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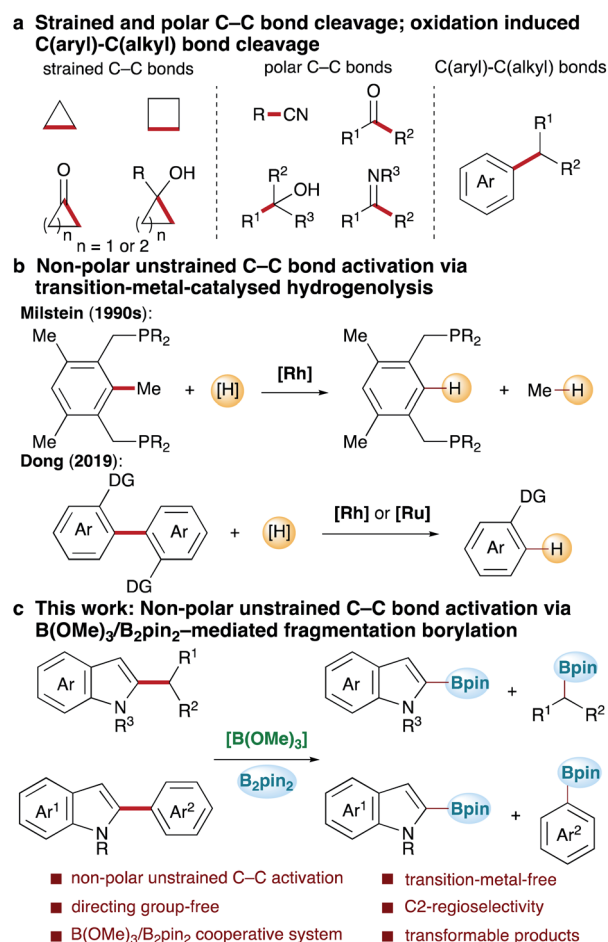
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Carbon–carbon bond activation by $B(OMe)_3/B_2pin_2$ -mediated fragmentation borylation†Li Wang,^{‡ab} Qi Zhong,^{‡ab} Youliang Zou,^b Youzhi Yin,^b Aizhen Wu,^b Quan Chen,^b Ke Zhang,^b Jiachen Jiang,^b Mengzhen Zhao^b and Hua Zhang^{†ab}

Selective carbon–carbon bond activation is important in chemical industry and fundamental organic synthesis, but remains challenging. In this study, non-polar unstrained Csp^2-Csp^3 and Csp^2-Csp^2 bond activation was achieved by $B(OMe)_3/B_2pin_2$ -mediated fragmentation borylation. Various indole derivatives underwent C2-regioselective C–C bond activation to afford two C–B bonds under transition-metal-free conditions. Preliminary mechanistic investigations suggested that C–B bond formation and C–C bond cleavage probably occurred in a concerted process. This new reaction mode will stimulate the development of reactions based on inert C–C bond activation.

Introduction

Carbon–carbon bond activation, which enables the direct production of valuable functionalized products from widely available and inexpensive raw materials obtained from natural resources, is the foundation of many important industrial processes and has wide-ranging applications in complex molecule synthesis.^{1–14} Owing to the ubiquity of carbon–carbon bonds in organic molecules, the study of transformations based on selective carbon–carbon bond activation will greatly help realize free molecular editing, thus stimulating growing interest in the synthetic community. In recent decades, the rapid development of synthetic methods based on strained C–C bond cleavage *via* strain release,^{15–23} polar C–C bond cleavage^{24–36} *via* transition-metal-catalysed oxidative addition and β -carbon elimination, and oxidation induced C–C cleavage of alkylarenes,^{37–39} among others, has been witnessed (Scheme 1a). Owing to a high bond dissociation energy and competitive C–H bond activation, the selective activation of non-polar unstrained C–C bonds is challenging, with reports remaining rare. Reported successes mainly rely on the directed transition-metal-catalysed reductive hydrogenolysis of substrates bearing two directing groups (Scheme 1b). In this context, Milstein and co-workers contributed the pioneering work, wherein the hydrogenolysis of non-polar unstrained Csp^2-Csp^3 bonds in pincer-type substrates with bidentate phosphine as the directing group was achieved *via* Rh catalysis (Scheme 1b).^{40–43} Recently, Dong



Scheme 1 (a) Strained and polar C–C bond cleavage; oxidation induced C(aryl)–C(alkyl) bond cleavage. (b) Non-polar unstrained C–C bond activation *via* transition-metal-catalysed hydrogenolysis. (c) This work: non-polar unstrained C–C bond activation *via* $B(OMe)_3/B_2pin_2$ -mediated fragmentation borylation.

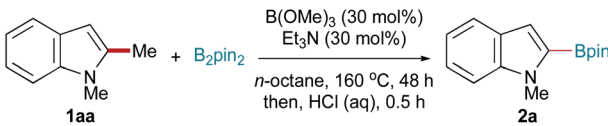
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Table 1 Effects of varying reaction parameters on the B(OMe)₃/B₂pin₂-mediated fragmentation borylation of **1aa**

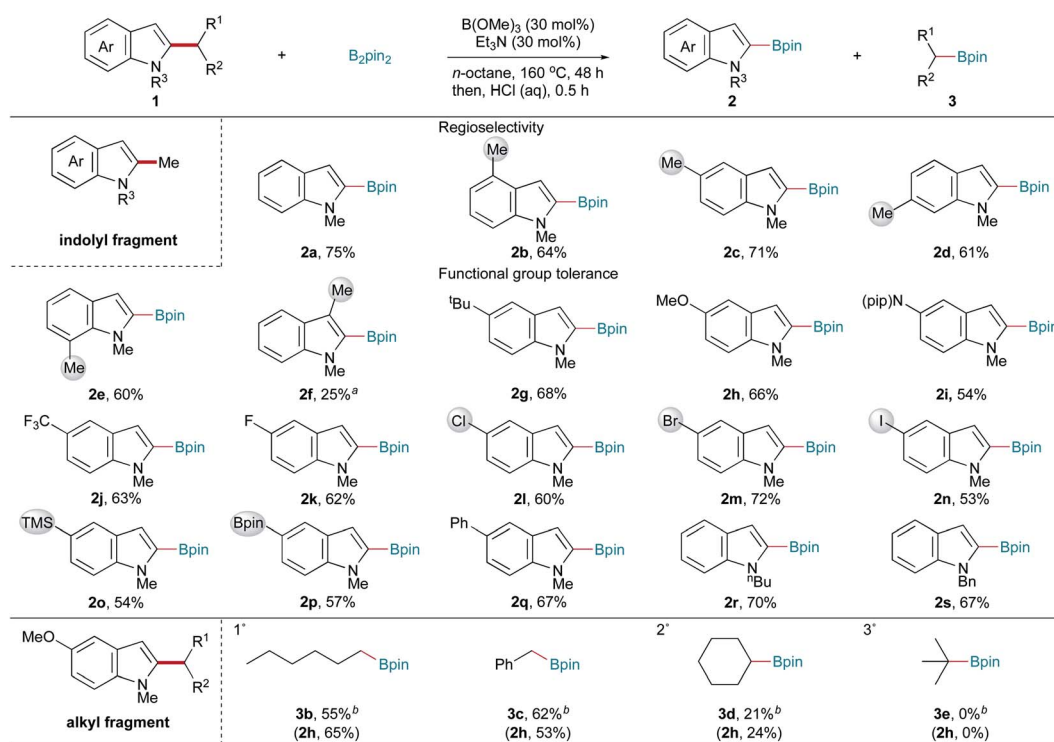
		
Entry	Deviation from standard reaction conditions ^a	Yield ^b (%)
1	None	83(75) ^c
2	No B(OMe) ₃	0
3	B(O ⁱ Pr) ₃ , instead of B(OMe) ₃	70
4	BPh ₃ , instead of B(OMe) ₃	59
5	PhB(OH) ₂ , instead of B(OMe) ₃	66
6 ^d	BF ₃ ·Et ₂ O, instead of B(OMe) ₃	Trace
7 ^{d,e}	BF ₃ ·Et ₂ O, instead of B(OMe) ₃	62
8	BBr ₃ , instead of B(OMe) ₃	0
9 ^f	B(C ₆ F ₅) ₃ , instead of B(OMe) ₃	Trace
10 ^g	Metal Lewis acids, instead of B(OMe) ₃	0
11	No Et ₃ N	59
12	ⁿ Bu ₃ N, instead of Et ₃ N	78
13	<i>n</i> -Hexane, instead of <i>n</i> -octane	68
14	16 h, instead of 48 h	Trace
15	180 °C, 16 h instead of 160 °C, 48 h	67
16	140 °C, instead of 160 °C	Trace

^a Standard reaction conditions: **1aa** (0.20 mmol), B₂pin₂ (0.50 mmol), B(OMe)₃ (0.06 mmol), Et₃N (0.06 mmol), *n*-octane (1.0 mL), 160 °C, and 48 h; HCl (1.0 mL, 6.0 M) and 0.5 h. ^b Yields determined by GC using naphthalene as the internal standard. ^c Isolated yield in parentheses. ^d THF (0.1 mL) was added. ^e No Et₃N. ^f 10 mol%. ^g Metal Lewis acids: Zn(OTf)₂, ZnCl₂, Sc(OTf)₃, AlCl₃, InCl₃, FeCl₃, CuCl₂, and NiCl₂.

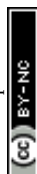
and co-workers made a significant advancement, achieving the activation of Csp²–Csp² bonds in a wide range of biaryl compounds bearing two *ortho*-directing groups using Rh and Ru catalysis (Scheme 1b).^{44–46} Although these studies proved that the selective cleavage of non-polar unstrained C–C bonds is feasible, the development of new systems to advance this field is needed. Herein, we describe the development of a B(OMe)₃/bis(pinacolato)diborane(B₂pin₂)-mediated non-polar unstrained C–C bond activation reaction (Scheme 1c). In this reaction, both Csp²–Csp³ and Csp²–Csp² bond activation occurred regioselectively at the C2-position in various substituted indoles, affording two C–B bond products under transition-metal-free conditions. This study not only provides a new approach to highly challenging selective carbon–carbon bond cleavage, but also provides new opportunities for further applications.

Results and discussion

As an extension of our previous study towards the Lewis acid-promoted C–H borylation of indoles,⁴⁷ we envisaged that installing substituents on the pyrrole core of indoles would provide opportunities for C–H borylation of the benzenoid moiety of indoles.^{48,49} This concept was initially investigated using the reaction of 1,2-dimethyl indole (**1aa**) and B₂pin₂. Surprisingly, no desired benzenoid C–H borylation products were obtained in the reaction, but C–C bond activation product **2a** was observed. Owing to the importance of C–C bond



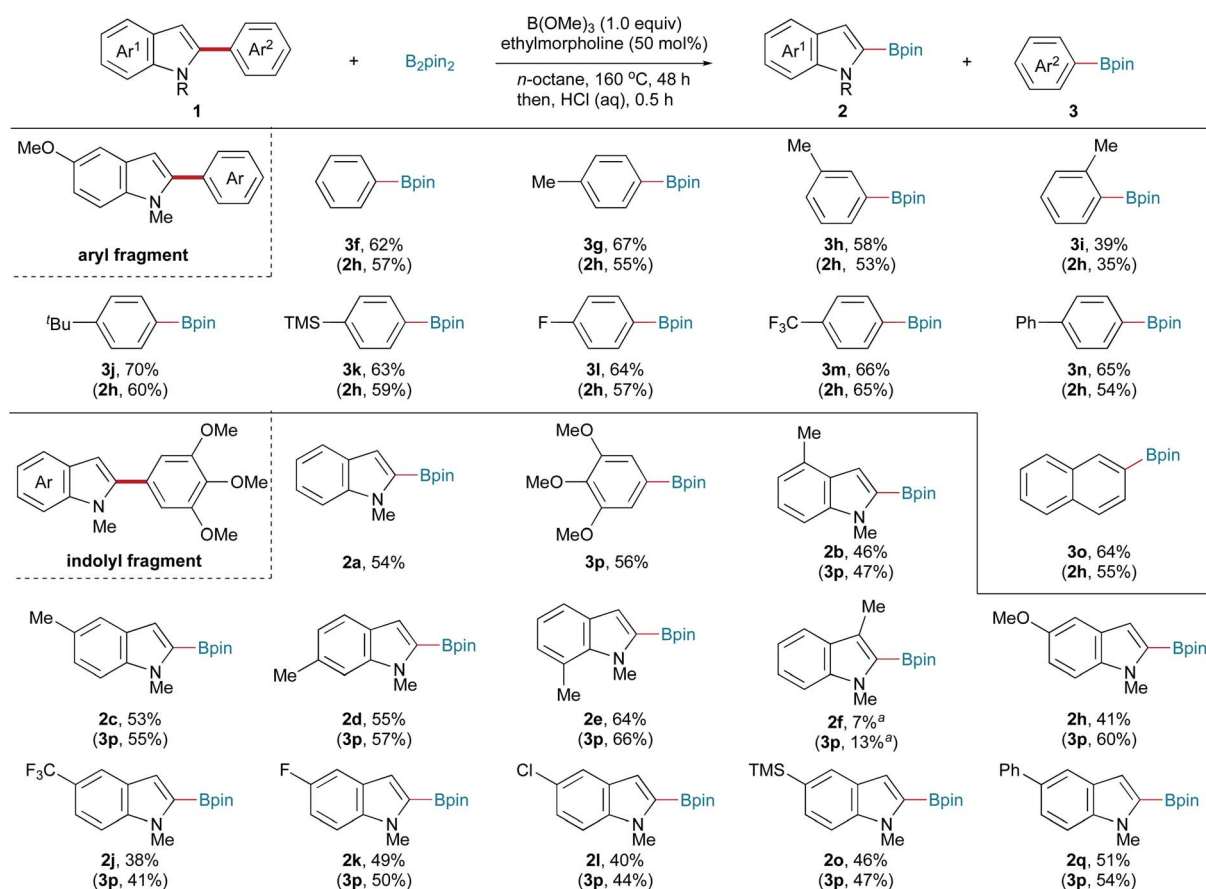
Scheme 2 Scope of Csp²–Csp³ bond fragmentation borylation. Reaction conditions: **1** (0.20 mmol), B₂pin₂ (0.50 mmol), B(OMe)₃ (0.06 mmol), Et₃N (0.06 mmol), *n*-octane (1.0 mL), 160 °C, and 48 h; HCl (1.0 mL, 6.0 M) and 0.5 h. Isolated yields. ^a B(OMe)₃ (0.20 mmol), B₂pin₂ (0.80 mmol), and 180 °C. ^b B(OMe)₃ (0.20 mmol), B₂pin₂ (0.80 mmol), Et₃N (0.06 mmol), *n*-octane (1.0 mL), 160 °C, and 48 h.



activation, we continued to optimize this $\text{Csp}^2\text{-Csp}^3$ bond activation reaction. Extensive screening showed that the best result was obtained when the reaction was conducted in the presence of B(OMe)_3 (30 mol%) and Et_3N (30 mol%) in *n*-octane at 160 °C for 48 h, affording 1-methyl-2-indolyl boronic pinacol ester (**2a**) in 75% isolated yield (Table 1, entry 1).⁵⁰ The results of varying the standard conditions are shown in Table 1. Compound **2a** was not detected in the absence of B(OMe)_3 , indicating that B(OMe)_3 catalysed this reaction (Table 1, entry 2). Using other boron Lewis acids, such as $\text{B(O}^i\text{Pr)}_3$, BPh_3 , PhB(OH)_2 , and $\text{BF}_3 \cdot \text{Et}_2\text{O}$, as catalysts gave lower yields (entries 3–7). Furthermore, BBr_3 and $\text{B(C}_6\text{F}_5)_3$ were ineffective (entries 8 and 9). No. **2a** was obtained using other metal Lewis acids as catalysts (entry 10). Lower yields of **2a** were obtained in the absence of Et_3N or in the presence of $n\text{-Bu}_3\text{N}$ (entries 11 and 12). Non-polar *n*-hexane was also a suitable solvent for this reaction (entry 13). Decreasing the reaction time resulted in only trace product, unless accompanied by an increased reaction temperature, which resulted in a moderate yield of **2a** (entries 14 and 15). Lowering the reaction temperature to 140 °C led to trace product formation (entry 16).

Having established optimal reaction conditions, the substrate scope of this C–C bond fragmentation borylation reaction was investigated. As shown in Scheme 2, the site-selectivity of this reaction was first studied. Exclusive C2-

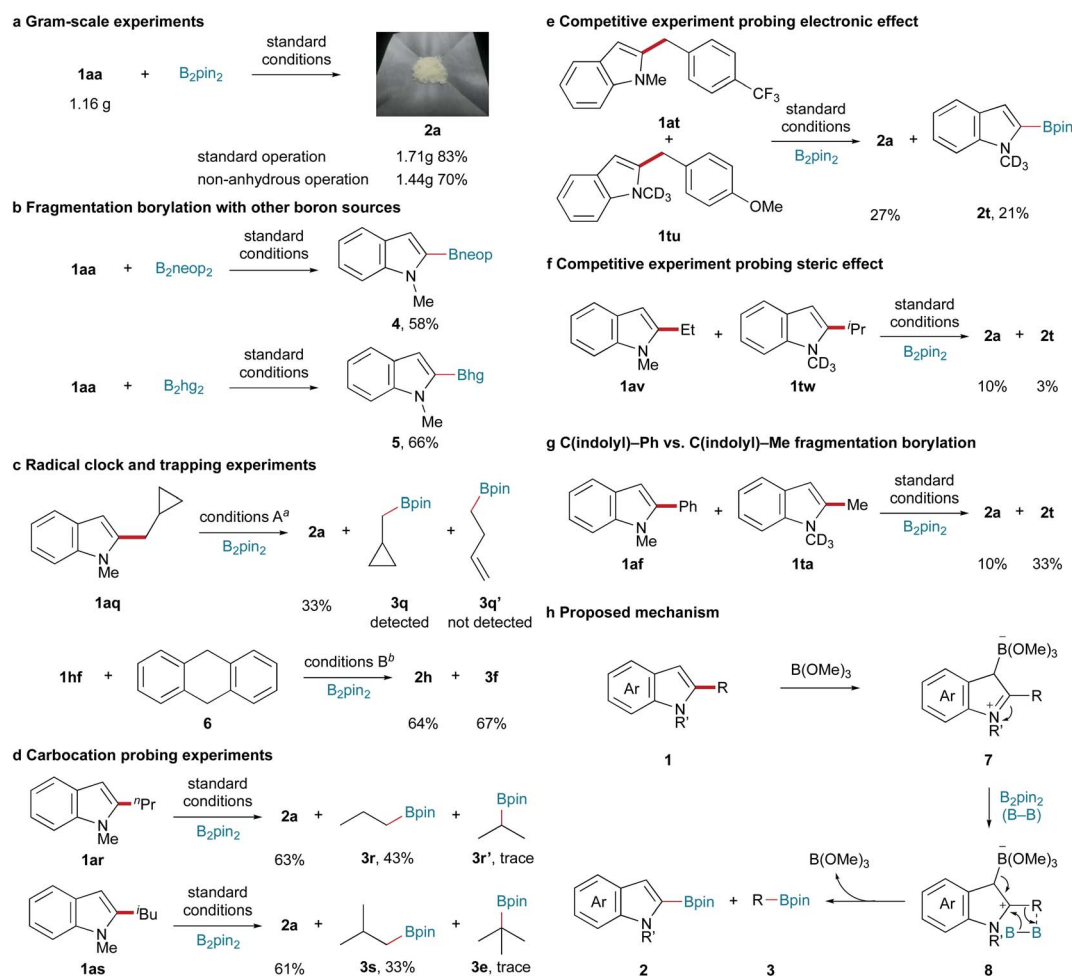
regioselectivity was observed, with the reactions of C4-, C5-, C6-, and C7-substituted 1,2-dimethyl indoles uniformly producing C2-borylated products (**2b–2e**) in good yields. Furthermore, C3-substituted 1,2-dimethyl indole afforded C2-borylated product **2f**, albeit in a lower yield under more harsh conditions. Next, the functional group tolerance of the indolyl fragment was examined. 1,2-Dimethyl indoles bearing *tert*-butyl, methoxy, piperidyl, and trifluoromethyl groups reacted well with B_2pin_2 , giving the corresponding borylation products (**2g–2j**) in good yields. Halogen substituents, such as F, Cl, Br, and I (**2k–2n**), were all tolerated in this C–C bond fragmentation borylation reaction, making further functionalization feasible. Transformable trimethylsilyl (**2o**) and (pinacolato)boryl (**2p**) groups, and a phenyl group (**2q**), were also well tolerated. Generally, both electron-donating and electron-withdrawing substituents on the indole ring did not affect the reaction efficiency. Different *N*-substituted indoles were also tested. Both *N*-butyl and *N*-benzyl indoles reacted well, giving the corresponding products (**2r** and **2s**) in good yields. However, electron-withdrawing protecting groups, such as acetyl and *tert*-butoxycarbonyl, resulted in no desired product formation. 2-Methyl-1-phenyl indole, 1-benzyl-2,5-dimethyl pyrrole, and 2-methyl benzothiophene gave trace or no desired products. The borylation of 5-methoxy-1-methyl indoles bearing alkyl C2-substituents other than a methyl group was performed to



examine the scope of the alkyl fragment (Scheme 2). 5-Methoxy-1-methyl indoles bearing primary alkyl C2-substituents, such as hexyl and benzyl groups, were suitable substrates, affording the corresponding indolyl boronic pinacol ester **2h** and alkyl boronic pinacol esters **3b** and **3c** in moderate yields under modified conditions. 5-Methoxy-1-methyl indole bearing a secondary alkyl C2-substituent (cyclohexyl) gave lower yields (**2h** and **3d**), while no desired products (**2h** and **3e**) were obtained when 5-methoxy-1-methyl indole bearing a tertiary alkyl C2-substituent (*tert*-butyl) was used as the substrate.

Encouraged by the above results, we investigated whether this protocol could be extended to $\text{Csp}^2\text{--Csp}^2$ bonds. To our delight, this transition-metal-free system also promoted $\text{Csp}^2\text{--Csp}^2$ bond cleavage. The reaction conditions were slightly optimized to ensure a satisfactory yield (for details, see Table S1†). The substrate scope was also carefully examined, with the results shown in Scheme 3. Various C2-aryl-substituted 5-methoxy-1-methyl indoles were subjected to this borylation reaction to examine the aryl fragment scope. Aryl moieties

bearing electronically diverse substituents all underwent C–C bond fragmentation borylation smoothly, affording the corresponding indolyl (**2h**) and aryl (**3f–3m**) boronic pinacol esters in moderate yields. Notably, the substrate with a (1,1'-biphenyl)-4-yl substituent (**1hn**) underwent C2-selective C–C bond activation, with the biphenyl moiety remaining intact (**3m**). Similarly, a C(indolyl)–C(2-naphthalenyl) bond (**1oh**) was also cleaved to give the corresponding boronic pinacol esters. Next, the indolyl fragment scope was investigated. 1-Methyl-2-(3,4,5-trimethoxyphenyl) indole (**1ap**) reacted well, affording the corresponding products **2a** and **3p** in moderate yields. The reactions of C4-, C5-, C6-, and C7-substituted indoles all produced the corresponding indolyl (**2b–2e**) and 3,4,5-trimethoxyphenyl (**3p**) boronic acid pinacol esters in moderate yields. The desired products were obtained in low yields from C3-substituted indole **1fp**, probably due to steric hindrance. Electron-donating (**1hp**) and electron-withdrawing (**1jp** and **1kp**) substituents on the indole ring were compatible with this C–C bond activation reaction. Transformable chloride (**1lp**) and trimethylsilyl (**1op**)



Scheme 4 Control experiments and proposed mechanism. (a) Gram-scale experiments. (b) Fragmentation borylation with other boron sources. (c) Radical clock and trapping experiments. (d) Carbocation probing experiments. (e) Competitive experiment probing the electronic effect. (f) Competition experiment probing the stereo effect. (g) C(indolyl)–Ph vs. C(indolyl)–Me fragmentation borylation. (h) Proposed mechanism. ^a Conditions A: B_2pin_2 (0.80 mmol), $\text{B}(\text{OMe})_3$ (0.20 mmol), *n*-octane (1.0 mL), 180 °C, 24 h; HCl (1.0 mL, 6.0 M), and 0.5 h. ^b Conditions B: B_2pin_2 (0.80 mmol), $\text{B}(\text{OMe})_3$ (0.20 mmol), ethylmorpholine (0.10 mmol), *n*-octane (1.0 mL), 160 °C, and 48 h; HCl (1.0 mL, 6.0 M) and 0.5 h.

groups were also tolerated. 1-Methyl-5-phenyl-2-(3,4,5-trimethoxyphenyl) indole (**1qp**) also reacted well with B_2pin_2 , affording the corresponding products **2q** and **3p** in moderate yields. Trace desired products were obtained using 1,2-diphenyl indole, 1-benzyl-2,5-diphenyl pyrrole, and 2-phenyl benzothio-
 phene as the substrate.

The scalability and practicability of this C–C bond fragmentation borylation reaction were also studied. Good yields were obtained from gram-scale experiments under both standard and non-anhydrous conditions (Scheme 4a). Furthermore, C–C bond fragmentation borylation was performed with bis(neopentyl glycolato)diboron (B_2neop_2) and bis(hexylene glycolato)diboron (B_2hg_2) as the boron source (Scheme 4b).

To obtain mechanistic insight into this $B(OMe)_3/B_2pin_2$ -mediated C–C bond activation reaction, a series of control experiments were designed and performed. When radical clock substrate **1aq** was used, only indolyl (**2a**) and cyclopropylmethyl (**3q**) boronic pinacol esters were obtained (Scheme 4c). The reaction of **1hf** with B_2pin_2 in the presence of a stoichiometric amount of radical scavenger 9,10-dihydroanthracene (**6**) afforded **2h** and **3f** in 64% and 67% yields, respectively (Scheme 4c). These results ruled out the possibility of this transformation involving a radical pathway. When **1ar** or **1as** was subjected to this C–C bond activation reaction, only trace amounts of isopropyl (**3r**) or *tert*-butyl (**3e**) boronic pinacol esters were detected (Scheme 4d). These results further ruled out the possibility of the mechanism involving a carbocation intermediate.

The competitive experiment of **1at** and **1tu** indicated that the electronic effect of the C2 substituent had no obvious influence on the C–C bond fragmentation borylation (Scheme 4e). However, the competitive experiment of **1av** and **1tw** indicated that the steric effect of the C2 substituent clearly influenced the C–C bond fragmentation borylation (Scheme 4f). The competitive experiment of **1af** and **1ta** indicated that C(indolyl)–Me bond activation was more favoured than C(indolyl)–Ph bond activation under the same conditions (Scheme 4g). Based on the above results and previous reports,⁵¹ we proposed the following mechanism for this $B(OMe)_3/B_2pin_2$ -mediated C–C bond activation reaction. $B(OMe)_3$ initially attacks the C3-position of **1**, affording intermediate **7**, which further reacts with B_2pin_2 to give products **2** and **3** via intermediate **8**. The cleavage of the C–C and B–B bonds and C–B bond formation probably occurred in a concerted process (Scheme 4h).

Conclusions

In conclusion, $B(OMe)_3/B_2pin_2$ -mediated C–C bond fragmentation borylation has been developed as a new transition-metal-free protocol for non-polar unstrained C–C bond activation. In this system, C2-regioselective C–C bond cleavage of indole derivatives was achieved, producing the corresponding boronic pinacol esters in moderate to good yields. Preliminary mechanistic studies suggested that C–C bond cleavage and C–B bond formation probably occurred in a concerted process. These results will help stimulate further interest in the exploration of C–C bond activation using transition-metal-free techniques. Efforts to gain further mechanistic insights and expand the

reaction mode to other C–C bonds are ongoing in our laboratories.

Data availability

All the experimental data have been included in the ESI.†

Author contributions

L. W., Q. Z., and H. Z. conceived and designed the experiments. L. W., Q. Z., Y. Z., Y. Y., A. W., Q. C., K. Z., J. J., and M. Z. performed the experiments. L. W. and Q. Z. analysed the data. L. W., Q. Z., and H. Z. prepared the manuscript with feedback from the other authors.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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References

- 1 B. Rybtchinski and D. Milstein, *Angew. Chem., Int. Ed.*, 1999, **38**, 870–883.
- 2 C.-H. Jun, *Chem. Soc. Rev.*, 2004, **33**, 610–618.
- 3 A. S. Goldman, *Nature*, 2010, **463**, 435–436.
- 4 M. Murakami and T. Matsuda, *Chem. Commun.*, 2011, **47**, 1100–1105.
- 5 K. Ruhland, *Eur. J. Org. Chem.*, 2012, 2683–2706.
- 6 G. Dong, *C–C Bond Activation*, Springer, Berlin, 2014.
- 7 L. Souillart and N. Cramer, *Chem. Rev.*, 2015, **115**, 9410–9464.
- 8 I. Marek, A. Masarwa, P.-O. Delaye and M. Leibeling, *Angew. Chem., Int. Ed.*, 2015, **54**, 414–429.
- 9 M. Murakami and N. Ishida, *J. Am. Chem. Soc.*, 2016, **138**, 13759–13769.
- 10 D.-S. Kim, W.-J. Park and C.-H. Jun, *Chem. Rev.*, 2017, **117**, 8977–9015.
- 11 Z. Nairoukh, M. Cormier and I. Marek, *Nat. Rev. Chem.*, 2017, **1**, 0035.
- 12 M. Wang and Z. Shi, *Chem. Rev.*, 2020, **120**, 7348–7398.
- 13 B. Zhao, T. Rogge, L. Ackermann and Z. Shi, *Chem. Soc. Rev.*, 2021, **50**, 8903–8953.
- 14 B. Zhao, B. Prabagar and Z. Shi, *Chem*, 2021, **7**, 2585–2634.
- 15 T. Seiser and N. Cramer, *Org. Biomol. Chem.*, 2009, **7**, 2835–2840.
- 16 T. Seiser, T. Saget, D. N. Tran and N. Cramer, *Angew. Chem., Int. Ed.*, 2011, **50**, 7740–7752.
- 17 C. Aïssa, *Synthesis*, 2011, 3389–3407.



- 18 D. J. Mack and J. T. Njardarson, *ACS Catal.*, 2013, **3**, 272–286.
- 19 P.-h. Chen and G. Dong, *Chem.–Eur. J.*, 2016, **22**, 18290–18315.
- 20 P.-h. Chen, B. A. Billett, T. Tsukamoto and G. Dong, *ACS Catal.*, 2017, **7**, 1340–1360.
- 21 G. Fumagalli, S. Stanton and J. F. Bower, *Chem. Rev.*, 2017, **117**, 9404–9432.
- 22 H. M. Ko and G. Dong, *Nat. Chem.*, 2014, **6**, 739–744.
- 23 Y. Wang, J. Bai, Y. Yang, W. Zhao, Y. Liang, D. Wang, Y. Zhao and Z. Shi, *Chem. Sci.*, 2021, **12**, 3599–3607.
- 24 F. Chen, T. Wang and N. Jiao, *Chem. Rev.*, 2014, **114**, 8613–8661.
- 25 A. Dermenci, J. W. Coe and G. Dong, *Org. Chem. Front.*, 2014, **1**, 567–581.
- 26 H. Liu, M. Feng and X. Jiang, *Chem.–Asian J.*, 2014, **9**, 3360–3389.
- 27 F. Song, T. Gou, B.-Q. Wang and Z.-J. Shi, *Chem. Soc. Rev.*, 2018, **47**, 7078–7115.
- 28 Y. Xia and G. Dong, *Nat. Rev. Chem.*, 2020, **4**, 600–614.
- 29 M. D. R. Lutz and B. Morandi, *Chem. Rev.*, 2021, **121**, 300–326.
- 30 C. He, S. Guo, L. Huang and A. Lei, *J. Am. Chem. Soc.*, 2010, **132**, 8273–8275.
- 31 Y. Xia, G. Lu, P. Liu and G. Dong, *Nature*, 2016, **539**, 546–550.
- 32 J. B. Roque, Y. Kuroda, L. T. Goettmann and R. Sarpong, *Science*, 2018, **361**, 171–174.
- 33 J. B. Roque, Y. Kuroda, L. T. Goettmann and R. Sarpong, *Nature*, 2018, **564**, 244–248.
- 34 V. T. Tran, J. A. Gurak Jr, K. S. Yang and K. M. Engle, *Nat. Chem.*, 2018, **10**, 1126–1133.
- 35 Y. Xu, X. Qi, P. Zheng, C. C. Berti, P. Liu and G. Dong, *Nature*, 2019, **567**, 373–378.
- 36 A. J. Smaligo, M. Swain, J. C. Quintana, M. F. Tan, D. A. Kim and O. Kwon, *Science*, 2019, **364**, 681–685.
- 37 Y. Adeli, K. Huang, Y. Liang, Y. Jiang, J. Liu, S. Song, C.-C. Zeng and N. Jiao, *ACS Catal.*, 2019, **9**, 2063–2067.
- 38 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, *Nat. Chem.*, 2019, **11**, 71–77.
- 39 S.-H. Shi, Y. Liang and N. Jiao, *Chem. Rev.*, 2021, **121**, 485–505.
- 40 M. Gozin, A. Weisman, Y. Ben-David and D. Milstein, *Nature*, 1993, **364**, 699–701.
- 41 M. Gozin, M. Alzenberg, S.-Y. Liou, A. Weisman, Y. Ben-David and D. Milstein, *Nature*, 1994, **370**, 42–44.
- 42 S.-Y. Liou, M. Gozin and D. Milstein, *J. Am. Chem. Soc.*, 1995, **117**, 9774–9775.
- 43 S.-Y. Liou, M. E. van der Boom and D. Milstein, *Chem. Commun.*, 1998, 687–688.
- 44 J. Zhu, J. Wang and G. Dong, *Nat. Chem.*, 2019, **11**, 45–51.
- 45 J. Zhu, P.-h. Chen, G. Lu, P. Liu and G. Dong, *J. Am. Chem. Soc.*, 2019, **141**, 18630–18640.
- 46 J. Zhu, R. Zhang and G. Dong, *Nat. Chem.*, 2021, **13**, 836–842.
- 47 Q. Zhong, S. Qin, Y. Yin, J. Hu and H. Zhang, *Angew. Chem., Int. Ed.*, 2018, **57**, 14891–14895.
- 48 J. Wen and Z. Shi, *Acc. Chem. Res.*, 2021, **54**, 1723–1736.
- 49 B. Prabagar, Y. Yang and Z. Shi, *Chem. Soc. Rev.*, 2021, **50**, 11249–11269.
- 50 Considerable yield of unstable C2,C3-diborylated indole **2a'** was obtained under fragmentation borylation conditions. C2,C3-diborylated indole **2a'** could occur C3-protodeboration by the treatment of aqueous hydrochloride solution to produce **2a** quantitatively. Methyl boronic pinacol ester **3a** was not detected by GCMS due to its instability under fragmentation borylation conditions. For details of **2a'**, see the ESI†
- 51 F. Focante, I. Camurati, D. Nanni, R. Leardini and L. Resconi, *Organometallics*, 2004, **23**, 5135–5141.

