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Triflic acid as an efficient Brønsted acid promoter for the umpolung of N-Ac indoles in hydroarylation reactions

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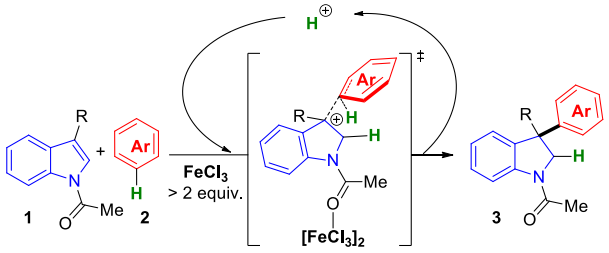
Abstract. We report that triflic acid, a strong Brønsted acid, is a very powerful alternative to $FeCl_3$ to mediate the hydroarylation of N-Ac indoles, which delivers regioselectively 3-arylindolines, 3,3-spiroindolines or 2-arylindolines. Mechanistic explorations point towards the existence of a highly electrophilic intermediate by simultaneous activation of the acetyl and of the C2=C3 bond by protons.

Keywords: Indole; Umpolung; Hydroarylation; Brønsted acid; Friedel-Crafts

The dearomative umpolung of the indole nucleus is an emerging topic with an important synthetic potential to access indoline derivatives of biological relevance.[1-8] Most of the time, this reversal of polarity[2a] involves the oxidation of the indole nucleus[2b-j,3] or the presence of strong electron-withdrawing groups.[2k-m] In this context, our group developed several methods[3,4] to generate electrophilic indoles to overturn the innate nucleophilicity of indoles,[1a,5] including the C3-regioselective $FeCl_3$-mediated hydroarylation of N-Ac indole **1** (Scheme 1)[3] which was inspired by preliminary findings from Nakatsuka and co-workers.[6]

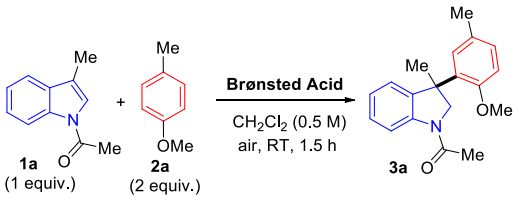


Scheme 1. Our $FeCl_3$-mediated regioselective hydroarylation of N-Ac indoles via a polyactivated intermediate.

We have recently demonstrated that this reaction proceeds via a polyactivated intermediate, in which the acetyl is activated by $FeCl_3$ to favour the delocalization of the nitrogen lone pair into the carbonyl system, and in which the C2=C3 bond is activated by a proton to induce a Friedel-Crafts reaction with arene **2** (Scheme 1).[7]

During the optimization process of the hydroarylation of N-Ac indoles, we screened several Lewis acids and $FeCl_3$ proved to be rather exclusive to promote the desired reaction. At that time, we ruled out the fact that a proton could be the sole promoter of the reaction. We recently started a more thorough evaluation of Brønsted acids as promoters (Table 1).

Table 1. Evaluation of Brønsted acids as promoter of the 3-hydroarylation of N-Ac skatole with 4-methylanisole.



Entry	Brønsted acid	Isolated Yield **3a**
1	HCl (excess)	0%
2	CF_3CO_2H (3 equiv.)	0%
3	H_2SO_4 (2.5 equiv.)	84%
4	CF_3SO_3H (2.5 equiv.)	95%
5	$MeSO_3H$ (3 equiv.)	0%
6	(+)-CSA (2.5 equiv.)	0%
7	$HNTf_2$ (2.2 equiv.)	0%

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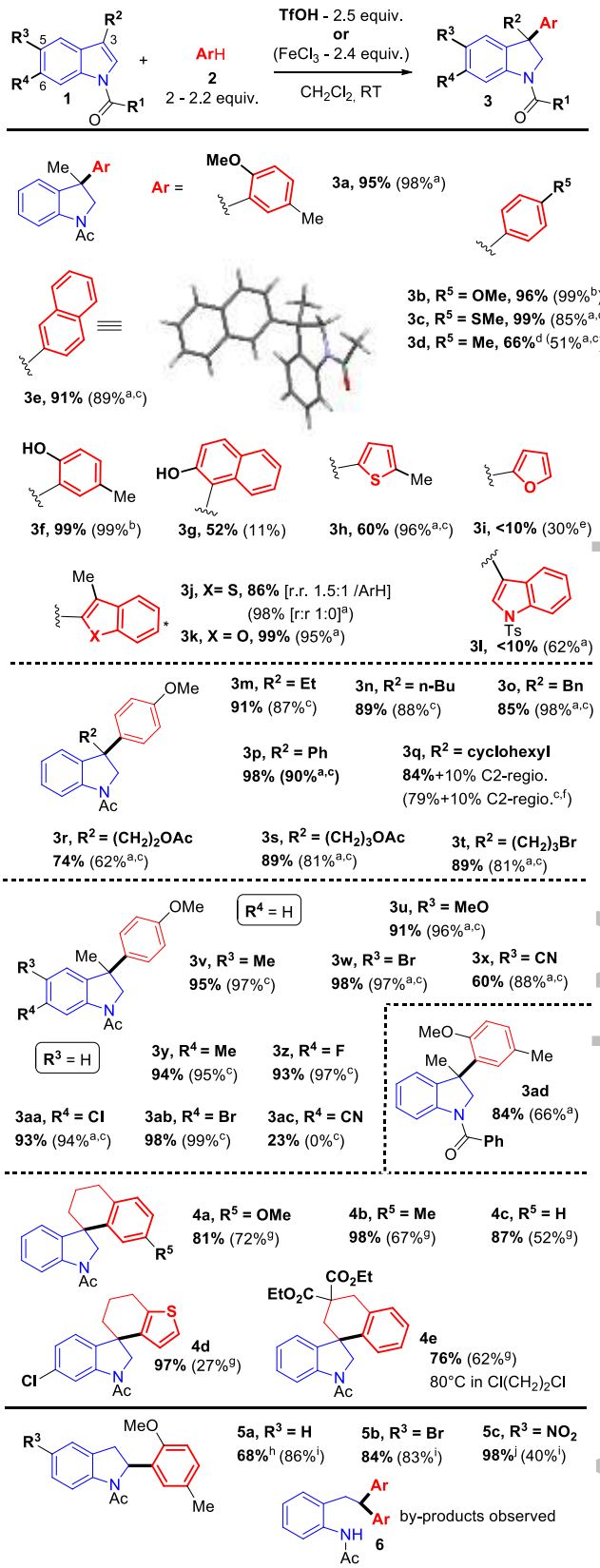
We indeed envisioned that hydrogen chloride could be generated from $FeCl_3$ in the reaction medium. Therefore, HCl gas was bubbled through a mixture of N-Ac skatole **1a** and anisole **2a**, yet **3a** was not detected (entry 1). We continued our study with strong Brønsted acids. Trifluoroacetic acid (entry 2) did not deliver any coupling product. However, 2.5 equivalents of sulfuric acid were able to promote the reaction and delivered **3a** in 84% yield (entry 3). Triflic acid (TfOH) was even better and provided the hydroarylated product in 95% yield (entry 4).[9] Other sulfonic acids or triflimine (entries 5-7) were ineffective.

Encouraged by this improved result, we decided to study the scope of the hydroarylation of N-Ac indoles with TfOH as promoter and compared it with $FeCl_3$ (Scheme 2). TfOH proved to be as efficient as $FeCl_3$ for the intermolecular regioselective 3-hydroarylation of N-Ac indoles substituted at the 3-position,[10] whether we used anisole derivatives, thioanisole, toluene, naphthalene[11] or phenols as the aromatic nucleophile (indolines **3a-g**). In the case of β-naphthol, a much better yield of **3g** was obtained with TfOH, because the oxidative dimerization of β-naphtol observed in the presence of $FeCl_3$ was suppressed. Heteroaromatic compounds were also evaluated Indoline **3h** was obtained from 2-methylthioanisole in 60% yield, while furan decomposed almost immediately in presence of TfOH leading to less than 10% of **3i**. Benzothiophene and benzofuran were excellent nucleophiles in presence of TfOH, leading to **3j** and **3k** in 86 and 99% yields. It is noteworthy that a mixture of two regioisomers of **3j** (relatively to the arene nucleophile) were observed with TfOH, which is in contrast with the $FeCl_3$ conditions. Surprisingly, N-Ts indole proved to be a poor nucleophile in these conditions (indoline **3l**). A similar efficiency between $FeCl_3$ and TfOH was noted when we investigated the substitution at positions 3, 5 or 6 of the indole nucleus (indolines **3m-ab**). TfOH was superior in the case of 6-cyanoindoline **3ac**. A better yield was also obtained with TfOH when the N-acetyl group on skatole was replaced by a N-benzoyl (**3ad**). Concerning the intramolecular reaction, TfOH proved to be a better promoter than $FeCl_3$ since 3,3-spirocycles **4a-e** were obtained with better yields. In particular the thiophene-containing spirocyclic derivative **4d** was obtained in 97% yield with TfOH in 2 hours, compared to 27% with $FeCl_3$. We recently established that if the N-Ac indole was unsubstituted at the C3-position, the aryl nucleophile reacted at the C2-position in presence of $FeCl_3$.[4e,8] The same regioselectivity was observed with TfOH for the reaction with *p*-methyl anisole **2a**, leading to **5a-c**. In the case of **5a**, it was necessary to use only one equivalent of the aromatic nucleophile to avoid the opening of the C2-N bond by a second aryl nucleophile which lead to **6**. Notably, a large increase of the yield was observed for 5-nitro indoline **5c**.



Scheme 2. Regioselective hydroarylation of 3-substituted N-Ac-indoles promoted by TfOH. a) reported in ref 4b; b) reported in ref 4a; c) 3.4 equiv. of $FeCl_3$ and 3 equiv. ArH; d) 3 equiv. of TfOH; e) 3 equiv. of TfOH; f) reported in ref 7; g) reported in ref 4d; h) 1.07 equiv. of **2**; i) reported in ref 4e; j) 2.75 equiv. of **2**.

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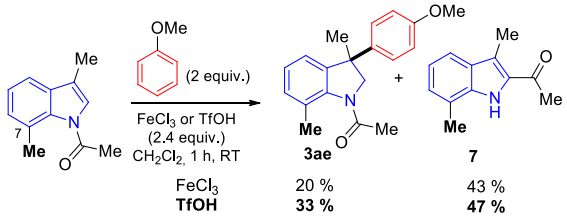
While studying the scope of the C3-hydroarylation, we turned our attention to a C-7 substituted indole and we observed an unexpected behaviour of the starting N-Ac indole (Scheme 3). 7-Methyl-N-Ac skatole gives the hydroarylated product **3ae** in only 20% and 33% with $FeCl_3$ and TfOH, respectively. The major product **7** is produced through the migration of the acetyl from the nitrogen to the C2-position. In absence of anisole, **7** was obtained in 90% yield with $FeCl_3$. This result informed us that to be fully operative, the amide bond should suffer no destabilization from the C7-substituent and even then, arylated indoline **3ae** can be isolated in moderate yield.



Scheme 3. Effect of the destabilization of the amide bond conformation on the reactivity.

Overall, some limitations of the $FeCl_3$ promoter in the hydroarylation of N-Ac indoles have been circumvented by the use of TfOH as an alternative and very efficient promoter. Having established that this reaction could operate with a Brønsted super acid (TfOH) or a Lewis acid ($FeCl_3$), we wondered whether a mechanism comparable to the one that we previously established for $FeCl_3$[7] was also operative with TfOH.

We conducted an *in situ* IR study to get insights into the course of the reaction (Figure 1).[7,12]

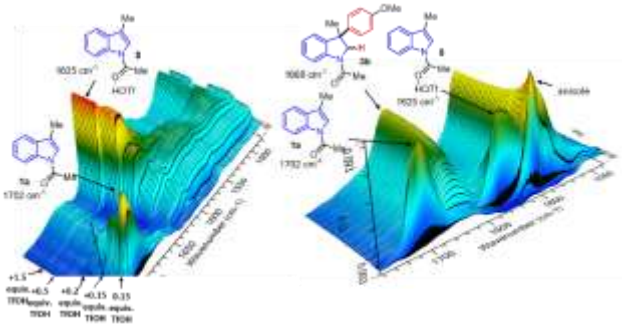


Figure 1. *in situ* IR monitoring of the reaction between N-Ac skatole **1a** and TfOH in 0.2M CH_2Cl_2 (left); reaction between N-Ac skatole **1a**, anisole **2b** (2 equiv.) and TfOH (2.5 equiv.) in 0.2M CH_2Cl_2 (right). .

We started to monitor the effect of TfOH towards N-Ac skatole **1a** in the absence of the aromatic nucleophile. Upon portion wise addition of TfOH to **1a**, we indeed noticed the progressive vanishing of the stretching absorption band of the carbonyl at 1702 cm^{-1} (Figure 1, left). In the meantime, no clear new band was observed, but rather a broad absorption between 1625 and 1500 cm^{-1}. Total disappearance of the stretching of the carbonyl of the starting N-Ac skatole was observed with 0.5 equivalent of TfOH with formation of a band at 1625 cm^{-1}. Upon addition of additional 0.5 equivalent of TfOH (1 equivalent in total) the broad absorption was transformed into a sharp strong band at 1625 cm^{-1}, which may represent the association of the acetyl of N-Ac skatole with TfOH in a 1:1 ratio (intermediate **8**). Further addition of TfOH did not induce any noteworthy change. We then recorded the *in situ* IR spectra in presence of anisole **2b** in the reaction conditions. As soon as 2.5 equivalents of TfOH were added, the carbonyl absorption band shifted from 1702 to 1625 cm^{-1} (Figure 1, right). The progressive disappearance of this band, attributed to 1:1 N-Ac skatole-TfOH intermediate **8**, is accompanied by the formation of the hydroarylation product carbonyl band at 1668 cm^{-1}.

A study of the activation of N-Ac skatole with the promoter by NMR was realized in order to improve our understanding of its effect on reactivity.[13] The proton NMR of N-Ac indole **1a** with several amounts of TfOH were recorded (Figure 2, top).

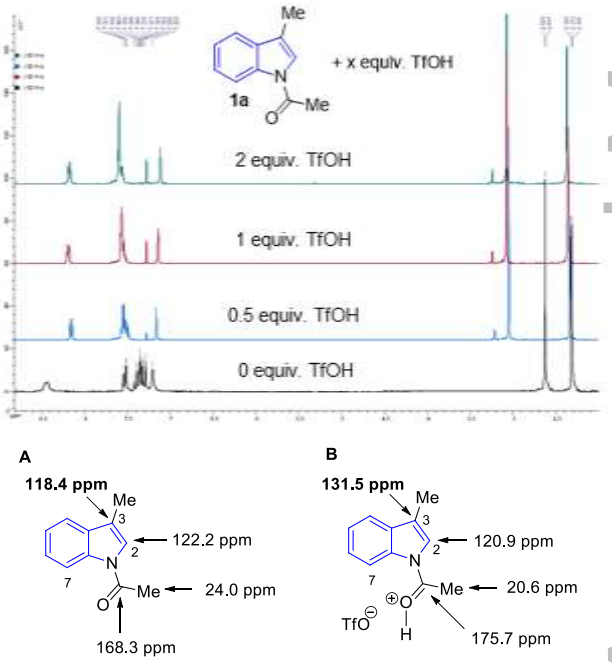


Figure 2. ^1H NMR of N-Ac skatole **1a** in presence of TfOH in $CDCl_3$ (top) and selected ^{13}C NMR data (bottom) of N-Ac skatole **1a** without triflic acid (A) and with 1 equivalent of TfOH (B) in $CDCl_3$.

Addition of 0.5 equivalent of TfOH had a major impact on the chemical shifts: the methyl of the acetyl moved downfield from 2.60 ppm to 3.05 ppm and the H7 proton moved upfield from 8.45 ppm to 8.15 ppm due to the probable association of the

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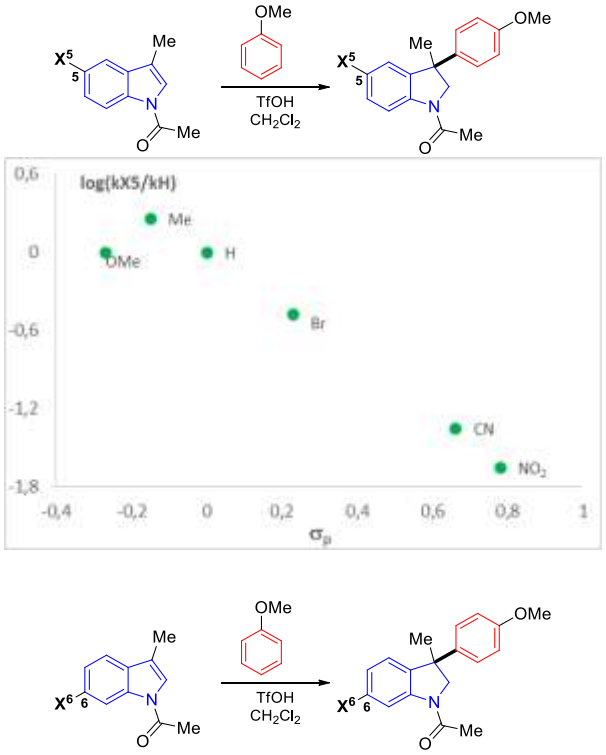
Brønsted acid with the basic oxygen of **1a**. In N-Ac indoles unsubstituted at C7, the C=O bond and benzene ring are in the same plane with the oxygen pointing towards the benzene ring to avoid steric interactions between the methyl of the acetyl and the hydrogen at position 7 of the indole.[14] Consequently, the latter displays a downfield ^{1}H NMR signal around 8.5 ppm because of the deshielding magnetic anisotropy of the carbonyl group. Obviously, the protonation of the oxygen of the acetyl diminished this effect. Upon addition of larger amounts of TfOH, no major changes were observed for the proton NMR. The carbon NMR of a mixture of 1:1 mixture of **1a** and TfOH was more instructive on the effect of this activation of the oxygen of the acetyl on the reactivity of the enamide system (Figure 2, bottom). Indeed, the carbonyl peak is downfield-shifted by 7.5 ppm in presence of TfOH. More interestingly, the chemical shift of the C3 carbon increases from 118.4 ppm to 131.5 ppm while at the same time a slight decrease of 1.3 ppm for the C2 carbon is observed. These experimental data were compared with theoretical ones predicted by DFT (GIAO method) and are in agreement.[15] We have demonstrated that the presence of the TfOH promoter triggers the Umpolung of the C2=C3 double in which the C3 carbon becomes the most electrophilic.



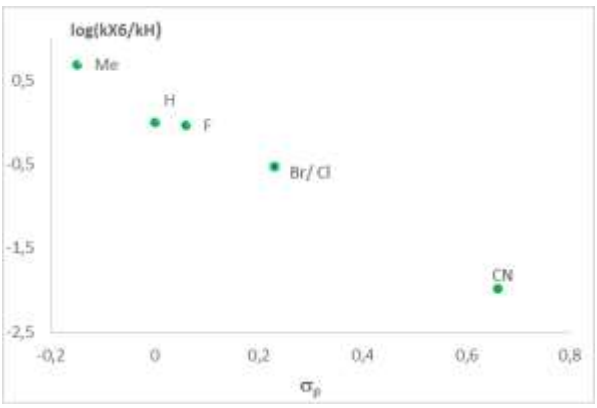


Figure 3. Hammett study of the hydroarylation reaction with 5-substituted N-Ac skatoles (top) and 6-substituted N-Ac skatoles (bottom).

Similarly to $FeCl_3$, the Hammett study conducted with TfOH showed that electron-withdrawing group at the C5 and C6 positions of N-Ac skatole is detrimental to the rate of the reaction (Figure 3). Rather linear correlations, with the exception of the methoxy group, were observed for both with significant negative ρ values which could be indicative of the existence of positive charges at the C3 position and at the nitrogen.[7,15,16]

Moreover, the observed proportional increase of the initial rate of the reaction with the amount of TfOH from 1.5 equivalents (Figure 4), led us to postulate that a polyactivated reactive species was involved as in the case of the $FeCl_3$-promoted reaction.[7]

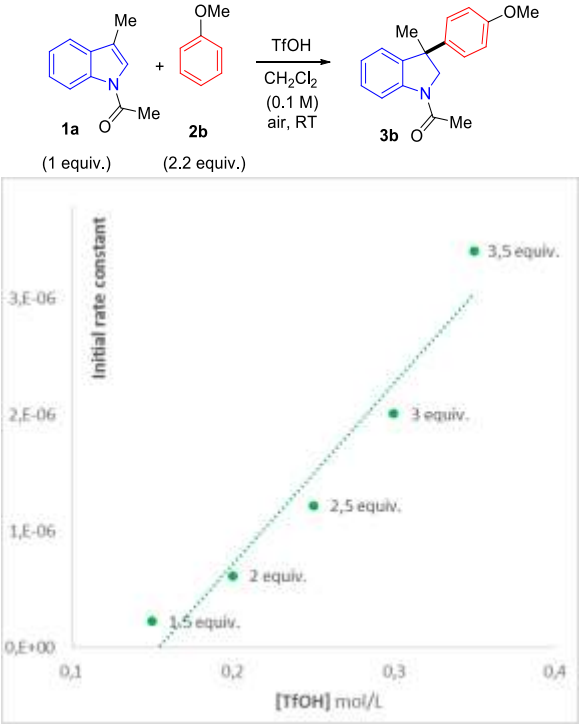
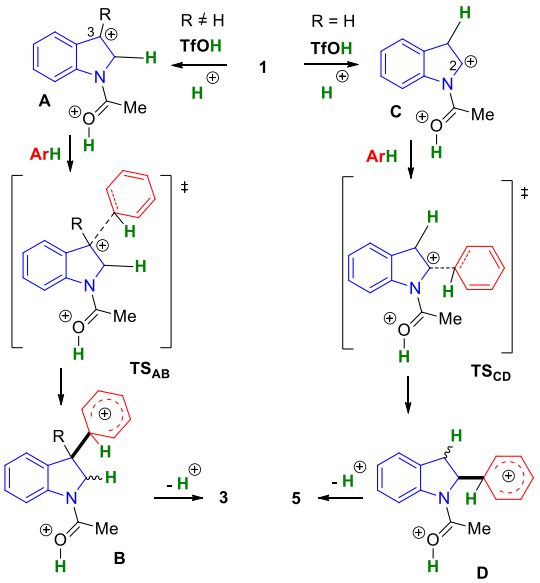


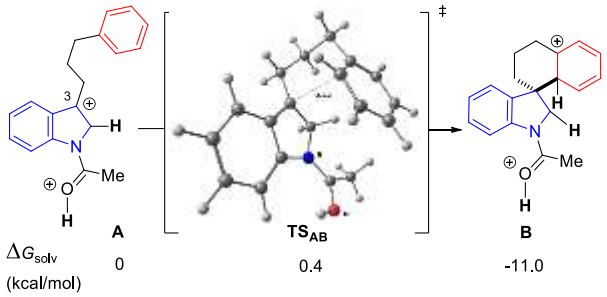
Figure 4. Influence of the stoichiometry of TfOH on the initial rate of the hydroarylation.

The following stepwise general mechanism could be presented (Scheme 4) which is similar to the one we reported for the $FeCl_3$-mediated reaction.[7] Protonation of the acetyl of the N-Ac indoles is accompanied by activation of the C2=C3 bond by a proton at the more nucleophilic position of the C3=C2 bond: C2 for 3-substituted N-Ac indoles or C3 for unsubstituted N-Ac indoles. The positive charge at C3 (**A**) or C2 (**C**) triggers the addition of the electron-rich arene respectively at C3 (TS_{AB}) or C2 (TS_{CD}). Aromatization of the resulting Wheland intermediate **B** or **D** delivers 3-arylindoline **3** or 2-arylindoline **5** and also releases a proton. The latter, as well as TfOH, could activate the C2=C3 bond of **1** as suggested by an experiment with deuterated triflic acid.[15,17]



Scheme 4. Postulated mechanism.

We then performed DFT computations at M06-2X level to evaluate the possibility of this dual activation with protons on the intramolecular hydorarylation leading to **4c** (Scheme 5). With one proton at the oxygen atom, a positive charge was found to be delocalized on the acetamide. Upon activation of the C2=C3 double bond with another proton, a second positive charge is formed at C3 and a C-H bond at C2. This polyactivated species **A** may be considered as a superelectrophile involved in a Friedel-Crafts mechanism.[18] The cyclization from **A** to Wheland intermediate **B** was found to be appreciably exergonic (11.0 kcal/mol with solvent correction) and the free energy of activation (0.4 kcal/mol, $\mathbf{TS_{AB}}$) as low as that found for the transition state of Scheme 1 with two $FeCl_3$ at the oxygen. The similarity between one proton at oxygen and two $FeCl_3$ at oxygen[7] was also established by the charge at C3 (0.294 vs 0.293) and the quite long C3-Cα distance of 2.52 Å (Scheme 5), which is actually even longer than with two $FeCl_3$ (2.22 Å). With two protons on the oxygen and one at the C2=C3 double bond, no cyclization transition state could be found. We could only observe a proton shift from the oxygen to the phenyl group.



Scheme 5. Computed Gibbs free energies of intermediates and transition states relatively to **A** with solvent correction (CH_2Cl_2) at M06-2X level.

In conclusion, we discovered that the promotion of the unusual hydroarylation of N-Ac indoles is not exclusively limited to the Lewis acid $FeCl_3$. A strong Brønsted acid such as TfOH is also very efficient to mediate this reaction and even superior in some cases. Similarly to the $FeCl_3$-promoted reaction, *in situ* IR monitoring, NMR and Hammett studies as well as DFT explorations point towards a Friedel-Crafts mechanism with an uncommon super electrophilic intermediate.

Experimental Section

General procedure A for the hydroarylation of N-Ac indoles with TfOH.

To a solution of the 3-substituted indole derivative **1** (1 equivalent) in CH_2Cl_2 (1.0 M), was successively added electron-rich arene **2** (2.2 equivalents) and TfOH (2.5 equivalents) in one portion. After completion of the reaction (checked by TLC) the reaction was quenched with a saturated $NaHCO_3$ aqueous solution and diluted with CH_2Cl_2. The phases were separated. The aqueous phase was then extracted twice with CH_2Cl_2. The combined organic phases were then dried over $MgSO_4$, filtered and concentrated under vacuum. The crude oil was then purified by flash column chromatography or preparative TLC.

General procedure B for the hydroarylation of N-Ac indoles with $FeCl_3$.

To a solution of the 3-substituted *N*-acetyl indole derivative **1** in CH_2Cl_2 (1.0 M), was successively added electron-rich arene **2** (2 or 3 equivalents) and $FeCl_3$ (2.4 or 3.6 equivalents) in one portion. After completion of the reaction (checked by TLC) the reaction was quenched with a saturated NaCl aqueous solution and diluted with EtOAc. The phases were separated. The aqueous phase was then extracted twice with EtOAc. The combined organic phases were then dried over Na_2SO_4, filtered and concentrated under vacuum. The crude oil was then purified by flash column chromatography.

The NMR of C3-hydroarylated products shows a mixture of two rotamers in a 9:1 ratio in $CDCl_3$ at 300K due to the slow rotation of the N-(CO) bond. Only, the major regioisomer is described in this experimental section. Upon

heating at 340K in DMSO, only one compound is observed.[15]

_N_-Acetyl-3-(5-methyl-2-methoxyphenyl)-3-methylindoline (3a)

TfOH: **3a** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), 4-methylanisole **2a** (135 mg, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3a** as a yellow solid (139.8 mg, 0.474 mmol, 95%).

$FeCl_3$: We reported the synthesis of **3a** with $FeCl_3$ with *General Procedure **B*** in ref 4b.

H_2SO_4: Compound **3a** was also obtained (248 mg, 0.84 mmol, 84%) by using H_2SO_4 (170 µL, 2.5 mmol) instead of TfOH in *General Procedure A* from 1-Acetyl-3-methylindole **1a** (173.3 mg, 1 mmol) and electron-rich arene 4-methylanisole **2a** (270 mg, 2.2 mmol).

See ref 4b for full characterization of **3a**.

_N_-Acetyl-3-(4-methoxyphenyl)-3-methylindoline (3b)

TfOH: **3b** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), anisole **2b** (118 mg, 1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3b** as a yellow solid (135 mg, 0.48 mmol, 96%).

$FeCl_3$: We reported the synthesis of **3b** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3b**.

_N_-Acetyl-3-(4-thiomethylphenyl)-3-methylindoline (3c)

TfOH: **3c** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), thioanisole **2c** (129 µL, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3c** as a yellow solid (148.0 mg, 0.499 mmol, 99%).

$FeCl_3$: We reported the synthesis of **3c** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3c**.

_N_-Acetyl-3-(4-methylphenyl)-3-methylindoline (3d)

TfOH: **3d** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), toluene **2d** (160 µL, 1.5 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3d** as a yellow oil (87.9 mg, 0.33 mmol, 66%).

$FeCl_3$: We reported the synthesis of **3d** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3d**.

_N_-Acetyl-3-(naphthalen-2-yl)-3-methylindoline (3e)

TfOH: **3e** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), naphthalene **2e** (192 mg, 1.5 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 7/3) led to **3e** as a red oil (137 mg, 0.45 mmol, 91%).

$FeCl_3$: We reported the synthesis of **3e** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3c.**

_N_-Acetyl-3-(2-hydroxy-5-methylphenyl)-3-methylindoline (3f)

TfOH: **3f** was obtained from 1-acetyl-3-methylindole **1a** (173 mg, 1 mmol), *p*-cresol **2f** (238 mg, 2.2 mmol) and TfOH (220 µL 2.5 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Flash column chromatography purification (Cyclohexane/EtOAc : 7/3 to 1/1) led to **3f** as a brown solid (280 mg, 0.99 mmol, 99%).

$FeCl_3$: We reported the synthesis of **3f** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3f**.

_N_-Acetyl-3-(2-hydroxynaphthalenyl)-3-methylindoline (3g)

TfOH: **3g** was prepared from 1-acetyl-3-methylindole **1a** (86.7 mg, 0.5 mmol), β-naphthol **2g** (144 mg, 1.0 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 1 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 6/4) led to **3g** as a brown solid (87 mg, 0.274 mmol, 55%).

$FeCl_3$: **3g** was prepared from 1-acetyl-3-methylindole **1a** (86.7 mg, 0.5 mmol), β-naphthol **2g** (150 mg, 1.04 mmol) as electron-rich arene and $FeCl_3$ (194 mg, 1.2 mmol) in 1 mL of CH_2Cl_2 following *General Procedure B*. Preparative TLC purification (Petroleum ether/EtOAc: 6/4) led to **3g** as a brown solid (17 mg, 0.053 mmol, 11%).

R_f: 0.27 (Petroleum ether/EtOAc: 3/2); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.41 (d, J = 8.2 Hz, 1H). 7.70 – 7.56 (m, 3H), 7.37 – 7.03 (m, 7H), 4.25 (d, J = 10.7 Hz, 1H), 4.08 (d, J = 10.7 Hz, 1H), 2.26 (s, 3H) 1.89 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm): 169.7, 154.8, 142.1, 141.0, 140.0, 133.6, 129.9, 128.3, 128.2, 127.2, 125.5, 124.8, 124.5, 124.3, 118.9, 117.4, 109.3, 65.8, 48.0, 27.3, 24.2; IR (neat) υ_{max} (cm^{-1}): 3436, 1641, 1489, 1425, 1299, 653; HRMS (ESI$^+$): calculated: 340.1308, ($[C_{21}H_{19}NNaO_2]^+$; $[M+Na]^+$); found: 340.1307.

_N_-Acetyl-3-(5-methylthiophen-2-yl)-3-methylindoline (3h)

TfOH: **3h** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), 2-methylthiophene **2h** (89.7 mg, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3h** as a yellow oil (81.0 mg, 0.30 mmol, 60%).

$FeCl_3$: We reported the synthesis of **3h** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3h**.

_N_-Acetyl-3-(3-methylbenzothiophen-2-yl)-3-methylindoline (3j)

TfOH: **3j** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), 3-methylbenzothiophene **2j** (163 mg, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3j** with 2 other regioisomers (in a 1.5:1: ratio

respectively to the benzothiophene nucleophile) as a yellow solid (138.0 mg, 0.43 mmol, 86%).

$FeCl_3$: We reported the synthesis of **3j** with $FeCl_3$ with *General Procedure B* in ref 4a.

See ref 4a for full characterization of **3j**.

_N_-Acetyl-3-(3-methylbenzofuran-2-yl)-3-methylindoline (3k)

TfOH: **3k** was prepared from 1-acetyl-3-methylindole **1a** (86.6 mg, 0.5 mmol), 3-methylbenzofuran **2k** (125 µL, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3k** as a yellow crystalline solid (151 mg, 0.49 mmol, 99%).

$FeCl_3$: We reported the synthesis of **3k** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3k**.

_N_-Acetyl-3-(4-methoxyphenyl)-3-ethylindoline (3m)

TfOH: **3m** was prepared from 1-acetyl-3-ethyllindole **1b** (47 mg, 0.25 mmol), anisole **2b** (60 mg, 0.55 mmol) as electron-rich arene and TfOH (55 µL, 0.625 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3m** as a pale yellow oil (68 mg, 0.226 mmol, 91%).

$FeCl_3$: **3m** was prepared from 1-acetyl-3-ethylindole **1b** (45.0 mg, 0.24 mmol) following *General Procedure B* using anisole **2b** (80 mg, 0.72 mmol) as electron-rich arene and $FeCl_3$ (132.3 mg, 0.816 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3m** as a pale yellow oil (62 mg, 0.21 mmol, 87%).

R_f: 0.14 (Cyclohexane/EtOAc: 8/2); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.32 (d, *J* = 7.7 Hz, 1H), 7.31 – 7.19 (m, 3H), 7.11 – 7.02 (m, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 4.08 (s, 2H), 3.80 (s, 3H), 2.22 (s, 3H), 2.14 (q, *J* = 7.2 Hz, 2H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ (ppm): 168.5, 158.1, 143.1, 138.1, 136.9, 128.1, 127.7 (2C), 124.7, 123.7, 116.9, 113.8 (2C), 63.4, 55.2, 51.5, 32.1, 24.3, 9.1; IR (NaCl), ν (cm^{-1}): 1666, 1596, 1512, 1481, 1402, 1252, 757; HRMS (ESI^+): calculated: 296.1645 ($[C_{19}H_{22}NO_2]^+$; $[M+H]^+$); found: 296.1640.

_N_-Acetyl-3-(4-methoxyphenyl)-3-butylindoline (3n)

TfOH: **3n** was prepared from 1-acetyl-3-butylindole **1c** (54 mg, 0.25 mmol), anisole **2b** (60 mg, 0.55 mmol) as electron-rich arene and TfOH (55 µL 0.625 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3n** as a pale yellow oil (72 mg, 0.222 mmol, 89%).

$FeCl_3$: **3n** was prepared from 1-acetyl-3-butylindole **1c** (55.1 mg, 0.256 mmol) following *General Procedure B* using anisole **2b** (85.5 mg, 0.768 mmol) as electron-rich arene and $FeCl_3$ (142 mg, 0.870 mmol) in 0.6 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3n** as a pale brown oil (73.2 mg, 0.226 mmol, 88%).

R_f: 0.2 (Petroleum ether/EtOAc: 8/2); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.32 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.19 (m, 3H), 7.11 – 7.06 (m, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.09 (s, 2H), 3.80 (s, 3H), 2.23 (s, 3H), 2.16 – 2.07 (m, 2H), 1.38 – 1.06 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ (ppm): 168.5, 158.1, 142.8, 138.3, 137.3, 128.0, 127.7 (2C), 124.7, 123.7, 116.9, 113.8 (2C), 63.7, 55.2, 51.1, 39.4, 26.7, 24.3, 23.1, 14.0; IR (NaCl), ν (cm^{-1}): 1662, 1596, 1513, 1479, 1403, 1254, 1035, 757; HRMS (ESI^+): calculated: 346.1778 ($[C_{21}H_{25}NNaO_2]^+$;$[M+Na]^+$); found: 346.1766.

_N_-Acetyl-3-(4-methoxyphenyl)-3-benzylindoline (3o)

TfOH: **3o** was prepared from 1-acetyl-3-benzylindole **1d** (125 mg, 0.5 mmol), anisole **2b** (120 mg, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3o** as a pale yellow oil (152 mg, 0.426 mmol, 85%).

$FeCl_3$: We reported the synthesis of **3o** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3o.**

_N_-Acetyl-3-(4-methoxyphenyl)-3-phenylindoline (3p)

TfOH: **3p** was prepared from 1-acetyl-3-phenylindole **1e** (59 mg, 0.25 mmol), anisole **2b** (60 mg, 0.55 mmol) as electron-rich arene and TfOH (55 µL 0.62 mmol) in 250 µL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 7/3) led to **3p** as a pale yellow oil (85 mg, 0.247 mmol, 99%).

$FeCl_3$: We reported the synthesis of **3p** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3p.**

_N_-Acetyl-3-(4-methoxyphenyl)-3-cyclohexylindoline (3q)

TfOH: **3q** was prepared from 1-acetyl-3-cyclohexylindole **1f** (120.5 mg, 0.5 mmol), anisole **2b** (120 mg, 1.1 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 1 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3q** as a pale brown oil (147 mg, 0.421 mmol, 84%) along with the C2-regioisomer (16.6 mg, 0.0498 mmol, 10%) as an inseparable mixture of *ortho/para* isomers.

$FeCl_3$: We reported the synthesis of **3q** with $FeCl_3$ with *General Procedure B* in ref 7.

See ref 7 for full characterization of **3q**.

2-(_N_-Acetyl-3-(4-methoxyphenyl)-indolin-3-yl)ethyl acetate (3r)

TfOH: **3r** was prepared from 2-(*N*-acetyl-indol-3-yl)ethyl acetate **1g** (122 mg, 0.50 mmol) anisole **2b** (120 mL, 1.1 mmol) as electron-rich arene and TfOH (150 µL 1.7 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3r** as a pale yellow oil (131.4 mg, 0.372 mmol, 74%).

$FeCl_3$: We reported the synthesis of **3r** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3r**.

2-(_N_-Acetyl-3-(4-methoxyphenyl)-indolin-3-yl)propyl acetate (3s)

TfOH: **3s** was prepared from 3-(*N*-acetyl-indol-3-yl)propyl acetate **1h** (131 mg, 0.5 mmol), anisole **2b** (120 µL, 1.1 mmol) as electron-rich arene and TfOH (150 µL 1.7 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*.

Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to acetate **3s** as a brownish oil (163 mg, 0.445 mmol, 89%).

$FeCl_3$: We reported the synthesis of **3s** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3s.**

_N_-Acetyl-3-(4-methoxyphenyl)-3-(3-bromopropyl)indoline (3t)

TfOH: **3t** was prepared from 1-acetyl-3-(3-bromopropyl)indole **1i** (106 mg, 0.378 mmol), anisole **2b** (90 µL, 0.83 mmol) as electron-rich arene and TfOH (84 µL 0.907 mmol) in 0.4 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3t** as a brownish oil (139 mg, 0.358 mmol, 95%).

$FeCl_3$: We reported the synthesis of **3t** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3t.**

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-5-methoxyindoline (3u)

TfOH: **3u** was prepared from 1-acetyl-3-methyl-5-methoxyindole **1k** (52 mg, 0.25 mmol), anisole **2b** (60 µL, 0.55 mmol) as electron-rich arene and TfOH (55 µL 0.62 mmol) in 400 µL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 7/3) led to **3u** as a pale yellow oil (73 mg, 0.234 mmol, 94%).

$FeCl_3$: We reported the synthesis of **3u** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3u.**

_N_-Acetyl-3-(4-methoxyphenyl)-3,5-dimethylindoline (3v)

TfOH: **3v** was prepared from 1-acetyl-3,5-dimethylindole **1k** (94 mg, 0.5 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 500 µL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3v** as a brown oil (140 mg, 0.474 mmol, 95%).

$FeCl_3$: **3v** was prepared from 1-acetyl-3,5-dimethylindole **1k** (82 mg, 0.438 mmol) following *General Procedure B* using anisole **2b** as electron-rich arene (142 mg, 1.314 mmol) and $FeCl_3$ (242 mg, 1.49 mmol) in 0.6 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2 to 7/3) led to **3v** as a brown oil (126 mg, 0.426 mmol, 97%).

R_f : 0.12 (Cyclohexane/EtOAc : 8/2); ^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm) : 8.14 (d, *J* = 8.3 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 6.8 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.77 (br s, 1H), 4.09 (d, *J* = 10.4 Hz, 1H), 3.98 (d, *J* = 10.4 Hz, 1H), 3.79 (s, 3H), 2.28 (s, 3H), 2.16 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) : 168.3, 158.3, 140.0, 139.9, 139.0, 133.7, 128.6, 127.6 (2C), 124.3, 116.8, 113.8 (2C), 66.1, 55.3, 47.3, 27.2, 24.2, 21.2; IR (NaCl), ν (cm^{-1}) : 2964, 2931, 2835, 1662, 1611, 1511, 1489, 1336, 1249, 1183, 1032, 830; HRMS (ESI^+) : calculated: 296.1645 ($[C_{19}H_{22}NO_2]^+$;$[M+H]^+$); found: 296.1643.

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-5-bromoindoline (3w)

TfOH: **3w** was prepared from 1-acetyl-3-methyl-5-bromoindole **1m** (125 mg, 0.5 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3w** as a white solid (177 mg, 0.494 mmol, 98%).

$FeCl_3$: We reported the synthesis of **3w** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3w**.

_N_-Acetyl-3-(4-methoxyphenyl)-5-cyano-3-methylindoline (3x)

TfOH: **3x** was prepared from 1-acetyl-3-methyl-5-cyanoindole **1n** (100 mg, 0.50 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (154 µL 1.74 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3x** as a pale yellow solid (92 mg, 0.298 mmol, 60%).

$FeCl_3$: We reported the synthesis of **3x** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3x.**

_N_-Acetyl-3-(4-methoxyphenyl)-3,6-dimethylindoline (3y)

TfOH: **3y** was also prepared from 1-acetyl-3,6-dimethylindole **1o** (94 mg, 0.5 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 500 µL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3y** as a brown oil (139 mg, 0.471 mmol, 94%).

$FeCl_3$: **3y** was prepared from 1-acetyl-3,6-dimethylindole **1o** (70 mg, 0.374 mmol) following *General Procedure B* using anisole **2b** as electron-rich arene (121 mg, 1.12 mmol) and $FeCl_3$ (206 mg, 1.17 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3y** as a brown oil (105 mg, 0.355 mmol, 95%).

R_f: 0.28 (Cyclohexane/EtOAc: 8/2); ^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm): 8.12 (s, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.87 (s, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 4.10 (d, *J* = 10.2 Hz, 1H), 3.99 (d, *J* = 10.2 Hz, 1H), 3.78 (s, 3H), 2.38 (s, 3H), 2.17 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ (ppm): 168.6, 158.4, 142.5, 139.2, 138.2, 137.0, 127.6 (2C), 124.9, 123.5, 117.8, 113.9 (2C), 66.4, 55.4, 47.1, 27.4, 24.3, 21.8; IR (NaCl), ν (cm^{-1}): 2963, 2931, 2835, 1663, 1608, 1511, 1398, 1250, 1183, 1031, 832, 812; HRMS (ESI^+): calculated: 296.1645 ($[C_{19}H_{21}NNaO_2]^+$;$[M+Na]^+$); found: 296.1635.

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-6-fluoroindoline (3z)

TfOH: **3z** was prepared from 1-acetyl-3-methyl-6-fluoroindole **1p** (95 mg, 0.497 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3z** brown oil (139 mg, 0.464 mmol, 93%).

$FeCl_3$: **3z** was prepared from 1-acetyl-3-methyl-6-fluoroindole **1p** (100 mg, 0.523 mmol) following *General Procedure B* using anisole **2b** as electron-rich arene (170 mg, 1.57 mmol) and $FeCl_3$ (288 mg, 1.78 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3z** as a brown oil (152 mg, 0.508 mmol, 97%).

R_f: 0.27 (Cyclohexane/EtOAc: 8/2); ^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm): 8.04 (dd, *J* = 10.7, 2.3 Hz, 1H), 7.14 (d, *J* = 8.9 Hz, 2H), 6.89 (dd, *J* = 8.3, 5.6 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.73 (td, *J* = 8.4, 2.3 Hz, 1H), 4.14 (d, *J* = 10.2 Hz, 1H), 4.03 (d, *J* = 10.2 Hz, 1H), 3.79 (s, 3H), 2.17 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ (ppm): 168.9, 162.6 (d, $^1J_{C-F}$ = 241 Hz), 158.6, 143.4 (d, $^3J_{C-F}$ = 12 Hz), 138.8, 135.3, 127.5 (2C), 124.3 ($^3J_{C-F}$ = 10 Hz), 114.1 (2C), 110.6 ($^2J_{C-F}$ = 23 Hz), 105.0 ($^2J_{C-F}$ = 29 Hz), 66.7, 55.4, 47.1, 27.6, 24.2; IR (NaCl), ν (cm^{-1}): 2966, 2934, 2836, 1668, 1610, 1512, 1439, 1399, 1251, 1183, 1032, 833; HRMS (ESI$^+$): calculated: 322.1214 ([$C_{18}H_{18}FNNaO_2$]$^+$;[M+Na]$^+$); found: 322.1208.

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-6-chloroindoline (3aa)

TfOH: **3aa** was prepared from 1-acetyl-3-methyl-6-chloroindole **1q** (104 mg, 0.497 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL, 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3aa** as pale brown oil (146 mg, 0.463 mmol, 93%).

$FeCl_3$: We reported the synthesis of **3aa** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3aa.**

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-6-bromoindoline (3ab)

TfOH: **3ab** was prepared from 1-acetyl-3-methyl-6-bromoindole **1r** (125 mg, 0.5 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (110 µL, 1.25 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3ab** as a yellow solid (176 mg, 0.491 mmol, 98%).

$FeCl_3$: **3ab** was prepared from 1-acetyl-3-methyl-6-bromoindole **1r** (45.5 mg, 0.180 mmol), using anisole **2b** as electron-rich arene (58.5 mg, 0.541 mmol) and $FeCl_3$ (99.5 mg, 0.614 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure B*. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3ab** as a yellow solid (64.0 mg, 0.180 mmol, 99%).

R_f: 0.31 (Petroleum ether/EtOAc: 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.47 (d, *J* = 1.8 Hz, 1H). 7.18 – 7.13 (m, 3H), 6.86 – 6.81 (m, 3H), 4.11 (d, *J* = 10.5 Hz, 1H), 4.01 (d, *J* = 10.5 Hz, 1H), 3.78 (s, 3H), 2.18 (s, 3H) 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 168.9, 158.4, 143.3, 139.0, 138.2, 127.5 (2C), 127.0, 125.1, 121.5, 120.1, 113.9 (2C), 66.1, 55.3, 47.1, 27.2, 24.2; IR (neat) υ_{max} (cm^{-1}): 2930, 1668, 1470, 1393, 1336, 1252, 1185, 1030, 834, 665; HRMS (ESI$^+$): calculated: 382.0413, ([$C_{18}H_{18}BrNNaO_2$]$^+$; [M+Na]$^+$); found: 382.0402.

_N_-Acetyl-3-(4-methoxyphenyl)-3-methyl-6-cyanoindoline (3ac)

TfOH: **3ac** was prepared from 1-acetyl-6-cyano-3-methylindole **1s** (99 mg, 0.5 mmol), anisole **2b** (120 µL, 1.10 mmol) as electron-rich arene and TfOH (150 µL, 1.7 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3ac** as a yellow solid (35 mg, 0.114 mmol, 23%).

R_f: 0.31(Petroleum ether/EtOAc: 7/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.59 (s, 1H). 7.35 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.14 (dd, *J* = 6.6, 2.1 Hz, 2H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.88 (dd, *J* = 6.6, 2.1 Hz, 2H) 4.20 (d, *J* = 10.5 Hz, 1H), 4.09 (d, *J* = 10.5 Hz, 1H), 3.80 (s, 3H), 2.22 (s, 3H) 1.76 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 169.2, 158.7, 145.3, 142.6, 137.4, 128.4, 127.5 (2C), 124.7, 120.2, 119.1, 114.2 (2C), 111.8, 65.9, 55.4, 47.8, 27.2, 24.2; IR (neat): υ_{max} (cm^{-1}): 1677, 1502, 1436, 1257, 1035, 735; HRMS (ESI$^+$): calculated: 329.1260, ([$C_{19}H_{18}N_2NaO_2$]$^+$; [M+Na]$^+$); found : 329.1257.

_N_-Benzoyl-3-(5-methyl-2-methoxyphenyl)-3-methylindoline (3ad)

TfOH: **3ad** was prepared from 1-benzoyl-3-methylindole **1s** (231 mg, 0.98 mmol) following *General Procedure A* using 4-methylanisole **2a** (264 mg, 2.16 mmol) as electron-rich arene and TfOH (220 µL 2.5 mmol) in 1 mL of CH_2Cl_2. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3ad** as a yellow solid (296 mg, 0.82 mmol, 84%).

$FeCl_3$: We reported the synthesis of **3ad** with $FeCl_3$ with *General Procedure B* in ref 4b.

See ref 4b for full characterization of **3ad.**

_N_-Acetyl-3-(4-methoxyphenyl)-3,7-dimethylindoline (3ae) and 2-Acetyl-3,7-dimethylindole (7)

TfOH: **3ae** was prepared from 1-acetyl-3,7-dimethylindole **1v** (47 mg, 0.25 mmol) using anisole **2b** as electron-rich arene and TfOH (55 µL 0.625 mmol) in 250 µL of CH_2Cl_2 following *General Procedure A*. Flash column chromatography purification (Cyclohexane/EtOAc : 9/1 to 8/2) led to **3ae** as a brownish oil (25 mg, 0.085 mmol, 34%) along with **7** as colourless crystals (22 mg, 0.117 mmol, 47%).

$FeCl_3$: **3ae** was prepared from 1-acetyl-3,7-dimethylindole **1v** (80 mg, 0.427 mmol) following *General Procedure B* using anisole **2b** as electron-rich arene (92 mg, 0.854 mmol) and $FeCl_3$ (166.3 mg, 1.025 mmol) in 0.6 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc : 9/1 to 8/2) led to **3ae** as a brownish oil (25 mg, 0.085 mmol, 20%) along with **7** as colourless crystals (34 mg, 0.182 mmol, 43%).

*Data for **3y**:* R_f: 0.14 (Cyclohexane/EtOAc: 8/2); ^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm): 7.14-7.07 (m, 4H), 6.90 (dd, *J* = 7.0, 1.9 Hz, 1H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.13 (br s, 1H), 3.96 (d, *J* = 10.4 Hz, 1H), 3.77 (s, 3H), 2.33 (s, 3H), 2.09 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (90.5 MHz, $CDCl_3$) δ (ppm): 169.6, 158.3, 142.5, 141.7, 137.3, 130.2, 129.2, 127.6 (2C), 125.7, 120.9, 113.8 (2C), 67.0, 55.2, 48.8, 24.9, 23.4, 20.3; IR (NaCl), ν (cm^{-1}): 2961, 2930, 2835, 1669, 1608, 1511, 1386, 1374, 1250, 1183, 1031; HRMS (ESI$^+$): calculated: 318.1465 ([$C_{19}H_{21}NNaO_2$]+;[M+Na]$^+$); found: 318.1455.

*Data for **7**:* R_f: 0.43 (Cyclohexane/EtOAc: 8/2); ^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm): 8.90 (br s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.17-7.04 (m, 2H), 2.64 (s, 3H), 2.64 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm): 190.6, 136.0, 132.7, 128.7, 126.8, 121.3, 120.5, 119.4, 119.0, 29.1 16.6, 11.4; IR (NaCl), ν (cm^{-1}): 3337, 2913, 1636, 1539, 1443, 1417, 1354, 1323, 1238, 971, 777, 744; HRMS (ESI$^+$): calculated: 210.0889 ([$C_{12}H_{13}NNaO$]$^+$; [M+Na]$^+$); found: 210.0889

1-(7'-methoxy-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-1-yl)ethanone (4a)

TfOH: **4a** was prepared from 1-acetyl-3-(3-(4-methoxyphenyl)-propyl)indole **1w** (154 mg, 0.5 mmol) and TfOH (110 µL 1.25 mmol) in 10 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc : 7/3) led to **4a** as a yellow solid (125 mg, 0.407 mmol, 81%).

$FeCl_3$: We reported the synthesis of **4a** with $FeCl_3$ with *General Procedure B* in ref 4d.

See ref 4d for full characterization of **4a**.

1-(7'-methyl-3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-1-yl)ethanone (4b)

TfOH: **4b** was prepared from 1-acetyl-3-(3-(4-methylphenyl)-propyl)indole **1x** (145.5 mg, 0.5 mmol) and TfOH (110 µL 1.25 mmol) in 10.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc:7/3) led to **5b** as a brownish solid (143 mg, 0.491 mmol, 98%).

$FeCl_3$: We reported the synthesis of **4b** with $FeCl_3$ with *General Procedure B* in ref 4d.

See ref 4d for full characterization of **4b**.

1-(3',4'-dihydro-2'H-spiro[indoline-3,1'-naphthalen]-1-yl)ethanone (4c)

TfOH: **4c** was prepared from 1-acetyl-3-(3-phenylpropyl)indole **1y** (139 mg, 0.5 mmol) and TfOH (110 µL 1.25 mmol) in 10.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc : 7/3) led to **4c** as a yellow solid (121 mg, 0.437 mmol, 87%).

$FeCl_3$: We reported the synthesis of **4c** with $FeCl_3$ with *General Procedure B* in ref 4d.

See ref 4d for full characterization of **4c**.

1-(6'-chloro-6,7-dihydro-5H-spiro[benzo[b]thiophene-4,3'-indolin]-1'-yl)ethanone (4d)

TfOH: **4d** was prepared from 1-acetyl-6-chloro-3-(3-(thiophen-2-yl)propyl)indole **1z** (80 mg, 0.25 mmol) and TfOH (55 µL, 0.625 mmol) in 5.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc : 7/3) led to **4d** as a white solid (77 mg, 0.242 mmol, 97%).

$FeCl_3$: We reported the synthesis of **4d** with $FeCl_3$ with *General Procedure B* in ref 4d.

See ref 4d for full characterization of **4d**.

Diethyl 1-acetyl-2'H-spiro[indoline-3,1'-naphthalene]-3',3'(4'H)-dicarboxylate (4e)

TfOH: **4e** was prepared from diethyl 2-((1-acetyl-1H-indol-3-yl)methyl)-2-benzylmalonate **1aa** (210 mg, 0.5 mmol) and TfOH (110 µL 1.25 mmol) in 10 mL of $ClCH_2CH_2Cl$ following *General Procedure A* at 80 °C. Preparative TLC purification (Petroleum ether/EtOAc: 7/3) led to **4e** as a colorless solid (159 mg, 0.378 mmol, 76%).

$FeCl_3$: We reported the synthesis of **4e** with $FeCl_3$ with *General Procedure B* at 80°C in ref 4d.

See ref 4d for full characterization of **4e**.

***N*-Acetyl-2-(2-methoxy-5-methylphenyl)indoline 5a**

TfOH: **5a** was prepared from 1-acetyl indole **1ab** (160 mg, 1.0 mmol), 4-methyl anisole **2a** (131 mg, 1.07 mmol) as electron-rich arene and TfOH (220 µL 2.5 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **5a** as a yellow solid (192 mg, 0.682 mmol, 68%) along with **6** as a yellow oil **(**19 mg, 0.047 mmol, 5%).

$FeCl_3$: We reported the synthesis of **5a** with $FeCl_3$ with *General Procedure B* in ref 4e.

See ref 4e for full characterization of **5a**.

*Data for **6**:* R_f: 0.11 (Petroleum ether/EtOAc: 8/2); ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.62 (d, *J* = 8.0 Hz, 1H), 7.18 – 6.98 (m, 7H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.59 (br s, 1H), 4.97 (t, *J* = 7.7 Hz, 1H), 3.52 (s, 6H), 3.19 (d, *J* = 7.7 Hz, 2H), 2.30 (s, 6H), 1.99 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 168.6, 155.4, 132.7, 132.6, 131.4, 131.3, 129.9, 129.1, 127.9, 126.6, 125.1, 124.1, 111.7, 56.1, 38.4, 37.5, 24.1, 21.0; HRMS (ESI^+): calculated: 426.2039 ($[C_{26}H_{29}NNaO_3]^+$;$[M+Na]^+$); found: 426.2026

N-Acetyl-2-(2-methoxy-5-methylphenyl)-5-bromoindoline (5b)

TfOH: **5b** was prepared from 1-acetyl-5-bromoindole **1ac** (119 mg, 0.5 mmol) 4-methyl anisole **2a** (136 mg, 1.11 mmol) as electron-rich arene and TfOH (110 µL, 1.25 mmol) in 1.0 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **7b** as a yellow solid (152 mg, 0.422 mmol, 84%).

$FeCl_3$: We reported the synthesis of **5b** with $FeCl_3$ with *General Procedure B* in ref 4e.

See ref 4e for full characterization of **5b**.

***N*-Acetyl-2-(2-methoxy-5-methylphenyl)-5-nitroindoline 5c**

TfOH: **5c** was prepared from 1-acetyl 5-nitroindole **1ad** (103 mg, 0.504 mmol), 4-methyl anisole **2a** (168 mg, 1.36 mmol) as electron-rich arene and TfOH (110 µL, 1.25 mmol) in 0.5 mL of CH_2Cl_2 following *General Procedure A*. Preparative TLC purification (Petroleum ether/EtOAc: 6/4) led to **5c** as a light brown solid (161 mg, 0.493 mmol, 98%).

$FeCl_3$: We reported the synthesis of **5c** with $FeCl_3$ with *General Procedure B* in ref 4e.

See ref 4e for full characterization of **5c**.

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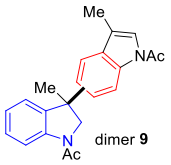

dimer **9**

[10] The regioselectivity was checked by 1H NMR of the crude after aqueous workup.

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UPDATE

Triflic acid as an efficient Brønsted acid promoter for the Umpolung of N-Ac indoles in hydroarylation reactions

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