






Cite this: *RSC Adv.*, 2017, 7, 30554

Rhodium(III)-catalyzed indole-directed carbenoid aryl C–H insertion/cyclization: access to 1,2-benzocarbazoles†

Zhenhui Zhang,^a Kunkun Liu,^b Xun Chen,^a Shi-Jian Su,^a ^{*b} Yuanfu Deng ^a and Wei Zeng ^{*a}

Received 1st May 2017
 Accepted 8th June 2017

DOI: 10.1039/c7ra04889k

rsc.li/rsc-advances

A rhodium(III)-catalyzed indole-directed aryl C–H bond carbenoid insertion cascade of 2-arylindoles with diazo compounds has been developed. This method provides a rapid access to 1,2-benzocarbazoles and isoquinoline-based polycyclic heteroaromatics with a broad range of functional group tolerance. The primary evaluation of the photoluminescence property of the novel extended π -systems indicated that these heteroarenes could be potentially used in the field of optoelectronic materials.

Introduction

Fused polycyclic heteroaromatics (FPHs) have been referred to as privileged structures in complex natural products, pharmaceuticals and organic functional materials.¹ Particularly, N-fused polycycles have attracted increasing interest for their diverse photophysical properties.² For example, carbazole-based FPHs (**A**, Fig. 1) could be employed to furnish green phosphorescent organic light-emitting diodes (OLED).³ Pyran-based FPHs (**B**, Fig. 1)-containing molecular devices⁴ exhibited red emission color. Moreover, spiro-annulated triarylamine-based polycyclic heteroarenes (**C**, Fig. 1)⁵ could be used to assemble deep-blue OLED devices because these spiro molecules can provide exciton blocking and hole-injection properties due to their deep HOMO and high triplet energy level. Thus it can be seen that different core subunits generally exhibited particular optical and electroluminescent properties. However, in the past decades, although many structural skeletons have been well evaluated for their optoelectronic applications,⁶ 1,2-benzocarbazoles, especially for isoquinolinocarbazole derivative (**D**, Fig. 1) which possess excellent conformational rigidity property from the molecular backbone, have rarely been reported owing to the restriction of synthetic access to these compounds (**D**, Fig. 1).⁷

Recently, the 1,2-benzocarbazoles could be assembled relying on the construction of ring **A** and ring **B** through cascade

cyclic strategies of alkynes⁸ (Scheme 1a) and others,⁹ but most of these methods suffer from the disadvantage of requiring pre-functionalized alkynes or tedious steps. Therefore, developing more efficient method to construct 1,2-benzocarbazoles utilizing easily materials remains highly desirable and challenging. On the other hand, transition metal-catalyzed C–H carbenoid functionalization provides an atom- and step-economic approach to construct C–C bonds.¹⁰ Moreover, the reactivity of acceptor moieties of carbenoids could also be fully utilized as an internal nucleophilic partner.¹¹ From the step economy as well as the functional group diversity point of view, cascade C–H carbenoid functionalization belongs to an innovative approach to complex heterocycles. For examples, we recently reported a Rh(III)-catalyzed relay Csp²–H bond carbenoid functionalization of *N*-aryl ketoimines, in which a nucleophilic enamine derived from imine/enamine-isomerization was trapped by an acceptor ketocarbonyl moiety of diazo compounds to assemble 1-azaphenalenenes (1-APLEs). These 1-APLEs showed promising potential in optoelectronic applications due to their low-lying HOMO levels (Scheme 1b).¹² Encouraged by this work and in combination with our interest in developing cascade C–H carbenoid functionalization toward photoelectrically interesting π -conjugated molecule synthesis, we proposed that a 2-arylindole molecule which contains a nucleophilic directing indole group, could also possibly

^aKey Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510641, China. E-mail: zengwei@scut.edu.cn; Fax: +86-20-2223-6337

^bState Key Laboratory of Luminescent Materials and Devices, Institute of Polymer Optoelectronic Materials and Devices, South China University of Technology, Guangzhou 510641, China. E-mail: mssjsu@scut.edu.cn

† Electronic supplementary information (ESI) available. CCDC 1511555 and 1511559. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra04889k

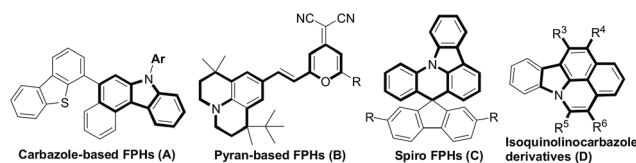
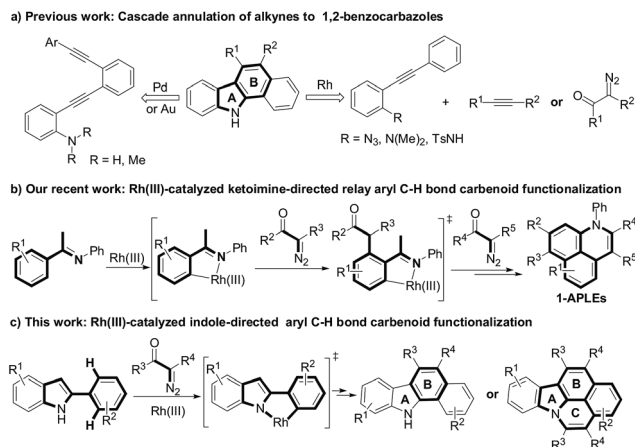


Fig. 1 Selected examples of N-fused polycycles.





Scheme 1 Aryl Csp²-H carbenoid functionalization strategies for assembling FPHs.

undergo relay carbenoid aryl C-H insertion/cyclization to furnish polycyclic heteroarenes through constructing ring B even ring C¹³ (Scheme 1c).

Results and discussion

To achieve this reaction, we commenced our study with 2-phenylindole (**1a**) and 2-diazo-3-oxobutanoic ethyl ester (**2a**) as a model reaction (Table 1). The effect of base on the cascade aryl C-H bond carbenoid insertion was first evaluated using [Cp**RhCl*₂]₂ (5 mol%) as a catalyst in combination with cocatalyst Cu(OAc)₂ (50 mol%) and additive KOAc (2.0 equiv.) in CH₃CN under an Ar atmosphere at 80 °C for 8 h (entries 1–4), and we quickly found that this catalytic system produced the major 5-ethoxycarbonyl-6-methyl-1,2-benzocarbazole **3a** under basic condition.¹⁴ Among them, Na₂CO₃ provided **3a** (62% yield) and isoquinoline-based carbazole **4a** (13% yield) (entry 2). Although the competitive aryl C-H carbenoid insertion led to poor chemoselectivity under Rh(III)/Cu(II) system, this positive result still encouraged us to conduct further optimization of the reaction conditions for achieving excellent selectivity. Low oxidation state copper(I) salt chemoselectively afforded **3a** in 84% yield under NaOAc/Na₂CO₃ system, and no **4a** was observed (compare entries 5–9 with 10). Interestingly, switching copper(I) cocatalysts into silver salts resulted in the formation of the major product **4a** when employing 2,2,2-trifluoroethanol (TFE) as solvent in the absence of Na₂CO₃ (entries 11–13). In particular, Rh(III)/AgOAc/PivOH system significantly increased the chemoselectivity of this transformation at 120 °C and provided 45% yield of **4a** (compare entries 11–13 with 14). When other alcohols such as *i*-PrOH were employed as solvents, no desired **3a** and **4a** were observed (entry 15).

With the optimized reaction conditions in hand, the scope of 2-arylindoles was then examined by employing 2-diazo-3-oxobutanoic ethyl ester (**2a**) as the coupling partner. As shown in Scheme 2, a variety of 2-arylindoles were smoothly converted to the corresponding multisubstituted 1,2-benzocarbazole derivatives in good to excellent yields. The substituents on the

Table 1 Optimization of the reaction parameters^a

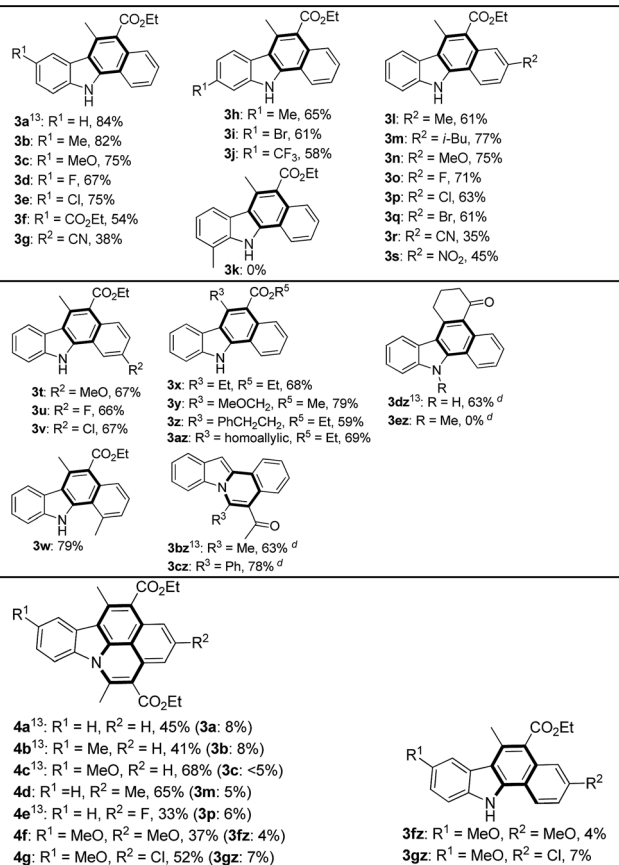
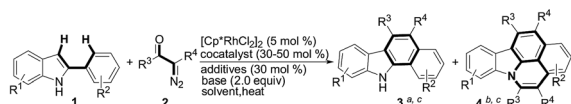
Entry	Cocatalyst	Additive	Base	Solvent	Yield (%) ^b
1	Cu(OAc) ₂	KOAc	—	CH ₃ CN	0/0
2	Cu(OAc) ₂	KOAc	Na ₂ CO ₃	CH ₃ CN	62/13
3	Cu(OAc) ₂	KOAc	NaHCO ₃	CH ₃ CN	53/19
4	Cu(OAc) ₂	KOAc	KHCO ₃	CH ₃ CN	48/28
5	CuOAc	KOAc	Na ₂ CO ₃	CH ₃ CN	61/7
6	CuBr	KOAc	Na ₂ CO ₃	CH ₃ CN	68/5
7	CuI	KOAc	Na ₂ CO ₃	CH ₃ CN	48/0
8	CuCN	KOAc	Na ₂ CO ₃	CH ₃ CN	67/20
9	CuCl	CsOAc	Na ₂ CO ₃	CH ₃ CN	58/18
10	CuCl	NaOAc	Na ₂ CO ₃	CH ₃ CN	84/0
11	Ag(NTf) ₂	AcOH	—	TFE	31/41 ^c
12	AgOAc	AcOH	—	TFE	28/39 ^c
13	AgOAc	PhCO ₂ H	—	TFE	29/35 ^c
14	AgOAc	PivOH	—	TFE	8/45 ^c
15	AgOAc	PivOH	—	<i>i</i> -PrOH	0/0 ^c

^a Unless otherwise noted, all the reactions were carried out using 2-phenylindole (**1a**) (0.20 mmol) and diazo compound (**2a**) (0.40 mmol) with [Cp**RhCl*₂]₂ catalysts (0.01 mmol, 5 mol%) in the presence of cocatalyst (copper salts: 0.10 mmol, 50 mol%; silver salts: 0.06 mmol, 30 mol%), base (0.40 mmol, 2.0 equiv.) and additives (0.06 mmol, 30 mol%) in solvent (2.0 mL) at 80 °C for 8 h under Ar in a sealed reaction tube. Followed by flash chromatography on SiO₂. ^b Isolated yield. ^c The reaction temperature was 120 °C; 0.80 mmol of diazo compound **2a** was used.

indole ring and the 2-indoly phenyl ring apparently exerts different electronic effects on the reactivity (**3a–3w**). For example, electron-rich substituents (Me, OMe) provided the corresponding 1,2-benzocarbazoles in 61–82% yields (**3b**, **3c**, **3h**, **3l**, **3n** and **3t**). On the contrary, electron-poor substituent such as CO₂Et, CN, NO₂ and CF₃ *etc.* showed poorer reactivity and afforded the target compounds in 35–58% yields (**3f**, **3g**, **3j**, **3r** and **3s**). It is worth noting that the reaction is sensitive to the substituent position in the indole rings. 5- or 6-Substituted 2-phenylindoles showed good reactivity (**3b–3j**), but 7-methyl 2-phenylindole did not furnish the desired carbazole, possibly due to steric factors (**3k**).

Moreover, the present cascade aryl C-H carbenoid insertion protocol was subsequently applied to a wide range of α -acyl-diazo compounds with particular 2-phenylindole (**1a**) as the coupling partner. As anticipated, α -alkylacyl, α -alkoxymethylacyl and α -homoallylic acyl substituted diazoacetates could easily enable assembly of 5-ethoxycarbonyl-1,2-benzocarbazoles in 59–79% yields (**3x–3az**). Meanwhile, linear α -acyl diazoketones produced the corresponding 1-indolo[2,1-*a*]isoquinolin-5-yl-ethanones **3bz** and **3cz** in 63% and 78% yields, respectively, but cyclic α -acyl diazoketones produced the desired 11*H*-benzo[*a*]carbazole **3dz** in 63% yield. If the indole





Scheme 2 Substrate scope. ^a For the synthetic procedure of product **3**: all the reactions were carried out using 2-arylimidoles (**1**) (0.20 mmol) and diazo compounds (**2**) (0.40 mmol) with [Cp*RhCl₂]₂ (5 mol%) in the presence of CuCl (50 mol%), NaOAc (30 mol%) and Na₂CO₃ (2.0 equiv.) in acetonitrile (2.0 mL) at 80 °C for 8 h under Ar in a sealed reaction tube. ^b For the synthetic procedure of product **4**: all the reactions were carried out using **1** (0.20 mmol) and **2** (0.80 mmol) with [Cp*RhCl₂]₂ (5 mol%) in the presence of AgOAc (30 mol%), PivOH (2.0 equiv.) in CF₃CH₂OH (2.0 mL) at 120 °C for 24 h under Ar in a sealed reaction tube. ^c Isolated yield. ^d Cu(OAc)₂ (50 mol%) was used.

nitrogen atom was blocked with a methyl group, this transformation did not occur (**3ez**).

Next, Rh(III)/Ag(I) system catalyzed double aryl C–H carbonyl insertion cyclization between 2-arylimidoles and 2-diazo-3-oxobutanoic ethyl ester (**2a**) was further investigated. As shown in Scheme 2 (**4a–4g**), various methyl, alkoxy and halo-substituted 2-aryl-indoles could be smoothly employed to furnish isoquinolinocarbazoles (**4a–4g**) in acceptable yields (33–56%).¹² It should be noted that around 5% yields of 1,2-benzocarbazoles (**3a–3c**, **3m**, **3p**, **3fz** and **3gz**) were observed.

Finally, the photo-physical properties, quantum yields and fluorescence lifetime spectrometer of partial molecules were explored systematically. The data of absorption and photoluminescence wavelength, the molar absorption coefficients (ϵ)

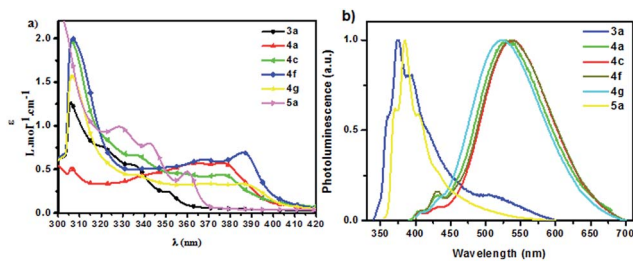


Fig. 2 UV-vis absorption (a) and emission spectra (b) of the compounds **3a**, **4a**, **4c**, **4f**, **4g** and **5a** in dichloromethane solutions (10^{-5} M).

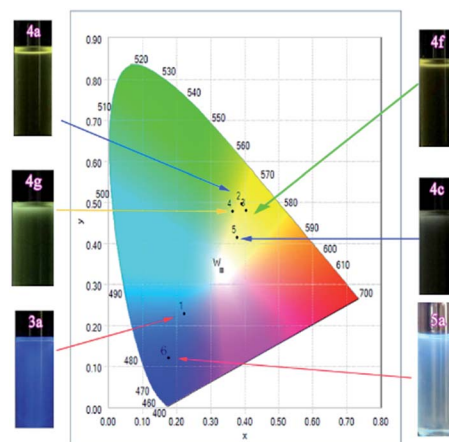


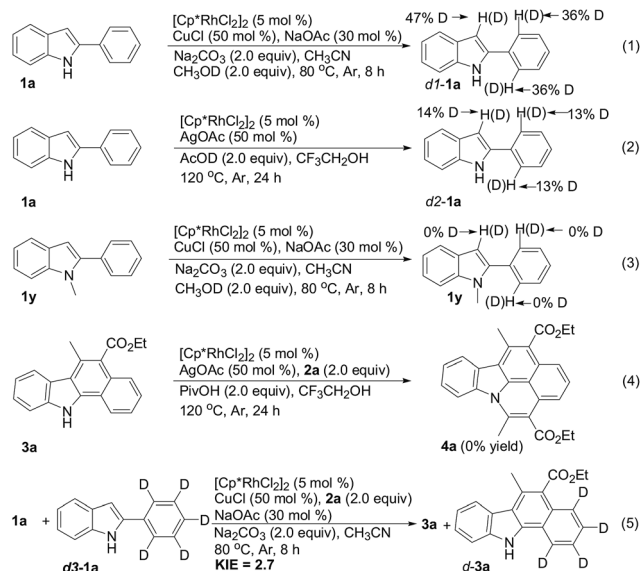
Fig. 3 Emission color change of **3a**, **4a**, **4c**, **4f**, **4g**, and **5a** in dichloromethane (10^{-5} M) upon excitation at 365 nm.

and the excited state lifetimes (τ) as well as quantum yields (Φ) of the selected compounds **3a**, **4a**, **4c**, **4f**, **4g** and **5a**¹⁵ in CH₂Cl₂ are listed in Table S-1.† As shown in Fig. 2, the emission spectra of **3a** and **5a** showed a peak at 374 nm and 386 nm, respectively. In contrast, the other compounds exhibited obvious bathochromic shifts (521–539 nm) in emission.¹⁶

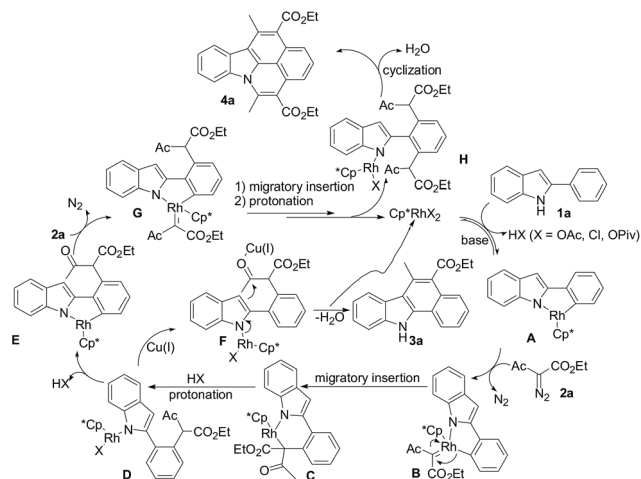
Their emission colour change in dichloromethane (10^{-5} M) under UV excitation (365 nm) further indicated that **3a** and **5a** showed blue light, while the others exhibited yellow light under UV excitation (Fig. 3). These results demonstrated molecules **4a**, **4c**, **4f** and **4g** were potential for furnishing white OLED devices.¹⁷

Several control experiments were performed to further explore the possible mechanism (Scheme 3). First, the H/D exchange of 2-phenylimidole **1a** was conducted in a Rh(III)/Cu(I)/CH₃OD or Rh(III)/Ag(I)/AcOD system in the absence of diazo compounds, and 36% and 13% deuterium incorporation at the 2-indolylphenyl ring C2- and C6-position was observed, respectively (eqn (1) and (2)). And also, the H/D exchange of C3-position from indole ring occurred possibly due to that indole C3-position possesses strong nucleophilic properties and easily attacks rhodium cation followed by metal protonation. On the contrary, no H/D exchange of *N*-methyl-2-phenylimidole **1y** was observed under the same conditions (eqn (3)), this fact implied that the indole NH moiety played a key role of chelation in





Scheme 3 Preliminary mechanistic studies.



Scheme 4 Proposed mechanism.

promoting 2-indolylphenyl ring C–H bond cleavage. Subsequently, treating 1,2-benzocarbazole 3a with diazo compound 2a under a Rh(III)/Ag(I)/PivOH system did not furnish the corresponding isoquinoline-based carbazole 4a. This control experiment also demonstrated that 1,2-benzocarbazole 3a was not the intermediate to form product 4a (eqn (4)). Finally, the competitive isotope effect ($k_H/k_D = 2.7$) further indicated that 2-indolylphenyl C–H bond-breaking was possibly involved in the rate-limiting step of 1,2-benzocarbazole-forming reaction (eqn (5)) (see ESI† for more details).

A proposed catalytic cycle is shown in Scheme 4. The initial N-coordination of 2-phenylindole 1a to Rh(III) catalyst followed by 2-indolylphenyl C–H bond activation afforded rhodacycle intermediate A to generate Rh-carbene species B, which would undergo migratory insertion and protonolysis to form rhodacycle intermediate C and complex D, respectively.^{18,19}

Subsequently, Rh(III)/Cu(I) system catalyzed cyclization of D to furnish 1,2-benzocarbazole 3a, in which Cu(I) salts played a role of Lewis acid to activate keto-carbonyl group of F. Meanwhile, complex D could also further undergo the secondary indole-directed phenyl C–H carbenoid insertion/cyclization cascade under Rh(III)/Ag catalytic system to produce isoquinoline-based carbazole 4a.

Conclusions

In summary, we have developed a Rh(III)-catalyzed, indole-directed phenyl C–H bond carbenoid insertion/cyclization of 2-phenylindoles²⁰ with alpha-acyl diazo compounds²¹ for rapid assembly of 1,2-benzocarbazoles and isoquinoline-based carbazoles. Further exploring the photoelectronic performance of isoquinoline-based carbazoles demonstrated that these compounds could be further assembled within promising optoelectronic devices.

Acknowledgements

The authors thank the National Key Research and Development Program of China (No. 2016YFA0602900), the NSFC (No. 21372085), and the Science and Technology Program of Guangzhou (No. 156300075) for financial support.

Notes and references

- For selected reviews, see: (a) W. Jiang, Y. Li and Z. Wang, *Chem. Soc. Rev.*, 2013, **42**, 6113; (b) C. Beemelmans and H. U. Reissig, *Chem. Soc. Rev.*, 2011, **40**, 2199 and reference therein.
- For selected examples, see: (a) Z. Q. Jiang, Z. Y. Liu, C. L. Yang, C. Zhong, J. G. Qin, G. Yu and Y. Q. Liu, *Adv. Funct. Mater.*, 2009, **19**, 3987; (b) M. S. Park and J. Y. Lee, *Chem. Mater.*, 2011, **23**, 4338; (c) Z. Q. Jiang, Y. H. Chen, C. Fan, C. L. Yang, Q. Wang, Y. T. Tao, Z. Q. Zhang, J. G. Qin and D. G. Ma, *Chem. Commun.*, 2009, **45**, 3398; (d) T. Mitsumori, M. Bendikov, O. Dautel, F. Wudl, T. Shioya, H. Sato and Y. Sato, *J. Am. Chem. Soc.*, 2004, **126**, 16793.
- Y. Chen, W. Liang, W. H. Choi, J. Huang, Q. Dong, F. Zhua and J. Su, *Dyes Pigm.*, 2015, **123**, 196.
- K. H. Lee, M. H. Park, C. S. Kim, Y. K. Kim and S. S. Yoon, *Thin Solid Films*, 2011, **520**, 510.
- M. Kim and J. Y. Lee, *Org. Electron.*, 2012, **13**, 1245.
- For selected examples, see: (a) X. Qin, X. Li, Q. Huang, H. Liu, D. Wu, Q. Guo, J. Lan, R. Wang and J. You, *Angew. Chem., Int. Ed.*, 2015, **54**, 7167; (b) T. H. Huang, W. T. Whang, J. Y. Shen, Y. S. Wen, J. T. Lin, T. H. Ke, L. Y. Chen and C. C. Wu, *Adv. Funct. Mater.*, 2006, **16**, 1449; (c) E. Ahmed, T. Earmme, G. Q. Ren and S. A. Jenekhe, *Chem. Mater.*, 2010, **22**, 5786; (d) T. Spehr, R. Pudzych, T. Fuhrmann and J. Salbeck, *Org. Electron.*, 2003, **4**, 61; (e) K. R. J. Thomas, J. T. Lin, Y. T. Tao and C. H. Chuen, *Adv. Mater.*, 2002, **14**, 822.
- (a) S. Ito, Y. Tokimaru and K. Nozaki, *Angew. Chem., Int. Ed.*, 2015, **54**, 7256; (b) Z. Shi, S. Ding, Y. Cui and N. Jiao, *Angew.*



- Chem., Int. Ed.*, 2009, **48**, 7895; (c) R. Xie, Y. Ling and H. Fu, *Chem. Commun.*, 2012, **48**, 12210.
- 8 (a) X. F. Xia, N. Wang, L. L. Zhang, X. R. Song, X. Y. Liu and Y. M. Liang, *J. Org. Chem.*, 2012, **77**, 9163; (b) N. Li, X. L. Lian, Y. H. Li, T. Y. Wang, Z. Y. Han, L. Zhang and L. Z. Gong, *Org. Lett.*, 2016, **18**, 4178.
- 9 For selected examples, see: (a) S. Protti, A. Palmieri, M. Petrini, M. Fagnoni, R. Ballini and A. Albini, *Adv. Synth. Catal.*, 2013, **355**, 643; (b) F. Sha, Y. Tao, C. Y. Tang, F. Zhang and X. Y. Wu, *J. Org. Chem.*, 2015, **80**, 8122; (c) N. J. Truax, F. B. Mejia, D. O. Kwansare, M. M. Lafferty, M. H. Kean and E. T. Pelkey, *J. Org. Chem.*, 2016, **81**, 6808.
- 10 For selected examples, see: (a) A. Gutierrez-Bonet, F. Julia-Hernandez, B. de Luis and R. Martin, *J. Am. Chem. Soc.*, 2016, **138**, 6384; (b) R. S. Phatake, P. Patel and C. V. Ramana, *Org. Lett.*, 2016, **18**, 2828; (c) W. W. Chan, S. F. Lo, Z. Zhou and W. Y. Yu, *J. Am. Chem. Soc.*, 2012, **134**, 13565; (d) K. Shibata and N. Chatani, *Chem. Sci.*, 2016, **7**, 240; (e) S. Yu, S. Liu, Y. Lan, B. Wan and X. Li, *J. Am. Chem. Soc.*, 2015, **137**, 1623; (f) Y. Xia, Z. Liu, Z. Liu, R. Ge, F. Ye, M. Hossain, Y. Zhang and J. Wang, *J. Am. Chem. Soc.*, 2014, **136**, 3013; (g) Z. Shi, D. C. Koester, M. Boultadakis-Arapinis and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 12204; (h) T. K. Hyster, K. E. Ruhl and T. Rovis, *J. Am. Chem. Soc.*, 2013, **135**, 5364.
- 11 For selected examples, see: (a) D. Zhao, J. H. Kim, L. Stegemann, C. A. Strassert and F. Glorius, *Angew. Chem., Int. Ed.*, 2015, **54**, 4508; (b) Y. Xia, Z. X. Liu, Z. Liu, R. Ge, F. Ye, M. Hossain, Y. Zhang and J. B. Wang, *J. Am. Chem. Soc.*, 2014, **136**, 3013; (c) Z. Shi, D. C. Koester, M. Boultadakis-Arapinis and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 12204; (d) X. Chen, X. Hu, Y. Deng, H. F. Jiang and W. Zeng, *Org. Lett.*, 2016, **18**, 4742; (e) J. Wang, M. Wang, K. Chen, S. Zha, C. Song and J. Zhu, *Org. Lett.*, 2016, **18**, 1178.
- 12 Y. Xie, X. Chen, X. Liu, S. J. Su, J. Li and W. Zeng, *Chem. Commun.*, 2016, **52**, 5856.
- 13 Unfortunately, during the period that we carried out this work, two similar works have been reported through constructing ring **B** and ring **C** of isoquinolinocarbazole derivatives through Ir(III) and Rh(III) catalytic system, see: (a) S. S. Li, Y. Q. Xia, F. Z. Hu, C. F. Liu, F. Su and L. Dong, *Chem.-Asian J.*, 2016, **11**, 3165; (b) B. Li, B. Zhang, X. Zhang and X. Fan, *Chem. Commun.*, 2017, **53**, 1297.
- 14 The structures of **3a** (CCDC No. 1511555) and **4e** (CCDC No. 1511559) were already unambiguously assigned by their crystal X-ray analysis, please see ESI† for the more details.
- 15 We made the compound **5a** through the *N*-methylation of **3a** in order to systematically study the emission properties. For the structure of **5a**, please see ESI†.
- 16 B. Li, J. Lan, D. Wu and J. You, *Angew. Chem., Int. Ed.*, 2015, **54**, 14008.
- 17 H. H. Chou and C. H. Cheng, *Adv. Mater.*, 2010, **22**, 2468.
- 18 K. Morimoto, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2010, **12**, 2068.
- 19 (a) W. Chan, S. F. Lo, Z. Zhou and W. Y. Yu, *J. Am. Chem. Soc.*, 2012, **134**, 13565; (b) S. Yu, S. Liu, Y. Lan, B. Wan and X. W. Li, *J. Am. Chem. Soc.*, 2015, **137**, 1623.
- 20 (a) Y. Wei, I. Deb and N. Yoshikai, *J. Am. Chem. Soc.*, 2012, **134**, 9098; (b) S. Gore, S. Baskaran and B. König, *Org. Lett.*, 2012, **14**, 4568; (c) S.-D. Yang, C.-L. Sun, Z. Fang, B.-J. Li, Y.-Z. Li and Z.-J. Shi, *Angew. Chem., Int. Ed.*, 2008, **47**, 1473.
- 21 (a) X. Chen, Y. Xie, X. Xiao, G. Li, Y. Deng, H. Jiang and W. Zeng, *Chem. Commun.*, 2015, **51**, 15328; (b) R. Pasceri, H. E. Bartrum, C. J. Hayes and C. J. Moody, *Chem. Commun.*, 2012, **48**, 12077.

