Green Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: D. Liu, J. Huang, Z. Fu and W. Huang, *Green Chem.*, 2019, DOI: 10.1039/C9GC00064J.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/green-chem

Journal Name

RSCPublishing View Article Online
DOI: 10.1039/C9GC00064J

PAPER

Direct Construction of Carbazoles from 2-Methyl-indole-3-carbaldehydes and Enals

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Dehai Liu,[a] Jie Huang,[a] Zhenqian Fu,*[a,b] and Wei Huang,*[a,b]

The direct and rapid construction of carbazoles was achieved via the reaction of 2-methyl-indole-3-carbaldehydes with enals promoted by LiCl/DBU in a single operation. This mild and green reaction proceeds through a [4+2] cycloaddition/dehydration/oxidative aromatization cascade to generate carbazoles in good to excellent yields. The reaction features mild reaction conditions, a broad substrate scope, and excellent functional group tolerance, using O_2 (1atm) as the sole oxidant and affording H_2O as the only byproduct. More importantly, 4-fluoroquinocarbazole, a significant bioactive compound, was generated in 80% yield in only one step from the obtained carbazole.

Introduction

Carbazoles, as a kind of the most privileged aza-heterocycles, are fundamental motifs in a large number of pharmaceuticals, alkaloid-based natural products,[1] as well as organic optoelectronic materials[2] due to a wide band gap and outstanding luminescent efficiency (Scheme 1a). For example, Carprofen[3] is a nonsteroidal anti-inflammatory pharmaceutical used to treat joint pain and postoperative pain. Carvedilol[4] is applied in treatment of congestive heart failure and high blood pressure. Midostaurin (Rydapt),[5] as a semi-synthetic derivative of an alkaloid Staurosporine,[6] is a FDA approved drug for treating acute myeloid leukemia, myelodysplastic syndrome and advanced systemic mastocytosis. Furthermore, 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN), containing four carbazolyl units, has been demonstrated as an excellent thermally activated delayed fluorescence material.[7] Owing to the significance of carbazole compounds, the facile and efficient synthesis of carbazoles has received continuous attention. Numerous elegant methods have been established,[8] mainly involving direct construction of the pyrrole ring moiety through C–C and C–N bond formation,[9] and direct construction of the aromatic ring moiety though p-extension of indoles (Scheme 1b).[10] However, they often cannot avoid the use of transition-metal catalysts, harsh conditions or multistep

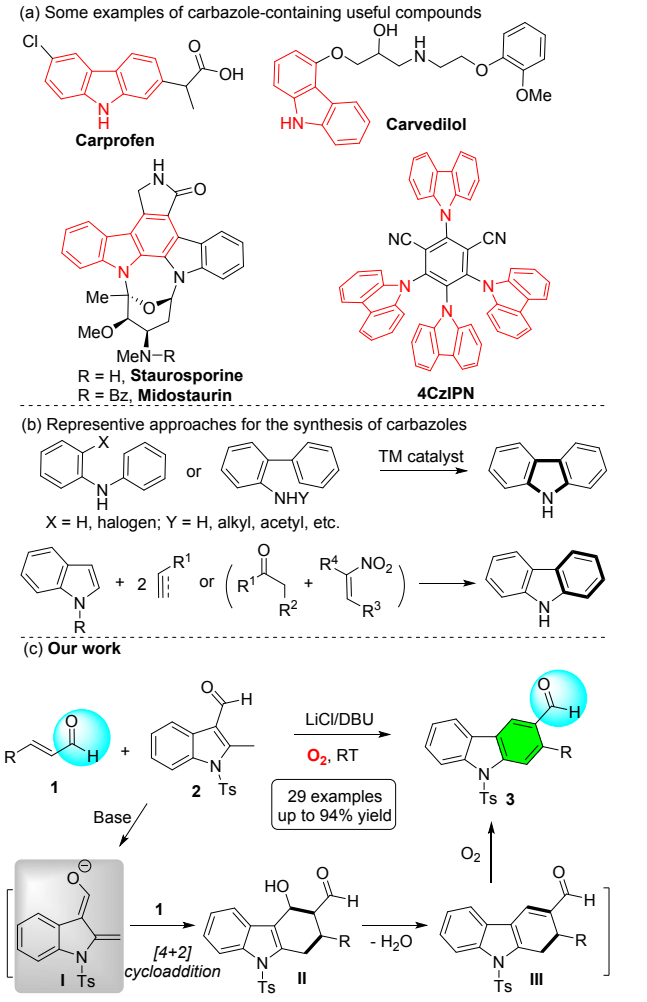


Figure 1 Examples of carbazole-containing useful compounds and synthetic methods for carbazoles.

[a] Key Laboratory of Flexible Electronics & Institute of Advanced Materials, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, 30 South Puzhu Road, Nanjing, 211816, China. E-mail: iamwhuang@njtech.edu.cn;iamzqfu@njtech.edu.cn.
[b] Shaanxi Institute of Flexible Electronics (SIFE), Northwestern Polytechnical University (NPU), 127 West Youyi Road, Xi'an, 710072, China.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

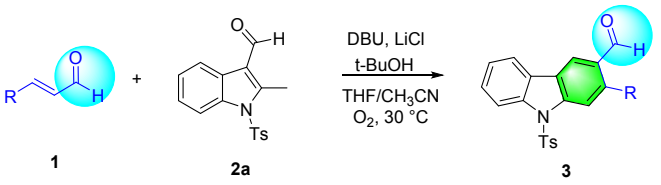
synthesis. Therefore, further development of simple and efficient strategies for the construction of carbazoles is highly desirable. In particular, an ideal synthetic route would be transition metal-free, start from simple and readily available raw materials, use green and mild reaction conditions, involve a single operation, and show excellent tolerance of various reactive functional groups for further derivatizations.

[4+2] cycloaddition has been proven as one of the most powerful and reliable strategies for the construction of a series of structurally diverse six-membered rings from simple raw materials.[11] Furthermore, although molecular oxygen (O_2) is an ideal oxidant, the direct use of O_2 as a sole oxidant remains a critical challenge in academia and industry.[12] As part of our ongoing interest in the synthesis of carbo- and heterocycles,[10j, 13] we envisaged a novel strategy for the synthesis of highly functionalized carbazoles might be achieved via the reaction of 2-methyl-indole-3-carbaldehydes and enals in a single operation (Scheme 1c). In fact, this strategy presents some apparent challenges, including (i) achieving the difficulty [4+2] cycloaddition of in situ-generated dienolate **I** with enals; (ii) ensuring all processes, including [4+2] cycloaddition, dehydration and aerobic oxidative aromatization, successively accomplished under identical conditions; (iii) retaining the highly reactive formyl moiety under basic and oxidative conditions. Herein, we present the successful development of a mild and green synthetic route to carbazoles based on the reaction of 2-methyl-indole-3-carbaldehydes and enals promoted by inexpensive Lewis acid LiCl and DBU in a single operation. Notably, this transition metal-free strategy avoids problematic heavy-metal residues, which should substantially promote its potential use in the preparation of pharmaceuticals and materials. More importantly, the formyl group in the obtained carbazoles can undergo subsequent derivatizations. Recently, the group of Wan[14] described an efficient method for the construction of polyfunctionalized benzaldehydes on the basis of [4+2] annulation of linear dienals and tertiary enaminones.

Results and discussion

We selected the reaction of cinnamaldehyde **1a** and readily available 2-methyl-1-tosyl-1H-indole-3-carbaldehyde **2a**[15] as the model reaction for optimizing conditions. The key results of reaction optimization were summarized in Table 1. Initial reaction attempts were unsuccessful, with no desired product afforded when several bases (including DBU, DBN, K_2CO_3, t-BuONa and Et_3N) were employed in THF at room temperature (entry 1). Several Lewis acids, including $Cu(OTf)_2$, $Zn(OTf)_2$, $Sc(OTf)_3$, $Mg(OTf)_2$, $FeCl_3$ and $ZnCl_2$ were then investigated, affording no product or < 10% yield of carbazole **3a** (entries 2–7). Inexpensive LiCl[16] is a weak Lewis acid known to activate cinnamaldehyde **1a**. Furthermore, lithium cations can stabilize oxygen anions. We envisaged that these synergetic effects might help the reaction to proceed. Pleasingly, when LiCl was added, desired carbazole **3a** was generated in 62% yield (entry 8). Replacing LiCl with LiF, LiBr, and NaCl led to a decreased product yield (entries 9–11). With a proper Lewis acid established, several bases and solvents were then investigated, wherein DBU and THF proving to be the best choices, respectively (see SI for details). To our delight, the product yield was considerably increased when the reaction was performed under O_2 (entry 12). Using a mixed solvent (THF/CH_3CN = 1:1, v/v) further increased the product yield (entry 13). Furthermore, adding *t*-BuOH improved the product yield up to 82% (entry 14). Without DBU, the desired product **3a** was not observed (entry 15).

Table 1. Optimization of reaction conditions[a]



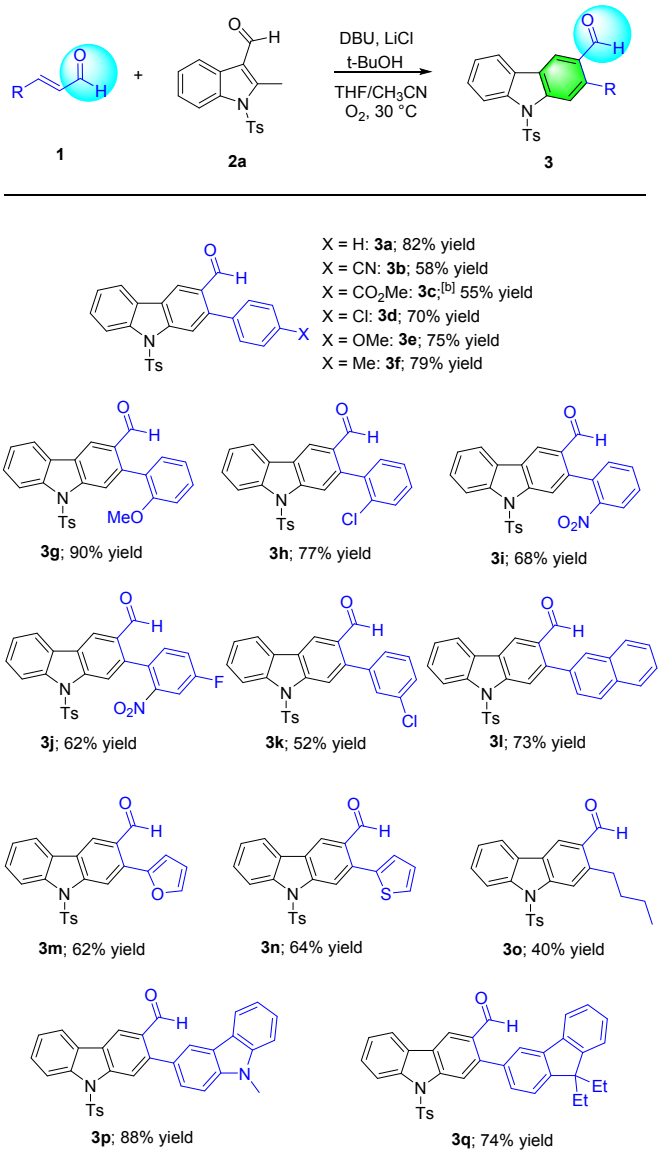
1 2a 3

Entry[a]	Base	Lewis acid	solvent	Yield(%)[b]
1	Several bases	-	THF	n.d.
2	DBU	$Cu(OTf)_2$	THF	<10
3	DBU	$Zn(OTf)_2$	THF	<10
4	DBU	$Sc(OTf)_2$	THF	<10
5	DBU	$Mg(OTf)_2$	THF	<10
6	DBU	$FeCl_3$	THF	n.d.
7	DBU	$ZnCl_2$	THF	n.d.
8	DBU	LiCl	THF	63
9	DBU	LiF	THF	30
10	DBU	LiBr	THF	57
11	DBU	NaCl	THF	<10
12[c]	DBU	LiCl	THF	75
13[c d]	DBU	LiCl	THF/CH_3CN	79
14[c e]	DBU	LiCl	THF/CH_3CN	82
15[c e]	-	LiCl	THF/CH_3CN	n.d.

[a] Reaction conditions: cinnamaldehyde **1a** (1.5 equiv), **2a** (0.1 mmol), base (2.0 equiv), Lewis acid (0.2 or 3.0 equiv), solvent (1.0 mL), 30 °C, 24 h. [b] Yields of products isolated after column chromatography. [c] Under an O_2 balloon. [d] THF/CH_3CN=1:1. [e] 100 μL of t-BuOH was added. n.d. = not detected.

With acceptable optimized conditions in hand (Table 1, entry 14), we then evaluated the reaction scope for enal substrates using **2a** as a model substrate (Table 2). Enals bearing various substituents with diverse electronic and steric properties on the β-aryl ring, reacted smoothly to generate the corresponding carbazole-3-carbaldehydes **3a–3k** in good to excellent yields. Gratifyingly, CHO, ester, CN, NO_2, and halide groups were well tolerated. Enals bearing β-2-naphthyl or heteroaromatic rings (such as 2-furyl or 2-thienyl rings) also reacted efficiently (**3l–n**). Notably, a β-alkyl enal also gave desired product **3o**, albeit in a lower yield. Pleasingly, β-carbazolyl and fluorenyl enals were suitable substrates, generating products **3i** and **3j** in good yields, respectively. Notably, no reaction occurred when N-Ts was replaced with N-Me for substrates **2**.

Table 2. Reaction Scope[a]

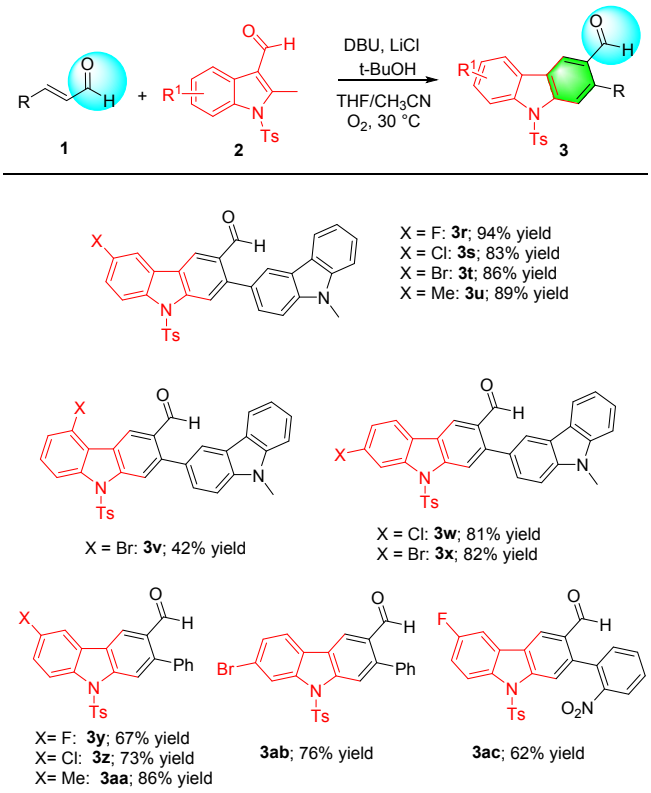


[a] Reaction conditions: **1** (1.5 equiv), cinnamaldehyde **2a** (0.1 mmol), DBU (2.0 equiv), LiCl (3.0 equiv), t-BuOH (100 µL), THF/CH_3CN=1:1 (1.0 mL), 30 °C, O_2, 24 h. Yields (after SiO2 chromatography purification) were based on 2.

We then investigated the generality of 2-methyl-3-formyl indoles **2** using β-carbazolyl enal **1x** as a model substrate under the optimized conditions. The reactions proceeded smoothly with a range of substituents at the 4, 5 and 6 positions on the indole ring, leading to the formation of diverse biscarbazoles (**3r–x**) in good to excellent yields. Other enals were also employed to evaluate the generality of 2-methyl-3-formyl indoles 2, leading to similar results (**3y–ac**) to β-carbazolyl enal 1x. N-tosyl 2-methyl 3-acetyl indole cannot give the desired carbazole. Notably, CHO, NO_2, F, Cl, and Br groups in the obtained carbazoles **3** significantly increased the possibility of further synthetic transformations.

Subsequent transformations of the obtained carbazole-3-carbaldehydes were performed, as shown in Scheme 2 and Table 4. Selective reduction of the nitro moiety of carbazoles **3**

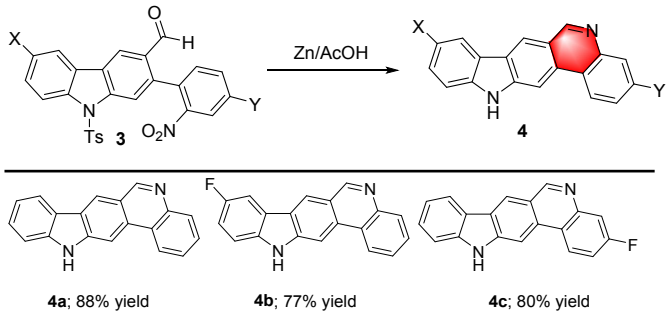
Table 3. Reaction Scope[a]



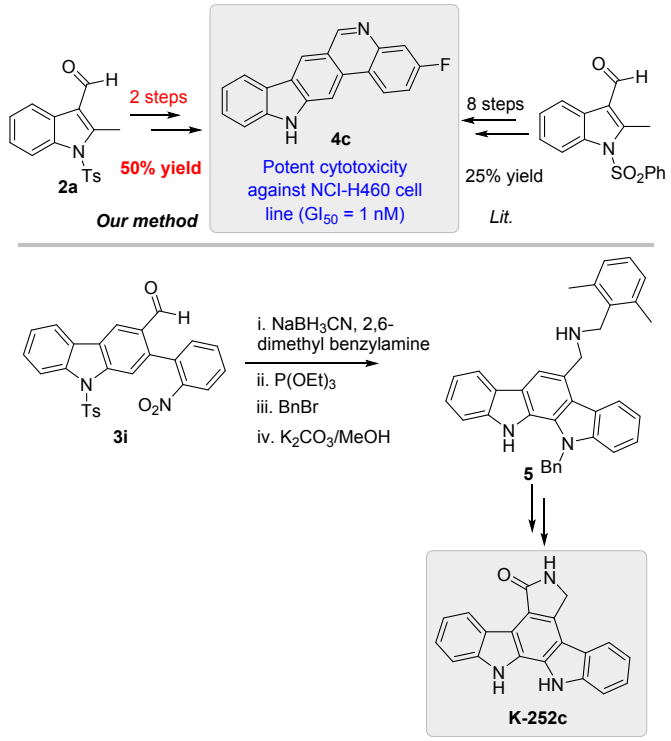
[a] Reaction conditions: **1** (1.5 equiv), cinnamaldehyde **2a** (0.1 mmol), DBU (2.0 equiv), LiCl (3.0 equiv), t-BuOH (100 µL), THF/CH_3CN=1:1 (1.0 mL), 30 °C, O_2, 24 h. Yields (after SiO2 chromatography purification) were based on 2.

using Zn/AcOH, followed by intramolecular cyclizationn and detosylation, efficiently delivered quinocarbazoles **4a–4c** in good yields. Furthermore, as analogues of alkaloid calothrixin B, quinocarbazoles **4** show a wide range of promising biological activities.[17] More importantly, 4-fluoroquinocarbazole **4c** has been demonstrated to exhibit potent cytotoxicity against the NCI-H460 cell line (GI_{50} =1 nM), and deserves further study. Notably, the previously reported synthesis of **4c** from 2-methyl-1-(phenylsulfonyl)-1H-indole-3-carbaldehyde required eight steps.[17] In constrast, using our strategy, **4c** was elegantly constructed in only one step (80% yield) from generated carbazole **3j**, and in only two steps from **2a** (50% overall yield). Furthermore, treating **3i** with 2,6-dimethyl benzylamine and $NaBH_3CN$, followed by a $P(OEt)_3$-promoted cyclization, benzylation, and detosylation afforded product **5** which can be converted into K-252c[18] (staurosporinone) **6** using a known process.[19]

Table 4. Synthetic transformations. [a]



[a] Reaction conditions: **3** (0.1 mmol), Zn (20 equiv.), AcOH (3.0 mL), reflux, overnight.



Scheme 2. Synthetic transformations.

Conclusions

In summary, we have successfully developed a mild and green method for the construction of carbazoles on the basis of the reaction of 2-methyl-indole-3-carbaldehydes and enals promoted by Lewis acid LiCl and DBU in a single operation. Notably, this transition metal-free strategy features mild and green reaction conditions, a broad substrate scope, and excellent functional group tolerance, using O_2 as the sole oxidant and giving H_2O as the only byproduct. More importantly, the obtained carbazoles were suitable for further derivatization. The important bioactive 4-fluoroquinocarbazole **4c** was constructed from the obtained carbazole in 80% yield in only one step using pesent strategy. Further exploration of this catalytic process is underway in our laboratory.

Acknowledgements

We acknowledge financial support by National Natural Science Foundation of China (21602105), National Key R&D Program of China (2017YFA0204704), Natural Science Foundation of Jiangsu Province (BK20171460) and National Key Basic Research Program of China (973) (2015CB932200). We thank Y. Guo in this group for reproducing the reactions of **3a**, **3j**, and **3s**.

Notes and references

1 For selected reviews, see: (a) A. W. Schmidt, K. R. Reddy, H. J. Knolker, *Chem. Rev.* 2012, **112**, 3193; (b) A. Gluszynska, *Eur. J. Med. Chem.* 2015, **94**, 405; (c) A. Caruso, D. Iacopetta, F. Puoci, A. R. Cappello, C. Saturnino, M. S. Sinicropi, *Mini-Rev. Med. Chem.* 2016, **16**, 630; (d) L. S. Tsutsumi, D. Gundisch, D. Q. Sun, *Curr. Top. Med. Chem.* 2016, **16**, 1290.

2 (a) J. L. Diaz, A. Dobarro, B. Villacampa, D. Velasco, *Chem. Mater.* 2001, **13**, 2528; (b) K. R. J. Thomas, J. T. Lin, Y. T. Tao, C. W. Ko, *J. Am. Chem. Soc.* 2001, **123**, 9404; (c) P. M. Beaujuge, J. R. Reynolds, *Chem. Rev.* 2010, **110**, 268; (d) J. Li, A. C. Grimsdale, *Chem. Soc. Rev.* 2010, **39**, 2399; (e) H. Huang, Q. Fu, B. Pan, S. Q. Zhuang, L. Wang, J. S. Chen, D. G. Ma, C. L. Yang, *Org. Lett.* 2012, **14**, 4786; (f) C. Wang, H. Dong, W. Hu, Y. Liu, D. Zhu, *Chem. Rev.*2012, **112**, 2208.

3 A. P. Ricketts, K. M. Lundy, S. B. Seibel, *Am. J. Vet. Res.* 1998, **59**, 1441.

4 R. B. Innis, F. M. A. Correa, S. H. Snyder, *Life Sci.* 1979, , 2255.

5 (a) E. Weisberg, C. Boulton, L. M. Kelly, P. Manley, D. Fabbro, T. Meyer, D. G. Gilliland, J. D. Griffin, *Cancer Cell.* 2002, **1**, 433; (b) P. W. Manley, E. Weisberg, M. Sattler, J. D. Griffin, *Blochem.* 2018, **57**, 477.

6 (a) V. Rialet, L. Meijer, *Anticancer Res.* 1991, **11**, 1581; (b) Y. Wada, H. Nagasaki, M. Tokuda, K. Orito, *J. Org. Chem.* 2007, **72**, 2008.

7 H. Uoyama, K. Goushi, K. Shizu, H. Nomura, C. Adachi, *Nature* 2012, **492**, 234.

8 (a) E. Fischer, F. Jourdan, *Berichte der deutschen chemischen Gesellschaft* 1883, **16**, 2241; (b) E. Drechsel, *Journal für Praktische Chemie* 1888, **38**, 65; (c) C. Graebe, F. Ullmann, *Justus Liebigs Annalen der Chemie* 1896, **291**, 8; (d) W. Borsche, *Justus Liebigs Annalen der Chemie* 1908, **359**, 49; (e) B. Robinson, *Chem. Rev.* 1963, 373; (f) B. Robinson, *Chem. Rev.* 1969, **69**, 227; (g) H. J. Knolker, K. R. Reddy, *Chem. Rev.* 2002, **102**, 4303; (h) I. Bauer, H. J. Knolker, in *Top. Curr. Chem., 309*, 2012, 203; (i) J. Roy, A. K. Jana, D. Mal, *Tetrahedron* 2012, **68**, 6099; (j) Y. Men, Z. Hu, J. Dong, X. Xu, B. Tang, *Org. Lett.* 2018, **20**, 5348.

9 For selected examples, see: (a) F. E. Goodson, S. I. Hauck, J. F. Hartwig, *J. Am. Chem. Soc.* 1999, **121**, 7527; (b) W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* 2005, **127**, 14560; (c) D. S. Surry, S. L. Buchwald, *J. Am. Chem. Soc.* 2007, **129**, 10354; (d) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* 2008, **130**, 16184; (e) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* 2010, **2**, 527; (f) S. H. Cho, J. Yoon, S. Chang, *J. Am. Chem. Soc.* 2011, **133**, 5996; (g) S. W. Youn, J. H. Bihn, B. S. Kim, *Org. Lett.* 2011, **13**, 3738; (h) S. Chakrabarty, I. Chatterjee, L. Tebben, A. Studer, *Angew. Chem. Int. Ed.* 2013, **52**, 2968; (i) A. C.

Hernandez-Perez, S. K. Collins, *Angew. Chem. Int. Ed.* 2013, **52**, 12696; (j) H. Gao, Q.-L. Xu, M. Yousufuddin, D. H. Ess, L. Kuerti, *Angew. Chem. Int. Ed.* 2014, **53**, 2701; (k) M. Bhanuchandra, K. Murakami, D. Vasu, H. Yorimitsu, A. Osuka, *Angew. Chem. Int. Ed.* 2015, **54**, 10234; (l) C. Suzuki, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* 2015, **17**, 1597; (m) N. Li, X. L. Lian, Y. H. Li, T. Y. Wang, Z. Y. Han, L. M. Zhang, L. Z. Gong, *Org. Lett.* 2016, **18**, 4178; (n) S. Maiti, T. K. Achar, P. Mal, *Org. Lett.* 2017, **19**, 2006; (o) S. Maiti, P. Mal, *Org. Lett.* 2017, **19**, 2454; (p) M. Wang, Q. Fan, X. Jiang, *Org. Lett.* 2018, **20**, 216.

10 For selected examples, see: (a) M. Yamashita, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* 2009, **11**, 2337; (b) Y. Qiu, W. Kong, C. Fu, S. Ma, *Org. Lett.* 2012, **14**, 6198; (c) K. Ozaki, H. Zhang, H. Ito, A. W. Lei, K. Itami, *Chem. Sci.* 2013, **4**, 3416; (d) S. Y. Wang, Z. Chai, Y. Wei, X. C. Zhu, S. L. Zhou, S. W. Wang, *Org. Lett.* 2014, **16**, 3592; (e) J. Wang, H. T. Zhu, Y. F. Qiu, Y. Niu, S. Chen, Y. X. Li, X. Y. Liu, Y. M. Liang, *Org. Lett.* 2015, **17**, 3186; (f) L. Zhou, B. Xu, J. Zhang, *Angew. Chem. Int. Ed.* 2015, **54**, 9092; (g) S. P. Chen, Y. X. Li, P. H. Ni, H. W. Huang, G. J. Deng, *Org. Lett.* 2016, **18**, 5384; (h) Y. W. Huang, X. Y. Li, L. N. Fu, Q. X. Guo, *Org. Lett.* 2016, **18**, 6200; (i) Y. L. Gu, W. B. Huang, S. M. Chen, X. Wang, *Org. Lett.* 2018, **20**, 4285. (j) D. Liu, Y. Gao, J. Huang, Z. Fu, W. Huang, *J. Org. Chem.* 2018, **83**, 14210.

11 (a) A. S. Mitchell, R. A. Russell, *Tetrahedron* 1995, **51,** 5207; (b) D. Mal, P. Pahari, *Chem. Rev.* 2007, **107**, 1892; (c) K. Rathwell, M. A. Brimble, *Synthesis* 2007, **643**; (d) A. Borovika, P.-I. Tang, S. Klapman, P. Nagorny, *Angew. Chem. Int. Ed.* 2013, **52**, 13424; (e) G. Masson, C. Lalli, M. Benohoud, G. Dagousset, *Chem. Soc. Rev.* 2013, **42**, 902; (f) F. Lopez, J. L. Mascarenas, *Chem. Soc. Rev.* 2014, **43**, 2904.

12 For selected reviews, see: (a) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* 2005, **105**, 2329; (b) S. S. Stahl, *Science* 2005, **309**, 1824; (c) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* 2012, **41**, 3381; (d) S. Song, Y. Zhang, A. Yeerlan, B. Zhu, J. Liu, N. Jiao, *Angew. Chem., Int. Ed.* 2017, **56**, 2487.

13 (a) G. J. Wang, Z. Q. Fu, W. Huang, *Org. Lett.* 2017, **19**, 3362; (b) Y. R. Gao, Y. F. Ma, C. Xu, L. Li, T. J. Yang, G. Q. Sima, Z. Q. Fu, W. Huang, *Adv. Synth. Catal.* 2018, **360**, 479; (c) G. J. Wang, W. Y. Hu, Z. L. Hu, Y. X. Zhang, W. Yao, L. Li, Z. Q. Fu, W. Huang, *Green Chem.* 2018, **20**, 3302; (d) Y. X. Zhang, J. Huang, Y. Y. Guo, L. Li, Z. Q. Fu, W. Huang, *Angew. Chem. Int. Ed.* 2018, **57**, 4594.

14 L. Yang, L. Wei, J.-P. Wan, *Chem. Commun.*, 2018, **54**, 7475.

15 (a) M. W. Robinson, J. H. Overmeyer, A. M. Young, P. W. Erhardt, *J. Med. Chem.* 2012, **55**, 1940; (b) L. Han, C. Liu, W. Zhang, X.-X. Shi, S.-L. You, *Chem. Commun.* 2014, **50**, 1231; (c) W. Gu, Y. Hao, G. Zhang, S.-F. Wang, T.-T. Miao, *Bioorg. Med. Chem. Lett.* 2015, **25**, 554; (d) Z. Deng, J. Wei, L. Liao, H. Huang, X. Zhao, *Org. Lett.* 2015, **17**, 1834; (e) S. K. Bhunia, A. Polley, R. Natarajan, R. Jana, *Chem. Eur. J.* 2015, **21**, 16786; (f) H. E. Colley, M. Muthana, S. J. Danson, L. V. Jackson, M. L. Brett, J. Harrison, S. F. Coole,; D. P. Mason, L. R. Jennings, M. Wong, V. Tulasi, D. Norman, P. M. Lockey, L. Williams, A. G. Dossetter, E. J. Griffen, M. J. Thompson, *J. Med. Chem.* 2015, **58**, 9309; (g) X. Song, C. Xu, D. Du, Z. Zhao, D. Zhu, M. Wang, *Org. Lett.* 2017, **19**, 6542.

16 (a) D. Seebach, *Angew. Chem. Int. Ed.* 1988, **27**, 1624; (b) L. Hong, W. Sun, D. Yang, G. Li, R. Wang, *Chem. Rev.* 2016, **116**, 4006.

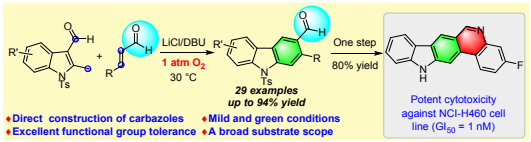
17 B. M. Ramalingam, N. D. Moorthy, S. R. Chowdhury, T. Mageshwaran, E. Vellaichamy, S. Saha, K. Ganesan, B. N. Rajesh, S. Iqbal, H. K. Majumder, K. Gunasekaran, R. Siva, A. K. Mohanakrishnan, *J. Med. Chem.* 2018, **61**, 1285.

18 (a) A. R. Howard-Jones, C. T. Walsh, *J. Am. Chem. Soc.* 2006, **128**, 12289; (b) G. G. Rajeshwaran, A. K. Mohanakrishnan, *Org. Lett.* 2011, **13**, 1418; (c) P. Raju, G. G. Rajeshwaran, A. K. Mohanakrishnan, *Eur. J. Org. Chem* 2015, 7131; (d) J. C. Fox, R. E. Gilligan, A. K. Pitts, H. R. Bennett, M. J. Gaunt, *Chem. Sci.* 2016, **7**, 2706.

19 Y. Wada, H. Nagasaki, M. Tokuda, K. Orito, *J. Org. Chem.* 2007, **72**, 2008.

View Article Online
DOI: 10.1039/C9GC00064J

Graphic Abstract



The direct and rapid construction of carbazoles was achieved based on the reaction of 2-methyl-indole-3-carbaldehydes and enals promoted by Lewis acid LiCl and DBU in a single operation.