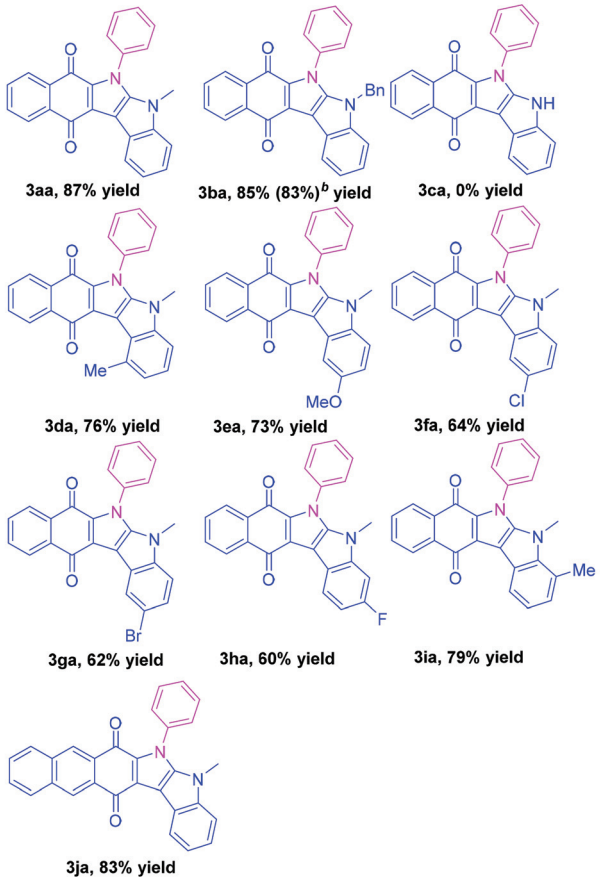




[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.6 mmol), CuCl (10 mol%), *t*-BuOK (2.0 equiv.), DMF (2.0 mL), 16 h, air, 120 °C. Isolated yield.

Table 3 Scope with respect to indolylquinones with aniline[a]

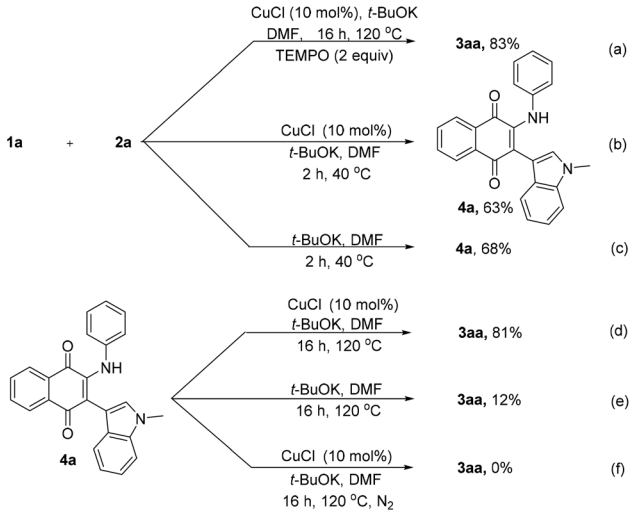




[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.6 mmol), CuCl (10 mol%), *t*-BuOK (2.0 equiv.), DMF (2.0 mL), 16 h, air, 120 °C. Isolated yield. N. R. = no reaction. [b] In a 5 mmol scale.

pleased to find that the position of the substituent on the indole moiety showed no obvious influence on the reaction outcome, and substituents at C4-(**3da**), C5-(**3ea–3ga**), C6-(**3ha**) or C7-(**3ia**) were all well tolerated in the reaction. 1,4-Anthraquinone-substituted indole **1j** was also employed, affording the corresponding product **3ja** in 83% yield.

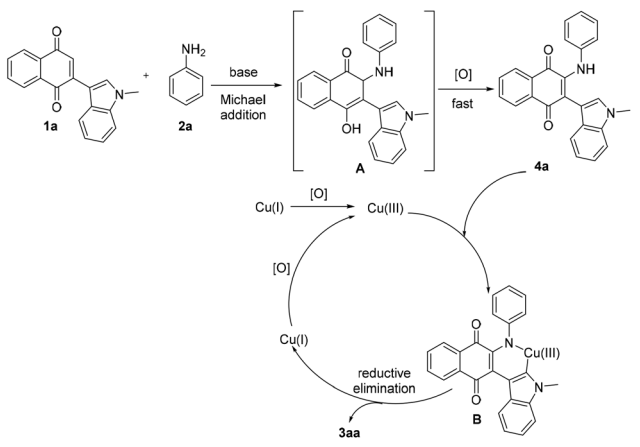
Control experiments were conducted to clarify the cycloamination reaction pathway (Scheme 2). The studies revealed that the radical scavenger TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) did not inhibit the reaction under standard conditions, ruling out the radical mechanism (Scheme 2a). At 40 °C for 2 h, the reaction of model compounds **1a** and **2a** generated the coupling product **4a** in a yield of 63% (Scheme 2b). The reaction of model compounds **1a** and **2a** generated the coupling



Scheme 2 Control experiments.

product **4a** without CuCl in a yield of 68% (Scheme 2c). The studies revealed the Michael addition process of the aniline to the quinone in the presence of a base at first. Under the standard conditions, the reaction of compound **4a** generated the product **3aa** in a yield of 81% (Scheme 2d). We surmised that the coupling product **4a** should be a key intermediate in this reaction. Without CuCl, the reaction of compound **4a** generated the product **3aa** in just 12% yield (Scheme 2e). The reaction of compound **4a** under N_2 delivered only a trace amount of the product (Scheme 2f). The studies demonstrated the importance of CuCl and O_2.

On the basis of this and previous reports, a possible reaction mechanism was proposed (Scheme 3). Initially, the Michael addition of indolylnaphthoquinone (**1a**) and aniline (**2a**) in the presence of a base gave the intermediate **A**, which was immediately oxidized to intermediate **4a** by O_2 or the oxidative naphthoquinone.[18] On the other hand, a copper salt was oxidized to the Cu(III) species in the presence of O_2, which then reacted with intermediate **4a** giving the Cu(III) species **B**.



Scheme 3 Plausible reaction mechanism.

Finally, the intermediate **B** underwent reductive elimination producing the desired product **3aa** and regenerating Cu(III) with the oxidant (O_2).[19]

Conclusions

In conclusion, we have successfully demonstrated Cu(I)-catalyzed cycloamination reaction between indolylquinones and various (hetero)aromatic amines to accomplish the polycyclic N-heterocyclic molecules. The significant aspects of our work allow modest functional group tolerance, including electron-donating and electron-withdrawing groups, which were compatible under the current methodology.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful for the financial support from the Foundation of Chengdu Normal University Talent Introduction Research Funding (2021YJRC202020), Applied Basic Research Project of Sichuan Provincial Science and Technology Department (2018JY0262) and the National Nature Science Foundation of China (grant number 21703020).

Notes and references

1 (*a*) K. Sun, Z. Shi, Z. Liu, B. Luan, J. Zhu and Y. Xue, Synthesis of (E)-β-Selenovinyl Sulfones through a Multicomponent Regio-and Stereospecific Selenosulfonation of Alkynes with Insertion of Sulfur Dioxide, *Org. Lett.*, 2018, **20**, 6687–6690; (*b*) K.-J. Li, K. Xu, Y.-G. Liu, C.-C. Zeng and B.-G. Sun, Electrochemical Dehydrogenative Cross-Coupling of Quinoxalin-2 (1H)-ones with Amines for the Synthesis of 3-Aminoquinoxalinones, *Adv. Synth. Catal.*, 2019, **361**, 1033–1041; (*c*) R. K. Konidena, W. J. Chung and J. Y. Lee, C1-, C2-, and C3-Modified Carbazole Derivatives as Promising Host Materials for Phosphorescent Organic Light-Emitting Diodes, *Org. Lett.*, 2020, **22**, 2786–2790; (*d*) D. Bader, J. Fröhlich and P. Kautny, Thienopyrrolo[3,2,1-jk]carbazoles: Building Blocks for Functional Organic Materials, *J. Org. Chem.*, 2020, **85**, 3865–3871.

2 (*a*) A. W. Schmidt, K. R. Reddy and H. J. Knolker, Occurrence, biogenesis, and synthesis of biologically active carbazole alkaloids, *Chem. Rev.*, 2012, **112**, 3193–3328; (*b*) Y. Wang, S. Wang, W. Shan and Z. Shao, Direct asymmetric N-propargylation of indoles and carbazoles catalyzed by lithium SPINOL phosphate, *Nat. Commun.*, 2020, **11**, 226.

3 A. Tomillero and M. Moral, Gateways to clinical trials, *Methods Find. Exp. Clin. Pharmacol.*, 2009, **31**, 661–700.
4 T. F. Molinski, Marine pyridoacridine alkaloids: structure, synthesis, and biological chemistry, *Chem. Rev.*, 1993, **93**, 1825–1838.
5 A. P. Salas, L. L. Zhu, C. Sanchez, A. F. Brana, J. Rohr, C. Mendez and J. A. Salas, Deciphering the late steps in the biosynthesis of the anti-tumour indolocarbazole staurosporine: sugar donor substrate flexibility of the StaG glycosyltransferase, *Mol. Microbiol.*, 2005, **58**, 17–27.
6 S. Routier, G. Coudert and J.-Y. Mérour, Synthesis of naphthopyrrolo[3,4-c]carbazoles, *Tetrahedron Lett.*, 2001, **42**, 7025–7028.
7 (*a*) K. P. Carter, A. M. Young and A. E. Palmer, Fluorescent sensors for measuring metal ions in living systems, *Chem. Rev.*, 2014, **114**, 4564–4601; (*b*) U. H. F. Bunz, J. U. Engelhart, B. D. Lindner and M. Schaffroth, Large N-Heteroacenes: New Tricks for Very Old Dogs?, *Angew. Chem., Int. Ed.*, 2013, **52**, 3810–3821.
8 (*a*) P. M. Beaujuge and J. R. Reynolds, Color control in π-conjugated organic polymers for use in electrochromic devices, *Chem. Rev.*, 2010, **110**, 268–320; (*b*) C. L. Wang, H. L. Dong, W. P. Hu, Y. Q. Liu and D. B. Zhu, Semiconducting π-conjugated systems in field-effect transistors: a material odyssey of organic electronics, *Chem. Rev.*, 2012, **112**, 2208–2267.
9 (*a*) E. E. Langdon-Jones and S. J. A. Pope, The coordination chemistry of substituted anthraquinones: Developments and applications, *Coord. Chem. Rev.*, 2014, **269**, 32–53; (*b*) R. M. F. Batista, S. P. G. Costa and M. M. M. Raposo, Selective colorimetric and fluorimetric detection of cyanide in aqueous solution using novel heterocyclic imidazoanthraquinones, *Sens. Actuators, B*, 2014, **191**, 791–799; (*c*) R. M. F. Batista, E. Oliveira, S. P. G. Costa, C. Lodeiro and M. M. M. Raposo, Synthesis and Ion Sensing Properties of New Colorimetric and Fluorimetric Chemosensors Based on Bithienyl-lmidazo-Anthraquinone Chromophores, *Org. Lett.*, 2007, **9**, 3201–3204.
10 M.-C. Jiang and C.-P. Chuang, Manganese (III) acetate initiated oxidative free radical reactions between 2-amino-1, 4-naphthoquinones and β-dicarbonyl compounds, *J. Org. Chem.*, 2000, **65**, 5409–5412.
11 (*a*) C. Jiang, M. Xu, S. Wang, H. Wang and Z.-J. Yao, Azaanthraquinone assembly from N-propargylamino quinone via a Au (I)-catalyzed 6-endo-dig cycloisomerization, *J. Org. Chem.*, 2010, **75**, 4323–4325; (*b*) N. Fei, H. Yin, S. Wang, H. Wang and Z.-J. Yao, CuCl2-Promoted 6-endo-dig Chlorocyclization and Oxidative Aromatization Cascade: Efficient Construction of 1-Azaanthraquinones from N-Propargylaminoquinones, *Org. Lett.*, 2011, **13**, 4208–4211; (*c*) C. Ding, S. Tu, Q. Yao, F. Li, Y. Wang, W. Hu and A. Zhang, One-Pot Three-Step Synthesis of Naphtho [2, 3-a] carbazole-5, 13-diones using a Tandem Radical Alkylation–Cyclization–Aromatization Reaction Sequence, *Adv. Synth. Catal.*, 2010, **352**, 847–853; (*d*) A. Borah, A. Sharma, H. Hazarika, K. Sharma and P. Gogoi, Synthesis of 1-Azaanthraquinone: Sequential C–N Bond Formation/Lewis Acid Catalyzed Intramolecular Cyclization Strategy, *J. Org. Chem.*, 2017, **82**, 8309–8316.
12 (*a*) C. B. D. Koning, J. P. Michael, J. M. Nhlapo, R. Pathak and W. A. L. V. Otterlo, The Synthesis of Naphtho[a]carbazoles and Benzo[c]carbazoles, *Synlett*, 2003, **2003**, 705–707; (*b*) R. Pathak, J. M. Nhlapo, S. Govender, J. P. Michael and C. B. D. Koning, A Concise Synthesis of Novel Naphtho[a] carbazoles and Benzo[c]carbazoles, *Tetrahedron*, 2006, **62**, 2820–2830.
13 (*a*) B. Liégault, D. Lee, M. P. Huestis, D. R. Stuart and K. Fagnou, Intramolecular Pd (II)-catalyzed oxidative biaryl synthesis under air: reaction development and scope, *J. Org. Chem.*, 2008, **73**, 5022–5028; (*b*) P. Patil, A. Nimonkar and K. G. Akamanchi, Aryl-Free Radical-Mediated Oxidative Arylation of Naphthoquinones Using o-Iodoxybenzoic Acid and Phenylhydrazines and Its Application toward the Synthesis of Benzocarbazoledione, *J. Org. Chem.*, 2014, **79**, 2331–2336; (*c*) V. Sridharan, M. A. Martin and J. C. Menendez, Acid-Free Synthesis of Carbazoles and Carbazolequinones by Intramolecular Pd-Catalyzed, Microwave-Assisted Oxidative Biaryl Coupling Reactions–Efficient Syntheses of Murrayafoline A, 2-Methoxy-3-methylcarbazole, and Glycozolidine, *Eur. J. Org. Chem.*, 2009, **2009**, 4614–4621.
14 (*a*) U. Pindur, N.-H. Kim and M. Eitel, The 3-vinylindole parent compound and its anion: New elactivity aspects, *Tetrahedron Lett.*, 1990, **31**, 1551–1552; (*b*) L. Zhou, B. Xu and J. Zhang, Metal-Free Dehydrogenative Diels–Alder Reactions of 2-Methyl-3-Alkylindoles with Dienophiles: Rapid Access to Tetrahydrocarbazoles, Carbazoles, and Heteroacenes, *Angew. Chem., Int. Ed.*, 2015, **54**, 9092–9096; (*c*) C.-W. Kuo, A. Konala, L. Lin, T.-T. Chiang, C.-Y. Huang, T.-H. Yang, V. Kavala and C.-F. Yao, Synthesis of benzo [a] carbazole derivatives from 3-ethylindoles by exploiting the dual character of benzoquinone as an oxidizing agent and dienophile, *Chem. Commun.*, 2016, **52**, 7870–7873; (*d*) Y. Guo, Z. Wang, Y. Zhu, Q. Zhang, D. Wei, X. Liu and Z. Fu, Access to polyfunctionalized carbazoles through π-extension of 2-methyl-3-oxoacetate indoles, *Org. Chem. Front.*, 2019, **6**, 3741–3745.
15 (*a*) T. Matsubara, S. Asako, L. Ilies and E. Nakamura, Synthesis of anthranilic acid derivatives through iron-catalyzed ortho amination of aromatic carboxamides with N-chloroamines, *J. Am. Chem. Soc.*, 2014, **136**, 646–649; (*b*) C. Zhu, M. Yi, D. Wei, X. Chen, Y. Wu and X. Cui, Copper-Catalyzed Direct Amination of Quinoline N-Oxides via C–H Bond Activation under Mild Conditions, *Org. Lett.*, 2014, **16**, 1840–1843; (*c*) J. Jiao, K. Murakami and K. Itami, Catalytic Methods for Aromatic C–H Amination: An Ideal Strategy for Nitrogen-Based Functional Molecules, *ACS Catal.*, 2016, **6**, 610–633.
16 (*a*) H. Kim, K. Shin and S. Chang, Iridium-catalyzed C-H amination with anilines at room temperature: compatibility of iridacycles with external oxidants, *J. Am. Chem. Soc.*, 2014, **136**, 5904–5907; (*b*) J. Roane and O. Daugulis, A

General Method for Aminoquinoline-Directed, Copper-Catalyzed sp2 C-H Bond Amination, *J. Am. Chem. Soc.*, 2016, **47**, 4601–4607; (*c*) C. Du, P.-X. Li, X. Zhu, J.-N. Han, J.-L. Niu and M.-P. Song, Cobalt-Catalyzed Oxidative C–H/N–H Cross-Coupling: Selective and Facile Access to Triarylamines, *ACS Catal.*, 2017, **7**, 2810–2814.

17 (*a*) Y. Dong, J. Yang, H. Zhang, X.-Y. Zhan, Z.-C. Shi, S. He, X.-M. Zhang and J.-Y. Wang, Cobalt-Catalyzed Cycloamination: Synthesis and Photophysical Properties of Polycyclic N-Heterocycles, *Org. Lett.*, 2020, **22**, 5151–5156; (*b*) Y. Dong, T. Mei, Q.-Q. Luo, Q. Feng, B. Chang, F. Yang, H.-w. Zhou, Z.-C. hi, J.-Y. Wang and B. He, t-BuOK mediated oxidative coupling amination of 1, 4-naphthoquinone and related 3-indolylnaphthoquinones with amines, *RSC Adv.*, 2021, **11**, 6776–6780.

18 C. d. S. Lisboa, V. G. Santos, B. G. Vaz, N. C. de Lucas, M. N. Eberlin and S. J. Garden, C–H Functionalization of 1,4-Naphthoquinone by Oxidative Coupling with Anilines in the Presence of a Catalytic Quantity of Copper(II) Acetate, *J. Org. Chem.*, 2011, **76**, 5264–5273.

19 (*a*) M. Fan, W. Zhou, Y. Jiang and D. Ma, Assembly of primary (hetero) arylamines via CuI/oxalic diamide-catalyzed coupling of aryl chlorides and ammonia, *Org. Lett.*, 2015, **17**, 5934–5937; (*b*) A. Casitas, A. E. King, T. Parella, M. Costas, S. S. Stahl and X. Ribas, Direct observation of CuI/CuIII redox steps relevant to Ullmann-type coupling reactions, *Chem. Sci.*, 2010, **1**, 326–330; (*c*) E. R. Strieter, B. Bhayana and S. L. Buchwald, Mechanistic studies on the copper-catalyzed N-arylation of amides, *J. Am. Chem. Soc.*, 2009, **131**, 78–88; (*d*) See ref. 17.