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Organocatalytic Enantioselective Friedel−Crafts Aminoalkylation of Indoles in the Carbocyclic Ring

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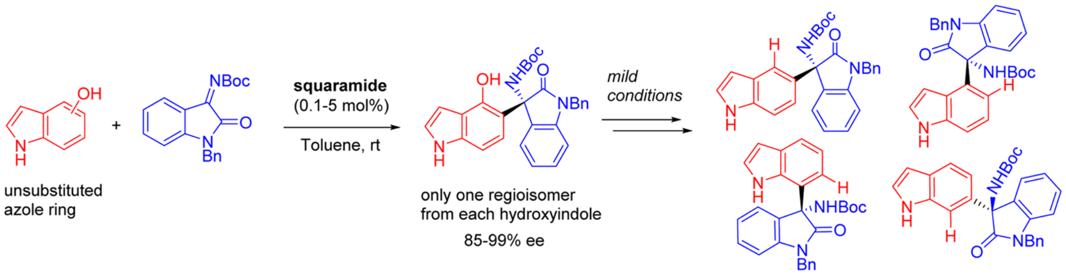
Supporting Information



ABSTRACT: The first general catalytic method for the, so far elusive, enantioselective Friedel−Crafts functionalization of indoles in the carbocyclic ring is presented. This transformation contrasts with the usual tendency of these heterocycles to react at the azole ring. For this purpose, the four regioisomeric hydroxy carbocyclic-substituted indoles were reacted with several isatin-derived ketimines, using a *Cinchona* alkaloid-based squaramide, in a low 0.5−5 mol % catalyst loading, as a bifunctional catalyst. This methodology allows the functionalization of indoles in every position of the carbocyclic ring in a regio- and enantioselective fashion, by switching only the position of the hydroxy group in the starting material. Furthermore, several transformations were carried out, including the reductive elimination of the hydroxy group.

KEYWORDS: *asymmetric catalysis, organocatalysis, Friedel−Crafts reaction, indoles, phenols, isatin-derived ketimines*

The indole scaffold is a privileged structure not only in medicinal chemistry but also in materials science and technology. In fact, over 10 000 indole derivatives with biological activity have been reported to date, and the number of drugs, either commercialized or in clinical trial stage, containing this scaffold is increasing.[1] The indole framework is also present in a multitude of natural products.[2] On account of this, the synthesis and modification of indoles has been intensively studied since the 19th century. Indoles are excellent nucleophiles prone to react by electrophilic aromatic substitution at the C-3 position of the azole ring including enantioselective transformations. Positions C-2 and N-1 can also be functionalized selectively using different strategies.[3]

However, general methods to carry out selectively the functionalization of indoles in the carbocyclic ring are scarce. Generally, this functionalization requires the presence of deactivating or blocking substituents in the 5-membered ring, the appropriate choice of a directing group on the N atom, and the use of a transition metal catalyst.[4−6] Alternatively, the enantioselective functionalization of indolines, followed by oxidation,[7] can provide functionalized indoles in the carbocyclic ring, although just at the C-5 position.[8]

Undoubtedly, there is a demand for a general method for the enantioselective electrophilic functionalization of the carbocyclic ring of indoles lacking a substituent in the azole system. On the basis of our recent work on the addition of naphthols and electron-rich phenols to isatin-derived ketimines,[9,10] we envisioned that the functionalization of the carbocyclic ring of indoles could be attained by introducing an activating/directing hydroxy group in the carbocyclic ring of the indole. This represents a diametrically opposed approach to the commonly applied methods, focused on the electronic or sterical deactivation of the 5-membered ring. Moreover, the hydroxyindole moiety is of high importance in medicinal chemistry as it is present in serotonine and other biologically active compounds (Figure 1).

However, although the activating/directing ability of the OH group in hydroxyindoles has been known for nearly 50 years,[11] this effect has not been exploited in enantioselective Friedel−Crafts reactions, and all the asymmetric reactions with hydroxyindoles have been reported occurring at the C-3 position (Scheme 1).[12] Only very recently, Jørgensen and co-workers have described just one example of Friedel−Crafts/

Received: January 26, 2016
Revised: March 11, 2016

DOI: 10.1021/acscatal.6b00260
ACS Catal. 2016, 6, 2689−2693

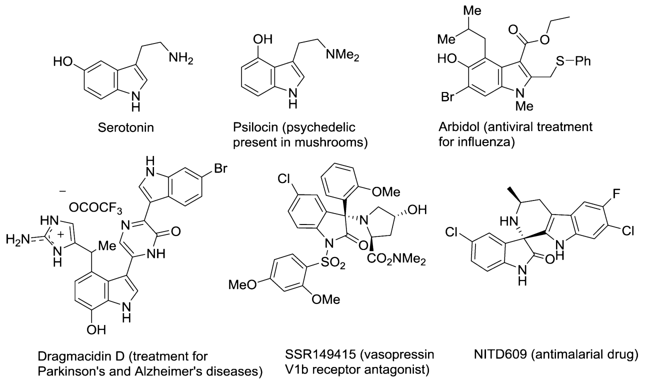
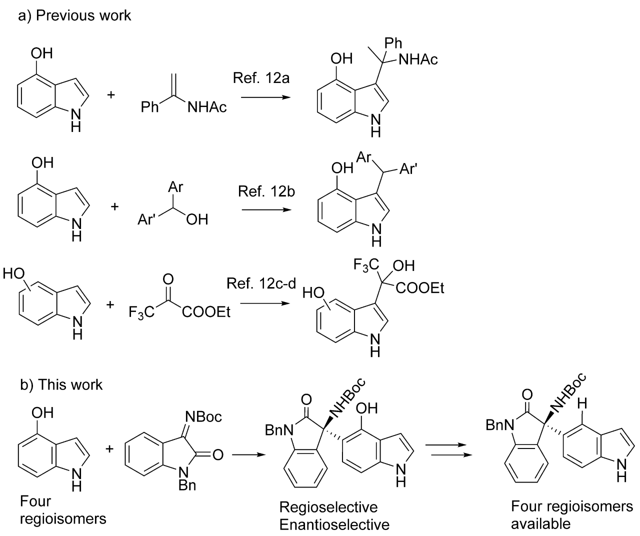


Figure 1. Biologically active indoles and oxindoles.

Scheme 1. Asymmetric Friedel–Crafts Reactions of Hydroxyindoles

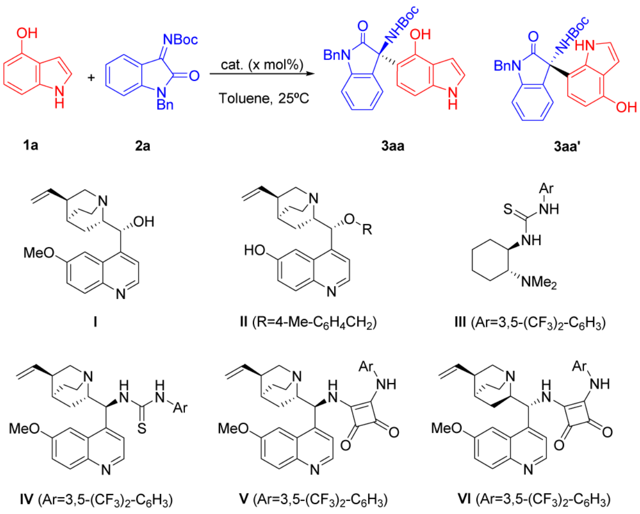


oxa-Michael reaction of 4-hydroxyindole occurring at the C-5 position of the carbocyclic ring, leading to an interesting chiral chroman.[13]

In this communication, we present the first regio- and enantioselective functionalization of each position of the carbocyclic ring in indoles. Our strategy involved three actions: (a) switching the reacting ring by activating the carbocyclic ring with a hydroxy group; (b) directing the regioselectivity by changing the position of the hydroxy group, and (c) removal of the OH group in the resulting products. Accordingly, we carried out the Friedel–Crafts reaction of the four regioisomeric hydroxyindoles, unsubstituted in the azole ring, using a bifunctional organocatalyst based on the quinine skeleton.[14] The electrophiles of choice were Boc-protected isatin-derived ketimines.[15] The catalyst activates both nucleophile and electrophile at the same time, providing an exquisite enantioselectivity and complete regioselectivity, to give highly enantioenriched tetrasubstituted 3-aminooxindoles. Interestingly, this motif is present in several biologically active compounds (Figure 1).

We started our study by testing the reaction of 4-hydroxyindole (**1a**) and *N*-Boc-protected ketimine **2a** with different bifunctional organocatalysts in toluene at 25 °C. First, we carried out the reaction with simple quinine (**I**) as a chiral base, obtaining a complex mixture of products. The desired product **3aa** was isolated in low yield (38%) and with low enantioselectivity (18% ee) (Table 1, entry 1). We also observed the formation of compound **3aa′** in comparable yield (35%) and low enantioselectivity (35% ee). Cupreine derivative **II** gave product **3aa** with good yield but still low enantiocontrol (Table 1, entry 2). With Takemoto's catalyst **III**, we reached excellent enantioselectivity (93% ee) but low yield (Table 1, entry 3). Interestingly, in this case, the major product of the reaction (65% yield) was product **3aa′**, which was isolated in excellent enantioselectivity (98% ee). To our delight, quinine-derived thiourea **IV** gave excellent results in terms of yield and enantioselectivity for compound **3aa** (Table 1, entry 4). Further improvement was achieved using squaramide **V** (Table 1, entry 5).[16] This catalyst also allowed us to reduce the catalyst loading as low as 1 mol %, keeping the enantiomeric excess in 99% (Table 1, entry 6). It should be pointed out that the reaction affords just one product, as observed by HPLC and ^{1}H NMR analysis of the crude mixture, demonstrating the high selectivity of the method. Finally, we also could access the opposite enantiomer by using squaramide **VI** as catalyst, which is based on the quinidine skeleton (Table 1, entry 7).

Table 1. Optimization of the Reaction Conditions[a]

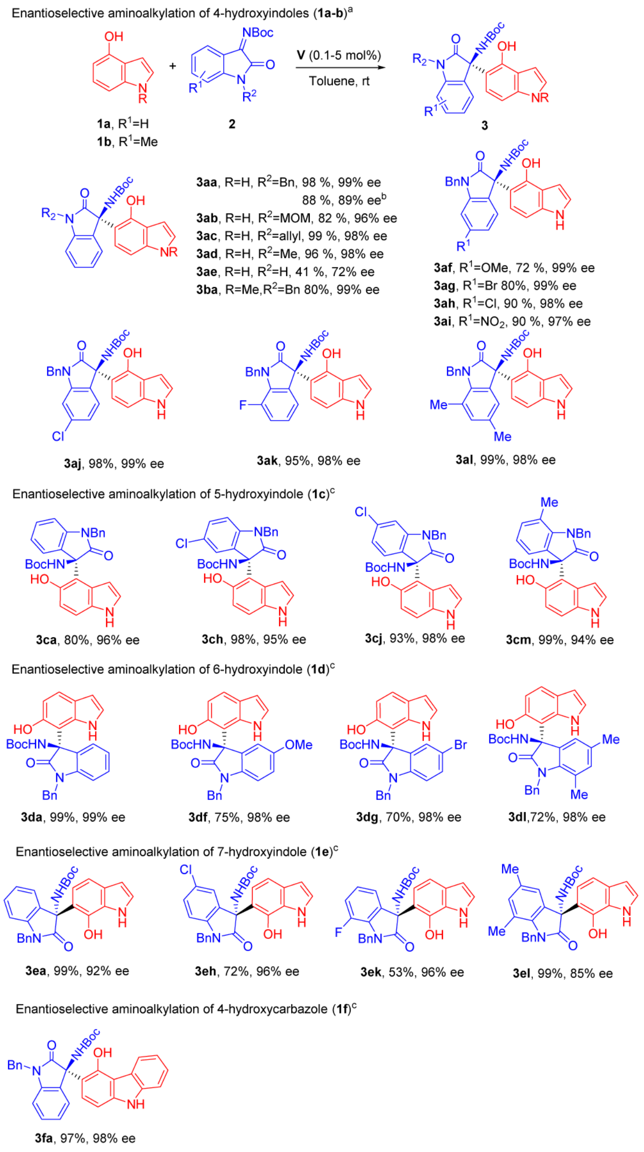


	catalyst (mol %)	time (h)	yield (%)[b]	ee (%)[c]
1	**I** (10 mol %)	5	38	18
2	**II** (10 mol %)	24	72	14[d]
3	**III** (10 mol %)	16	32	93[d]
4	**IV** (10 mol %)	5	91	98
5	**V** (10 mol %)	2	95	>99
6	**V** (1 mol %)	12	98	99
7	**VI** (10 mol %)	12	93	92[d]

[a] Reaction conditions: catalyst (*x* mol %), **1a** (0.2 mmol), **2a** (0.21 mmol), and dry toluene (2 mL) at 25 °C. [b] Isolated yields are reported. [c] Enantiomeric excess (ee) was determined by chiral HPLC. [d] Opposite enantiomer.

Then, we examined the generality of our methodology by reacting 4-hydroxyindole (**1a**) with different isatin-derived ketimines (Scheme 2). Different protecting groups at isatin N-1, such as methoxymethyl, allyl, and methyl, were well-tolerated, the corresponding products **3ab**–**3ad** being obtained with high yields and excellent enantioselectivities (Scheme 1). Unfortunately, the unprotected ketimine **2e** gave the expected product **3ae** in low yield (41%) and moderate enantioselectivity (72% ee). We attribute this result to the formation of nonproductive hydrogen bonds caused by the presence of the

Scheme 2. Substrate Scope



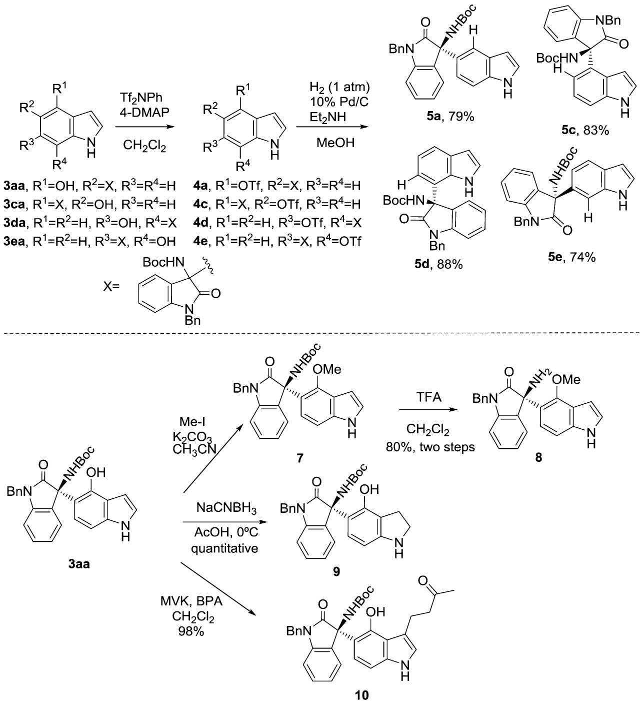
[a] Reaction with 4-hydroxyindole: **V** (1 mol %), 4-hydroxyindole (**1a**, 0.2 mmol), imine **2** (0.21 mmol), toluene (2 mL), 25 °C, 12 h. [b] Gram-scale reaction: **V** (0.1 mol %), 4-hydroxyindole (**1a**, 3.0 mmol), imine **2a** (3.05 mmol), toluene (16 mL), 25 °C, 36 h. [c] Reaction with hydroxyindoles **1c**–**f**: V (5 mol %), hydroxyindole **1** (0.1 mmol), imine **2** (0.105 mmol), toluene (1 mL), 25 °C, 12 h.

free NH group and the poor solubility of **2e** in the reaction solvent. High yields and excellent enantioselectivities (97−99% ee) were also obtained with isatin-derived ketimines having different substituents in the carbocyclic ring, independently of their position or electronic nature (**3af**−**3al** and **3ba**, Scheme 1). Remarkably, good yield and enantioselectivity were reached even with just a 0.1 mol % of catalyst **V** in a gram-scale reaction between 4-hydroxyindole (**1a**) and ketimine **2a**.

After having proved the efficiency of our method for the enantioselective aminoalkylation of 4-hydroxyindoles at the C-5 position, we examined the scope of the reaction with indoles bearing a hydroxy group in other positions of the carbocyclic ring (Scheme 2). Our aim was to achieve the functionalization of every position in this ring by simply changing the position of the directing group. Delightfully, 5-hydroxyindole (**1c**) reacted with ketimine **2a** to give product **3ca** substituted at C-4 with very good regioselectivity and high enantiocontrol (96% ee), although we had to increase the catalyst loading to 5 mol %. Excellent results (**3ch**, **3cj**, **3 cm**) were obtained also with different ketimines. In a similar manner, 6-hydroxyindole (**1d**) was functionalized selectively in the C-7 position using this method. Distinct ketimines were also introduced with outstanding selectivity leading to the corresponding products (**3da**, **3df**, **3dg**, **3dl**). Furthermore, 7-hydroxyindole (**1e**) reacted with several ketimines **2**, which yielded the desired 6-substituted 7-hydroxyindoles (**3ea**, **3eh**, **3ek**, and **3el**) with good enantioselectivities (85−96% ee). In this latter case, a slight decrease of enantioselectivity was observed, probably due to the presence of the vicinal NH. Finally, when 4-hydroxycarbazole (**1f**) was used as a nucleophile the product **3fa** was obtained with excellent yield and enantiomeric excess. It is interesting to note that hydroxyindoles **1c** and **1d** are specially challenging substrates, as they have two available *ortho* positions for the substitution reaction. Our method allows the regioselective aminoalkylation in only one *ortho* position, leading to the desired product.

Although hydroxyindoles are interesting targets *per se*, it is important that the activating/directing hydroxy group could also be removed or used in further transformations (Scheme 3).

Scheme 3. Removal of the Hydroxy Group and Other Synthetic Transformations[a]



[a] See Supporting Information for details.

After some optimization, compounds **3aa**, **3ca**, **3da**, and **3ea** were transformed into their corresponding triflates **4a**, **4c**, **4d**, and **4e**, respectively, which were catalytically hydrogenated at 1 atm to give hydroxy group-free products **5a**, **5c**, **5d**, and **5e** respectively, in high overall yields. All of these four aminoalkylated indoles exhibit distinct chromatographic behavior and spectroscopic properties (see SI), demonstrating we had accessed every aminoalkylated regioisomer. Moreover, triflates **4c**, **4e**, and mesylate **6** (prepared from product **3aa**, see SI) were successfully crystallized and their structures established by X-ray crystal analysis (see SI), unambiguously confirming the structures of their precursors **3ca**, **3ea**, and **3aa**, and hence, that of **3da**. The X-ray analysis of crystals from **6** and **4c** also revealed the *R* configuration for the stereogenic center in both compounds. For the rest of the compounds **3**, we assumed a uniform stereochemical mechanism. Interestingly, when compound **aa′** was subjected to the triflation/hydrogenation sequence, *ent*-**5d** was isolated (see SI).

Furthermore, different synthetic transformations were conducted with product **3aa**, proving the utility of the method (Scheme 3). Thus, compound **3aa** was selectively methylated to compound **7**, which was deprotected with trifluoroacetic acid, obtaining the corresponding free amine **8**. Hydroxyindole **3aa** was also easily transformed into hydroxyindoline **9** by reduction with $NaCNBH_3$ in the presence of acetic acid. Moreover, compound **3aa** reacted with methylvinylketone under acidic catalysis to give product **10**, following a classical Friedel−Crafts reaction at C-3 position of the indole nucleus.

In order to rationalize the observed regio- and stereochemistry, we propose a tentative transition state (Figure 2). As a model, we have followed the activation mode proposed by Khan, Ganguly, and co-workers for the thiourea-catalyzed reaction between 1-naphthols and isatin-derived ketimines.[10a] This model explains the *ortho*-regioselectivity for the nucleophiles and the *R* absolute configuration of the final products. The influence of the catalyst/OH-group interaction can be ascertained by the fact that the 5-methoxyindole does not react under the optimized reaction conditions.

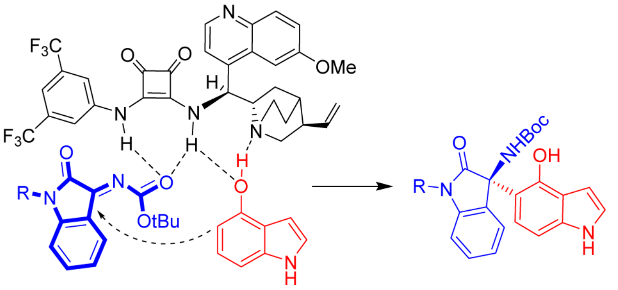


Figure 2. Proposed stereochemical model.

In summary, we have developed the first general method for the enantioselective Friedel−Crafts reaction of hydroxyindoles with isatin-derived ketimines, using an squaramide based on the quinine skeleton as bifunctional organocatalyst (catalyst loading 0.1−5 mol %). Under our reaction conditions, hydroxyindoles react in the carbocyclic ring rather than in the azole system to give the desired aminoalkylated products with high enantioselectivity. Unlike conventional Friedel−Crafts reactions, this approach enables the introduction of substituents in every position of the carbocyclic ring of indole in a regioselective manner, by just switching the position of the activating/directing hydroxy group. Besides the importance of the hydroxyindole moiety in medicinal chemistry, the hydroxy group could be removed under mild reductive elimination conditions in high overall yield. We envision this procedure provides a general strategy for the less explored enantioselective functionalization of indoles in the carbocyclic ring.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.6b00260.

Experimental procedures and spectroscopic data (PDF)
X-ray data for compound **4c** (CIF)
X-ray data for compound **4e** (CIF)
X-ray data for compound **6** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from MINECO (Gobierno de España; CTQ2013-47494-P) and from Generalitat Valenciana (ISIC2012/001) is gratefully acknowledged. M.M-M. thanks Universitat de València for a predoctoral grant, and C.V. thanks MINECO for a JdC contract. Access to NMR, X-ray, and MS facilities from SCSIE-UV is also acknowledged.

■ REFERENCES

(1) (a) Sundberg, R. J. *Indoles*; Academic Press: San Diego, 1996; pp 1−175. (b) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893−930. (c) Zhou, G.; Wu, D.; Snyder, B.; Ptak, R. G.; Kaur, H.; Gochin, M. *J. Med. Chem.* **2011**, *54*, 7220−7231. (d) Zhang, M. Z.; Chen, Q.; Yang, G.-F. *Eur. J. Med. Chem.* **2015**, *89*, 421−441. (e) Sherer, C.; Snape, T. J. *Eur. J. Med. Chem.* **2015**, *97*, 552−560.

(2) (a) Lancianesi, S.; Palmieri, A.; Petrini, M. *Chem. Rev.* **2014**, *114*, 7108−7149. (b) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. *Nat. Prod. Rep.* **2015**, *32*, 1389−1471.

(3) For selected reviews, see: (a) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608−9644. (b) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Chem. Soc. Rev.* **2010**, *39*, 4449−4465. (c) Zeng, M.; You, S.-L. *Synlett* **2010**, *2010*, 1289−1301. (d) Dalpozzo, R. *Chem. Soc. Rev.* **2015**, *44*, 742−778. (e) Wu, H.; He, Y.-P.; Shi, F. *Synthesis* **2015**, *47*, 1990−2016. For some recent examples of enantioselective Friedel−Crafts reactions of indoles, see: (f) Bi, B.; Lou, Q.-X.; Ding, Y.-Y.; Chen, S.-W.; Zhang, S.-S.; Hu, W.-H.; Zhao, J.-L. *Org. Lett.* **2015**, *17*, 540−543. (g) Li, M.-L.; Chen, D.-F-; Luo, S.-W.; Wu, X. *Tetrahedron: Asymmetry* **2015**, *26*, 219−224. (h) Fang, F.; Hua, G.; Shi, F.; Li, P. *Org. Biomol. Chem.* **2015**, *13*, 4395−4398. (i) Frías, M.; Padrón, J. M.; Alemán, J. *Chem. - Eur. J.* **2015**, *21*, 8237−8241. (j) Liu, R.-R.; Ye, S.-C.; Lu, C.-J.; Zhuang, G.-L.; Gao, J.-R.; Jia, Y.-X. *Angew. Chem., Int. Ed.* **2015**, *54*, 11205−11208. (k) Romanini, S.; Galletti, E.; Caruana, L.; Mazzanti, A.; Himo, F.; Santoro, S.; Fochi, M.; Bernardi, L. *Chem. - Eur. J.* **2015**, *21*, 17578−17582. (l) Kato, M.; Hirao, S.; Nakano, K.; Sato, M.; Yamanaka, M.; Sohtome, Y.; Nagasawa, K. *Chem. - Eur. J.* **2015**, *21*, 18606−18612. (m) Pan, J.; Wanga, Y.; Chen, S.; Zhang, X.; Wang, Y.; Zhou, Z. *Tetrahedron* **2016**, *72*, 240−246.

(4) For functionalization of indoles by lithiation, see: (a) Iwao, M.; Ishibashi, F. *Tetrahedron* **1997**, *53*, 51−58. (b) Fukuda, T.; Maeda, R.; Iwao, M. *Tetrahedron* **1999**, *55*, 9151−9162. (c) Hartung, C. G.; Fecher, A.; Chapell, B.; Snieckus, V. *Org. Lett.* **2003**, *5*, 1899−1902.

(5) For a review about C-H activation with indoles, see: (a) Sandtorv, A. H. *Adv. Synth. Catal.* **2015**, *357*, 2403−2435. For selected examples, see: (b) Lanke, V.; Prabhu, K. R. *Org. Lett.* **2013**, *15*, 6262−6265. (c) Liu, Q.; Li, Q.; Ma, Y.; Jia, Y. *Org. Lett.* **2013**, *15*, 4528−4531. (d) Paul, S.; Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E., Jr.; Smith, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 15552−15553. (e) Feng, Y.; Holte, D.; Zoller, J.; Umemiya, S.; Simke, L. R.; Baran, P. S. *J. Am. Chem. Soc.* **2015**, *137*, 10160−10163. (f) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 4068−

4069. (g) Yang, Y.; Qiu, X.; Zhao, Y.; Mu, Y.; Shi, Z. *J. Am. Chem. Soc.* **2016**, *138*, 495−498.

(6) For F−C reactions of substituted indoles, see: (a) Xu, Q.-L.; Dai, L.-X.; You, S.-L. *Chem. Sci.* **2013**, *4*, 97−102. (b) Liu, H.; Zheng, C.; You, S.-L. *J. Org. Chem.* **2014**, *79*, 1047−1054. (c) Zhou, L.-J.; Zhang, Y.-C.; Zhao, J.-J.; Shi, F.; Tu, S.-J. *J. Org. Chem.* **2014**, *79*, 10390−10398.

(7) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Fong, K. C.; He, Y.; Yoon, W. H.; Choi, H.-S. *Angew. Chem., Int. Ed.* **1999**, *38*, 1676−1678.

(8) For enantioselective F−C reactions of indolines, see: (a) Gathergood, N.; Zhuang, W.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2000**, *122*, 12517−12522. (b) Saaby, S.; Fang, X.; Gathergood, N.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 4114−4116. (c) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 7894−7895. (d) Yuan, Y.; Wang, X.; Li, X.; Ding, K. *J. Org. Chem.* **2004**, *69*, 146−149. For selected C−H activation processes of indolines, see: (e) Talwar, D.; Gonzalez-de-Castro, A.; Li, H. Y.; Xiao, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 5223−5227. (f) Yang, X.-F.; Hu, X.-H.; Feng, C.; Loh, T.-P. *Chem. Commun.* **2015**, *51*, 2532−2535. (g) Yang, G.; Lindovska, P.; Zhu, D.; Kim, J.; Wang, P.; Tang, R.-Y.; Movassaghi, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 10807−10813. (h) Wang, X.; Tang, H.; Feng, H.; Li, Y.; Yang, Y.; Zhou, B. *J. Org. Chem.* **2015**, *80*, 6238−6249.

(9) (a) Montesinos-Magraner, M.; Vila, C.; Cantón, R.; Blay, G.; Fernández, I.; Muñoz, M. C.; Pedro, J. R. *Angew. Chem., Int. Ed.* **2015**, *54*, 6320−6324.

(10) For more examples of enantioselective F−C reactions with hydroxyarenes and ketimines, see: (a) Kumari, P.; Barik, S.; Khan, N. H.; Ganguly, B.; Kureshy, R. I.; Abdi, S. H. R.; Bajaj, H. C. *RSC Adv.* **2015**, *5*, 69493−69−501. (b) Zhou, D.; Huang, Z.; Yu, X.; Wang, Y.; Li, J.; Wang, W.; Xie, H. *Org. Lett.* **2015**, *17*, 5554−5557. For a review on enantioselective F−C reactions with naphthols and phenols, see: (c) Montesinos-Magraner, M.; Vila, C.; Blay, G.; Pedro, J. R. *Synthesis* **2016**, manuscript accepted.

(11) (a) Monti, S. A.; Johnson, W. O.; White, D. H. *Tetrahedron Lett.* **1966**, *7*, 4459−4464. (b) Troxler, F.; Bormann, G.; Seemann, F. *Helv. Chim. Acta* **1968**, *51*, 1203−1213.

(12) (a) Jia, Y.-X.; Zhong, J.; Zhu, S.-F.; Zhang, C.-M.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5565−5567. (b) Saha, S.; Alamsetti, S. K.; Schneider, C. *Chem. Commun.* **2015**, *51*, 1461−1464. (c) Han, X.; Ouyang, W.; Liu, B.; Wang, W.; Tien, P.; Wu, S.; Zhou, H.-B. *Org. Biomol. Chem.* **2013**, *11*, 8463−8475. (d) Wolf, C.; Zhang, P. *Adv. Synth. Catal.* **2011**, *353*, 760−766.

(13) During our investigation, Jørgensen and co-workers reported a very stimulating 1,6-Friedel-Crafts/1,4-oxa-Michael reaction, in which they described a single example with 4-hydroxyindole (7 days; 43% yield, 97% ee). Poulsen, P. H.; Feu, K. S.; Paz, B. M.; Jensen, F.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2015**, *54*, 8203−8207.

(14) For selected reviews: (a) Alemán, J.; Parra, A.; Jiang, H.; Jørgensen, K. A. *Chem. - Eur. J.* **2011**, *17*, 6890−6899. (b) Chauhan, P.; Mahajan, S.; Kaya, U.; Hack, D.; Enders, D. *Adv. Synth. Catal.* **2015**, *357*, 253−281.

(15) For recent reviews, see: (a) Kaur, J.; Chimni, S. S.; Mahajan, S.; Kumar, A. *RSC Adv.* **2015**, *5*, 52481−52496. (b) Yu, J.-S.; Zhou, F.; Liu, Y.-L.; Zhou, J. *Synlett* **2015**, *26*, 2491−2504. For stereoselective F−C reaction of indoles, see: (c) Feng, J.; Yan, W.; Wang, D.; Li, P.; Sun, Q.; Wang, R. *Chem. Commun.* **2012**, *48*, 8003−8005. (d) Chen, J.-P.; Chen, W.-W.; Li, Y.; Xu, M.-H. *Org. Biomol. Chem.* **2015**, *13*, 3363−3370. For recent examples, see: (e) Bao, X.; Wang, B.; Cui, L.; Zhu, G.; He, Y.; Qu, J.; Song, Y. *Org. Lett.* **2015**, *17*, 5168−5171. (f) Arai, T.; Tsuchiya, K.; Matsumura, E. *Org. Lett.* **2015**, *17*, 2416−2419. (g) Holmquist, M.; Blay, G.; Muñoz, M. C.; Pedro, J. R. *Adv. Synth. Catal.* **2015**, *357*, 3857−3862. (h) Engl, O. D.; Fritz, S. P.; Wennemers, H. *Angew. Chem., Int. Ed.* **2015**, *54*, 8193−8197. (i) Zheng, H.; Liu, X.; Xu, C.; Xia, Y.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 10958−10962. (j) He, Q.; Wu, L.; Kou, X.; Butt, N.; Yang, G.; Zhang, W. *Org. Lett.* **2016**, *18*, 288−291. (k) Beceño, C.; Chauhan, P.; Rembiak, A.; Wang, A.; Enders, D. *Adv. Synth. Catal.* **2015**, *357*, 672−676. (l) Zhao, J.; Fang, B.; Luo, W.; Hao, X.; Liu, X.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 241−244.

(16) For seminal examples: (a) Malerich, J. P.; Hagihara, K.; Rawal, V. H. *J. Am. Chem. Soc.* **2008**, *130*, 14416−14417. (b) Yang, W.; Du, D.-M. *Org. Lett.* **2010**, *12*, 5450−5453.

DOI: 10.1021/acscatal.6b00260
ACS Catal. 2016, 6, 2689−2693