Enantioselective synthesis of 2-amino-1,1-diarylalkanes bearing a carbocyclic ring substituted indole through asymmetric catalytic reaction of hydroxyindoles with nitroalkenes

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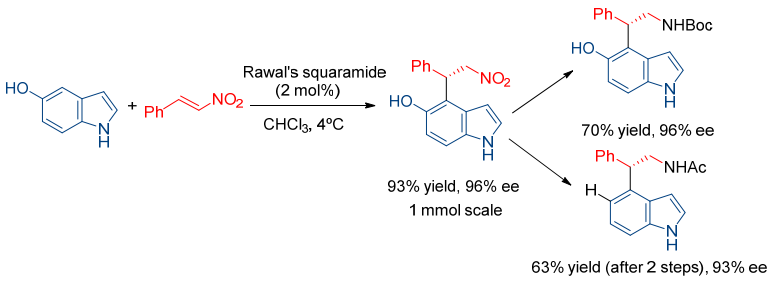


ABSTRACT:

An asymmetric catalytic reaction of hydroxyindoles with nitroalkenes leading to the Friedel-Crafts alkylation in the carbocyclic ring of indole is presented. The method is based in the activating/directing effects of the hydroxy group situated in the carbocyclic ring of the indole providing nitroalkylated indoles functionalizated at the C-4, C-5 and C-7 positions with high yield, regio- and enantioselectivity. The optically enriched nitroalkanes were transformed efficiently in optically enriched 2-amino-1,1-diarylalkanes bearing a carbocyclic ring substituted indole.

INTRODUCTION

The arylethylamine moiety is present as basic skeleton of a series of compounds that exhibit significant pharmaceutical properties.[1] The installation of a second arene moiety at the benzylic position of this arylethylamine scaffold leads to a new structural motif, 2-amino-1,1-diarylalkane, with interesting biological functions (Figure 1).[2] Among them, the heteroaryl substituted derivatives represent an important class, particularly those incorporating an indole[3] core because the importance of this heterocyclic in medicinal[4] and agrochemical chemistry[5] and material science.[6] Consequently, the enantioselective synthesis of this kind of compounds constitutes a major theme of recent research using asymmetric catalytic reactions (ACR).[7,8] Taking into consideration that nitroalkenes represent a notable class of electrophiles for ACR,[9] since to the versatility of the resulting nitroalkanes as valuable intermediates in organic synthesis,[10] we envisioned a procedure for the synthesis of 2-amino-1,1-diarylalkanes (Scheme 1). The procedure involves the introduction of an indole framework in the β-position of a nitrostyrene via a Friedel–Crafts alkylation followed by reduction of the nitro group to amine.

The majority of methods on the enantioselective Friedel-Crafts reaction of indoles involve the azole ring.[8] This fact can be explained by the inherent reactivity of indoles where the azole ring possesses a high nucleophilicity, being the C-3 position the most reactive. Additionally, different methodologies to perform the asymmetric functionalization at C-2 position or the nitrogen atom have been described recently.[11,12]

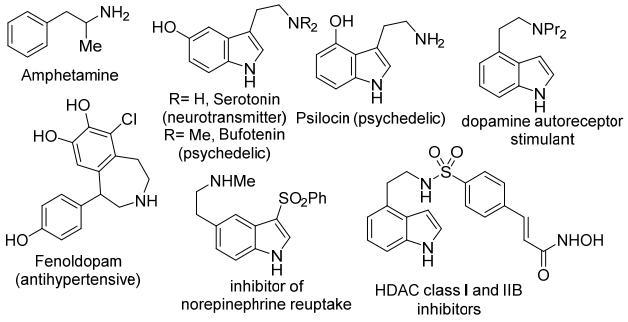
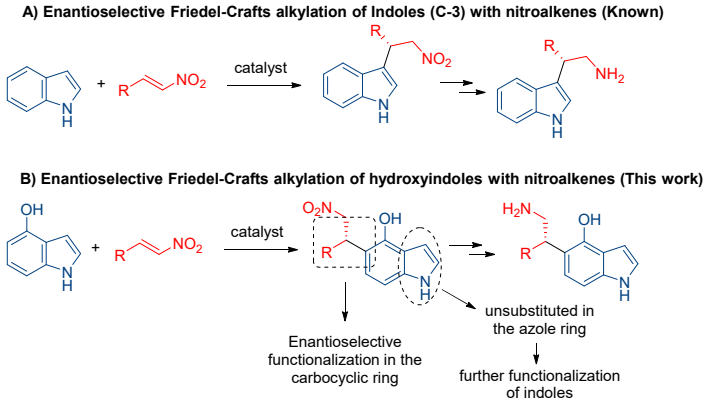


Figure 1. Examples of biologically active 2-amino-1-aryl alkanes, 2-amino-1,1-diarylalkanes and hydroxyindoles.

In contrast, the functionalization of the carbocyclic ring is more challenging and only some non-enantioselective methodologies have been described.[13] However, the enantioselective functionalizations of positions C-4, C-5, C-6 and C-7 are seldom studied in the literature. Therefore, the development of methodologies that enable the asymmetric functionalization of the carbocyclic ring of indoles is a great challenge in asymmetric catalysis. We have recently presented a methodology for the organocatalytic

enantioselective functionalization of the carbocyclic ring of indoles using an hydroxy group as an activating/directing group.[14-16] Hydroxindoles, using bifunctional organocatalysts, act as phenols, even when the positions in the azole ring of indole remained unsubstituted. Given the outstanding potential of chiral indoles and hydroxyindoles, the development of new methodologies for the enantioselective functionalization of indoles is of great interest.

In this paper, we described the enantioselective alkylation of hydroxyindoles with β-nitrostyrenes. Several enantioselective Friedel-Crafts reaction of indoles with nitroalkenes[17,18] have been described in the literature for the synthesis of chiral triptamines (Scheme 1A). However, these examples are limited to the functionalization of the azole ring. The corresponding functionalization in the carbocyclic ring with nitroalkenes is unprecedented, to the best of our knowledge (Scheme 1B). The corresponding chiral nitroalkylated indoles in the carbocyclic ring are significant because of the possibility of reducing the nitro group and to synthesize 2-amino-1,1-diarylalkanes.



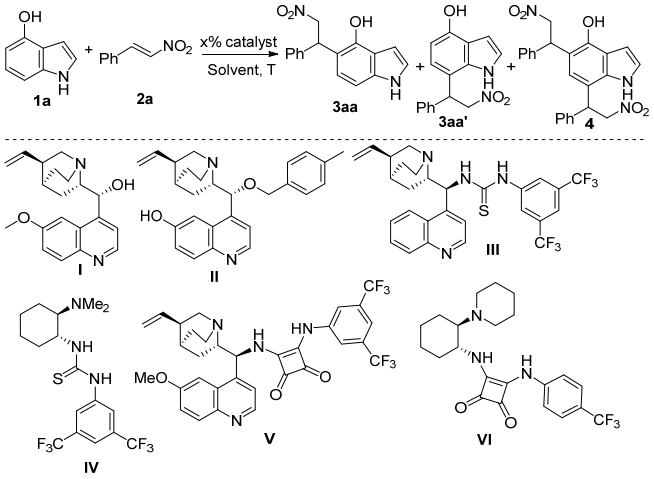
Scheme 1. Enantioselective functionalization of indoles and hydroxyindoles with α,β-unsaturated nitroalkenes.

RESULTS AND DISCUSSION

We started our studies with the Friedel-Crafts reaction of 4-hydroxyindole (**1a**) with β-nitrostyrene (**2a**) in the presence of chiral bifunctional organocatalysts[19] in toluene as a solvent at room temperature (Table 1). When quinine was used as a catalyst, full conversion was observed after 24 h and 3 products were identified in the crude reaction mixture: the corresponding alkylated products at C-5 position (**3aa**) and C-7 position (**3aa'**) and the dialkylated hydroxyindole at C-5 and C-7 positions (**4**), in a ratio 1:0.06:1.6 (**3aa**:**3aa'**:**4**) respectively. We could isolate pure product **3aa** in 18% yield as a racemate (entry 1, Table 1). With catalyst **II** we could increase the yield and the ee of product **3aa** (entry 2), but still were very poor. When the

thiourea derived from quinine **III** (entry 3) was used as catalyst, the reaction was more selective toward product **3aa**, which was gained with 56% yield and 31% ee. The use of thiourea **IV** as catalyst (entry 4) gave worse results than thiourea **III**. However, the squaramide **V** proved to be superior than the thiourea **III**, obtaining the best regioselectivity (63% yield for **3aa**) and enantioselectivity (83% ee, entry 5). While squaramide **VI** (entry 7), introduced by Rawal,[20] gave the best enantiomeric excess (86% ee), and good yield (58%), although was not sufficient for us. A solvent screening (entries 7–11) with catalyst **VI** showed that chlorinated solvents performed the reaction with the best enantioselectivities. Chloroform afforded the product **3aa** with the best enantiomeric excess (93 % *ee*), and the best yield (86 %, entry 10). In order to avoid the polyalkylated product **4** and increase the selectivity of product **3aa**, we increased the ratio between **1a** and **2a** (entry 12), obtaining a slight decrease in the enantioselectivity. After, we screened the catalyst loading and we found that we could decrease the catalyst loading to 2 mol % (entry 13) without compromising the yield (80%) and enantiomeric excess (92% ee). Furthermore, in these conditions the dialkylation product **4** was not observed by ^{1}H NMR in the reaction mixture.

Table 1. Optimization of the reaction conditions

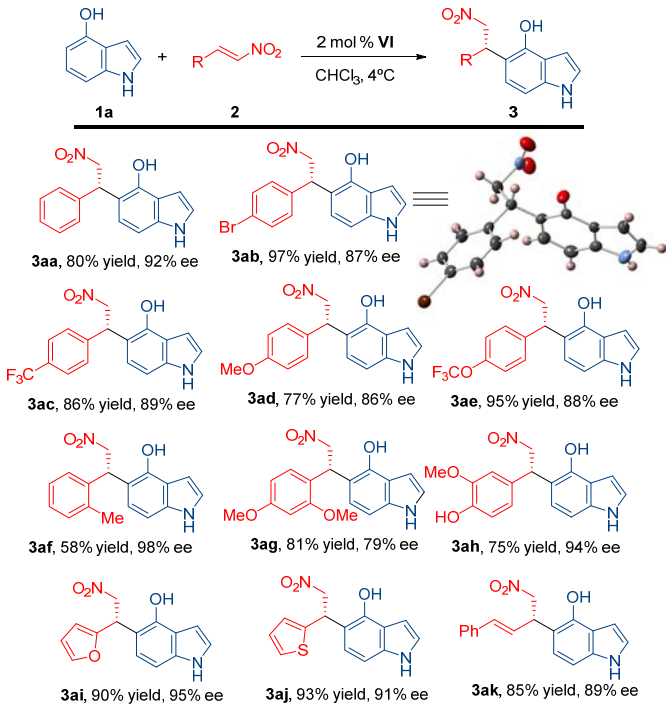


Entry	Catalyst	Solvent	t (h)	Percentage[d] **3aa**:**3aa'**:**4**	Yield of **3aa** (%)[e]	Ee of **3aa**[f]
1[a]	**I** (10 %)	Toluene	24	38:2:68	18	2
2[a]	**II** (10 %)	Toluene	23	53:10:37	25	9
3[a]	**III** (10 %)	Toluene	6	76:2:22	56	31
4[a]	**IV** (10 %)	Toluene	5	53:2:45	43	3
5[a]	**V** (10 %)	Toluene	2	90:2:8	63	83
6[a]	**V** (5 %)	Toluene	7	92:2:6	56	80
7[a,b]	**VI** (5 %)	Toluene	24	86:3:10	58	86
8[a,b]	**VI** (5 %)	CH_2Cl_2	17	95:0:5	71	91
9[a,b]	**VI** (5 %)	$ClCH_2CH_2Cl$	17	1:0:0.07	70	90
10[a,b]	**VI** (5 %)	$CHCl_3$	24	93:1:6	86	93
11[a,b]	**VI** (5 %)	MTBE	48	55:31:14	25	n.d.[g]
12[b,c]	**VI** (5 %)	$CHCl_3$	8	98:0:2	93	90
13[b,c]	**VI** (2 %)	$CHCl_3$	22	100:0:0	80	92
14[b,c]	**VI** (1 %)	$CHCl_3$	22	100:0:0	70	90

[a] Reaction conditions: 0.1 mmol of **1a**, 0.1 mmol **2a**, x mol % de catalyst in 1 mL of solvent at rt; [b] The temperature was 4 °C; [c] Reaction conditions: 0.15 mmol of **1a**, 0.1 mmol of **2a**, x mol % of catalyst in 1 mL of solvent; [d] Determined by ^{1}H NMR; [e] Isolated yield of **3aa**; [f] Determined by chiral HPLC; [g]No determined.

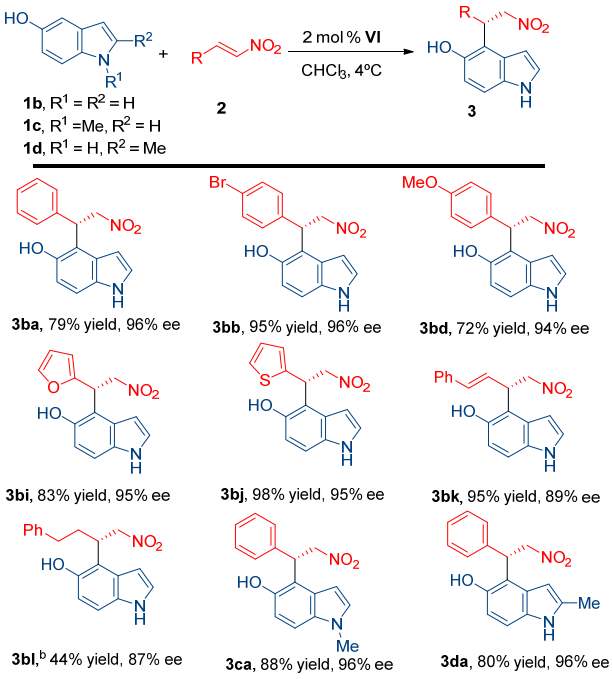
With the optimized reaction conditions established, the scope of the reaction was explored with respect to the 4-hydroxyindole **1a** and different β-nitrostyrenes **2** (Scheme 2). A range of β-arylnitroalkenes were

suitable for this reaction obtaining good yields and enantioselectivities. Electron-withdrawing (Br, CF_3) and electron-donating groups (MeO, CF_3O) in *para* position were well tolerated. The presence of substituents at *ortho* position (Me) led to an excellent enantioselectivity (98% ee) although with a decrease in the conversion (58% yield). When β-heteroarylnitroalkenes **2i** and **2j** were used excellents yields and enantioselectivities were obtained. Remarkably, when (*E*)-2-methoxy-4-(2-nitrovinyl)phenol **2h**, with an hydroxyl group that may interfere in the catalysis, was used as an electrophile the corresponding product **3ah** was gained with excellent regio- and enantioselectivity (94% ee). Finally, with ((1*E*,3*E*)-4-nitrobuta-1,3-dien-1-yl)benzene **2k**, product **3ak** was obtained regioselectively with 85% yield and 89% ee. This result is particularly noteworthy, due to the possible regioisomers than can be obtained in this reaction. From the point of view of the nucleophile, hydroxyindole **1a** can be alkylated at C-3, C-5 or C-7, but we only observe alkylation at C-5. And from the point of view of the electrophile, we can have 1,4 or 1,6 addition, but we only observed the 1,4-addition product. The absolute configuration of product **3ab** was determined by X-ray analysis,[21] and for the rest of compounds **3**, we assumed a uniform stereochemical mechanism.



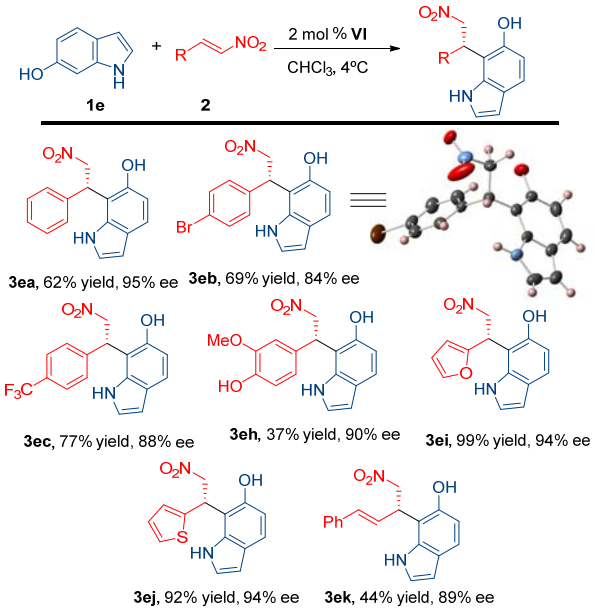
Scheme 2. Scope of the Friedel-Crafts reaction with 4-hydroxyindole **1a**. Reaction conditions: **1a** (0.15 mmol), **2** (0.1 mmol) and **VI** (2 mol%) in 1 mL of $CHCl_3$ at 4 °C. Isolated yields after column chromatography. Enantiomeric excesses were determined by HPLC using chiral stationary phase.

After having proved the efficiency of our methodology for the regio- and enantioselective Friedel-Crafts alkylation of 4-hydroxyindole with nitroalkenes 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. In this way, we wanted to explore if we could achieve the enantioselective functionalization of every position in this ring by simply changing the position of the directing group. Pleasingly, 5-hydroxyindole (**1b**) reacted with β-nitrostyrene (**2a**) to give regioselectivity C-4 alkylated product **3ba** with good yield (79% yield) and high enantiocontrol (96% ee) (Scheme 3). We carried out the reaction of **1b** with several β-aryl and β-heteroarylnitroalkenes obtaining high yields and better enantioselectivities (up to 96% ee) than the reactions with **1a**. Moreover, the reaction with ((1*E*,3*E*)-4-nitrobuta-1,3-dien-1-yl)benzene **2k** procced with excellent regioselectivity (only one product was observed) and high enantioselectivity and product **3bk** was gained with 95% yield and 89% ee. Furthermore, the reaction was carried out with one β-alkylnitroalkene. In this case, the reactivity was very low and we need to increase the temperature to 50 °C and the catalyst loading to 5 mol% for several days. In these conditions, the reaction of **1b** with (*E*)-(4-nitrobut-3-en-1-yl)benzene gave regioselectively compound **3bl** with moderate 44% yield, but good enantioselectivity (87% ee). 5-hydroxyindoles with alkyl substituents at the pyrrole ring were also tested, and products **3ca** and **3da** were isolated in high yields with excellent enantioselectivities (96% ee). Although in the reaction with 5-hydroxy-2-methyl-indole **1d** we also observed the C-3 alkylated product (15% yield) as a racemic mixture.



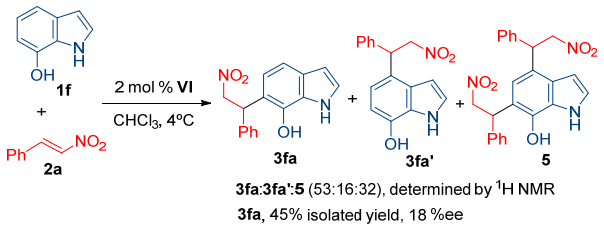
Scheme 3. Scope of the Friedel-Crafts reaction with 5-hydroxyindole derivatives. Reaction conditions: **1** (0.15 mmol), **2** (0.1 mmol) and **VI** (2 mol%) in 1 mL of $CHCl_3$ at 4 °C. Isolated yields after column chromatography. Enantiomeric excesses were determined by HPLC using chiral stationary phase. [a] The reaction was performed at 50 °C using 5 mol% of **VI**.

We also extend our methodology to 6-hydroxyindole **1e** (Scheme 4), which was regio- and enantioselectively alkylated at the C-7 position with good yields and excellent enantiomeric excess. 6-hydroxyindole **1e** proved to be less reactive than **1a** and **1b**, and in general, we obtain lower conversions but the products were obtained with excellent enantiomeric excesses. Again, the conjugated nitrodiene derived from cinnamaldehyde **2k** gave excellent regioselectivity and good ee value (89%), although with a moderate yield (44%).



Scheme 4. Scope of the Friedel-Crafts reaction with 6-hydroxyindole **1e**: **1e** (0.15 mmol), **2** (0.1 mmol) and **VI** (2 mol%) in 1 mL of $CHCl_3$ at 4 ºC. Isolated yields after column chromatography. Enantiomeric ratio were determined by HPLC using chiral stationary phase.

Finally, 7-hydroxyindole **1f** was also tested under the optimized reaction conditions (Scheme 5). Unfortunately, the regioselectivity was low obtaining a ratio (53:16:32), determined by ^{1}H NMR, of product alkylated at C-6 (**3da**), at C-4 (**3da'**) and also the product of double alkylation **5**, and the enantiomeric excess of compound **3da** was also very poor (18% ee). We attribute these results to an interference between the NH of the indole nucleous and the hydroxyl group.



Scheme 5. Friedel-Crafts alkylation of 7-hydroxyindole **1f** with **2a**. Reaction conditions: **1f** (0.15 mmol), **2a** (0.1 mmol) and **VI** (2 mol%) in 1 mL of $CHCl_3$ at 4 °C. Enantiomeric excesses were determined by HPLC using chiral stationary phase.

In order to rationalize the observed regio- and enantioselectivity, we propose a tentative transition state (Figure 2). The squaramide acts as bifunctional organocatalyst responsible for the preorientation and the activation of the substrates. While the nitroalkene is activated upon formation of hydrogen bonds between nitro group and the squaramide,[22] the hydroxyindole undergoes nucleophilic activation by hydrogen bonding with the tertiary amine moiety of the catalyst. This model explains the *ortho*-regioselectivity for the nucleophiles and the *S* absolute configuration of the final products. The influence of the catalyst/OH-group interaction can be ascertained by the fact that the 5-methoxyindole reacts very slowly under the optimized reaction conditions (7% yield after 7 days), and the corresponding Friedel-Crafts alkylation takes place at C-3.

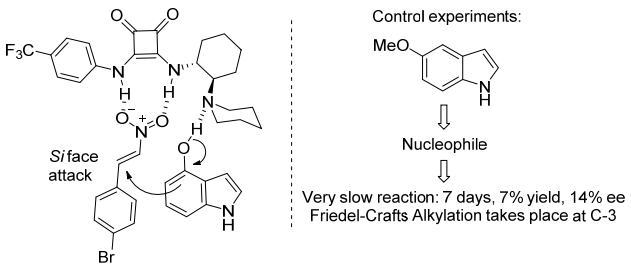
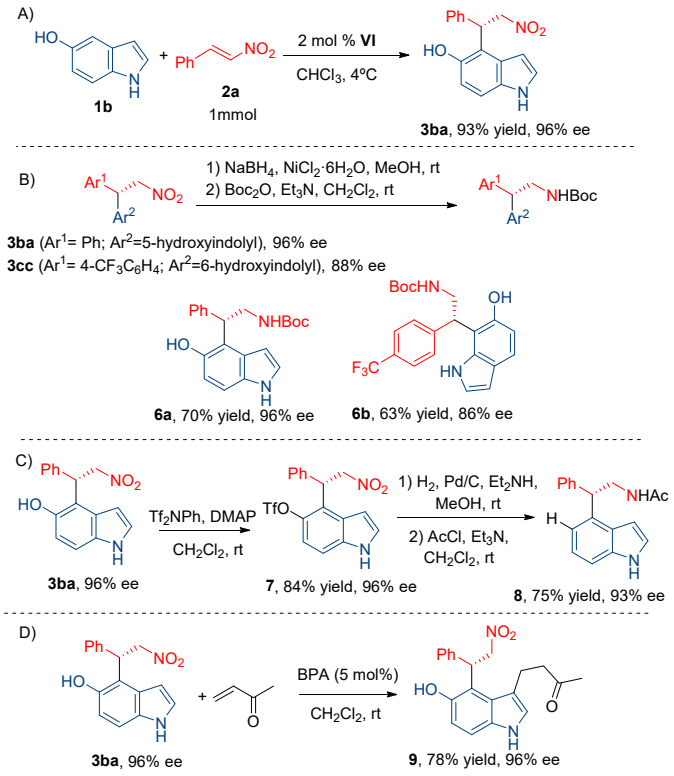


Figure 2 Proposed stereochemical model.

To showcase the utility of our catalytic protocol for the synthesis of chiral 2-amino-1,1-diarylalkanes, we performed first the reaction of 5-hydroxyindole **1b** and nitroalkene **2a** at 1 mmol scale, obtaining the product **3ba** with better yield (93%) and the same ee (96%) than when the reaction was carried out using 0.1 mmol of **2a** (Scheme 6A). Next, we carried out the selective reduction of the nitro group present in the alkylated indoles **3ba** and **3cc** with $NaBH_4$-$NiCl_2.6H_2O$, obtaining the corresponding 2-amino-1,1-

diarylalkanes with good yields and preserving the ee, which were isolated as Boc-derivatives **6a** and **6b** (Scheme 6B). In order to eliminate the activating-directing hydroxy group we have also transformed compound **3ba** in the corresponding triflate **7**. Triflates can be considered as privileged synthetic intermediates for the synthesis of a large number of molecules.[23] So, triflate **7** was catalytically hydrogenated with Pd/C at 1 atm affording the corresponding chiral 2-amino-1,1-diarylalkane **8** with a C-4 indolyl substituent in good yield and without erosion in the enantiomeric excess (Scheme 6C). In this procedure the nitro group was simultaneously reduced to the corresponding amine which was protected with AcCl to facilitate the isolation. With this transformation we demonstrate that the activating/directing hydroxy group could be posteriorly removed obtaining the chiral hydroxy group-free indole. Finally, we performed the reaction of compound **3ba** with methylvinylketone under acidic catalysis to obtain product **9**, following a classical Friedel–Crafts alkylation at C-3 position of the indole scaffold, proving that our method can provide highly functionalized chiral indoles (Scheme 6D) and consequently 2-amino-1,1-diarylalkanes.



Scheme 6. Synthetic transformations. Isolated yields after column chromatography. Enantiomeric excesses were determined by HPLC using chiral stationary phase.

CONCLUSION

In summary, we have described an enantioselective synthesis of 2-amino-1,1-diarylalkanes bearing a carbocyclic ring substituted indole through asymmetric catalytic reaction of hydroxyindoles with nitroalkenes followed by reduction of the nitro group to amine. The asymmetric catalytic reaction described here is the first regio- and enantioselective alkylation in the carbocyclic ring of indoles with nitroalkenes as electrophiles, which was catalysed by the commercially available Rawal squaramide **VI** (2 mol% catalyst). Under our reaction conditions, hydroxyindoles react in the carbocyclic ring rather than in the azole system because the hydroxy group acts as an activating group but also directing group. We can introduce regioselectively the electrophile at C-4, C-5 and C-7 with high levels of enantioselectivity, by using 5-hydroxyindole, 4-hydroxyindole and 6-hydroxyindole, respectively.[24] The selective reduction of the nitro group present in the alkylated indoles was carried with $NaBH_4$-$NiCl_2.6H_2O$, obtaining the corresponding 2-amino-1,1-diarylalkanes with good yield and preserving the ee. In addition, we have performed the removal of the hydroxy group, through of the corresponding triflate, simultaneously to the reduction of nitro group under mild reductive elimination conditions in high overall yield. Studies to further extend the scope of this reaction are currently underway in our laboratory.

EXPERIMENTAL SECTION:

General methods:

Reactions were carried out in 5 mL vials under air. Comercial reagents were used as purchased. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm and visualized using both a UV lamp (254 nm) and then a CAM solution (an aqueous solution of ceric ammonium molybdate). Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for ^1H and 75 MHz for ^{13}C using residual nondeuterated solvent as internal standard ($CHCl_3$: δ 7.26 and 77.00 ppm, respectively, MeOH: δ 3.34 ppm and δ 49.87 ppm, respectively). Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a AB SCIEX Triple TOF™ spectrometer equipped with an electrospray source with a capillary voltage of 4.5 kV (ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using columns with chiral stationary phases from Daicel. Catalysts **I**, **IV** and **VI** were commercially available. Catalyst **II** was prepared from quinine using Deng's procedure.[25] Catalyst **III** was prepared from cinchonidine using Soós'

procedure.[26] Catalyst **V** was prepared from quinine using Du's procedure.[27] Nitroalkenes **2a-j** were commercially available. Nitroalkenes **2l** and **2k** were prepared following a procedure described by Lam.[28] 5-hydroxy-1-methyl-indole **1c** was synthesized from 5-hydroxyindole **1b** as described in the literature.[29]

General procedure for the non enantioselective Friedel-Crafts reaction:

In a 5 mL vial were placed the proper hydroxyindole (**1**, 0.1 mmol), the proper nitroalkene (**2**, 0.1 mmol) and 1-(3,5-bis(trifluoromethyl)phenyl)-3-(3-(dimethylamino)propyl) thiourea (3.7 mg, 0.01 mmol). Then, the mixture was dissolved in toluene (1 mL) and it was stirred at room temperature for 24 h and purified by column chromatography using hexane:AcOEt mixtures (95:5 to 70:30) to afford the product **3** as a racemic mixture.

General procedure for the enantioselective Fridel-Crafts reaction:

In a 5 mL vial were placed the proper hydroxyindole (**1**, 0.15 mmol), the proper nitroalkene (**2**, 0.10 mmol) and Rawal squaramide (**VI**, 0.84 mg, 0.002 mmol). Then, the mixture was dissolved in $CHCl_3$ (1 mL) and it was stirred at 4 ºC until the reaction was complete (TLC). Finally, the reaction mixture was directly poured to the column chromatography, using hexane:AcOEt mixtures (95:5 to 70:3) as eluent to afford the product **3** as an enantioenriched mixture.

Specific procedure for the enantioselective Friedel-Crafts reaction with nitroalkene 2l:

In a 5 mL flask equipped with a refrigerant were placed 5-hydroxyindole (**1b**, 0.15 mmol), (*E*)-(4-nitrobut-3-en-1-yl)benzene (**2l**, 0.10 mmol) and Rawal Squaramide (**VI**, 2.1 mg, 0.005 mmol). Then, the mixture was dissolved in $CHCl_3$ (1 mL) and it was stirred at 50 oC until the reaction was complete (TLC). Finally, the reaction mixture was directly poured to the column chromatography, using hexane:AcOEt mixtures (95:5 to 70:3) as eluent to afford the product **3al** as an enantioenriched mixture.

Scope of the reaction with 4-hydroxyindole:

(*S*)-5-(1-phenyl-2-nitroethyl)-1*H*-indol-4-ol (3aa)

The product **3aa** was obtained as a dark oil (22.6 mg, 0.08 mmol, 80% yield). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 70:30, 1.0 mL/min, major enantiomer t_r = 14.55 min, minor enantiomer t_r = 16.10 min. $[\alpha]_D^{20}$ -79.2 (*c*=0.55, $CHCl_3$) (92% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.38 – 7.23 (m, 4H), 7.26 – 7.15 (m, 1H), 7.09 (dd, J = 3.3, 2.3 Hz, 1H), 6.93 (dd, J = 8.4, 0.7 Hz, 1H), 6.89 (d, J = 8.5 Hz, 1H), 6.49 – 6.40 (m, 1H), 5.36 (dd, J = 8.7, 7.5 Hz, 1H), 5.18 (s, 1H), 5.17 – 5.03 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 145.9 (C), 139.8 (C), 136.7 (C), 128.7 (CH),

127.8 (CH), 127.1 (CH), 123.8 (CH), 122.7 (CH), 118.0 (C), 114.8 (C), 104.6 (CH), 97.8 (CH), 78.5 (CH_2), 43.2 (CH). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_3$ 283.1077; Found 283.1083.

(*S*)-5-(1-(4-bromophenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ab)

The product **3ab** was obtained as a yellow solid (35.0 mg, 0.097 mmol, 97% yield); m.p. 133-138 ºC. Enantiomeric excess (87% and 90% after crystallization) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 28.39 min, minor enantiomer t_r = 31.20 min. $[\alpha]_D^{20}$ -45.2 (*c*=0.29, $CHCl_3$) (87% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 7.14 (dd, *J* = 3.3, 2.3 Hz, 1H), 6.95 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.46 (ddd, *J* = 3.2, 2.0, 0.9 Hz, 1H), 5.30 (dd, *J* = 9.0, 7.2 Hz, 1H), 5.13 (s, 1H), 5.11 – 5.03 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7 (C), 138.8 (C), 131.7 (CH), 131.2 (C), 129.4 (CH), 128.2 (C), 125.6 (CH), 120.9 (C), 115.0 (C), 112.9 (CH), 111.3 (CH), 100.6 (CH), 77.7 (CH_2), 42.9 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{14}N_2O_3Br$ 361.0182; Found 361.0192.

(*S*)-5-(1-(4-(trifluoromethyl)phenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ac)

The product **3ac** was obtained as a dark oil (30.1 mg, 0.086 mmol, 86% yield). Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 19.35 min, minor enantiomer t_r = 17.81 min. $[\alpha]_D^{20}$ -55.2 (*c*=0.65, $CHCl_3$) (89% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.15 (t, *J* = 2.8 Hz, 1H), 6.96 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.46 (s, 1H), 5.40 (t, *J* = 8.1 Hz, 1H), 5.16 (s, 1H), 5.13 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 145.9 (C), 144.1 (C), 136.8 (C), 129.3 (q, J_{C-F} = 32.4 Hz, C), 128.2 (CH), 125.6 (q, J_{C-F} = 3.8 Hz, CH), 124.1 (CH), 124.4 (d, J_{C-F} = 272.1 Hz, CF_3), 122.7 (CH), 117.9 (C), 114.0 (C), 104.8 (CH), 97.7 (CH), 78.0 (CH_2), 43.3 (CH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -63.0 (s, CF_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{14}N_2O_3F_3$ 351.0951; Found 351.0963.

(*S*)-5-(1-(4-methoxyphenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ad)

The product **3ad** was obtained as a green solid (24.1 mg, 0.077 mmol, 77% yield); m.p: 169-173. Enantiomeric excess (86%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 28.81 min, minor enantiomer t_r = 41.49 min. $[\alpha]_D^{20}$ -48.9 (c=1.16, MeOH) (86% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.13 (dd, *J* = 3.4, 2.4 Hz, 1H), 6.95 (dd, *J* = 8.5, 0.9 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.47 (td, *J* = 2.3, 1.1 Hz, 1H), 5.28 (dd, *J* = 8.7, 7.5 Hz, 1H), 5.14 – 5.06 (m, 2H), 5.02 (dd, *J* = 12.7, 8.9 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7 (C), 145.9 (C), 136.7 (C), 131.7 (C), 128.8 (CH), 123.8 (CH), 122.7

(CH), 118.1 (C), 115.1 (C), 114.2 (CH), 104.5 (CH), 97.9 (CH), 78.8 (CH_2), 55.2 (CH_3), 42.6 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_4$ 313.1183; Found 313.1192.

(*S*)-5-(1-(4-(trifluoromethoxy)phenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ae)

The product **3ae** was obtained as a dark oil (34.8 mg, 0.095 mmol, 95% yield); Enantiomeric excess (88%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 17.28 min, minor enantiomer t_r = 14.72 min. $[\alpha]_D^{20}$ -39.2 (c=0.91, $CHCl_3$) (88% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.15 – 7.06 (m, 3H), 6.96 (d, *J* = 8.5 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.57 – 6.40 (m, 1H), 5.35 (dd, *J* = 8.9, 7.3 Hz, 1H), 5.20 (s, 1H), 5.16 – 5.01 (m, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2 (C), 145.9 (C), 138.7 (C), 136.8 (C), 129.2 (CH), 124.0 (CH), 122.7 (CH), 121.1 (CH), 120.4 (d, J_{C-F} = 257.1 Hz, CF_3), 118.0 (C), 114.3 (C), 104.7 (CH), 97.8 (CH), 78.3 (CH_2), 42.9 (CH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -58.3 (s, CF_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{14}N_2O_4F_3$ 367.0900; Found 367.0916.

(*S*)-5-(1-(*o*-tolyl)-2-nitroethyl)-1*H*-indol-4-ol (3af)

The product **3af** was obtained as a green solid (17.2 mg, 0.058 mmol, 58% yield); m.p: 160-165. Enantiomeric excess (98%) was determined by chiral HPLC (Chiralpak IC), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 4.88 min, minor enantiomer t_r = 7.33 min. $[\alpha]_D^{20}$ -65.9 (c=0.44, $CHCl_3$) (98% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.23 – 7.11 (m, 4H), 6.89 (dd, *J* = 8.5, 0.7 Hz, 1H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.48 (ddd, *J* = 3.0, 1.9, 0.8 Hz, 1H), 5.59 – 5.52 (m, 1H), 5.23 (s, 1H), 5.03 – 4.99 (m, 2H), 2.28 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0 (C), 137.6 (C), 137.1 (C), 136.7 (C), 131.1 (CH), 127.1 (CH), 126.1 (CH), 125.9 (CH), 123.8 (CH), 122.9 (CH), 117.8 (C), 113.9 (C), 104.6 (CH), 97.9 (CH), 77.9 (CH_2), 38.9 (CH), 19.4 (CH_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_3$ 297.1234; Found 297.1225.

(*S*)-5-(1-(2,4-dimethoxyphenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ag)

The product **3ag** was obtained as a dark oil (27.7 mg, 0.081 mmol, 81% yield). Enantiomeric excess (79%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 48.84 min, minor enantiomer t_r = 30.42 min. $[\alpha]_D^{20}$ -73.2 (c=0.55, $CHCl_3$) (79% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.07 (dd, *J* = 3.3, 2.3 Hz, 1H), 6.98 – 6.89 (m, 2H), 6.53 (ddd, *J* = 3.1, 2.1, 0.8 Hz, 1H), 6.47 – 6.39 (m, 2H), 6.10 (s, 1H), 5.51 (t, *J* = 8.2 Hz, 1H), 5.19 – 4.95 (m, 2H), 3.87 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0 (C), 157.1 (C), 146.5 (C), 136.7 (C), 128.3 (CH), 123.5 (CH), 121.5 (CH), 120.1 (C), 118.5 (C), 114.3 (C), 105.1 (CH), 104.4 (CH), 99.1

(CH), 99.0 (CH), 77.8 (CH_2), 55.9 (CH_3), 55.4 (CH_3), 35.8 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{19}NO_5$ 343.1288; Found 343.1285.

(*S*)-5-(1-(4-hydroxy-3-methoxyphenyl)-2-nitroethyl)-1*H*-indol-4-ol (3ah)

The product **3ah** was obtained as a dark oil (27.2 mg, 0.075 mmol, 75% yield). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 70:30, 1.0 mL/min, major enantiomer t_r = 27.50 min, minor enantiomer t_r = 17.22 min. $[\alpha]_D^{20}$ -78.2 (c=0.47, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (bs, 1H), 7.12 (dd, *J* = 3.3, 2.4 Hz, 1H), 6.94 (dd, *J* = 8.5, 0.9 Hz, 1H), 6.88 (s, *J* = 8.4 Hz, 1H), 6.84 (m, 2H), 6.80 (s, 1H), 6.48 (ddd, *J* = 3.2, 2.1, 0.9 Hz, 1H), 5.53 (bs, 1H), 5.30 – 5.22 (m, 2H), 5.12 – 4.97 (m, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7 (C), 145.9 (C), 144.8 (C), 136.7 (C), 131.6 (C), 123.9 (CH), 122.6 (CH), 120.1 (CH), 118.1 (C), 115.0 (C), 114.5 (CH), 110.8 (CH), 104.5 (CH), 98.0 (CH), 78.7 (CH_2), 55.9 (CH_3), 43.0 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_5$ 329.1132; Found 329.1143.

(*S*)-5-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indol-4-ol (3ai)

The product **3ai** was obtained as a yellow oil (24.5 mg, 0.09 mmol, 90% yield). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 23.48 min, minor enantiomer t_r = 25.76 min. $[\alpha]_D^{20}$ -52.14 (*c*=0.66, $CHCl_3$) (95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.191-7.151 (m, 3H), 7.02 (dt, *J* = 3.5, 1.1 Hz, 1H), 6.91 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.52 (ddd, *J* = 3.1, 2.1, 0.9 Hz, 1H), 5.72 (td, *J* = 7.7, 0.9 Hz, 1H), 5.38 (dd, *J* = 13.0, 7.8 Hz, 1H), 5.27 (dd, *J* = 13.0, 7.5 Hz, 1H), 4.82 (bs, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 152.8 (C), 146.1 (C), 142.1 (CH), 137.0 (C), 123.9 (CH), 123.0 (CH), 118.0 (C), 112.4 (C), 110.4 (CH), 107.1 (CH), 104.7 (CH), 98.1 (CH), 77.2 (CH_2), 37.7 (CH); HRMS (ESI) *m/z:* $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_4$ 273.0870; Found 273.0877.

(*S*)-5-(2-nitro-1-(thiophen-2-yl)ethyl)-1*H*-indol-4-ol (3aj)

The product **3aj** was obtained as a colorless oil (26.8 mg, 0.093 mmol, 93% yield). Enantiomeric excess (91%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 20.50 min, minor enantiomer t_r = 34.27 min. $[\alpha]_D^{20}$ -0.15 (*c*=1.45, $CHCl_3$) (91% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (bs, 1H), 7.19 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.12 (dd, *J* = 3.3, 2.4 Hz, 1H), 7.04 – 6.89 (m, 4H), 6.48 (dd, *J* = 2.8, 2.0 Hz, 1H), 5.69 – 5.51 (m, 1H), 5.32 (bs, 1H), 5.12 – 5.04 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 145.9 (C), 143.4 (C), 136.9 (C), 126.8 (CH), 124.9 (CH), 124.8 (CH), 124.0

(CH), 122.7 (CH), 118.0 (C), 114.4 (C), 104.3 (CH), 98.0 (CH), 79.2 (CH_2), 39.1 (CH); HRMS (ESI) *m/z:* $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_3S$ 289.0641; Found 289.0650.

(*S*,*E*)-5-(1-nitro-4-phenylbut-3-en-2-yl)-1*H*-indol-4-ol (3ak)

The product **3ak** was obtained as a colorless oil (26.3 mg, 0.085 mmol, 85% yield). Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 19.36 min, minor enantiomer t_r = 21.63 min. $[\alpha]_D^{20}$ -17.79 (*c*=1.04, $CHCl_3$) (89% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (bs, 1H), 7.52 – 7.19 (m, 5H), 7.14 (dd, *J* = 3.3, 2.4 Hz, 1H), 7.06 – 6.94 (m, 2H), 6.57 – 6.54 (m, 2H), 6.53 – 6.50 (m, 1H), 5.38 (bs, 1H), 4.94 – 4.87 (m, 2H), 4.77 (ddd, *J* = 8.7, 4.3, 2.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.1 (C), 136.8 (C), 136.7 (C), 132.2 (CH), 128.5 (CH), 127.6 (CH), 127.3 (CH), 126.4 (CH), 123.9 (CH), 123.1 (CH), 118.1 (C), 113.6 (C), 104.7 (CH), 97.8 (CH), 78.9 (CH_2), 42.8 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{17}N_2O_3$ 309.1234; Found 309.1237.

Scope of the reaction with 5-hydroxyindole:

(*S*)-4-(1-phenyl-2-nitroethyl)-1H-indol-5-ol (3ba)

The product **3ba** was obtained as a dark oil (0.1 mmol scale reaction: 22.4 mg, 0.079 mmol, 79% yield; 1 mmol scale reaction: 262.7 mg, 0.93 mmol, 93% yield). Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 15.30 min, minor enantiomer t_r = 13.88 min. $[\alpha]_D^{20}$ -48.8 (*c*=1.07, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (bs, 1H), 7.43 – 7.36 (m, 2H), 7.30 – 7.25 (m, 2H), 7.27 – 7.10 (m, 3H), 6.63 (d, *J* = 8.7 Hz, 1H), 6.51 (ddd, *J* = 3.2, 2.1, 1.0 Hz, 1H), 5.51 – 5.21 (m, 3H), 4.68 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9 (C), 139.6(C), 131.3 (C), 128.7 (CH), 128.4 (C), 127.6 (CH), 127.1 (CH), 125.4 (CH), 115.7 (C), 113.1 (CH), 111.1 (CH), 100.8 (CH), 77.9 (CH_2), 43.3 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_3$ 283.1077; Found 283.1089.

(*S*)-4-(1-(4-bromophenyl)-2-nitroethyl)-1H-indol-5-ol (3bb)

The product **3bb** was obtained as a dark oil (34.3 mg, 0.095 mmol, 95% yield). Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 13.90 min, minor enantiomer t_r = 11.78 min. $[\alpha]_D^{20}$ -49.1 (c=1.12, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (bs, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.15 (dd, *J* = 3.2, 2.5 Hz, 1H), 7.12 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 1H), 6.48 (ddd, *J* = 3.0, 2.0, 0.8 Hz, 1H), 5.42 – 5.32 (m, 2H), 5.29 – 5.18 (m, 1H), 4.77 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7 (C), 138.8 (C), 131.7 (CH),

131.2 (C), 129.4 (CH), 128.2 (C), 125.6 (CH), 120.9 (C), 115.0 (C), 112.9 (CH), 111.3 (CH), 100.6 (CH), 77.7 (CH_2), 42.9 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{14}N_2O_3Br$ 361.0182; Found 361.0195.

(*S*)-4-(1-(4-methoxyphenyl)-2-nitroethyl)-1H-indol-5-ol (3bd)

The product **3bd** was obtained as a brown solid (22.5 mg, 0.072 mmol, 72% yield); m.p: 128-132 ºC. Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 19.50 min, minor enantiomer t_r = 22.35 min. $[\alpha]_D^{20}$ -11.3 (c=0.67, MeOH) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (bs, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.20 – 7.09 (m, 2H), 6.80 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 8.5 Hz, 1H), 6.52 (ddd, *J* = 3.0, 2.0, 0.9 Hz, 1H), 5.45 – 5.16 (m, 3H), 4.63 (bs, 1H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5 (C), 146.8 (C), 131.6 (C), 131.3 (C), 128.6 (CH), 125.4 (CH), 116.0 (C), 114.1 (CH), 113.2 (CH), 111.0 (CH), 100.9 (CH), 78.1 (CH_2), 55.2 (CH_3), 42.7 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_4$ 313.1183; Found 313.1193.

(*S*)-4-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indol-5-ol (3bi)

The product **3bi** was obtained as a colorless oil (22.6 mg, 0.083 mmol, 83% yield). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 19.99 min, minor enantiomer t_r = 16.94 min. $[\alpha]_D^{20}$ -32.11 (c=1.06, $CHCl_3$) (95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (bs, 1H), 7.36 – 7.34 (m, 1H), 7.21 – 7.15 (m, 2H), 6.71 (d, J = 8.6 Hz, 1H), 6.39 (ddd, J = 3.1, 2.1, 0.9 Hz, 1H), 6.31 (dd, J = 3.3, 1.9 Hz, 1H), 6.16 (dt, J = 3.3, 0.9 Hz, 1H), 5.62 (t, J = 8.0 Hz, 1H), 5.33 (dd, J = 13.1, 8.2 Hz, 1H), 5.07 (dd, J = 13.0, 7.0 Hz, 1H), 5.04 (bs, 1H);^{13}C NMR (75.5 MHz, $CDCl_3$) δ 152.3 (C), 147.1 (C), 141.9 (CH), 131.4 (C), 127.9 (C), 125.5 (CH), 113.1 (CH), 113.0 (C), 111.6 (CH), 110.6 (CH), 107.0 (CH), 100.6 (CH), 76.1 (CH_2), 37.1 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_4$ 273.0870; Found 273.0876.

(*S*)-4-(2-nitro-1-(thiophen-2-yl)ethyl)-1*H*-indol-5-ol (3bj)

The product **3bj** was obtained as a colorless oil (28.4 mg, 0.098 mmol, 98% yield). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 24.18 min, minor enantiomer t_r = 17.67 min. $[\alpha]_D^{20}$ -10.61 (*c*=0.15, $CHCl_3$) (95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (bs, 1H), 7.20 – 7.17 (m, 2H), 7.15 (t, *J* = 1.0 Hz, 1H), 7.02 (dt, *J* = 3.5, 1.1 Hz, 1H), 6.91 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.52 (ddd, *J* = 3.1, 2.1, 0.9 Hz, 1H), 5.72 (td, *J* = 7.7, 0.9 Hz, 1H), 4.82 (bs, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.8 (C), 142.7 (C), 131.3 (C), 128.0 (C), 126.7 (CH), 125.5 (CH), 124.9 (CH), 124.7 (CH), 115.1 (C), 113.0 (CH), 111.5 (CH), 100.6

(CH), 78.4 (CH_2), 39.0 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_3S$ 289.0641; Found 289.0650.

(*S*,*E*)-4-(1-nitro-4-phenylbut-3-en-2-yl)-1*H*-indol-5-ol (3bk)

The product **3bk** was obtained as a colorless oil (29.3 mg, 0.095 mmol, 95% yield). Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 66.76 min, minor enantiomer t_r = 78.59 min. $[\alpha]_D^{20}$ -66.12 (*c*=0.80, $CHCl_3$) (89% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.37 – 7.09 (m, 7H), 6.80 – 6.45 (m, 5H), 5.14 (dd, J = 14.1, 10.9 Hz, 1H), 4.95 (dt, J = 6.5, 5.0 Hz, 2H), 4.84 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.9 (C), 136.7 (C), 132.4 (CH), 131.4 (C), 128.4 (CH), 127.9 (C), 127.6 (CH), 126.4 (CH), 126.4 (CH), 125.5 (CH), 114.2 (C), 112.8 (CH), 111.1 (CH), 100.7 (CH), 77.9 (CH_2), 42.2 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{17}N_2O_3$ 309.1234; Found 309.1247.

(*S*)-4-(1-nitro-4-phenylbutan-2-yl)-1*H*-indol-5-ol (3bl)

The product **3bl** was obtained as a colorless oil (13.8 mg, 0.044 mmol, 44% yield). Enantiomeric excess (87%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 12.79 min, minor enantiomer t_r = 10.96 min. $[\alpha]_D^{20}$ -13.53 (*c*=0.67, $CHCl_3$) (87% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (bs, 1H), 7.25-7.12 (m, 5H), 7.12-7.04 (m, 2H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.50 (ddd, *J* = 3.1, 2.0, 0.9 Hz, 1H), 5.03-4.83 (m, 2H), 4.66 (bs, 1H), 4.21-4.08 (m, 1H), 2.57-2.45 (m, 2H), 2.19-2.00 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 147.3 (C), 141.7 (C), 131.3 (C), 128.3 (CH), 128.3 (CH), 125.8 (CH), 125.2 (CH), 114.9 (C), 112.8 (CH), 110.8 (CH), 101.0 (CH), 78.7 (CH_2), 33.6 (CH_2), 32.6 (CH_2), 30.3 (CH); HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{19}N_2O_3$ 311.1390; Found 311.1397.

(*S*)-1-methyl-4-(2-nitro-1-phenylethyl)-1*H*-indol-5-ol (3ca)

The product **3ca** was obtained as a colorless oil (26.1 mg, 0.088 mmol, 88% yield). Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak IC), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 7.17 min, minor enantiomer t_r = 6.50 min. $[\alpha]_D^{20}$ -48.4 (c=1.30, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.36 (m, 2H), 7.34-7.15 (m, 4H), 7.08 (d, J = 8.6 Hz, 1H), 7.02 (d, J = 3.1 Hz, 1H), 6.67 (d, J = 8.6 Hz, 1H), 6.44 (d, J = 2.6 Hz, 1H), 5.51-5.23 (m, 3H), 4.58 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.6 (C), 139.6 (C), 132.4 (C), 129.9 (CH), 128.9 (C), 128.7 (CH), 127.5 (CH), 127.0 (CH) , 115.8 (C), 112.7 (CH), 109.4 (CH), 98.9 (CH), 77.8 (CH_2), 43.2 (CH), 33.0 (CH_3); HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{17}N_2O_3$ 297.1234; Found 297.1239.

(*S*)-2-methyl-4-(2-nitro-1-phenylethyl)-1H-indol-5-ol (3da)

The product **3da** was obtained as a colorless oil (27.1 mg, inseparable mixture of C-4 alkylated product: C-3 alkylated product, (5.4:1 by ^{1}H NMR), 80% yield). Enantiomeric excess (96%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 13.47 min, minor enantiomer t_r = 11.02 min. $[\alpha]_D^{20}$ -64.1 (c=1.43, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.37 (d, J = 7.2 Hz, 2H), 7.22 (t, J = 3.7 Hz, 3H), 6.96 (d, J = 8.5 Hz, 1H), 6.49 (d, J = 8.5 Hz, 1H), 6.17 (s, 1H), 5.45-5.19 (m, 3H), 4.60 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.7 (C), 139.7 (C), 136.5 (C), 131.4 (C), 129.5 (C), 128.6 (CH), 127.5 (CH), 127.0 (CH), 114.9 (C), 111.5 (CH), 110.2 (CH), 98.8 (CH), 77.9 (CH_2), 43.3 (CH), 13.8 (CH_3). HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{17}N_2O_3$ 297.1234; Found 297.1242.

Scope of the reaction with 6-hydroxyindole

(*S*)-7-(1-phenyl-2-nitroethyl)-1*H*-indol-6-ol (3ea)

The product **3ea** was obtained as a dark oil (17.6 mg, 0.062 mmol, 62% yield). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer t_r = 42.21 min, minor enantiomer t_r = 49.20 min. $[\alpha]_D^{20}$ -67.5 (c=0.92, $CHCl_3$) (95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.41 – 7.25 (m, 6H), 6.94 (dd, *J* = 3.3, 2.4 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.41 (dd, *J* = 3.3, 2.0 Hz, 1H), 5.45 – 5.37 (m, 1H), 5.35 – 5.17 (m, 2H), 4.92 (s, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0 (C), 138.7 (C), 135.7 (C), 129.1 (CH), 127.6 (CH), 127.4 (CH), 123.7 (CH), 123.3 (C), 120.8 (CH), 110.7 (CH), 107.6 (C), 102.9 (CH), 77.2 (CH_2), 41.3 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_3$ 283.1077; Found 283.1088.

(*S*)-7-(1-(4-bromophenyl)-2-nitroethyl)-1*H*-indol-6-ol (3eb)

The product **3eb** was obtained as a yellow solid (24.9 mg, 0.069 mmol, 69% yield); m.p. 190-194 ºC. Enantiomeric excess (84%; 99% after crystallization) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 8.97 min, minor enantiomer t_r = 10.10 min. $[\alpha]_D^{20}$ -0.17 (c=1.085, $CHCl_3$) (84% *ee*); ^{1}H NMR (300 MHz, CD_3OD) δ 7.50 – 7.36 (m, 4H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 3.2 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.36 (d, *J* = 3.2 Hz, 1H), 5.53 – 5.39 (m, 2H), 5.34 (dd, *J* = 11.5, 3.7 Hz, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 152.7 (C), 141.7 (C), 138.3 (C), 133.2 (CH), 131.9 (CH), 125.2 (CH), 124.6 (C), 122.4 (C), 122.0 (C), 112.1 (C), 109.3 (C), 103.7 (CH), 79.7 (CH_2), 43.8 (CH). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{14}N_2O_3Br$ 361.0182; Found 361.0199.

(*S*)-7-(1-(4-(trifluoromethyl)phenyl)-2-nitroethyl)-1H-indol-6-ol (3ec)

The product **3ec** was obtained as a brown solid (27.0 mg, 0.077 mmol, 77% yield); m.p: 152-157. Enantiomeric excess (88%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 6.58 min, minor enantiomer t_r = 7.50 min. $[\alpha]_D^{20}$ -46.7 (c=0.85, $CHCl_3$) (88% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.04 (dd, *J* = 3.3, 2.4 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.45 (dd, *J* = 3.3, 1.9 Hz, 1H), 5.41 – 5.19 (m, 3H), 4.89 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1 (C), 143.0 (C), 135.6 (C), 129.8 (J_{C-F} =32.3 Hz, C), 127.9 (CH), 125.9 (J_{C-F} =3.5 Hz, C), 123.89 (CH), 123.88 (d, J_{C-F} = 272.0 Hz, CF_3), 123.3 (C), 121.3 (CH), 110.7 (CH), 106.6 (C), 103.4 (CH), 77.12(CH_2), 41.5 (CH). ^{19}F NMR (282.4 MHz, $CDCl_3$) δ - 63.11 (s, CF_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{13}N_2O_3F_3$ 351.0951; Found 351.0953.

(*S*)-7-(1-(4-hydroxy-3-methoxyphenyl)-2-nitroethyl)-1H-indol-6-ol (3eh)

The product **3eh** was obtained as a dark oil (12.2 mg, 0.037 mmol, 37% yield). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralpak IC), hexane-iPrOH 70:30, 1.0 mL/min, major enantiomer t_r = 7.78 min, minor enantiomer t_r = 5.26 min. $[\alpha]_D^{20}$ -48.7 (c=0.33, $CHCl_3$) (90% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 6.96 – 6.91 (m, 2H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 2.0 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.39 (dd, *J* = 3.3, 2.0 Hz, 1H), 5.58 (s, 1H), 5.39 (dd, *J* = 8.9, 6.4 Hz, 1H), 5.22 (dd, *J* = 13.3, 8.9 Hz, 1H), 5.12 (dd, *J* = 13.2, 6.5 Hz, 1H), 4.93 (s, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2 (C), 147.7 (C), 145.7 (C), 136.1 (C), 130.9 (C), 124.1 (CH), 123.9 (C), 121.2 (CH), 119.7 (CH), 115.1 (CH), 111.1 (CH), 110.9 (CH), 103.2 (CH), 77.7 (CH_2), 56.4 (CH_3), 41.4 (CH). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}N_2O_5$ 329.1132; Found 329.1129.

(*S*)-7-(1-(furan-2-yl)-2-nitroethyl)-1*H*-indol-6-ol (3ei)

The product **3ei** was obtained as a colorless oil (26.9 mg, 0.099 mmol, 99% yield). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 90:10, 1.0 mL/min, major enantiomer t_r = 25.78 min, minor enantiomer t_r = 28.51 min. $[\alpha]_D^{20}$ -45.8 (c=1.05, $CHCl_3$) (94% *ee*); **¹**H NMR (300 MHz, CDCl3) δ 8.03 (bs, 1H), 7.43 (t, *J* =0.9 Hz, 1H), 7.41 (dd, *J* =5.4, 0.7 Hz, 1H), 7.02 (dd, *J* =3.2, 2.4 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.45 (dd, *J* = 3.3, 2.0 Hz, 1H), 6.39 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.31 (dt, *J* = 3.3, 0.9 Hz, 1H), 5.65 (ddd, *J* = 9.2, 6.1, 0.6 Hz, 1H), 5.22 (dd, *J* = 13.2, 9.2 Hz, 1H), 5.08 (bs, 1H), 4.97 (dd, *J* = 13.2, 6.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 151.8 (C), 148.8 (C), 142.3 (CH), 135.3 (C), 123.8 (CH), 123.5 (C), 121.1 (CH), 111.0 (CH), 110.3 (CH), 107.7 (CH), 105.3 (C), 102.9 (CH), 75.4 (CH_2), 35.1 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_4$ 273.0870; Found 273,0877.

(*S*)-7-(2-nitro-1-(thiophen-2-yl)ethyl)-1*H*-indol-6-ol (3ej)

The product **3ej** was obtained as a colorless oil (26.6 mg, 0.092 mmol, 92% yield). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 11.71 min, minor enantiomer t_r = 10.25 min. $[\alpha]_D^{20}$ -8.84 (c=0.91, $CHCl_3$) (94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (bs, 1H), 7.42 (dd, *J*=8.4, 0.6 Hz, 1H), 7.24 (dd, *J* =5.1, 1.2 Hz, 1H), 7.06 (dt, *J* =3.5, 1.2 Hz, 1H), 7.00 (dd, *J* = 3.2, 2.4 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.62 (d, *J* =8.4 Hz, 1H), 6.45 (dd, *J* =3.3, 2.0 Hz, 1H) ,5.73–5.62 (m, 1H), 5.29 (dd, *J* =13.3, 8.3 Hz, 1H), 5.17 (dd, *J* = 13.3, 6.6 Hz, 1H), 5.07 (bs, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 148.8 (C), 142.2 (C), 135.4 (C), 126.9 (CH), 125.5 (CH), 124.8 (CH), 123.8 (CH), 123.4 (C), 121.2 (CH), 110.6 (CH), 107.1 (C), 103.0 (CH), 77.7 (CH_2), 37.1 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_3S$ 289.0641; Found 289.0650.

(S,*E*)-7-(1-nitro-4-phenylbut-3-en-2-yl)-1*H*-indol-6-ol (3ek)

The product **3ek** was obtained as a colorless oil (13.6 mg, 0.044 mmol, 44% yield). Enantiomeric excess (89%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 66.76 min, minor enantiomer t_r = 78.59 min. $[\alpha]_D^{20}$ -66.12 (c=0.80, $CHCl_3$) (89% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.38 – 7.26 (m, 4H), 7.26 – 7.18 (m, 1H), 7.13 – 7.08 (m, 1H), 6.72 – 6.54 (m, 3H), 6.49 (dd, J = 3.2, 2.0 Hz, 1H), 5.09 (dd, J = 12.6, 8.4 Hz, 1H), 4.96 (dd, J = 12.5, 6.4 Hz, 1H), 4.93 (s, 1H), 4.82 (dt, J = 8.4, 6.2 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 149.3 (C), 136.3 (C), 135.5 (C), 132.5 (CH), 128.6 (CH), 127.9 (CH), 126.5 (CH), 125.9 (CH), 123.7 (CH), 123.2 (C), 120.8 (CH), 110.7 (CH), 106.1 (C), 103.2 (CH), 77.4 (CH_2), 40.2 (CH); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{17}N_2O_3$ 309.1234; Found 309.1247.

Scope of the reaction with 7-hydroxyindole

(*S*)-6-(1-phenyl-2-nitroethyl)-1H-indol-7-ol (3fa)

The product **3fa** was obtained as a dark oil (12.7 mg, 0.045 mmol, 45% yield). Enantiomeric excess (18%) was determined by chiral HPLC (lux-amylose-1), hexane-iPrOH 80:20, 1.0 mL/min, major enantiomer t_r = 11.50min, minor enantiomer t_r = 12.55 min. $[\alpha]_D^{20}$ -10.2 (c=0.26, $CHCl_3$) (18% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.35 – 7.25 (m, 5H), 7.23 (d, *J* = 8.7 Hz, 1H), 7.14 (s, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.49 – 6.45 (m, 1H), 5.27 (m, 2H), 5.09 (d, *J* = 7.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (C), 139.1 (C), 129.3 (C), 129.2 (CH), 127.7 (CH), 127.6 (CH), 127.4 (C), 124.7 (CH), 119.2 (CH), 118.2 (C), 114.5 (CH), 103.0 (CH), 78.9 (CH_2), 42.6 (CH). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_2O_3$ 283.1077; Found 283.1107.

Dialkylation product when 4-hydroxyindole is used

Products **3aa'** and **4** were obtained as an unseparable mixture. But, in some cases, **4** was obtained pure after column chromatography.

5,7-bis(1-phenyl-2-nitroethyl)-1H-indol-4-ol (4)

Dark oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.35 – 7.17 (m, 10H), 6.99 (t, J = 2.9 Hz, 1H),6.82 (s, 0.5H)*, 6.78 (s, 0.5H)*, 6.42 (ddd, J = 3.1, 2.0, 1.0 Hz, 1H), 5.39-5.29 (m, 1H), 5.22 (s, 1H), 5.22 – 4.87 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 145.8*, 139.4, 139.3*, 138.2, 134.8, 129.4, 129.3*, 128.9, 128.8*, 128.12, 128.07*, 127.72, 127.71*, 127.6, 127.5*, 127.4, 127.3*, 124.3, 120.7, 120.2*, 118.8, 115.10, 115.06*, 114.9, 114.7*, 98.5, 78.82, 78.81*, 78.4, 78.3*, 44.64, 44.60*, 43.7, 43.3*. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}N_3O_5$ 432.1554; Found 432.1565.* Presence of rotamers.

Procedures and characterization data for compounds 6

***tert*-Butyl (*S*)-(2-(5-hydroxy-1*H*-indol-4-yl)-2-phenylethyl)carbamate (6a)**

Compound **3ba** (28.1 mg, 0.1 mmol) and $NiCl_2 \cdot 6H_2O$ (23.8 mg, 0.1 mmol, 1 eq) were placed in a 10 mL round bottomed flask and MeOH (1 mL) was added. After stirring the suspension, $NaBH_4$ (18.9 mg, 0.5 mmol, 5 eq) was added at 0 ºC and the mixture was stirred at room temperature for 1.5 h. After which, the mixture was quenched with sat. NH_4Cl at 0 ºC and extracted with CH_2Cl_2. The organic layers were washed with brine and dried over $MgSO_4$. After filtered and concentrated under vacuum, the crude product was used in the next step as obtained. The crude amine and Boc_2O (21.8 mg, 0.1 mmol, 1 eq) were placed in a 10 mL round bottomed flask and they were disoslved in CH_2Cl_2 (1 mL). Then, Et_3N (14 µL, 0.1 mmol, 1 eq) was added. The mixture was stirred overnight and after that was purified by flash chromatography on silica gel using hexane/EtOAc mixtures (90:10 to 80:20) to afford the product **6a** (24.7 mg, 0.070 mmol) in 70 % yield.

Enantiomeric excess (97%) was determined by chiral HPLC (Chiralcel OD-H), hexane-^{i}PrOH 90:10, 1.0 mL/min, major enantiomer t_r = 40.96 min, minor enantiomer t_r = 51.38 min. Brown oil; $[\alpha]_D^{20}$ -9.77 (c=1.37, $CHCl_3$) (97% *ee*); ^{1}H NMR (300 MHz, CD_3OD) δ 7.43 (d, *J* = 7.5 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.19 – 7.07 (m, 3H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.31 (d, *J* = 3.1 Hz, 1H), 4.92 (m, 1H), 4.27 – 4.04 (m, 1H), 3.87 (dd, *J* = 13.3, 8.7 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ 159.3 (C), 149.9 (C), 145.3 (C), 133.7 (C), 130.7 (C), 130.2 (CH), 129.8 (CH), 127.6 (CH), 126.5 (CH), 119.7 (C), 114.1 (CH), 112.1 (CH), 102.1 (CH), 80.8 (C), 46.4 (CH), 45.5 (CH_2), 29.6 (CH_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{25}N_2O_3$ 353.1865; Found 353.1862.

***tert*-Butyl (*S*)-(2-(6-hydroxy-1*H*-indol-7-yl)-2-(4-(trifluoromethyl)phenyl)ethyl) carbamate (6b)**

Compound **3cc** (24.5 mg, 0.07 mmol) and $NiCl_2 \cdot 6H_2O$ (17.0 mg, 0.07 mmol, 1 eq) were placed in a 10 mL round bottomed flask and MeOH (1 mL) was added. After stirring the suspension, $NaBH_4$ (13.2 mg, 0.35 mmol, 5 eq) was added at 0 ºC and the mixture was stirred at room temperature for 1.5 h. After which, the mixture was quenched with sat. NH_4Cl at 0 ºC and extracted with CH_2Cl_2. The organic layers were washed with brine and dried over $MgSO_4$. After filtered and concentrated under vacuum, the crude product was used in the next step as obtained. The crude amine and Boc_2O (15.3 mg, 0.07 mmol, 1 eq) were placed in a 10 mL round bottomed flask and they were disoslved in CH_2Cl_2 (1 mL). Then, Et_3N (10 µL, 0.07 mmol, 1 eq) was added. The mixture was stirred overnight and after that was purified by flash chromatography on silica gel using hexane/EtOAc mixtures (90:10 to 80:20) to afford the product **6b** (18.2 mg, 0.043 mmol) in 62 % yield.

Enantiomeric excess (88%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 80:20, 1.0 mL/min, major enantiomer t_r = 18.0 min, minor enantiomer t_r = 20.76 min. Colorless oil; $[\alpha]_D^{20}$ -36.7 (c=0.56, $CHCl_3$) (86% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.50 (d, J = 8.3 Hz, 3H), 7.42 (d, J = 8.3 Hz, 3H), 7.37 (d, J = 8.3 Hz, 1H), 6.93 (t, J = 2.8 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.41 (dd, J = 3.3, 1.9 Hz, 1H), 5.55 (s, 1H), 5.00 – 4.83 (m, 2H), 4.04 (m, 1H), 3.84 (ddd, J = 13.7, 8.4, 5.4 Hz, 1H), 1.36 (s, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7 (C), 149.7 (C), 145.2 (C), 136.0 (C), 129.0 (q, $J_{C\text{-}F}$ = 32 Hz, C), 128.2 (CH), 125.7 (q, $J_{C\text{-}F}$ = 3.4 Hz, CH), 124.1 (q, $J_{C\text{-}F}$ = 272.0 Hz, CF_3), 123.5 (CH), 123.0 (C), 120.4 (CH), 111.1 (CH), 109.1 (C), 102.8 (CH), 80.1 (C) 43.0 (CH_2), 42.2 (CH), 28.3 (CH_3). HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{24}F_3N_2O_3$ 421,1734; Found 421,1739.

Procedure and characterization data for compound 7

Compound **3ba** (28.1 mg, 0.1 mmol) and 4-dimethylaminopyridine (36.7 mg, 0.3 mmol, 3 eq) were placed in a 10 mL round bottomed flask. Then, the flask was purged with N_2 and CH_2Cl_2 (2 mL) was added. After 5 minutes, *N*-phenyl-bis(trifluoromethane sulfonimide (71.4 mg, 0.2 mmol, 2 eq) was added and the mixture was stirred at room temperature. The reaction was monitored by thin layer chromatography eluting with CH_2Cl_2. When the starting material was consumed, H_2O was added (5 mL) and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (30 mL) and dried under anhydrous Na_2SO_4. The organic solvents were removed under reduced pressure and the residue was purified by column chromatography eluting with hexane:CH_2Cl_2 mixtures (50:50 to 30:70) to afford the triflated product **6** (38.8 mg, 0.084 mmol) in 84% yield.

(*S*)-4-(2-nitro-1-phenylethyl)-1*H*-indol-5-yl trifluoromethanesulfonate (7)

Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 80:20, 1.0 mL/min, major enantiomer t_r = 7.19 min, minor enantiomer t_r = 8.19 min. Brown oil; $[\alpha]_D^{20}$ -55.71 (c=0.53, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (bs, 1H), 7.37 – 7.23 (m, 7H), 7.23 – 7.20 (m, 1H), 7.16 (d, *J* = 8.9 Hz, 1H), 6.34 (ddd, *J* = 3.2, 2.0, 0.9 Hz, 1H), 5.69 (dd, *J* = 8.1, 7.3 Hz, 1H), 5.43 (dd, *J* = 13.4, 8.4 Hz, 1H), 5.12 (dd, *J* = 13.4, 7.0 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 141.1 (C), 137.8 (C), 135.0 (C), 128.9 (CH), 127.4 (CH), 127.3 (CH), 127.0 (C), 126.9 (CH), 123.6 (C), 118.6 (q, $J_{C\text{-}F}$ = 320.2 Hz, C), 115.6 (CH), 112.1 (CH), 102.5 (CH), 77.0 (CH_2), 41.3 (CH); ^{19}F RMN (282 MHz, $CDCl_3$) δ -74.16 (s); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{14}F_3N_2O_5S$ 415.0570; Found 415.0577.

Procedure and characterization data for compound 8:

Compound **7** (22.4 mg, 0.054 mmol) was placed in a 25 mL round bottomed flask, which was purged with N2. Then, MeOH (3 mL) was added, followed by 10% Pd/C (5 mg) and Et_2NH (6.7 µL, 0.065 mmol, 1.2 eq). Then, the reaction vessel was repeatedly purged with H_2 using a balloon and a needle as a vent. Finally, the reaction was stirred at room temperature under H_2 (1 atm, balloon). The reaction was monitored by thin layer chromatography eluting with CH_2Cl_2. When the reaction was complete, the suspension was passed through a pad of Celite and the organic solvents were removed under vacuum. Then, the residue was placed in a 10 mL round bottomed flask, which was purged with N_2. Then, CH_2Cl_2 was added (1.5 mL) and, when was dissolved, AcCl (5.8 µL, 0.081 mmol, 1.5 eq) and Et_3N (12.0 µL, 0.086 mmol, 1.6 eq) were carefully added via syringe and the mixture was stirred at room temperature until completion (TLC). The reaction mixture was quenched by addition of H_2O at 0 ºC and extracted 3 times with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the filtrate was concentrated to dryness in vacuo. The crude was purified by column chromatography eluting with hexane:AcOEt mixtures (95:5 to 80:20) to obtain the product **8** (11.3 mg, 0.041 mmol) in 75% yield.

(*S*)-*N*-(2-(1*H*-indol-4-yl)-2-phenylethyl)acetamide (8)

Enantiomeric excess (93%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 85:15, 1.0 mL/min, major enantiomer tr = 35.04 min, minor enantiomer tr = 38.99 min. Transparent oil; $[\alpha]_D^{20}$ -16.73 (c=0.53, $CHCl_3$) (93% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.35 – 7.27 (m, 5H), 7.24 – 7.14 (m, 3H), 6.99 (d, J = 7.2 Hz, 1H), 6.57 (ddd, J = 3.1, 2.0, 0.9 Hz, 1H), 5.48 (s, 1H), 4.62 (t, J = 7.9 Hz, 1H), 4.10 – 3.96 (m, 2H), 1.86 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.1 (C), 142.0 (C), 136.0 (C), 135.0 (C), 128.6 (CH), 128.1 (CH), 127.5 (C), 126.6 (CH), 124.1 (CH), 122.1 (CH), 117.7 (CH), 110.0(CH),

101.1 (CH), 47.9 (CH), 43.5 (CH_2), 23.4 (CH_3); HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{19}N_2O$ 279.1492; Found 279.1491.

Procedure and characterization data for compound 9

Compound **3ba** (28.1 mg, 0.1 mmol) and racemic 1,1′-Binaphthyl-2,2′-diyl hydrogenphosphate (2.8 mg, 0.01 mmol, 0.1 eq) were placed in a 10 mL flask. Then, the flask was purged with N_2 and CH_2Cl_2 (1 mL) was added. After stirring for 10 minutes, methylvinylketone (9.8 μL, 0.12 mmol, 1.2 eq) was added via syringe. The mixture was stirred at room temperature for 24 h. Then, H2O (5 mL) was added and the mixture extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Finally, the residue was purified by column chromatography eluting with hexane:AcOEt mixtures (95:5 to 75:25) and the C-3 alkylated product **9** (27.5 mg, 0.078 mmol) was obtained in 78 % yield.

(*S*)-4-(5-hydroxy-4-(2-nitro-1-phenylethyl)-1*H*-indol-3-yl)butan-2-one (9)

Enantiomeric excess (96%) was determined by chiral HPLC (Chiralpak AS-H), hexane-^{i}PrOH 80:20, 1.0 mL/min, major enantiomer t_r = 19.52 min, minor enantiomer t_r = 24.65 min. Colorless oil; $[\alpha]_D^{20}$ -40.88 (c=1.07, $CHCl_3$) (96% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.34 – 7.19 (m, 5H), 7.13 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.65 (d, *J* = 8.6 Hz, 1H), 5.73 (t, *J* = 7.4 Hz, 1H), 5.46 (dd, *J* = 12.9, 7.5 Hz, 1H), 5.31 (dd, *J* = 12.9, 7.3 Hz, 1H), 4.84 (s, 1H), 3.24 (td, *J* = 7.6, 3.9 Hz, 2H), 2.96 – 2.66 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9 (C), 147.7 (C), 139.7 (C), 132.7 (C), 128.7 (CH), 127.5 (CH), 127.0 (CH), 126.4 (C), 124.3 (CH), 116.2 (C), 114.9 (C), 113.3 (CH), 111.5 (CH), 78.7 (CH_2), 44.6 (CH_2), 42.3 (CH), 29.8 (CH_3), 21.8 (CH_2); HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{20}N_2O_4Na$ 375.1315; Found 375.1322.

Control experiment with 5-methoxyindole

In a 5 mL vial were placed 5-methoxyindole (0.15 mmol), *trans*-β-nitrostyrene **2a** (0.10 mmol) and Rawal squaramide (**VI**, 0.84 mg, 0.02 mmol). Then, the mixture was dissolved in $CHCl_3$ (1 mL) and it was stirred at 4 ^{o}C until the reaction was complete (TLC). Finally, the reaction mixture was directly poured to the column chromatography using hexane:AcOEt mixtures (90:10 to 80:20) as eluent to afford the product **10** as an enantioenriched mixture.

5-methoxy-3-(1-phenyl-2-nitroethyl)-1H-indole (10)

The product **10** was obtained as a colorless oil (3 mg, 0.007 mmol, 7% yield). Enantiomeric excess (14%) was determined by chiral HPLC (Chiralpak AD-H), hexane-^{i}PrOH 90:10, 1.0 mL/min, major enantiomer t_r

= 29.92 min, minor enantiomer t_r = 44.34 min. The HPLC conditions were previously described in the literature.[30] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.33 – 7.24 (m, 5H), 7.22 (d, *J* = 1.0 Hz, 1H), 7.01 – 6.99 (m, 1H), 6.86 – 6.80 (m, 2H), 5.12 (t, *J* = 7.5 Hz, 1H), 5.03 (dd, *J* = 12.2, 7.4 Hz, 1H), 4.92 (dd, *J* = 12.2, 8.4 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2 (C), 139.1 (C), 131.6 (C), 128.9 (CH), 127.8 (CH), 127.6 (CH), 126.6 (C), 122.3 (CH), 114.2 (C), 112.8 (CH), 112.1 (CH), 100.9 (CH), 79.5 (CH_2), 55.8 (CH_3), 41.5 (CH).

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. ^{1}H and ^{13}C NMR spectra, and HPLC chromatograms for all compounds. Crystallographic data for compounds **3ab** and **3eb**.

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