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FULL PAPER

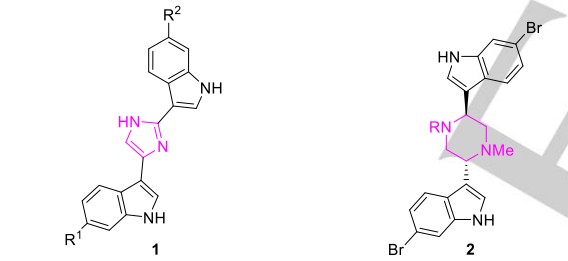
Asymmetric organocatalytic synthesis of Bisindoles – Scope and Derivatizations

Christina Retich,[a] and Stefan Bräse*[a, b]

Abstract: Starting from 3-vinylindoles and glyoxolate imines we created a library of diverse 4,6-bis(1*H*-indole-3-yl)piperidine 2-carboxylates using 10 mol% of a chiral phosphoric acid. Utilising electron withdrawing groups on the starting material during the reaction led to the formation of Povarov-type structures, which extended the previous library of molecules. Furthermore we could demonstrate that consecutive reactions like reductions, cross coupling reactions or click reactions on bisindoles are feasible.

Introduction

Bisindole alkaloids such as nortopsentins (**1**)[1] and dragmacidins (**2**)[2] (Figure 1) are widely found in nature, exhibiting various interesting biological activities. Many compounds of marine origin bear two isolated indoles on one heterocycle. Nortopsentins and their analogs exhibit antitumor,[1d, 3] antiproliferative, antifungal[4] and antiplasmodial[5] activities. Besides, dragmacidins show phosphatase inhibitory,[6] antiviral,[7] and antitumor[8] effects.



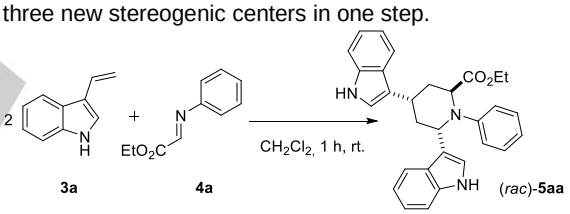
nortopsentin A: $R^1 = R^2$ = Br (**1a**)
nortopsentin B: R^1 = Br, R^2 = H (**1b**)
nortopsentin C: R^1 = H, R^2 = Br (**1c**)
nortopsentin D: $R^1 = R^2$ = H (**1d**)

dragmacidin A: R = H (**2a**)
dragmacidin B: R = Me (**2b**)

Figure 1. Structures of nortopsentins (**1**) and dragmacidins (**2**) represent alkaloids which contain two isolated indole moieties.

Due to the fact that 3-vinylindole can act as a diene in the Diels-Alder reaction with various electrondeficient olefins[9] or can be utilized in the synthesis of carbazoles, [9a, 10] it is a versatile building block for the synthesis of heterocycles. In the last few years, the first asymmetric organocatalytic reactions of 3-vinylindoles including thiourea-catalyzed reactions with maleimides or indolones, were reported.[11] When reacted with electron-rich arylamines the reactivity of 3-vinylindole can be that of a dienophile, furnishing Povarov-type products.[12] Although Ricci et al. could trap the intermediate which was a bisindole-piperidine-hybrid by an excess of 3-vinylindole (5.00 equiv.), they focused mainly on the asymmetric Povarov reaction.

Recently we developed a powerful three-component, enantioselective, and organocatalytic synthesis of 4,6-bis(1*H*-indole-3-yl)piperidine 2-carboxylates (**5**) utilizing easily accessible 3-vinylindoles (**3**) and imino esters (**4**) and a chiral phosphoric acid (Scheme 1).[13] The reaction proceeds within 1 h and diastereosectively at room temperature, building three new bonds and three new stereogenic centers in one step.



Scheme 1. Racemic synthesis of bisindole (*rac*)-**5aa** with imino ester **4a** and 3-vinylindole **3a**.

The mechanism of the bisindole formation is shown in Scheme 2. After the first addition of one equivalent 3-vinylindole (**3a**) to the imino ester **4a**, the second molecule of **3a** is able to attack the stabilized intermediate. An intramolecular ring closure of **6** finally yields (*rac*)-**5aa** as product. To proceed the reaction, a free NH group on the indole moiety is necessary, as in previous studies with *N*-methylated derivatives no product could be isolated.[13]

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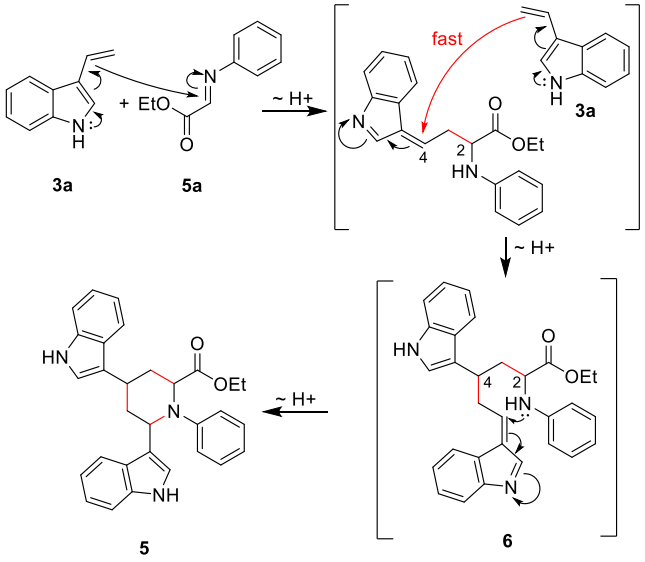


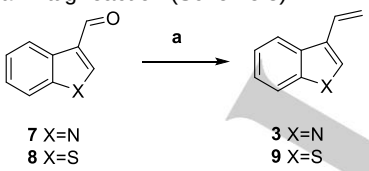
Scheme 2. Mechanism for the formation of (*rac*)-**5aa**.

Based on our preliminary work we report the synthesis of several bisindoles bearing new substitution patterns and heterocycles to study the scope of the reaction. Furthermore we will perform consecutive reactions on selected bisindoles.

Results and Discussion

Starting material synthesis

3-Vinylindoles (**3**) and 3-vinylbenzothiophene (**9**) were synthesized *via* Wittig reaction (Scheme 3).[11a]



Scheme 3. Synthesis of 3-vinylindoles (**3**) and 3-vinylbenzothiophene (**9**). **a** methyltriphenylphophonium iodide, *n*-BuLi, THF, –50 °C → 0 °C; then indole-3-carboxaldehyde (**7**)/bezothiophene-3-carboxaldehyde (**8**), NaHMDS, THF, –30 °C → rt., 1-5 h, 34–95%.

3-Vinylbenzofuran (**10**) was synthesized in four steps starting with benzofuran-3(2*H*)-one according to a literature known procedure.[14] Another heterocycle which should be introduced during the three-component reaction is 4-vinyl-1*H*-imidazole (**11**). We obtained the compound after decarboxylation of urocanic acid by distillation in vacuo.[15] 3-Vinyl-1*H*-indazole (**12**) was synthesized out of 3-bromo-1*H*-indazole *via* Stille coupling.[16] 3-vinyl-1*H*-pyrrole (**13**) was obtained in five steps out of commercially available pyrrole.[17]

Figure 2 shows the synthesized building blocks for the multicomponent reaction.

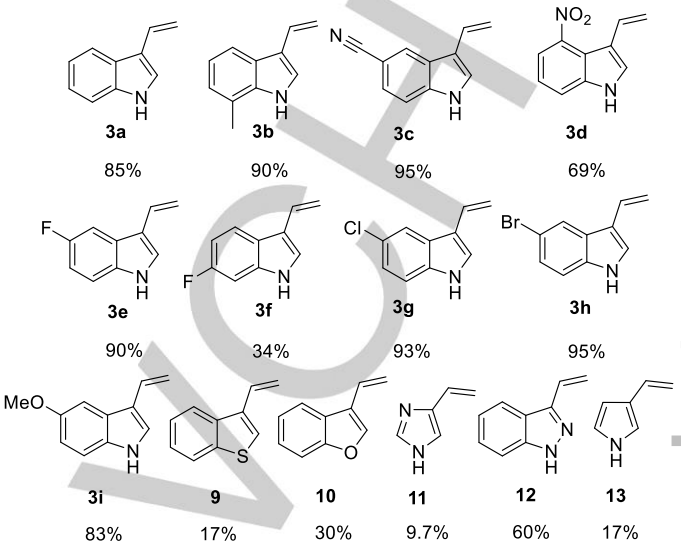


Figure 2. Synthesized heterocycles and their yields.

Imino esters (Figure 3) were prepared according to an established procedure.[18]

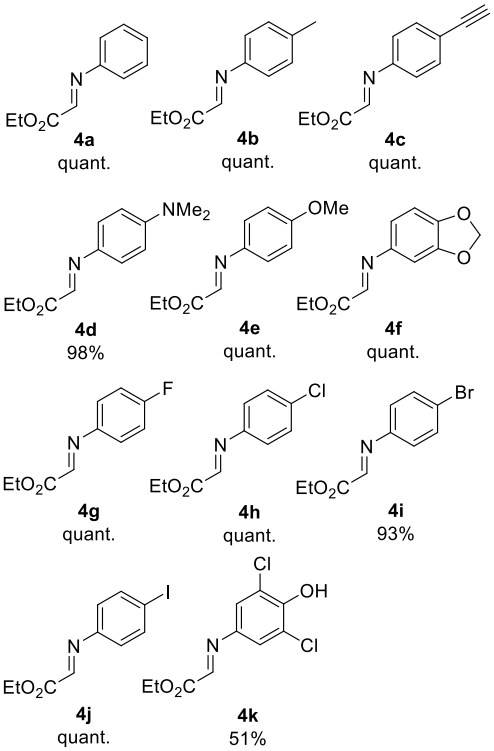
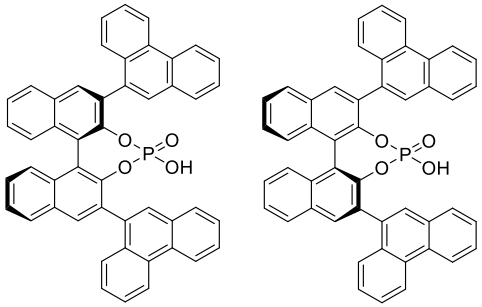


Figure 3. Synthesized imino esters and their yields.

In previous work it was envisioned that chiral thiourea catalysts, would be able to interact strongly with an imine *via* H-bond catalysis.[11, 19] But employing these catalysts did not lead to satisfying results. There was almost no enantioinduction (7.5% ee) observed and the yields were mostly diminished compared to those without applying any catalyst.[13] Therefore we chose another widely used catalyst class in organic chemistry – chiral phosphoric acids, also used by Ricci et al. in the aforementioned paper.[12] Having found an efficient catalyst (Figure 4) for the enantioselective reaction, we accomplished the synthesis according to a literature known procedure in comparable yields.[20]



14$^{(R)}$ **14**$^{(S)}$

Figure 4. Catalysts (*R*)-**14** and (*S*)-**14**.

(Asymmetric) Reaction between 3-vinylindoles (3) and glyoxalate imines (4)

The synthesis of various bisindole-derivatives was accomplished by applying one equivalent of an imino ester and two equivalents of 3-vinylindole. Table 1 shows the synthesized bisindoles in a non-catalyzed racemic and also catalyzed asymmetric reaction procedure. The yields in table 1 refer to the 2 diastereomers (F1 and F2) that could be isolated for some bisindoles.

Entries 17–23 (Table 1) show the results while using a chloro substituted vinylindole (**3g**) during the reaction. Thereby a fluoro substituted imino ester (**4g**) led to the highest yields, either in a racemic or asymmetric reaction. In general, the yields are good except of entry 19. We could only isolate 8.4% of the desired product during the racemic reaction. However the addition of the phosphoric acid as a catalyst (**14**) led to an increase of the yield to 36% or rather 64%. Considering the results of entries 17–23 we can record that electron withdrawing groups on R^2 lead to higher yields.

Previous studies are confirmed by entries 1-7 (Table 1). At this point the unsubstituted 3-vinylindole (**3a**) was used to perform the reaction. In this case the highest yield was obtained with a chloro substituted imino ester (**4h**) – but only for the racemic reaction (entry 5). Continuously high yields were reported for the racemic and asymmetric reaction for the fluoro substituted imino ester (**4g**) cumulated for both diastereomers (entry 4). Surprisingly the usage of a methyl substituted imino ester (**4b**) led to high yields for the racemic as well as for the asymmetric reaction (entry 2). For the entries 1–7 we could prove that the addition of the catalyst increased the yield of the bisindoles.

The results for the reaction with 5-fluoro-3-vinyl-1*H*-indole (**3e**) and 6-fluoro-3-vinyl-1*H*-indole (**3f**) are shown in entries 13–16 (Table 1). Thereby we can note high yields for every substitution during the asymmetric reaction. The racemic reaction with a methoxy substituted imino ester (**4e**) yielded 9.8% (entry 15) and 10% (entry 13). Both yields could be improved through an addition of a phosphoric acid catalyst up to 64%.

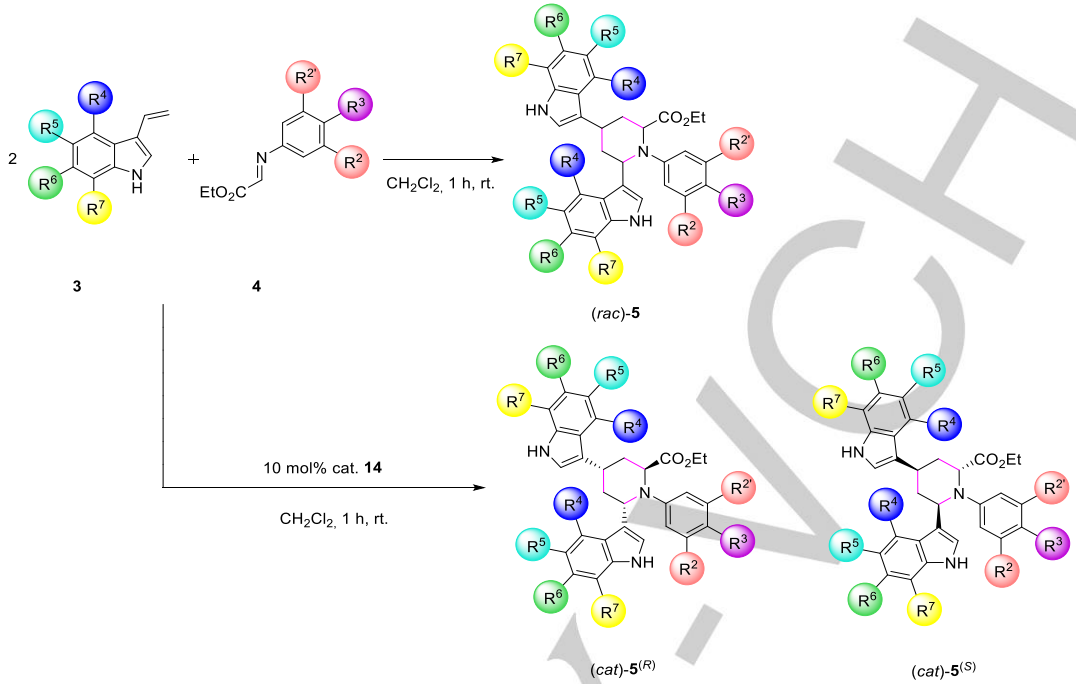
Furthermore, we investigated the reaction of a 7-methyl-3-vinyl-1*H*-indole (**3b**) (entries 8–10) and 5-bromo-3-vinyl-1*H*-indole (**3h**) with the corresponding imino esters (entries 24–27). The yields of the obtained bisindoles are not as high as the previously reported yields. But it was important to functionalize the products with functional groups like methoxy (**4e**, entry 27) or ethynyl (**4c**, entry 8 and 26) to expand the substrate spectrum.

Further functionalizations were accomplished while using 5-nitrile-3-vinyl-1*H*-indole (**3c**) and 4-nitro-3-vinyl-1*H*-indole (**3d**) (entries 11, 12) as starting material. Conclusively the yields for the asymmetric reaction were also higher than for the racemic one.

Entries 21 and 24 show significantly low yields during the asymmetric synthesis while using **14**$^{(R)}$. In these cases we used a preparative TLC as purification method and could observe that some derivatives were not stable throughout the purification process *via* preparative TLC. Furthermore a long purification process, as it is common for preparative TLC was unfortunately not suitable for all of the bisindoles and led to lower yields. In general we detected that methoxy substituted bisindoles **5de**, **5ee**, **5fe**, **5ge**, **5he** do not lead to high yields and are not stable, even while storing under inert atmosphere at –18 °C.

Furthermore it is interesting to mention, that there was no successful reaction while using imino esters with a substitution pattern on the R^1 and R^2 position – only imino ester **4k** reacted to the desired bisindole. In addition we tried to investigate further derivatives of the bisindoles by changing the CO_2Et-group to CO_2Bn, CO_2Me or CF_3 or using pyridine as a heterocyle instead of the aromatic ring. Unfortunately none of the attempts was successful.

Table 1. Racemic and asymmetric synthesis of bisindole derivatives.



Entry	$R^{2/2'}$	R^3	R^4	R^5	R^6	R^7	product	Yield[a] [%] rac F1	Yield[a] [%] rac F2	Yield[a] [%] cat-(*S*)-**14** F1	Yield[a] [%] cat-(*S*)-**14** F2	Yield[a] [%] cat-(*R*)-**14** F1	Yield[a] [%] cat-(*R*)-**14** F2
1	H	H	H	H	H	H	**5aa**	69$^{(A)}$	-[b]	57$^{(A)}$	18$^{(A)}$	40$^{(B)}$	-[b]
2	H	CH_3	H	H	H	H	**5ab**	57$^{(B)}$	-[b]	57$^{(A)}$	16$^{(A)}$	79$^{(B)}$	-[b]
3	H	$N(CH_3)_2$	H	H	H	H	**5ad**	17$^{(A)}$	-[b]	43$^{(A)}$	26$^{(A)}$	46$^{(A)}$	21$^{(A)}$
4	H	F	H	H	H	H	**5ag**	29$^{(A)}$	29$^{(A)}$	56$^{(A)}$	28$^{(A)}$	56$^{(A)}$	16$^{(A)}$
5	H	Cl	H	H	H	H	**5ah**	36$^{(B)}$	-[b]	50$^{(A)}$	49$^{(A)}$	39$^{(B)}$	-[b]
6	H	Br	H	H	H	H	**5ai**	28$^{(A)}$	-[b]	49$^{(A)}$	-[b]	22$^{(B)}$	-[b]
7	H	I	H	H	H	H	**5aj**	22$^{(B)}$	28$^{(B)}$	46$^{(A)}$	11$^{(A)}$	38$^{(A)}$	15$^{(A)}$
8	H	Ethynyl	H	H	H	CH_3	**5bc**	18$^{(B)}$	-[b]	29$^{(A)}$	-[b]	47$^{(A)}$	-[b]
9	H	Cl	H	H	H	CH_3	**5bh**	33$^{(A)}$	17$^{(A)}$	50$^{(A)}$	-[b]	30$^{(B)}$	-[b]
10	Cl	OH	H	H	H	CH_3	**5bk**	25$^{(A)}$	25$^{(A)}$	27$^{(A)}$	-[b]	62$^{(A)}$	-[b]
11	H	CH_3	H	CN	H	H	**5cb**	12$^{(B)}$	-[b]	33$^{(A)}$	-[b]	46$^{(B)}$	-[b]
12	H	OCH_3	NO_2	H	H	H	**5de**	13$^{(A)}$	-[b]	24$^{(A)}$	-[b]	37$^{(B)}$	-[b]
13	H	OCH_3	H	F	H	H	**5ee**	10$^{(A)}$	-[b]	37$^{(A)}$	39$^{(A)}$	30$^{(B)}$	-[b]
14	H	H	H	H	F	H	**5fa**	58$^{(A)}$	-[b]	51$^{(A)}$	19$^{(A)}$	32$^{(B)}$	-[b]
15	H	OCH_3	H	H	F	H	**5fe**	9.8$^{(A)}$	-[b]	64$^{(A)}$	-[b]	36$^{(B)}$	-[b]
16	H	Cl	H	H	F	H	**5fh**	37$^{(A)}$	-[b]	51$^{(A)}$	20$^{(A)}$	30$^{(B)}$	19$^{(B)}$
17	H	H	H	Cl	H	H	**5ga**	28$^{(A)}$	-[b]	67$^{(A)}$	-[b]	32$^{(A)}$	-[b]
18	H	CH_3	H	Cl	H	H	**5gb**	41$^{(B)}$	-[b]	42$^{(A)}$	-[b]	67$^{(B)}$	-[b]
19	H	OCH_3	H	Cl	H	H	**5ge**	8.4$^{(A)}$	-[b]	36$^{(A)}$	-[b]	64$^{(A)}$	-[b]
20	H	F	H	Cl	H	H	**5gg**	53$^{(A)}$	41$^{(A)}$	57$^{(A)}$	23$^{(A)}$	67$^{(A)}$	32$^{(A)}$
21	H	Cl	H	Cl	H	H	**5gh**	44$^{(A)}$	43$^{(A)}$	92$^{(A)}$	-[b]	29$^{(B)}$	-[b]
22	H	Br	H	Cl	H	H	**5gi**	41$^{(A)}$	23$^{(A)}$	35$^{(A)}$	41$^{(A)}$	47$^{(A)}$	15$^{(A)}$
23	Cl	OH	H	Cl	H	H	**5gk**	48$^{(A)}$	-[b]	47$^{(A)}$	-[b]	39$^{(A)}$	-[b]
24	H	H	H	Br	H	H	**5ha**	67$^{(A)}$	-[b]	42$^{(A)}$	-[b]	7.9$^{(B)}$	-[b]
25	H	CH_3	H	Br	H	H	**5hb**	28$^{(A)}$	-[b]	24$^{(A)}$	-[b]	34$^{(A)}$	-[b]
26	H	Ethynyl	H	Br	H	H	**5hc**	10$^{(B)}$	-[b]	30$^{(A)}$	-[b]	57$^{(A)}$	-[b]
27	H	OCH_3	H	Br	H	H	**5he**	23$^{(A)}$	-[b]	28$^{(B)}$	-[b]	36$^{(A)}$	-[b]

[a] Isolated yields. Method A: column chromatography; Method B: preparative TLC. [b] not found/traces (<5%).

Relative and absolute configuration

We observed the appearance of two fractions with different polarities for most of the synthesized bisindoles. The less polar fraction (Fraction 1) has an R_f = 0.30 (cyclohexane/EtOAc 2:1) and the more polar fraction (Fraction 2) has an R_f = 0.10 (cyclohexane/EtOAc 2:1). The isolated fractions differ in ^{1}H and ^{13}C NMR spectra through the chemical shifts and split of the signals of the piperidine ring. The characterization approves that two diastereomers were synthesized which vary in their polarity and so could be separated through column chromatography.
The relative configuration was identified through NOE correlations (Figure 5). In previous work we could prove through NOE correlation experiment, X-ray crystallography and electronic circular dichroism (CD) spectrum the appearance of the shown (2*S*,4*S*,6*S*) configuration. [13] Therefore we performed a NOE correlation with fraction 2 of bisindole **5gg**. This spectrum showed some interesting correlations between protons which lead to the conclusion that as in fraction 1 both indole-3-yl groups are standing in the equatorial position. In contrast to fraction 1 the ethyl ester group is also standing in the equatorial position leading to a (2*R*,4*S*,6*S*) configuration of this diastereomer (Figure 5).

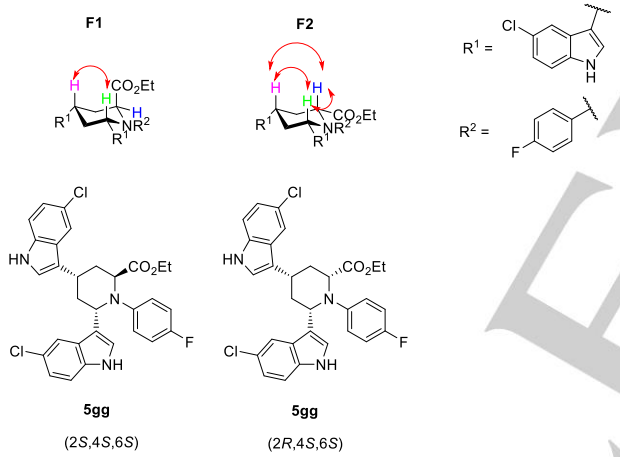
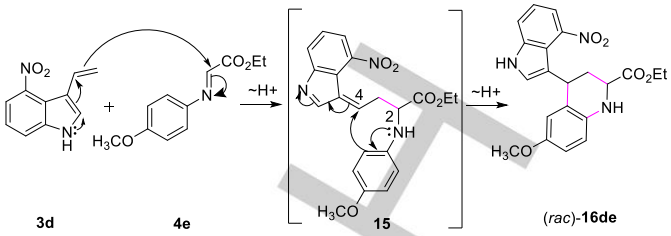


Figure 5. Configurations of bisindole **5gg**, above: experimentally determined NOE correlations; below: Configurations of F1 and F2.

Substitution effects – the Povarov product

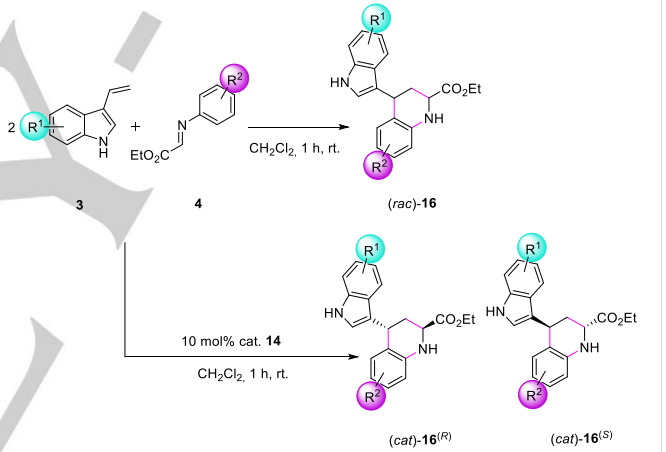
A close observation of the entries 11 and 12 (Table 1) shows a significant decrease in the yields compared to other entries. This could be explained by the appearance of a competing reaction – the Povarov reaction.[12, 21] Scheme 4 shows the postulated mechanism for the formation of the Povarov product.



Scheme 4. Postulated mechanism for the formation of the Povarov product (*rac*)-**16de**.

After first addition of the 3-vinylindole **3d** to the imine **4e** to form the intermediate **15**, the aromatic phenyl ring proceeds a nucleophilic attack at position 4 to give the Povarov product (*rac*)-**16de**. Table 2 shows the synthesized products.

Table 2. Racemic and asymmetric synthesis of Povarov products.



Entry	R^1	R^2	product	Yield[a] [%] rac	Yield[a] [%] cat-(*S*)	Yield[a] [%] cat-(*R*)
1	H	1,3-Dioxolyl	**16af**	60	90	66
2	5-CN	4-CH_3	**16cb**	80	56	51
3	4-NO_2	4-OCH_3	**16de**	63	49	63
4	5-Cl	4-CH_3	**16gb**	47	-	-
5	5-Cl	1,3-Dioxolyl	**16gf**	99	99	80

[a] Isolated yield.

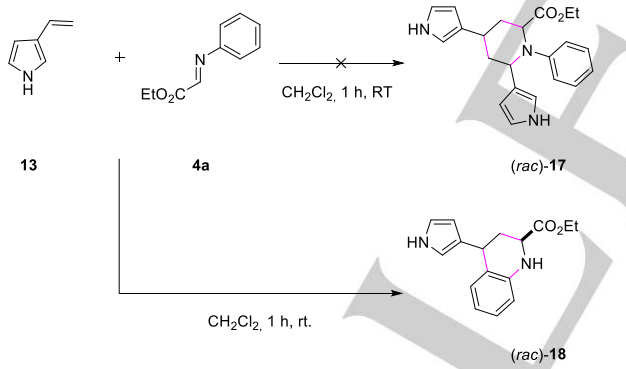
Entries 1–5 (Table 2) demonstrate that the Povarov products could be obtained in good to very good yields in racemic as well as in asymmetric reactions. The reaction between a 5-chloro-3-vinyl-1*H*-indole (**3g**)/ 3-vinyl-1*H*-indole (**3a**) and an imino ester containing an electron withdrawing like an 1,3-dioxolylring (**4f**) only leads in both reactions (racemic and asymmetric) to the formation of the Povarov product in very good yields (entries 1 and 5). Comparable to the bisindole synthesis,

entry 1 (Table 2) shows an increase in the yield during the asymmetric reaction. Unfortunately this observation cannot be transferred to the other entries of table 2. The conclusion is that the synthesis of bisindoles is a catalytic reaction in contrast to the Povarov reaction which proceeds also non-catalytical, which is obvious while comparing the yields of the enantiomeric catalysts. To confirm our assumption we analysed entry 4 (table 2). In this case we obtained the Povarov product (*rac*)-**16gb** during the racemic reaction. While performing the reaction with the phosphoric catalyst we isolated the corresponding bisindole (*cat*)-**5gb** (entry 18, table 1). Furthermore, entry and 3 (table 2) and entry 12 (table 1) demonstrate a reaction of a 3-vinylindole **3d** with an electron withdrawing group reacting with an electronrich imine **4e**. In contrast to the Povarov product, where the yields did not change by modifying the racemic conditions to asymmetric ones (63%), the yields of the bisindoles increased through the addition of the catalyst from 13% to 37%.

Derivatisation of Bisindoles

Previously synthesized heterocycles 3-vinylbenzothiophene (**9**), 3-vinylbenzofuran (**10**), 4-vinyl-1*H*-imidazole (**11**) and 3-vinyl-1*H*-indazole (**12**) could not be implemented in the bisindole synthesis – even by changing the electron character of the imines.

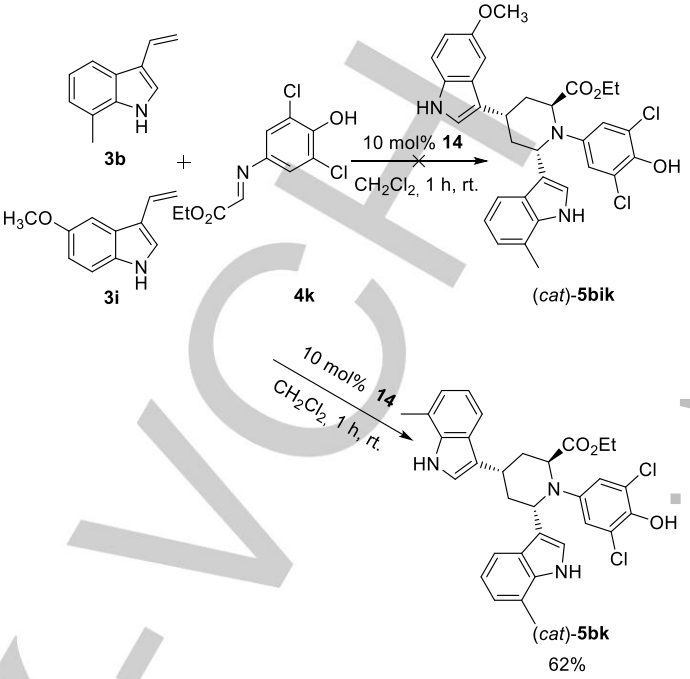
After a successful synthesis of 3-vinyl-1*H*-pyrrole (**13**) we analyzed its reactivity during a racemic bispyrrole synthesis (Scheme 5).



Scheme 5. Racemic reaction of 3-vinyl-1*H*-pyrrole (**13**) with imine **4a**.

As described in Scheme 5 we could obtain the Povarov product **18** instead of the desired bispyrrole **17**. The Povarov product (*rac*)-**18** could be isolated in 77% yield. Because of the lower resonant energy of pyrrole, the nucleophilic attack of the phenyl ring in position 4 proceeds faster than the addition of the second molecule 3-vinyl-1*H*-pyrrole (**13**).

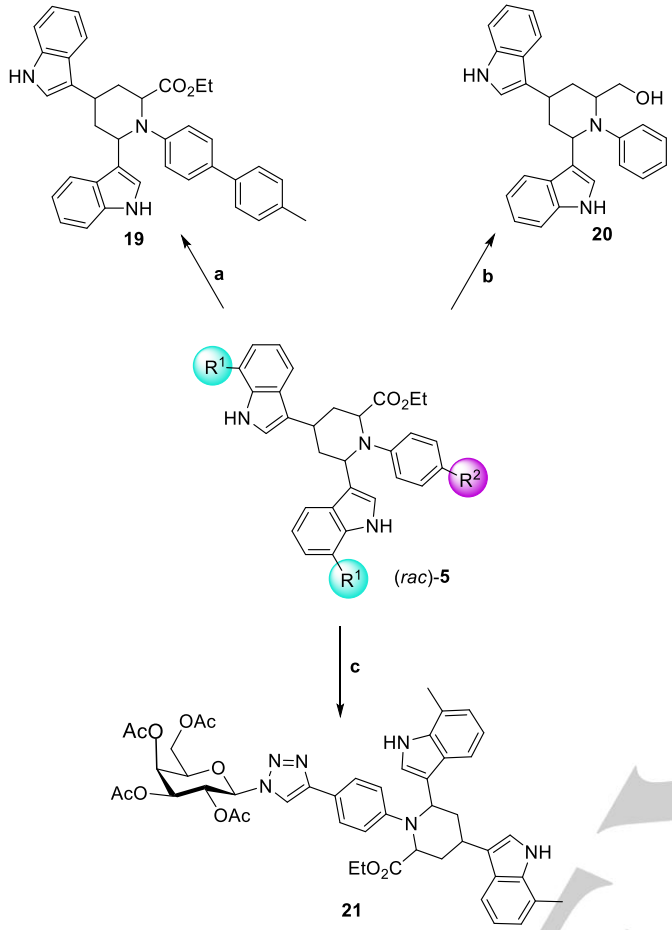
An introduction of two different indole moieties on one piperidine ring was impossible to perform. We chose two indoles, which differ significantly in their polarity, for the reaction (Scheme 6).



Scheme 6. Synthesis of a bisindole with different substituted 3-vinylindoles.

However this reaction did not lead to the formation of the desired product (*cat*)-**5bik**. Product (*cat*)-**5bk** was synthesized – a bisindole with the same heterocycles on the piperidine ring.

Furthermore we tried to investigate consecutive reactions with 3 types of bisindoles – the completely unsubstituted one ((*rac*)-**5aa**) and the ethynyl ((*rac*)-**5bc**)/bromo ((*rac*)-**5ai**) substituted on the imine position (Scheme 7).



Scheme 7. Derivatisation of the bisindoles (*rac*)-**5aa/ai/bc**. Synthesis: **a** *p*-tolylboronic acid, potassium phosphate, $Pd(OAc)_2$, Sphos, argon atmosphere, degassed THF/H_2O = 3:1, 80 °C, 16 h, 57%; **b** $LiAlH_4$, Et_2O, argon atmosphere, reflux, 6 h, 31%; **c** Acetyl-2,3,4,6-tetra-O-acetyl-D–galactopyranosylazide, 1 M $CuSO_4 \times 5\ H_2O$, 1 M sodium ascorbate, *t*-BuOH/H_2O = 1:1, 70 °C, 16 h, traces.

The derivatization experiments shown in Scheme 7 were successful. Product **19** was obtained *via* a Suzuki cross coupling reaction using *p*-tolylbronic acid in 57% yield. The reduction of (*rac*)-**5aa** was realized with $LiAlH_4$ in 31% yield. The provided sugar azide could be successfully introduced in a Click-reaction. Product **21** could be obtained in 24% yield.

Conclusions

In conclusion, we could create a diverse library of bisindoles based on previous investigations on the powerful three-component, enantioselective, and organocatalytic synthesis of 4,6-bis(1*H*-indole-3-yl)piperidine 2-carboxylates. Furthermore we could observe a formation of an interesting side product – the Povarov product – while using electron withdrawing groups on the starting material. Both products are highly functionalized and they resemble medicinally interesting natural products. Their activity towards various test organisms is currently under investigation. Subsequently we could also prove that it is possible to perform consecutive reactions (reduction, cross coupling and click reaction) with selected bisindoles.

Experimental Section

For information concerning the measurements and working techniques as well as the analytical data of all the other compounds please use our supporting information.

*Ethyl (2S,4S,6S) 4,6 bis(1H indol 3 yl) 1 phenylpiperidine-2-carboxylate (**5aa**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5aa** as a yellow oil (cat-(R): 18.5 mg, 39.8 µmol, 40%; cat-(S): F1: 26.6 mg, 57.3 µmol, 57%, F2: 8.40 mg, 18.1 µmol, 18%).
The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 309 mg, 2.16 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 191 mg, 1.08 mmol, 1.00 Equiv.) without a catalyst in 30 mL dichloromethane. The product **5aa** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a colorless oil (345 mg, 0.744 mmol, 69%).

fraction 1 (F1): R_f = 0.48 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.19–1.24 (m, 3H, CH_2CH_3), 2.16–2.30 (m, 1H, NCHC*H*H), 2.38–2.51 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.65 (dq, ^3J = 13.2, ^4J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.36 (tt, ^3J = 12.5, ^3J = 3.1 Hz, 1H, CH_2CHCH_2), 4.05–4.12 (m, 1H, C*H*HCH$_3$), 4.13–4.23 (m, 1H, CH*H*CH$_3$), 4.82 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.65 (dd, ^3J = 11.2, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.63–6.71 (m, 1H, C*H*$_{Ar}$), 6.92–7.04 (m, 5H, C*H*$_{Ar}$), 7.06–7.11 (m, 1H, C*H*$_{Ar}$), 7.15 (dd, ^3J = 6.4, ^3J = 2.2 Hz, 2H, C*H*$_{Ar}$), 7.22 (ddd, ^3J = 9.7, ^3J = 7.6, ^4J = 1.1 Hz, 3H, C*H*$_{Ar}$), 7.37 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.62 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.88–7.96 (m, 1H, C*H*$_{Ar}$), 9.84 (sbr, 1H, N*H*), 10.00 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.4 (+, CH_2CH_3), 20.6 (+, CH_2CHCH_2), 36.9 (–, $CHCH_2$), 43.4 (–, $CHCH_2$), 52.8 (+, NCHC$_{Ind}$), 60.6 (–, CH_2CH_3), 65.7 (+, NCHCO$_2$Et), 112.0 (+, C*H*$_{Ar}$), 112.3 (+, C*H*$_{Ar}$), 119.1 (+, C*H*$_{Ar}$), 119.2 (+, C*H*$_{Ar}$), 119.3 (+, C*H*$_{Ar}$), 119.8 (C$_q$, C$_{Ar}$), 120.4 (C$_q$, C$_{Ar}$), 120.7 (+, C*H*$_{Ar}$), 121.0 (+, C*H*$_{Ar}$), 121.8 (+, C*H*$_{Ar}$), 122.1 (+, C*H*$_{Ar}$), 122.2 (+, C*H*$_{Ar}$), 123.7 (+, C*H*$_{Ar}$), 125.3 (+, 2 × C*H*$_{Ar}$), 126.9 (C$_q$, C$_{Ar}$), 127.6 (C$_q$, C$_{Ar}$), 128.2 (+, 2 × C*H*$_{Ar}$), 137.7 (C$_q$, C$_{Ar}$), 137.9 (C$_q$, C$_{Ar}$), 151.9 (C$_q$, C$_{Ar}$), 173.7 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3410, 2932, 2540, 1697, 1595, 1492, 1455, 1336, 1245, 1176, 1093, 1023, 931, 845, 810, 740, 696, 581, 477, 424 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 464 (64) [*M*+H]$^+$, 390 (69), 347 (43); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{30}O_2N_3$ [*M*+H]$^+$: 464.2333; found: 464.2334.
fraction 2 (F2): R_f = 0.33 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.81 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.14 (q, ^3J = 12.3 Hz, 1H, NCHC*H*H), 2.20–2.31 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.38 (q, ^3J = 12.3 Hz, 1H,

CH*H*CHCO$_2$Et), 3.31 (tt, ^3J = 12.5, ^3J = 3.6 Hz, 1H, CH$_2$C*H*CH$_2$), 3.73 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 3.97 (dd, ^3J = 11.0, ^3J = 2.9 Hz, 1H, NC*H*CO$_2$Et), 4.53 (dd, ^3J = 11.0, ^3J = 2.9 Hz, 1H, NC*H*C$_{Ind}$), 6.71 (t, ^3J = 7.3 Hz, 1H, C*H*$_{Ar}$), 6.82–6.98 (m, 7H, C*H*$_{Ar}$), 7.06–7.11 (m, 4H, C*H*$_{Ar}$), 7.25 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.58 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.85–7.90 (m, 1H, C*H*$_{Ar}$), 9.65 (sbr, 1H, N*H*), 9.90 (sbr, 1H, N*H*) ppm.

*Ethyl 4,6-bis(1H-indol-3-yl)-1-(4-tolyl)piperidine-2-carboxylate (**5ab**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ab** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (cat-(R): 37.9 mg, 79.0 µmol, 79%; cat-(S): F1: 27.2 mg, 56.9 µmol, 57%, F2: 7.40 mg, 15.5 µmol, 16%).
The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5ab** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (27.0 mg, 56.6 µmol, 57%).

fraction 1 (F1): R_f = 0.41 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.22 (t, ^3J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 2.04 (s, 3H, C*H*$_3$), 2.17–2.28 (m, 1H, NCHC*H*H), 2.38–2.49 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.63 (dq, ^3J = 13.2, ^3J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.37 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH$_2$C*H*CH$_2$), 4.04–4.11 (m, 1H, C*H*HCH$_3$), 4.13–4.24 (m, 1H, CH*H*CH$_3$), 4.74 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.65 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.76 (d, ^3J = 8.2 Hz, 2H, C*H*$_{Ar}$), 6.93–7.04 (m, 3H, C*H*$_{Ar}$), 7.06–7.12 (m, 3H, C*H*$_{Ar}$), 7.14 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 2H, C*H*$_{Ar}$), 7.23 (dd, ^3J = 6.9, ^3J = 1.5 Hz, 1H, C*H*$_{Ar}$), 7.37 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.62 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.91–7.97 (m, 1H, C*H*$_{Ar}$), 9.81 9.98 (sbr, 1H, N*H*), 9.98 9.98 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH$_2$CH$_3$), 20.6 (+, *C*H$_3$), 27.5 (+, CH$_2$CHCH$_2$), 37.0 (–, CHCH$_2$), 43.4 (–, CHCH$_2$), 52.8 (+, NCHC$_{Ind}$), 60.5 (–, *C*H$_2$CH$_3$), 65.9 (+, NCHCO$_2$Et), 112.0 (+, *C*H$_{Ar}$), 112.3 (+, *C*H$_{Ar}$), 119.1 (+, *C*H$_{Ar}$), 119.2 (+, *C*H$_{Ar}$), 119.3 (+, *C*H$_{Ar}$), 119.9 (C$_q$, *C*$_{Ar}$), 120.4 (C$_q$, *C*$_{Ar}$), 120.8 (+, *C*H$_{Ar}$), 121.1 (+, *C*H$_{Ar}$), 121.7 (+, *C*H$_{Ar}$), 122.1 (+, *C*H$_{Ar}$), 123.7 (+, *C*H$_{Ar}$), 125.4 (+, 2 × *C*H$_{Ar}$), 126.9 (C$_q$, *C*$_{Ar}$), 127.6 (C$_q$, *C*$_{Ar}$), 128.9 (+, 2 × *C*H$_{Ar}$), 131.3 (C$_q$, *C*$_{Ar}$), 137.7 (C$_q$, *C*$_{Ar}$), 137.9 (C$_q$, *C*$_{Ar}$), 149.4 (C$_q$, *C*$_{Ar}$), 173.8 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3395, 3347, 2920, 2851, 1708, 1618, 1509, 1452, 1339, 1274, 1209, 1188, 1094, 1040, 1007, 933, 848, 816, 741, 673, 615, 592, 561, 515, 466, 423 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 477 (46) [*M*]$^+$, 404 (24), 337 (29), 307 (28), 271 (49), 192 (53), 154 (100), 136 (67), 118 (35), 91 (26); HRMS (EI): calcd for C$_{31}$H$_{31}$O$_2$N$_3$ [*M*]$^+$: 477.2411; found: 477.2414.
fraction 2 (F2): R_f = 0.26 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 0.96 (t, ^3J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 2.08 (s, 3H, C*H*$_3$), 2.19–2.30 (m, 1H, NCHC*H*H), 2.30–2.42 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.44–2.54 (m, 1H, CH*H*CHCO$_2$Et), 3.43 (tt, ^3J = 12.1, ^3J = 3.5 Hz, 1H, CH$_2$C*H*CH$_2$), 3.86 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 4.03 (dd, ^3J = 11.2, ^3J = 2.8 Hz, 1H, NC*H*CO$_2$Et), 4.63 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, NC*H*C$_{Ind}$), 6.79 (d, ^3J = 8.1 Hz, 2H, C*H*$_{Ar}$), 6.97–7.15 (m, 7H, C*H*$_{Ar}$), 7.19–7.25 (m, 2H, C*H*$_{Ar}$), 7.38 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.71 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 8.00–8.06 (m, 1H, C*H*$_{Ar}$), 9.76 (sbr, 1H, N*H*), 10.02 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.2 (+, CH$_2$CH$_3$), 20.8 (+, *C*H$_3$), 27.5 (+, CH$_2$CHCH$_2$), 38.4 (–, CHCH$_2$), 42.8 (–, CHCH$_2$), 60.4 (–, *C*H$_2$CH$_3$), 61.4 (+, NCHC$_{Ind}$), 69.9 (+, NCHCO$_2$Et), 112.0 (+, *C*H$_{Ar}$), 112.3 (+, *C*H$_{Ar}$), 118.8 (C$_q$, *C*$_{Ar}$), 119.1 (+, *C*H$_{Ar}$), 119.3 (+, *C*H$_{Ar}$), 119.5 (+, *C*H$_{Ar}$), 120.5 (C$_q$, *C*$_{Ar}$), 121.1 (+, *C*H$_{Ar}$), 121.2 (+, *C*H$_{Ar}$), 121.8 (+, *C*H$_{Ar}$), 122.1 (+, *C*H$_{Ar}$), 124.0 (+, *C*H$_{Ar}$), 127.4 (C$_q$, *C*$_{Ar}$), 127.6 (C$_q$, *C*$_{Ar}$), 127.8 (+, 2 × *C*H$_{Ar}$), 129.2 (+, 2 × *C*H$_{Ar}$), 134.9 (C$_q$, *C*$_{Ar}$), 137.7 (C$_q$, *C*$_{Ar}$), 137.9 (C$_q$, *C*$_{Ar}$), 149.5 (C$_q$, *C*$_{Ar}$), 172.9 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3408, 2921, 2851, 1723, 1696, 1618, 1509, 1456, 1338, 1224, 1176, 1094, 1030, 815, 738, 582, 548, 477, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 477 (50) [*M*]$^+$, 271 (73), 192 (100), 154 (78), 147 (76), 91 (83); HRMS (FAB, 3-NBA): calcd for C$_{31}$H$_{31}$O$_2$N$_3$ [*M*]$^+$: 477.2411; found: 477.2411.

*Ethyl 4,6-bis(1H-indol-3-yl)-1-(4-(dimethylamino)-phenyl)piperidine-2-carboxylate (**5ad**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-dimethylaminophenyl)imino)acetate (**4d**, 22.0 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ad** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (cat-(*R*): F1: 23.4 mg, 46.2 µmol, 46%, F2: 10.6 mg, 20.9 µmol, 21%; cat-(*S*): F1: 21.6 mg, 42.6 µmol, 43%, F2: 12.9 mg, 25.5 µmol, 26%).
The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-dimethylaminophenyl)imino)acetate (**4d**, 22.0 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5ad** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (8.38 mg, 16.5 µmol, 17%).

fraction 1 (F1): R_f = 0.28 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.23 (t, ^3J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 2.22 (q, ^3J = 12.6 Hz, 1H, NCHC*H*H), 2.37–2.48 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.54–2.62 (m, 1H, CH*H*CHCO$_2$Et), 2.71 (s, 6H, N(C*H*$_3$)$_2$), 3.41 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH$_2$C*H*CH$_2$), 4.04–4.11 (m, 1H, C*H*HCH$_3$), 4.13–4.24 (m, 1H, CH*H*CH$_3$), 4.57 (d, ^3J = 3.8 Hz, 1H, NC*H*CO$_2$Et), 5.68 (dd, ^3J = 11.1, ^3J = 2.6 Hz, 1H, NC*H*C$_{Ind}$), 6.41 (d, ^3J = 8.8 Hz, 2H, C*H*$_{Ar}$), 6.94–7.04 (m, 3H, C*H*$_{Ar}$), 7.06–7.15 (m, 5H, C*H*$_{Ar}$), 7.22 (dd, ^3J = 6.3, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.37 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.62 (d, ^3J = 8.0 Hz, 1H, C*H*$_{Ar}$), 7.96 (dd, ^3J = 6.1, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 9.77 (sbr, 1H, N*H*), 9.98 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH$_2$CH$_3$), 27.5 (+, CH$_2$CHCH$_2$), 37.0 (–, CHCH$_2$), 40.9 (+, N(CH$_3$)$_2$), 43.6 (–, CHCH$_2$), 52.9 (+, NCHC$_{Ind}$), 60.4 (–, *C*H$_2$CH$_3$), 66.2 (+, NCHCO$_2$Et), 112.0 (+, *C*H$_{Ar}$), 112.3 (+, *C*H$_{Ar}$), 113.0 (+, 2 × *C*H$_{Ar}$), 119.0 (+, *C*H$_{Ar}$), 119.3 (+, 2 × *C*H$_{Ar}$), 120.1 (C$_q$, *C*$_{Ar}$), 120.6 (C$_q$, *C*$_{Ar}$), 120.9 (+, *C*H$_{Ar}$), 121.0 (+, *C*H$_{Ar}$), 121.6 (+, *C*H$_{Ar}$), 122.1 (+, *C*H$_{Ar}$), 123.7 (+, *C*H$_{Ar}$), 126.7 (+, 2 × *C*H$_{Ar}$), 127.1 (C$_q$, *C*$_{Ar}$), 127.6 (C$_q$, *C*$_{Ar}$), 137.7 (C$_q$, *C*$_{Ar}$), 137.9 (C$_q$, *C*$_{Ar}$), 141.9 (C$_q$, *C*$_{Ar}$), 147.2

(C_q, C_{Ar}), 174.2 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3408, 3053, 2922, 2851, 1720, 1695, 1613, 1514, 1455, 1338, 1246, 1223, 1173, 1113, 1092, 1038, 1022, 1010, 945, 818, 764, 739, 694, 580, 552, 476, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 506 (100) $[M]^+$, 271 (51), 147 (57); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{34}O_2N_4$ $[M]^+$: 506.2676; found: 506.2675.

fraction 2 (F2): R_f = 0.18 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.97 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.23 (q, ^3J = 12.3 Hz, 1H, NCHCHH), 2.28–2.39 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 2.45 (q, ^3J = 12.3 Hz, 1H, CHHCHCO$_2$Et), 2.72 (s, 6H, N(CH_3)$_2$), 3.40 (tt, ^3J = 12.3, ^3J = 3.5 Hz, 1H, CH_2CHCH_2), 3.86 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 3.98 (dd, ^3J = 11.3, ^3J = 2.7 Hz, 1H, NCHCO$_2$Et), 4.58 (dd, ^3J = 11.1, ^3J = 2.8 Hz, 1H, NCHC_{Ind}), 6.33–6.40 (m, 2H, CH_{Ar}), 6.97–7.04 (m, 4H, CH_{Ar}), 7.05–7.12 (m, 3H, CH_{Ar}), 7.18–7.23 (m, 2H, CH_{Ar}), 7.37 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.71 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 8.02–8.08 (m, 1H, CH_{Ar}), 9.72 (sbr, 1H, NH), 10.01 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.4 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 38.5 (–, $CHCH_2$), 40.7 (+, N(CH_3)$_2$), 43.0 (–, $CHCH_2$), 60.3 (–, CH_2CH_3), 61.7 (+, NCHC_{Ind}), 70.5 (+, NCHCO$_2$Et), 112.0 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 112.7 (+, 2 × CH_{Ar}), 119.0 (+, CH_{Ar}), 119.1 (C_q, C_{Ar}), 119.3 (+, CH_{Ar}), 119.5 (+, CH_{Ar}), 120.6 (C_q, C_{Ar}), 121.2 (+, CH_{Ar}), 121.3 (+, CH_{Ar}), 121.7 (+, CH_{Ar}), 122.1 (+, CH_{Ar}), 123.9 (+, CH_{Ar}), 127.5 (C_q, C_{Ar}), 127.6 (C_q, C_{Ar}), 128.6 (+, 2 × CH_{Ar}), 137.7 (C_q, C_{Ar}), 137.9 (C_q, C_{Ar}), 141.2 (C_q, C_{Ar}), 149.2 (C_q, C_{Ar}), 173.0 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3400, 3054, 2921, 2850, 1722, 1695, 1612, 1515, 1456, 1339, 1245, 1177, 1095, 1028, 1010, 950, 855, 817, 740, 581, 549, 477, 425 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 506 (100) $[M]^+$, 271 (62), 132 (87); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{34}O_2N_4$ $[M]^+$: 506.2676; found: 506.2676.

*Ethyl 4,6-bis(1H-indol-3-yl)-1-(4-fluorophenyl)piperidine-2-carboxylate (**5ag**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-fluorophenyl)imino)acetate (**4g**, 19.5 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ag** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (cat-(*R*): F1: 27.1 mg, 56.2 µmol, 56%, F2: 7.70 mg, 16.0 µmol, 16%; cat-(*S*): F1: 27.1 mg, 56.2 µmol, 56%, F2: 13.7 mg, 28.4 µmol, 28%).

The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-fluorophenyl)imino)acetate (**4g**, 19.5 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5ag** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 14.0 mg, 29.1 µmol, 29%; F2: 14.2 mg, 29.4 µmol, 29%).

fraction 1 (F1): R_f = 0.39 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.23 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.25 (q, ^2J = 12.5 Hz, 1H, NCHCHH), 2.39–2.50 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 2.66 (dq, ^2J = 13.2, ^3J = 2.5 Hz, 1H, CHHCHCO$_2$Et), 3.36 (tt, ^3J = 12.5, ^3J = 2.9 Hz, 1H, CH_2CHCH_2), 4.04–4.14 (m, 1H, CHHCH$_3$), 4.15–4.25 (m, 1H, CHHCH$_3$), 4.72 (dd, ^3J = 5.6, ^3J = 2.2 Hz, 1H, NCHCO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NCHC_{Ind}), 6.71 (t, ^3J = 8.8 Hz, 2H, CH_{Ar}), 6.92–7.04 (m, 3H, CH_{Ar}), 7.07–7.11 (m, 1H, CH_{Ar}), 7.14 (d, ^3J = 2.3 Hz, 1H, CH_{Ar}), 7.18 (d, ^3J = 2.3 Hz, 1H, CH_{Ar}), 7.21–7.25 (m, 3H, CH_{Ar}), 7.38 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.62 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.93 (d, ^3J = 7.3 Hz, 1H, CH_{Ar}), 9.86 (sbr, 1H, NH), 10.00 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.9 (–, $CHCH_2$), 42.2 (–, $CHCH_2$), 53.1 (+, NCHC_{Ind}), 60.7 (–, CH_2CH_3), 65.9 (+, NCHCO$_2$Et), 112.0 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 114.5 (+, CH_{Ar}), 114.7 (+, CH_{Ar}), 119.2 (+, 2 × CH_{Ar}), 119.3 (+, CH_{Ar}), 119.4 (C_q, C_{Ar}), 120.3 (C_q, C_{Ar}), 120.8 (+, CH_{Ar}), 121.1 (+, CH_{Ar}), 121.8 (+, CH_{Ar}), 122.2 (+, CH_{Ar}), 123.9 (+, CH_{Ar}), 126.8 (C_q, C_{Ar}), 127.2 (+, CH_{Ar}), 127.3 (+, CH_{Ar}), 127.6 (C_q, C_{Ar}), 137.7 (C_q, C_{Ar}), 137.9 (C_q, C_{Ar}), 148.2 (C_q, C_{Ar}), 159.6 (C_q, d, ^1J = 235.6 Hz, CF), 173.6 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –127.8 ppm; IR (ATR): $\tilde{\nu}$ = 3409, 2923, 2851, 2539, 1697, 1504, 1454, 1337, 1246, 1210, 1175, 1093, 1010, 932, 832, 815, 739, 708, 581, 565, 549, 476, 424 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 482 (14) $[M]^+$, 271 (23), 196 (32), 154 (44), 137 (43), 109 (35), 97 (67), 95 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3F$ $[M]^+$: 481.2160; found: 481.2158.

fraction 2 (F2): R_f = 0.24 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.83 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.06–2.17 (m, 1H, NCHCHH), 2.16–2.31 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 2.40 (q, ^3J = 12.4 Hz, 1H, CHHCHCO$_2$Et), 3.31 (tt, ^3J = 12.2, ^3J = 3.4 Hz, 1H, CH_2CHCH_2), 3.74 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 3.94 (dd, ^3J = 11.2, ^3J = 2.7 Hz, 1H, NCHCO$_2$Et), 4.45 (dd, ^3J = 11.2, ^3J = 2.7 Hz, 1H, NCHC_{Ind}), 6.60 (t, ^3J = 8.8 Hz, 2H, CH_{Ar}), 6.83–6.99 (m, 5H, CH_{Ar}), 7.08–7.13 (m, 4H, CH_{Ar}), 7.25 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.58 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.82–7.88 (m, 1H, CH_{Ar}), 9.68 (sbr, 1H, NH), 9.91 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2CH_3), 34.3 (+, CH_2CHCH_2), 38.3 (–, $CHCH_2$), 42.5 (–, $CHCH_2$), 60.6 (–, CH_2CH_3), 61.8 (+, NCHC_{Ind}), 69.7 (+, NCHCO$_2$Et), 112.2 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 114.9 (+, CH_{Ar}), 115.1 (+, CH_{Ar}), 118.3 (C_q, C_{Ar}), 119.2 (+, CH_{Ar}), 119.4 (+, CH_{Ar}), 119.5 (+, CH_{Ar}), 120.4 (C_q, C_{Ar}), 121.0 (+, CH_{Ar}), 121.3 (+, CH_{Ar}), 121.9 (+, CH_{Ar}), 122.1 (+, CH_{Ar}), 124.1 (+, CH_{Ar}), 127.3 (C_q, C_{Ar}), 127.6 (C_q, C_{Ar}), 129.9 (+, CH_{Ar}), 130.0 (+, CH_{Ar}), 137.7 (C_q, C_{Ar}), 137.9 (C_q, C_{Ar}), 148.2 (C_q, C_{Ar}), 159.6 (C_q, d, ^1J = 235.6 Hz, CF), 172.8 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –123.5 ppm.

*Ethyl 4,6-bis(1H-indol-3-yl)-1-(4-chlorophenyl)piperidine-2-carboxylate (**5ah**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ah** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 19.7 mg, 39.4 µmol, 39%; cat-(*S*): F1: 24.9 mg, 50.0 µmol, 50%, F2: 24.4 mg, 49.0 µmol, 49%).

The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4a**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl

acetate = 4:1) to give **5ah** as a yellow oil (18.0 mg, 36.0 µmol, 36%).

fraction 1 (F1): R_f = 0.51 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.24 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.24 (q, ^2J = 12.5 Hz, 1H, NCHC*H*H), 2.40–2.49 (m, 2H, CH_2CHCO_2Et), 2.69 (q, ^2J = 12.5 Hz, 1H, NCHCH*H*), 3.32 (tt, ^2J = 12.5, ^3J = 3.1 Hz, 1H, CH_2CHCH_2), 4.02–4.09 (m, 1H, C*H*HCH$_3$), 4.17–4.24 (m, 1H, CH*H*CH$_3$), 4.83 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.57 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.94–6.98 (m, 3H, CH_{Ar}), 6.97–7.04 (m, 2H, CH_{Ar}), 7.06–7.10 (m, 1H, CH_{Ar}), 7.14 (d, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.18–7.26 (m, 4H, CH_{Ar}), 7.38 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 7.62 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 7.90 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 9.90 (sbr, 1H, N*H*), 10.01 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.8 (–, $CHCH_2$), 43.1 (–, $CHCH_2$), 53.0 (+, NCHC$_{Ind}$), 60.8 (–, CH_2CH_3), 65.5 (+, NCHCO$_2$Et), 112.1 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 119.2 (+, CH_{Ar}), 119.3 (+, 2 × CH_{Ar}), 120.2 (C$_q$, C$_{Ar}$), 120.7 (+, CH_{Ar}), 121.1 (+, CH_{Ar}), 121.9 (+, CH_{Ar}), 122.2 (+, CH_{Ar}), 123.9 (+, CH_{Ar}), 126.6 (C$_q$, C$_{Ar}$), 126.7 (C$_q$, C$_{Ar}$), 126.9 (+, 2 × CH_{Ar}), 127.6 (C$_q$, C$_{Ar}$), 128.1 (+, 2 × CH_{Ar}), 137.7 (C$_q$, C$_{Ar}$), 137.9 (C$_q$, C$_{Ar}$), 150.9 (C$_q$, 2 × C$_{Ar}$), 173.5 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3400, 2929, 1724, 1696, 1596, 1490, 1455, 1369, 1337, 1275, 1246, 1177, 1091, 1009, 932, 819, 766, 740, 671, 581, 503, 477, 424 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 498 (15) [*M*]$^+$, 381 (15), 271 (56), 212 (66), 153 (57), 137 (56), 97 (63), 95 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{29}O_2N_3{}^{35}Cl$ [*M*+H]$^+$: 498.1943; found: 498.1941.

fraction 2 (F2): R_f = 0.32 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.98 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.21–2.31 (m, 1H, NCHC*H*H), 2.35 (dq, ^2J = 13.0, ^3J = 3.0 Hz, C*H*HCHCO$_2$Et), 2.43 (dq, ^2J = 13.0, ^3J = 3.0 Hz, CH*H*CHCO$_2$Et), 2.48–2.58 (m, 1H, NCHCH*H*), 3.45 (tt, ^2J = 12.2, ^3J = 3.6 Hz, 1H, CH_2CHCH_2), 3.90 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 4.10 (dd, ^3J = 11.0, ^3J = 2.9 Hz, 1H, NC*H*CO$_2$Et), 4.63 (dd, ^3J = 11.0, ^3J = 2.9 Hz, 1H, NC*H*C$_{Ind}$), 6.99–7.05 (m, 5H, CH_{Ar}), 7.06–7.11 (2H, CH_{Ar}), 7.18–7.26 (m, 4H, CH_{Ar}), 7.38 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.71 (d, ^3J = 8.0 Hz, 1H, CH_{Ar}), 7.98 (dd, ^3J = 5.4, ^3J = 3.7 Hz, 1H, CH_{Ar}), 9.83 (sbr, 1H, N*H*), 10.04 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2CH_3), 34.0 (+, CH_2CHCH_2), 38.1 (–, $CHCH_2$), 42.2 (–, $CHCH_2$), 60.7 (–, CH_2CH_3), 61.4 (+, NCHC$_{Ind}$), 69.0 (+, NCHCO$_2$Et), 112.1 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 118.2 (C$_q$, C$_{Ar}$), 119.3 (+, CH_{Ar}), 119.4 (+, CH_{Ar}), 119.5 (+, CH_{Ar}), 120.4 (C$_q$, C$_{Ar}$), 120.9 (+, CH_{Ar}), 121.3 (+, CH_{Ar}), 121.9 (+, CH_{Ar}), 122.1 (+, CH_{Ar}), 124.2 (+, CH_{Ar}), 127.3 (C$_q$, C$_{Ar}$), 127.6 (C$_q$, C$_{Ar}$), 128.6 (+, 2 × CH_{Ar}), 129.4 (+, 2 × CH_{Ar}), 130.3 (C$_q$, C$_{Ar}$), 137.7 (C$_q$, C$_{Ar}$), 137.9 (C$_q$, C$_{Ar}$), 151.0 (C$_q$, C$_{Ar}$), 172.8 (C$_q$, CO$_2$Et) ppm.

*Ethyl (2S,4S,6S)-4,6-bis(1H-indol-3-yl)-1-(4-bromophenyl)-piperidine-2-carboxylate (**5ai**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-bromophenyl)imino)acetate (**4i**, 25.6 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ai** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (cat-(*R*): 12.0 mg, 22.1 µmol, 22%; cat-(*S*): 26.5 mg, 48.9 µmol, 49%).

The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 100 mg, 1.40 mmol, 2.00 Equiv.) and ethyl 2-((4-bromophenyl)imino)acetate (**4i**, 179 mg, 0.698 mmol, 1.00 Equiv.) without a catalyst in 10 mL dichloromethane. The product **5ai** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (108 mg, 0.198 mmol, 28%).

R_f = 0.28 (cyclohexane/EtOAc 3:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.24 (q, ^3J = 12.6 Hz, 1H, NCHC*H*H), 2.40–2.49 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.69 (dq, ^3J = 13.2, ^3J = 3.0 Hz, 1H, CH*H*CHCO$_2$Et), 3.32 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 4.07–4.15 (m, 1H, C*H*HCH$_3$), 4.17–4.25 (m, 1H, CH*H*CH$_3$), 4.84 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.56 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.93–7.04 (m, 3H, CH_{Ar}), 7.06–7.12 (m, 3H, CH_{Ar}), 7.13–7.15 (m, 2H, CH_{Ar}), 7.16 (t, ^4J = 1.7 Hz, 1H, CH_{Ar}), 7.19 (d, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.24 (d, ^3J = 7.6 Hz, 1H, CH_{Ar}), 7.37 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 7.62 (d, ^3J = 7.9 Hz, 1H, CH_{Ar}), 7.90 (d, ^3J = 7.6 Hz, 1H, CH_{Ar}), 9.90 (sbr, 1H, N*H*), 10.01 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.8 (–, $CHCH_2$), 43.0 (–, $CHCH_2$), 53.0 (+, NCHC$_{Ind}$), 60.8 (–, CH_2CH_3), 65.5 (+, NCHCO$_2$Et), 112.1 (+, CH_{Ar}), 112.3 (+, CH_{Ar}), 114.3 (C$_q$, C$_{Ar}$), 116.9 (+, CH_{Ar}), 119.2 (+, CH_{Ar}), 119.3 (+, CH_{Ar}), 119.3 (C$_q$, C$_{Ar}$), 120.2 (C$_q$, C$_{Ar}$), 120.7 (+, CH_{Ar}), 121.1 (+, CH_{Ar}), 121.9 (+, CH_{Ar}), 122.2 (+, CH_{Ar}), 123.9 (+, CH_{Ar}), 126.6 (C$_q$, C$_{Ar}$), 127.5 (C$_q$, C$_{Ar}$), 127.8 (+, CH_{Ar}), 131.0 (+, CH_{Ar}), 131.9 (+, CH_{Ar}), 132.4 (+, CH_{Ar}), 137.7 (C$_q$, C$_{Ar}$), 137.9 (C$_q$, C$_{Ar}$), 151.4 (C$_q$, C$_{Ar}$), 173.4 (C$_q$, CO$_2$Et) ppm.

*Ethyl 4,6-bis(1H-indol-3-yl)-1-(4-iodophenyl)piperidine-2-carboxylate (**5aj**):* This compound was synthesized following the **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-iodophenyl)imino)acetate (**4j**, 30.3 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5aj** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a colorless oil in two fractions (cat-(*R*): F1: 22.6 mg, 38.3 µmol, 38%, F2: 8.60 mg, 14.6 µmol, 15%; cat-(*S*): F1: 26.8 mg, 45.5 µmol, 46%, F2: 6.30 mg, 10.7 µmol, 11%).

The racemic compound was obtained following **GP C** with 3-vinylindole (**3a**, 28.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-iodophenyl)imino)acetate (**4j**, 30.3 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 30 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 4:1) to give **5aj** as a yellow oil in two fractions (F1: 13.1 mg, 22.1 µmol, 22%, F2: 16.3 mg, 27.6 µmol, 28%).

fraction 1 (F1): R_f = 0.49 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.23 (q, ^2J = 12.5 Hz, 1H, NCHC*H*H), 2.39–2.50 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.69 (dq, ^2J = 13.3, ^3J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.31 (tt, ^2J = 12.4, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 4.07–4.15 (m, 1H, C*H*HCH$_3$), 4.16–4.25 (m, 1H, CH*H*CH$_3$), 4.85

(dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO_2Et), 5.55 (dd, ^3J = 11.3, ^3J = 3.7 Hz, 1H, NC*H*C_{Ind}), 6.93–6.98 (m, 1H, C*H*$_{Ar}$), 7.00–7.05 (m, 3H, C*H*$_{Ar}$), 7.06–7.11 (m, 1H, C*H*$_{Ar}$), 7.13 (d, ^3J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.19 (d, ^3J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.22–7.30 (m, 3H, C*H*$_{Ar}$), 7.34–7.41 (m, 2H, C*H*$_{Ar}$), 7.61 (d, ^3J = 7.8 Hz, 1H, C*H*$_{Ar}$), 7.89 (d, ^3J = 7.8 Hz, 1H, C*H*$_{Ar}$), 9.90 (sbr, 1H, N*H*), 10.00 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2*C*H_3), 27.5 (+, CH_2*C*HCH_2), 36.8 (–, CH*C*H_2), 43.1 (–, CH*C*H_2), 52.8 (+, NC*H*C$_{Ind}$), 60.8 (–, *C*H_2CH$_3$), 65.4 (+, N*C*HCO_2Et), 84.7 (C_q, *C*I), 112.1 (+, *C*H$_{Ar}$), 112.3 (+, *C*H$_{Ar}$), 119.2 (+, *C*H$_{Ar}$), 119.3 (C_q, *C*$_{Ar}$), 119.4 (+, 2 × *C*H$_{Ar}$), 120.2 (C_q, *C*$_{Ar}$), 120.7 (+, *C*H$_{Ar}$), 121.1 (+, *C*H$_{Ar}$), 121.9 (+, *C*H$_{Ar}$), 122.2 (+, *C*H$_{Ar}$), 123.8 (+, *C*H$_{Ar}$), 126.6 (C_q, *C*$_{Ar}$), 127.5 (C_q, *C*$_{Ar}$), 127.6 (+, 2 × *C*H$_{Ar}$), 137.1 (+, 2 × *C*H$_{Ar}$), 137.7 (C_q, *C*$_{Ar}$), 137.8 (C_q, *C*$_{Ar}$), 152.0 (C_q, *C*$_{Ar}$), 173.4 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3402, 2922, 1722, 1694, 1581, 1483, 1455, 1337, 1246, 1177, 1093, 1009, 952, 818, 740, 651, 581, 477, 424 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 589 (7) [*M*]$^+$, 304 (46), 271 (57), 109 (59), 95 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3{}^{127}$I [*M*]$^+$: 589.1221; found: 589.1219.

fraction 2 (F2): R_f = 0.36 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.00 (t, ^3J = 7.1 Hz, 3H, CH_2C*H*$_3$), 2.22–2.32 (m, 1H, NCHC*H*H), 2.34–2.46 (m, 2H, C*H*HCHCO_2Et, NCHCH*H*), 2.46–2.57 (m, 1H, CH*H*CHCO_2Et), 3.44 (tt, ^3J = 11.9, ^3J = 3.8 Hz, 1H, CH_2C*H*CH_2), 3.91 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 4.12 (dd, ^3J = 10.9, ^3J = 3.1 Hz, 1H, NC*H*CO_2Et), 4.66 (dd, ^3J = 11.0, ^3J = 3.1 Hz, 1H, NC*H*C$_{Ind}$), 6.98–7.04 (m, 5H, C*H*$_{Ar}$), 7.06–7.11 (m, 2H, C*H*$_{Ar}$), 7.19–7.26 (m, 2H, C*H*$_{Ar}$), 7.30–7.40 (m, 3H, C*H*$_{Ar}$), 7.70 (d, ^3J = 7.9 Hz, 1H, C*H*$_{Ar}$), 7.96–7.99 (m, 1H, C*H*$_{Ar}$), 9.83 (sbr, 1H, N*H*), 10.03 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2*C*H_3), 27.5 (+, CH_2*C*HCH_2), 37.9 (–, CH*C*H_2), 42.1 (–, CH*C*H_2), 60.7 (–, *C*H_2CH$_3$), 61.0 (+, NC*H*C$_{Ind}$), 68.6 (+, N*C*HCO_2Et), 89.1 (C_q, *C*I), 112.2 (+, *C*H$_{Ar}$), 112.3 (+, *C*H$_{Ar}$), 118.3 (C_q, *C*$_{Ar}$), 119.3 (+, *C*H$_{Ar}$), 119.4 (+, *C*H$_{Ar}$), 119.5 (+, *C*H$_{Ar}$), 120.4 (C_q, *C*$_{Ar}$), 120.9 (+, *C*H$_{Ar}$), 121.3 (+, *C*H$_{Ar}$), 121.9 (+, *C*H$_{Ar}$), 122.1 (+, *C*H$_{Ar}$), 124.2 (+, *C*H$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 127.6 (C_q, *C*$_{Ar}$), 129.7 (+, 2 × *C*H$_{Ar}$), 137.7 (+, 2 × *C*H$_{Ar}$), 137.9 (C_q, *C*$_{Ar}$), 138.4 (C_q, *C*$_{Ar}$), 152.1 (C_q, *C*$_{Ar}$), 172.9 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3402, 2922, 2851, 1723, 1693, 1583, 1486, 1456, 1337, 1246, 1178, 1094, 1005, 812, 739, 654, 581, 476, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 589 (7) [*M*]$^+$, 304 (27), 271 (31), 154 (21), 133 (100), 95 (57); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3{}^{127}$I [*M*]$^+$: 589.1221; found: 589.1220.

*Ethyl (2S,4S,6S)-4,6-bis(7-methyl-1H-indol-3-yl)-1-(4-ethynylphenyl)-piperidine-2-carboxylate (**5bc**):* This compound was synthesized following the **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-ethynylphenyl)imino)acetate (**4c**, 20.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5bc** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 24.3 mg, 47.1 µmol, 47%; cat-(*S*): 14.9 mg, 28.9 µmol, 29%).

The racemic compound was obtained following **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-ethynylphenyl)imino)acetate (**4c**, 20.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5bc** as a yellow oil (9.12 mg, 18.0 µmol, 18%).

R_f = 0.47 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.24 (t, ^3J = 7.0 Hz, 3H, CH_2C*H*$_3$), 2.22 (q, ^3J = 12.2 Hz, 1H, NCHC*H*H), 2.37 (s, 3H, C*H*$_3$), 2.39–2.44 (m, 2H, C*H*HCHCO_2Et, NCHCH*H*), 2.46 (s, 3H, C*H*$_3$), 2.66–2.73 (m, 1H, CH*H*CHCO_2Et), 3.29 (tt, ^3J = 12.9, ^3J = 2.5 Hz, 1H, CH_2C*H*CH_2), 3.37 (s, 1H, C*H*), 4.06–4.15 (m, 1H, C*H*HCH_3), 4.17–4.24 (m, 1H, CH*H*CH_3), 4.92 (dd, ^3J = 5.5, ^3J = 2.2 Hz, 1H, NC*H*CO_2Et), 5.55 (dd, ^3J = 11.1, ^3J = 3.7 Hz, 1H, NC*H*C$_{Ind}$), 6.80 (d, ^3J = 6.7 Hz, 1H, C*H*$_{Ar}$), 6.84–6.97 (m, 4H, C*H*$_{Ar}$), 7.06–7.12 (m, 2H, C*H*$_{Ar}$), 7.13–7.22 (m, 3H, C*H*$_{Ar}$), 7.45 (d, ^3J = 7.4 Hz, 1H, C*H*$_{Ar}$), 7.72 (d, ^3J = 7.4 Hz, 1H, C*H*$_{Ar}$), 9.85 (sbr, 1H, N*H*), 9.96 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2*C*H_3), 16.8 (+, *C*H$_3$), 16.9 (+, *C*H$_3$), 27.5 (+, CH_2*C*HCH_2), 36.8 (–, CH*C*H_2), 43.0 (–, CH*C*H_2), 53.0 (+, NC*H*C$_{Ind}$), 60.9 (–, *C*H_2CH$_3$), 65.1 (+, NC*H*CO_2Et), 77.3 (+, *C*H), 84.7 (C_q, *C*CH), 115.1 (C_q, *C*$_{Ar}$), 117.0 (+, *C*H$_{Ar}$), 118.3 (+, *C*H$_{Ar}$), 119.6 (+, *C*H$_{Ar}$), 119.7 (+, *C*H$_{Ar}$), 120.0 (C_q, *C*$_{Ar}$), 120.7 (C_q, *C*$_{Ar}$), 120.8 (+, *C*H$_{Ar}$), 121.2 (C_q, *C*$_{Ar}$), 121.5 (C_q, *C*$_{Ar}$), 122.6 (+, *C*H$_{Ar}$), 122.8 (+, *C*H$_{Ar}$), 123.4 (+, *C*H$_{Ar}$), 124.6 (+, 2 × *C*H$_{Ar}$), 126.3 (C_q, *C*$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 132.1 (+, 2 × *C*H$_{Ar}$), 137.1 (C_q, *C*$_{Ar}$), 137.3 (C_q, *C*$_{Ar}$), 152.8 (C_q, *C*$_{Ar}$), 173.5 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3401, 3278, 2923, 2853, 2100, 1724, 1695, 1602, 1508, 1435, 1370, 1342, 1291, 1244, 1175, 1108, 1061, 1021, 940, 829, 782, 746, 645, 571, 533, 476, 408 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 516 (31) [*M*+H]$^+$, 299 (42), 202 (64), 95 (100); HRMS (FAB, 3-NBA): calcd for $C_{34}H_{34}O_2N_3$ [*M*+H]$^+$: 516.2646; found: 516.2647.

*Ethyl 4,6-bis(7-methyl-1H-indol-3-yl)-1-(4-chlorophenyl)-piperidine-2-carboxylate (**5bh**):* This compound was synthesized following the **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5bh** as a yellow oil (cat-(*R*): 15.6 mg, 29.7 µmol, 30%; cat-(*S*): 26.2 mg, 49.8 µmol, 50%).

The racemic compound was obtained following **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5bh** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 17.6 mg, 33.5 µmol, 33%; F2: 8.90 mg, 16.9 µmol, 17%).

fraction 1 (F1): R_f = 0.49 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.24 (t, ^3J = 7.0 Hz, 3H, CH_2C*H*$_3$), 2.23 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.37 (s, 3H, C*H*$_3$), 2.39–2.45 (m, 2H, C*H*HCHCO_2Et, NCHCH*H*), 2.46 (s, 3H, C*H*$_3$), 2.68 (dd, ^3J =13.2, ^4J = 2.7 Hz, 1H, CH*H*CHCO_2Et), 3.30 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH_2C*H*CH_2), 4.06–4.12 (m, 1H, C*H*HCH_3), 4.18–4.24 (m, 1H, CH*H*CH_3), 4.81 (dd, ^3J = 5.6,

^3J = 2.3 Hz, 1H, NC*H*CO_2Et), 5.55 (dd, ^3J = 11.2, ^3J = 3.6 Hz, 1H, NC*H*C_{Ind}), 6.78–6.88 (m, 2H, C*H*$_{Ar}$), 6.89–6.93 (m, 2H, C*H*$_{Ar}$), 6.94–6.99 (m, 2H, C*H*$_{Ar}$), 7.08–7.15 (m, 2H, C*H*$_{Ar}$), 7.16 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.17–7.22 (m, 1H, C*H*$_{Ar}$), 7.45 (d, ^3J = 7.7 Hz, 1H, C*H*$_{Ar}$), 7.74 (d, ^3J = 7.7 Hz, 1H, C*H*$_{Ar}$), 9.84 (sbr, 1H, N*H*), 9.96 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2*C*H_3), 16.8 (+, *C*H_3), 16.9 (+, *C*H_3), 27.5 (+, CH_2*C*HCH_2), 36.9 (–, CH*C*H_2), 43.1 (–, CH*C*H$_2$), 53.1 (+, N*C*HC_{Ind}), 60.8 (–, *C*H_2CH$_3$), 65.5 (+, N*C*HCO$_2$Et), 116.0 (+, *C*H$_{Ar}$), 117.0 (+, *C*H$_{Ar}$), 118.4 (+, *C*H$_{Ar}$), 119.7 (+, *C*H$_{Ar}$), 119.8 (C_q, *C*$_{Ar}$), 120.6 (C_q, *C*$_{Ar}$), 120.7 (+, *C*H$_{Ar}$), 121.2 (C_q, *C*$_{Ar}$), 121.5 (C_q, *C*$_{Ar}$), 122.6 (+, *C*H$_{Ar}$), 122.7 (+, *C*H$_{Ar}$), 123.5 (+, *C*H$_{Ar}$), 123.9 (+, *C*H$_{Ar}$), 126.3 (C_q, *C*$_{Ar}$), 126.6 (C_q, *C*$_{Ar}$), 126.8 (+, *C*H$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 128.1 (+, *C*H$_{Ar}$), 129.6 (+, *C*H$_{Ar}$), 137.1 (C_q, *C*$_{Ar}$), 137.3 (C_q, *C*$_{Ar}$), 150.9 (C_q, *C*$_{Ar}$), 173.5 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3397, 2930, 1725, 1697, 1596, 1490, 1442, 1369, 1343, 1245, 1176, 1091, 1062, 1021, 940, 818, 782, 746, 716, 683, 582 564, 503, 477 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 525 (25) [*M*]$^+$, 299 (66), 212 (89), 135 (78); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{32}O_2N_3{}^{35}Cl$ [*M*]$^+$: 525.2178; found: 525.2178.

fraction 2 (F2): R_f = 0.31 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.98 (t, ^3J = 7.1 Hz, 3H, CH_2C*H*$_3$), 2.20–2.30 (m, 1H, NCHC*H*H), 2.30–2.45 (m, 5H, C*H*HCHCO$_2$Et, NCHCH*H*, C*H*$_3$), 2.47 (s, 3H, C*H*$_3$), 2.48–2.56 (m, 1H, CH*H*CHCO$_2$Et), 3.42 (tt, ^3J = 12.0, ^3J = 3.5 Hz, 1H, CH_2C*H*CH_2), 3.90 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 4.08 (dd, ^3J = 11.1, ^3J = 3.0 Hz, 1H, NC*H*CO_2Et), 4.62 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, NC*H*C_{Ind}), 6.83 (d, ^3J = 7.1 Hz, 1H, C*H*$_{Ar}$), 6.88–6.97 (m, 3H, C*H*$_{Ar}$), 6.98–7.04 (m, 2H, C*H*$_{Ar}$), 7.06 (d, ^3J = 2.5 Hz, 1H, C*H*$_{Ar}$), 7.18 (d, ^3J = 2.5 Hz, 1H, C*H*$_{Ar}$), 7.20–7.25 (m, 2H, C*H*$_{Ar}$), 7.54 (d, ^3J = 7.6 Hz, 1H, C*H*$_{Ar}$), 7.82 (d, ^3J = 7.6 Hz, 1H, C*H*$_{Ar}$), 9.77 (sbr, 1H, N*H*), 9.99 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2*C*H_3), 16.8 (+, *C*H_3), 16.9 (+, *C*H_3), 27.5 (+, CH_2*C*HCH_2), 34.1 (–, CH*C*H_2), 38.1 (–, CH*C*H$_2$), 42.3 (+, N*C*HC_{Ind}), 60.7 (–, *C*H_2CH$_3$), 69.1 (+, N*C*HCO$_2$Et), 117.2 (+, *C*H$_{Ar}$), 118.6 (+, *C*H$_{Ar}$), 118.7 (C_q, *C*$_{Ar}$), 119.6 (+, *C*H$_{Ar}$), 119.7 (+, *C*H$_{Ar}$), 120.8 (C_q, *C*$_{Ar}$), 120.9 (+, *C*H$_{Ar}$), 121.2 (C_q, *C*$_{Ar}$), 121.4 (C_q, *C*$_{Ar}$), 122.6 (+, *C*H$_{Ar}$), 122.7 (+, *C*H$_{Ar}$), 123.9 (+, *C*H$_{Ar}$), 126.9 (C_q, *C*$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 128.6 (+, 2 × *C*H$_{Ar}$), 129.4 (+, 2 × *C*H$_{Ar}$), 130.3 (C_q, *C*$_{Ar}$), 137.1 (C_q, *C*$_{Ar}$), 137.3 (C_q, *C*$_{Ar}$), 151.0 (C_q, *C*$_{Ar}$), 172.8 (C_q, *C*O_2Et) ppm.

*Ethyl 4,6-bis(7-methyl-1H-indol-3-yl)-1-(3,5-dichloro-4-hydroxyphenyl)–piperidine-2-carboxylate (**5bk**):*

This compound was synthesized following the **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((3,5-dichloro-4-hydroxyphenyl)imino)acetate (**4k**, 26.2 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5bk** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 36.6 mg, 61.8 µmol, 62%; cat-(*S*): 15.5 mg, 26.9 µmol, 27%).

The racemic compound was obtained following **GP C** with 7-methyl-3-vinylindole (**3b**, 31.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((3,5-dichloro-4-hydroxyphenyl)imino)acetate (**4k**, 26.2 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5bk** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 14.4 mg, 25.0 µmol, 25%; F2: 14.5 mg, 25.0 µmol, 25%).

fraction 1 (F1): R_f = 0.40 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.27 (t, ^3J = 7.1 Hz, 3H, CH_2C*H*$_3$), 2.24–2.33 (m, 1H, 1H, NCHC*H*H), 2.36 (s, 3H, C*H*$_3$), 2.37–2.45 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.46 (s, 3H, C*H*$_3$), 2.67 (dq, ^3J = 13.2, ^3J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.28 (tt, ^3J = 12.5, ^3J = 3.1 Hz, 1H, CH_2C*H*CH_2), 4.07–4.18 (m, 1H, C*H*HCH$_3$), 4.20–4.30 (m, 1H, CH*H*CH$_3$), 4.71 (dd, ^3J = 5.5, ^3J = 2.3 Hz, 1H, NC*H*CO_2Et), 5.48 (dd, ^3J = 11.1, ^3J = 3.8 Hz, 1H, NC*H*C_{Ind}), 6.79 (d, ^3J = 7.0 Hz, 1H, C*H*$_{Ar}$), 6.85–6.97 (m, 3H, C*H*$_{Ar}$), 7.11 (d, ^3J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.24 (s, 2H, C*H*$_{Ar}$), 7.28 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.45 (d, ^3J = 7.4 Hz, 1H, C*H*$_{Ar}$), 7.77 (d, ^3J = 7.9 Hz, 1H, C*H*$_{Ar}$), 8.10 (sbr, 1H, O*H*), 9.88 (sbr, 1H, N*H*), 9.97 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2C*H*$_3$), 16.8 (+, *C*H_3), 16.9 (+, *C*H_3), 27.5 (+, CH_2*C*HCH_2), 36.9 (–, CH*C*H_2), 42.8 (–, CH*C*H$_2$), 53.4 (+, N*C*HC_{Ind}), 60.9 (–, *C*H_2CH$_3$), 65.8 (+, N*C*HCO$_2$Et), 117.0 (+, *C*H$_{Ar}$), 118.7 (+, *C*H$_{Ar}$), 119.5 (C_q, 2 × *C*$_{Ar}$), 119.6 (+, *C*H$_{Ar}$), 119.7 (+, *C*H$_{Ar}$), 120.6 (C_q, *C*$_{Ar}$), 120.7 (+, *C*H$_{Ar}$), 121.2 (C_q, 2 × *C*$_{Ar}$), 121.5 (C_q, *C*$_{Ar}$), 122.6 (+, *C*H$_{Ar}$), 122.7 (+, *C*H$_{Ar}$), 123.8 (+, *C*H$_{Ar}$), 126.3 (+, 2 × *C*H$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 137.3 (C_q, 2 × *C*$_{Ar}$), 144.7 (C_q, *C*$_{Ar}$), 145.3 (C_q, 2 × *C*$_{Ar}$), 173.5 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3396, 2921, 2852, 1722, 1694, 1613, 1563, 1479, 1404, 1370, 1343, 1294, 1225, 1160, 1132, 1111, 1092, 1019, 943, 857, 826, 784, 748, 711, 655, 584, 540, 516 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 576 (7) [*M*+H]$^+$, 299 (13), 154 (34), 132 (100), 91 (72); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{32}O_3N_3{}^{35}Cl_2$ [*M*+H]$^+$: 576.1815; found: 576.1813.

fraction 2 (F2): R_f = 0.30 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.02 (t, ^3J = 7.1 Hz, 3H, CH_2C*H*$_3$), 2.22 (q, ^3J = 12.3 Hz, 1H, NCHC*H*H), 2.28–2.41 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.37 (s, 3H, C*H*$_3$), 2.42–2.52 (m, 1H, CH*H*CHCO$_2$Et), 2.47 (s, 3H, C*H*$_3$), 3.42 (tt, ^3J = 12.2, ^3J = 3.3 Hz, 1H, CH_2C*H*CH_2), 3.94 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 4.02 (dd, ^3J = 11.2, ^3J = 2.6 Hz, 1H, NC*H*CO_2Et), 4.60 (dd, ^3J = 11.2, ^3J = 2.6 Hz, 1H, NC*H*C_{Ind}), 6.83 (d, ^3J = 7.1 Hz, 1H, C*H*$_{Ar}$), 6.87–6.99 (m, 3H, C*H*$_{Ar}$), 7.13 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.19 (d, ^3J = 2.2 Hz, 1H, C*H*$_{Ar}$), 7.25 (s, 2H, C*H*$_{Ar}$), 7.53 (d, ^3J = 7.6 Hz, 1H, C*H*$_{Ar}$), 7.82 (d, ^3J = 7.9 Hz, 1H, C*H*$_{Ar}$), 8.40 (sbr, 1H, O*H*), 9.83 (sbr, 1H, N*H*), 10.00 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2C*H*$_3$), 16.8 (+, *C*H_3), 16.9 (+, *C*H_3), 34.2 (+, CH_2*C*HCH_2), 38.3 (–, CH*C*H_2), 42.5 (–, CH*C*H$_2$), 60.7 (–, *C*H_2CH$_3$), 61.5 (+, N*C*HC_{Ind}), 69.8 (+, N*C*HCO$_2$Et), 117.2 (+, *C*H$_{Ar}$), 118.4 (+, *C*H$_{Ar}$), 118.5 (C_q, *C*$_{Ar}$), 119.7 (+, 2 × *C*H$_{Ar}$), 120.7 (C_q, *C*$_{Ar}$), 120.9 (+, *C*H$_{Ar}$), 121.2 (C_q, *C*$_{Ar}$), 121.3 (C_q, 2 × *C*$_{Ar}$), 121.5 (C_q, *C*$_{Ar}$), 122.6 (+, *C*H$_{Ar}$), 122.7 (+, *C*H$_{Ar}$), 123.9 (+, *C*H$_{Ar}$), 127.2 (C_q, *C*$_{Ar}$), 128.8 (+, 2 × *C*H$_{Ar}$), 137.1 (C_q, *C*$_{Ar}$), 137.3 (C_q, *C*$_{Ar}$), 144.9 (C_q, 2 × *C*$_{Ar}$), 147.4 (C_q, *C*$_{Ar}$), 172.6 (C_q, *C*O_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3396, 2920, 2851, 2529, 1722, 1611, 1558, 1477, 1371, 1344, 1226, 1161, 1132, 1110, 1093, 1060, 1019, 942, 857, 823, 783, 746, 710, 679, 654, 584, 515, 487 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 576 (7) [*M*+H]$^+$, 299 (13), 154 (34), 132 (100), 91 (72); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{32}O_3N_3{}^{35}Cl_2$ [*M*+H]$^+$: 576.1737; found: 576.1735.

*Ethyl (2S,4S,6S)-4,6-bis(5-cyano-1H-indol-3-yl)-1-(4-tolyl)piperidine-2-carboxylate (**5cb**):* This compound was synthesized following the **GP C** with 5-cyano-3-vinylindole (**3c**, 33.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5cb** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 24.3 mg, 46.0 µmol, 46%; cat-(*S*): 17.2 mg, 32.6 µmol, 33%).
The racemic compound was obtained following **GP C** with 5-cyano-3-vinylindole (**3c**, 33.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5cb** as a yellow oil (6.10 mg, 11.6 µmol, 12%).

R_f = 0.18 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.23 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.14–2.26 (m, 1H, NCHC*H*H), 2.46 (dq, ^2J = 13.0, ^3J = 3.3 Hz, 1H, CH*H*CHCO$_2$Et), 2.52–2.64 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.87 (s, 3H, CH_3), 3.43 (tt, ^2J = 12.5, ^3J = 3.5 Hz, 1H, CH_2CHCH_2), 4.04–4.11 (m, 1H, C*H*HCH$_3$), 4.16–4.24 (m, 1H, CH*H*CH$_3$), 4.77 (dd, ^3J = 5.3, ^3J = 2.6 Hz, 1H, NC*H*CO$_2$Et), 5.69 (dd, ^3J = 11.4, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.78 (d, ^3J = 8.2 Hz, 2H, C*H*$_{Ar}$), 7.14 (d, ^3J = 8.4 Hz, 2H, C*H*$_{Ar}$), 7.26 (dd, ^3J = 8.4, ^4J = 1.5 Hz, 1H, C*H*$_{Ar}$), 7.37–7.43 (m, 3H, C*H*$_{Ar}$), 7.47 (d, ^3J = 2.3Hz, 1H, C*H*$_{Ar}$), 7.56 (d, ^3J = 8.4 Hz, 1H, C*H*$_{Ar}$), 8.07 (s, 1H, C*H*$_{Ar}$), 8.40–8.42 (m, 1H, C*H*$_{Ar}$), 10.44 (sbr, 1H, N*H*), 10.63 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 20.6 (+, $C_{Ar}CH_3$), 27.5 (+, CH_2CHCH_2), 36.4 (–, $CHCH_2$), 43.4 (–, $CHCH_2$), 52.8 (+, $NCHC_{Ind}$), 60.7 (–, CH_2CH_3), 65.7 (+, $NCHCO_2Et$), 102.3 (C_q, $C_{Ar}CN$), 102.5 (C_q, $C_{Ar}CN$), 113.3 (+, CH_{Ar}), 113.6 (+, CH_{Ar}), 120.9 (C_q, C_{Ar}), 121.3 (C_q, C_{Ar}), 121.4 (C_q, C_{Ar}), 121.5 (C_q, C_{Ar}), 124.0 (+, CH_{Ar}), 124.5 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 124.9 (+, CH_{Ar}), 125.6 (+, 2 × CH_{Ar}), 126.5 (C_q, C_{Ar}), 126.6 (+, CH_{Ar}), 127.0 (+, CH_{Ar}), 127.4 (C_q, C_{Ar}), 129.0 (+, 2 × CH_{Ar}), 131.8 (C_q, C_{Ar}), 139.3 (C_q, C_{Ar}), 139.4 (C_q, C_{Ar}), 149.0 (C_q, C_{Ar}), 173.6 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3321, 2921, 2851, 2217, 1695, 1616, 1509, 1469, 1438, 1350, 1245, 1223, 1174, 1087, 1020, 936, 920, 882, 804, 697, 640, 578, 477, 418 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 527 (7) [*M*]$^+$, 321 (57), 133 (100); HRMS (FAB, 3-NBA): calcd for $C_{33}H_{29}O_2N_5$ [*M*]$^+$: 527.2316; found: 527.2318.

*Ethyl (2S,4S,6S)-4,6-bis(4-nitro-1H-indol-3-yl)-1-(4-methoxyphenyl)piperidine-2-carboxylate (**5de**):* This compound was synthesized following the **GP C** with 4-nitro-3-vinylindole (**3d**, 37.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 1:1) to give **5de** as a brown oil (cat-(*R*): 21.5 mg, 40.0 µmol, 37%; cat-(*S*): 13.7 mg, 23.5 µmol, 24%).
The racemic compound was obtained following **GP C** with 4-nitro-3-vinylindole (**3d**, 37.6 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 1:1) to give **5de** as a brown oil (7.70 mg, 10.0 µmol, 13%).

R_f = 0.28 (cyclohexane/EtOAc 1:1); IR (ATR): $\tilde{\nu}$ = 3354, 2927, 1726, 1620, 1508, 1358, 1318, 1249, 1191, 1041, 977, 885, 799, 732, 463 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 584 (24) [*M*+H]$^+$, 506 (23), 396 (49), 395 (100); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{30}O_7N_5$ [*M*]$^+$: 584.2140; found: 584.2138.

*Ethyl 4,6-bis(5-fluoro-1H-indol-3-yl)-1-(4-methoxyphenyl)-piperidine-2-carboxylate (**5ee**):* This compound was synthesized following the **GP C** with 5-fluoro-3-vinylindole (**3e**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 4:1) to give **5ee** as a yellow oil (cat-(*R*): 16.0 mg, 30.0 µmol, 30%; cat-(*S*): F1: 19.8 mg, 37.4 µmol, 37%; F2: 20.6 mg, 38.9 µmol, 39%).
The racemic compound was obtained following **GP C** with 5-fluoro-3-vinylindole (**3e**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 4:1) to give **5ee** as a yellow oil (5.40 mg, 10.2 µmol, 10%).

fraction 1 (F1): R_f = 0.38 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.10 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.06 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.20–2.37 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.44 (dq, ^2J = 13.2, ^3J = 2.5 Hz, 1H, CH*H*CHCO$_2$Et), 3.18 (tt, ^2J = 12.5, ^3J = 3.2 Hz, 1H, CH_2CHCH_2), 3.44 (s, 3H, OCH_3), 3.88–3.99 (m, 1H, C*H*HCH$_3$), 4.01–4.10 (m, 1H, CH*H*CH$_3$), 4.49 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.45 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.38–6.44 (m, 2H, C*H*$_{Ar}$), 6.56–6.66 (m, 1H, C*H*$_{Ar}$), 6.70–6.80 (m, 1H, C*H*$_{Ar}$), 7.00–7.08 (m, 3H, C*H*$_{Ar}$), 7.11–7.18 (m, 3H, C*H*$_{Ar}$), 7.21–7.30 (m, 1H, C*H*$_{Ar}$), 7.51 (dd, ^3J = 10.3, ^3J = 2.5 Hz, 1H, C*H*$_{Ar}$), 9.80 (sbr, 1H, N*H*), 10.00 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.7 (–, $CHCH_2$), 43.0 (–, $CHCH_2$), 53.1 (+, $NCHC_{Ind}$), 55.2 (+, OCH_3), 60.5 (–, CH_2CH_3), 66.0 (+, $NCHCO_2Et$), 103.9 (+, d, ^2J = 23.4 Hz, CH_{Ar}), 105.7 (+, d, ^2J = 23.7 Hz, CH_{Ar}), 110.0 (+, dd, ^2J = 37.6, ^2J = 26.4 Hz, CH_{Ar}), 113.0 (+, dd, ^2J = 46.7, ^3J = 9.8 Hz, CH_{Ar}), 113.5 (+, 2 × CH_{Ar}), 114.9 (C_q, C_{Ar}), 115.4 (+, CH_{Ar}), 120.0 (C_q, ^3J = 4.9 Hz, C_{Ar}), 120.6 (C_q, ^3J = 4.8 Hz, C_{Ar}), 121.3 (C_q, C_{Ar}), 123.4 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 126.0 (+, CH_{Ar}), 127.0 (+, 2 × CH_{Ar}), 134.4 (C_q, ^3J = 4.2 Hz, C_{Ar}), 144.8 (C_q, C_{Ar}), 149.2 (C_q, C_{Ar}), 155.8 (C_q, C_{Ar}), 156.8 (C_q, d, ^1J = 236.6 Hz, *C*F), 159.6 (C_q, d, ^1J = 235.6 Hz, *C*F), 173.9 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –131.3, –131.4 ppm; IR (ATR): $\tilde{\nu}$ = 3379, 2924, 2852, 1718, 1623, 1579, 1507, 1482, 1346, 1259, 1240, 1160, 1091, 1021, 934, 795, 751, 700, 614, 570, 512, 428 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 529 (13) [*M*]$^+$, 316 (25), 132 (100), 107 (19), 91 (31); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{29}O_3N_3F_2$ [*M*]$^+$: 529.2172; found: 529.2170.

fraction 2 (F2): R_f = 0.18 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 0.99 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.22 (q, ^2J = 12.1 Hz, 1H, NCHCHH), 2.27–2.45 (m, 3H, CH_2CHCO_2Et, NCHCHH), 3.43 (tt, ^2J = 12.1, ^3J = 3.3 Hz, 1H, CH_2CHCH_2), 3.60 (s, 3H, OCH_3), 3.87 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 4.02 (dd, ^3J = 11.2, ^3J = 2.6 Hz, 1H, $NCHCO_2Et$), 4.59 (dd, ^3J = 11.2, ^3J = 2.9 Hz, 1H, $NCHC_{Ind}$), 6.50–6.60 (m, 2H, CH_{Ar}), 7.08–7.22 (m, 6H, CH_{Ar}), 7.30–7.38 (m, 2H, CH_{Ar}), 7.89 (d, ^4J = 1.7 Hz, 1H, CH_{Ar}), 8.12–8.24 (m, 1H, CH_{Ar}), 10.00 (sbr, 1H, NH), 10.27 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.3 (+, CH_2CH_3), 33.9 (+, CH_2CHCH_2), 38.2 (–, $CHCH_2$), 42.7 (–, $CHCH_2$), 55.3 (+, OCH_3), 60.5 (–, CH_2CH_3), 61.3 (+, $NCHC_{Ind}$), 70.0 (+, $NCHCO_2Et$), 112.2 (C_q, C_{Ar}), 112.3 (C_q, C_{Ar}), 113.8 (+, 2 × CH_{Ar}), 113.9 (+, CH_{Ar}), 114.1 (+, CH_{Ar}), 118.6 (C_q, C_{Ar}), 120.3 (C_q, C_{Ar}), 122.0 (+, CH_{Ar}), 123.1 (+, CH_{Ar}), 123.6 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 125.7 (+, CH_{Ar}), 129.1 (+, 2 × CH_{Ar}), 129.2 (C_q, C_{Ar}), 129.4 (C_q, C_{Ar}), 136.3 (C_q, C_{Ar}), 136.4 (C_q, C_{Ar}), 144.5 (C_q, C_{Ar}), 158.0 (C_q, C_{Ar}), 172.8 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –131.4, –131.5 ppm.

*Ethyl 4,6-bis(6-fluoro-1H-indol-3-yl)-1-phenylpiperidine-2carboxylate (**5fa**):* This compound was synthesized following the **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5fa** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 16.2 mg, 32.3 µmol, 32%; cat-(*S*): F1: 25.4 mg, 50.8 µmol, 51%; F2: 9.40 mg, 18.8 µmol, 19%).

The racemic compound was obtained following **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5fa** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (29.0 mg, 58.0 µmol, 58%).

fraction 1 (F1): R_f = 0.37 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.06 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3), 2.06 (q, ^3J = 12.6 Hz, 1H, NCHCHH), 2.23–2.37 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 2.48 (dd, ^3J =13.4, ^4J = 2.7 Hz, 1H, CHHCHCO$_2$Et), 3.20 (tt, ^3J = 12.5, ^3J = 3.1 Hz, 1H, CH_2CHCH_2), 3.89–3.97 (m, 1H, CHHCH$_3$), 3.99–4.07 (m, 1H, CHHCH$_3$), 4.66 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, $NCHCO_2Et$), 5.47 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, $NCHC_{Ind}$), 6.52–6.64 (m, 2H, CH_{Ar}), 6.71 (ddd, ^3J = 9.8, ^3J = 8.8, ^3J = 2.4 Hz, 1H, CH_{Ar}), 6.80–6.86 (m, 3H, CH_{Ar}), 6.96–7.08 (m, 5H, CH_{Ar}), 7.45 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, CH_{Ar}), 7.78 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, CH_{Ar}), 9.81 (sbr, 1H, NH), 9.98 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.7 (–, $CHCH_2$), 43.3 (–, $CHCH_2$), 52.8 (+, $NCHC_{Ind}$), 60.6 (–, CH_2CH_3), 65.7 (+, $NCHCO_2Et$), 98.09 (+, dd, ^2J = 32.2, ^2J = 25.8 Hz, 2 × CH_{Ar}), 107.7 (+, dd, ^2J = 24.5, ^2J = 20.1 Hz, 2 × CH_{Ar}), 119.8–120.3 (+, m, 2 × CH_{Ar}), 120.6 (C_q, 2 × C_{Ar}), 121.5–121.8 (+, m, CH_{Ar}), 121.9 (+, CH_{Ar}), 123.5 (C_q, 2 × C_{Ar}), 124.4 (+, CH_{Ar}), 125.4 (+, 2 × CH_{Ar}), 128.3 (+, 2 × CH_{Ar}), 137.5 (C_q, dd, ^3J = 18.2, ^3J = 12.5 Hz, C_qCHCF), 151.8 (C_q, 2 × C_{Ar}), 159.2 (C_q, d, ^1J = 25.8 Hz, *C*F), 161.5 (C_q, d, ^1J = 26.1 Hz, *C*F), 173.7 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –128.1, –128.5 ppm; IR (ATR): $\tilde{\nu}$ = 3415 (w), 2932 (w), 1697 (m), 1625 (w), 1595 (w), 1553 (w), 1493 (m), 1453 (m), 1342 (w), 1248 (m), 1219 (m), 1177 (m), 1137 (m), 1112 (m), 1090 (m), 1023 (m), 951 (m), 834 (w), 799 (m), 764 (w), 697 (m), 572 (w), 476 (m), 434 (w), 386 (vw) cm^{-1}; MS (EI, 70 eV): *m/z* (%): 499 (13) [*M*]$^+$, 178 (50), 135 (100); HRMS (EI): calcd for $C_{30}H_{27}O_2N_3F_2$ [*M*]$^+$: 499.2066; found: 499.2067.

fraction 2 (F2): R_f = 0.20 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.72 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 3.03 (q, ^3J = 12.2 Hz, 1H, NCHCHH), 3.09–3.20 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 3.20–3.30 (m, 1H, CHHCHCO$_2$Et), 4.22 (tt, ^3J = 11.9, ^3J = 3.6 Hz, 1H, CH_2CHCH_2), 4.64 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 4.87 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, $NCHCO_2Et$), 5.42 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, $NCHC_{Ind}$), 7.57–7.67 (m, 3H, CH_{Ar}), 7.72–7.81 (m, 3H, CH_{Ar}), 7.85 (d, ^3J = 2.3 Hz, 1H, CH_{Ar}), 7.91 (dd, ^3J = 10.0, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.97–8.03 (m, 3H, CH_{Ar}), 8.48 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, CH_{Ar}), 8.77 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, CH_{Ar}), 10.66 (sbr, 1H, NH), 10.93 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.2 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 33.9 (–, $CHCH_2$), 38.1 (–, $CHCH_2$), 42.4 (+, $NCHC_{Ind}$), 61.1 (–, CH_2CH_3), 69.3 (+, $NCHCO_2Et$), 98.1 (+, dd, ^2J = 28.8, ^2J = 25.7 Hz, 2 × CH_{Ar}), 107.6 (+, dd, ^2J = 24.4, ^2J = 21.5 Hz, 2 × CH_{Ar}), 118.7 (C_q, 2 × C_{Ar}), 120.2–120.7 (+, m, CH_{Ar}), 121.7–122.1 (+, m, 2 × CH_{Ar}), 124.1 (C_q, C_{Ar}), 124.4 (C_q, C_{Ar}), 124.6 (+, d, ^2J = 3.5 Hz, CH_{Ar}), 125.7 (+, CH_{Ar}), 127.8 (+, 2 × CH_{Ar}), 128.6 (+, 2 × CH_{Ar}), 137.6 (C_q, dd, ^3J = 23.7, ^3J = 12.6 Hz, C_qCHCF), 151.9 (C_q, 2 × C_{Ar}), 159.2 (C_q, d, ^1J = 26.1 Hz, *C*F), 161.5 (C_q, d, ^1J = 26.3 Hz, *C*F), 172.9 (C_q, CO_2Et) ppm; ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): δ = –128.2, –128.5 ppm; IR (ATR): $\tilde{\nu}$ = 3357, 2924, 1722, 1696, 1626, 1594, 1553, 1493, 1455, 1372, 1342, 1248, 1220, 1177, 1137, 1092, 1027, 951, 834, 799, 771, 698, 602, 476, 434 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 500 (27) [*M*+H]$^+$, 178 (55), 135 (89); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3F_2$ [*M*+H]$^+$: 500.2144; found: 500.2146.

*Ethyl (2S,4S,6S)-4,6-bis(6-fluoro-1H-indol-3-yl)-1-(4-methoxyphenyl)-piperidine-2-carboxylate (**5fe**):* This compound was synthesized following the **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 4:1) to give **5fe** as a yellow oil (cat-(*R*): 19.3 mg, 36.0 µmol, 36%; cat-(*S*): 33.7 mg, 63.6 µmol, 64%).

The racemic compound was obtained following **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5fe** was obtained after column chromatography (cyclohexane/ethyl acetate = 4:1) as a yellow oil (5.20 mg, 9.81 µmol, 9.8%).

R_f = 0.37 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.21 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3), 2.19 (q, ^3J = 12.6 Hz, 1H, NCHCHH), 2.34–2.49 (m, 2H, CHHCHCO$_2$Et,

NCHCH*H*), 2.57 (dq, ^3J =13.2, ^4J = 2.5 Hz, 1H, CH*H*CHCO$_2$Et), 3.36 (tt, ^2J = 12.5, ^3J = 2.8 Hz, 1H, CH$_2$C*H*CH$_2$), 3.58 (s, 3H, OC*H*$_3$), 4.03–4.12 (m, 1H, C*H*HCH$_3$), 4.12–4.24 (m, 1H, CH*H*CH$_3$), 4.60 (dd, ^3J = 5.6, ^3J = 2.2 Hz, 1H, NC*H*CO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.51–6.57 (m, 2H, C*H*$_{Ar}$), 6.75 (ddd, ^3J = 9.8, ^3J = 8.9, ^4J = 2.3 Hz, 1H, C*H*$_{Ar}$), 6.84 (ddd, ^3J = 9.8, ^3J = 8.9, ^4J = 2.3 Hz, 1H, C*H*$_{Ar}$), 6.95 (dd, ^3J = 10.1, ^4J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.09–7.19 (m, 5H, C*H*$_{Ar}$), 7.58 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, C*H*$_{Ar}$), 7.93 (dd, ^3J = 8.7, ^3J = 5.6 Hz, 1H, C*H*$_{Ar}$), 9.91 (sbr, 1H, N*H*), 10.10 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH$_2$*C*H$_3$), 27.5 (+, CH$_2$*C*HCH$_2$), 36.8 (–, CH*C*H$_2$), 43.3 (–, CH*C*H$_2$), 53.0 (+, NC*H*C$_{Ind}$), 55.2 (+, O*C*H$_3$), 60.5 (–, *C*H$_2$CH$_3$), 66.0 (+, NCHCO$_2$Et), 98.1 (+, dd, ^2J = 33.8, ^2J = 25.7 Hz, 2 × *C*H$_{Ar}$), 106.2–106.8 (+, m, 2 × *C*H$_{Ar}$), 113.5 (+, 2 × *C*H$_{Ar}$), 119.6 (+, d, ^3J = 10.3 Hz, *C*H$_{Ar}$), 120.7 (C$_q$, *C*$_{Ar}$), 121.7 (+, d, ^4J = 3.5 Hz, *C*H$_{Ar}$), 121.9 (+, d, ^3J = 10.1 Hz, *C*H$_{Ar}$), 123.6 (C$_q$, *C*$_{Ar}$), 124.3–124.5 (+, m, *C*H$_{Ar}$), 127.0 (+, 2 × *C*H$_{Ar}$), 137.7 (C$_q$, dd, ^3J = 16.4, ^3J = 12.6 Hz, 2 × *C*$_q$CHCF), 144.8 (C$_q$, 2 × *C*$_{Ar}$), 155.7 (C$_q$, 2 × *C*$_{Ar}$), 159.2 (C$_q$, d, ^1J = 27.6 Hz, *C*F), 161.5 (C$_q$, d, ^1J = 27.9 Hz, *C*F), 173.9 (C$_q$, *C*O$_2$Et) ppm; ^{19}F NMR (376 MHz, acetone-d$_6$, 25 °C): δ = –128.1, –128.6 ppm; IR (ATR): $\tilde{\nu}$ = 3396, 2923, 2540, 1705, 1623, 1553, 1506, 1486, 1451, 1342, 1217, 1176, 1107, 1026, 953, 829, 798, 609, 571, 471, 435 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%):(100) [*M*+H]$^+$, 395 (54), 109 (59), 97 (68); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{30}O_3N_3F_2$ [*M*+H]$^+$: 530.2250; found: 530.2250.

*Ethyl 4,6-bis(6-fluoro-1H-indol-3-yl)-1-(4-chlorophenyl)-piperidin e-2-carboxylate (**5fh**):* This compound was synthesized following the **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5fh** as a yellow oil in two fractions (cat-(*R*): F1: 15.8 mg, 29.6 µmol, 30%; F2: 10.3 mg, 19.3 µmol, 19%; cat-(*S*): F1: 27.3 mg, 51.1 µmol, 51%; F2: 10.7 mg, 20.0 µmol, 20%).

The racemic compound was obtained following **GP C** with 6-fluoro-3-vinylindole (**3f**, 32.2 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5fh** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (20.0 mg, 37.4 µmol, 37%).

fraction 1 (F1): R_f = 0.44 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.23 (t, ^3J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 2.20 (q, ^2J = 12.5 Hz, 1H, NCHCH*H*), 2.37–2.48 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.65 (dq, ^2J = 13.2, ^3J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.29 (tt, ^2J = 12.5, ^3J = 3.0 Hz, 1H, CH$_2$C*H*CH$_2$), 4.05–4.15 (m, 1H, C*H*HCH$_3$), 4.16–4.25 (m, 1H, CH*H*CH$_3$), 4.80 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.53 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.74 (ddd, ^3J = 9.8, ^3J = 8.9, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 6.84 (ddd, ^3J = 9.8, ^3J = 8.9, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 6.94–7.00 (m, 3H, C*H*$_{Ar}$), 7.12 (dd, ^3J = 10.0, ^3J = 2.3 Hz, 1H, C*H*$_{Ar}$), 7.15 (d, ^3J = 1.9 Hz, 1H, C*H*$_{Ar}$), 7.18–7.24 (m, 3H, C*H*$_{Ar}$), 7.58 (dd, ^3J = 8.7, ^3J = 5.5 Hz, 1H, C*H*$_{Ar}$), 7.88 (dd, ^3J = 8.7, ^3J = 5.5 Hz, 1H, C*H*$_{Ar}$), 10.00 (sbr, 1H, N*H*), 10.12 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH$_2$*C*H$_3$), 27.5 (+, CH$_2$*C*HCH$_2$), 36.6 (–, CH*C*H$_2$), 43.0 (–, CH*C*H$_2$), 53.0 (+, NC*H*C$_{Ind}$), 60.9 (–, *C*H$_2$CH$_3$), 65.5 (+, NCHCO$_2$Et), 98.2 (+, dd, ^2J = 25.7, ^2J = 22.9 Hz, 2 × *C*H$_{Ar}$), 107.7 (+, dd, ^2J = 24.5, ^3J = 8.2 Hz, 2 × *C*H$_{Ar}$), 116.4 (+, CH$_{Ar}$), 119.5 (C$_q$, *C*$_{Ar}$), 120.1 (+, d, ^3J = 10.3 Hz, *C*H$_{Ar}$), 120.4 (C$_q$, *C*$_{Ar}$), 121.7 (+, *C*H$_{Ar}$), 121.8 (C$_q$, *C*$_{Ar}$), 123.3 (C$_q$, *C*$_{Ar}$), 124.3 (+, *C*H$_{Ar}$), 124.5 (C$_q$, *C*$_{Ar}$), 126.8 (C$_q$, *C*$_{Ar}$), 126.9 (+, 2 × *C*H$_{Ar}$), 128.1 (+, 2 × *C*H$_{Ar}$), 137.7 (C$_q$, t, ^3J = 12.5 Hz, *C*$_q$CHCHF), 150.7 (C$_q$, *C*$_{Ar}$), 159.2 (C$_q$, d, ^1J = 235.2 Hz, *C*F), 161.6 (C$_q$, d, ^1J = 235.6 Hz, *C*F), 173.4 ppm; ^{19}F NMR (376 MHz, acetone-d$_6$, 25 °C): δ = –128.0, –128.3 ppm; IR (ATR): $\tilde{\nu}$ = 3370, 2930, 1697, 1625, 1592, 1554, 1489, 1454, 1370, 1342, 1248, 1219, 1177, 1137, 1090, 1022, 951, 800, 754, 718, 669, 605, 569, 476, 433 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 534 (9) [*M*]$^+$, 106 (37), 95 (34); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}ClF_2$ [*M*+H]$^+$: 534.1754; found: 534.1754.

fraction 2 (F2): R_f = 0.28 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 0.85 (t, ^3J = 7.1 Hz, 3H, CH$_2$C*H*$_3$), 2.10 (q, ^3J = 12.3 Hz, 1H, NCHCH*H*), 2.16–2.28 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.29–2.41 (m, 1H, CH*H*CHCO$_2$Et), 3.30 (tt, ^3J = 12.1, ^3J = 3.6 Hz, 1H, CH$_2$C*H*CH$_2$), 3.76 (q, ^3J = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 3.95 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, NC*H*CO$_2$Et), 4.47 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, NC*H*C$_{Ind}$), 6.66–6.74 (m, 2H, C*H*$_{Ar}$), 6.82–6.91 (m, 3H, C*H*$_{Ar}$), 6.95 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 6.99 (dd, ^3J = 10.1, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.03–7.11 (m, 3H, C*H*$_{Ar}$), 7.55 (dd, ^3J = 8.7, ^3J = 5.4 Hz, 1H, C*H*$_{Ar}$), 7.83 (dd, ^3J = 8.7, ^3J = 5.5 Hz, 1H, C*H*$_{Ar}$), 9.80 (sbr, 1H, N*H*), 10.02 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.2 (+, CH$_2$*C*H$_3$), 33.8 (+, CH$_2$*C*HCH$_2$), 37.9 (–, CH*C*H$_2$), 42.1 (–, CH*C*H$_2$), 60.7 (–, *C*H$_2$CH$_3$), 61.2 (+, NC*H*C$_{Ind}$), 69.0 (+, NCHCO$_2$Et), 98.1 (+, d, ^3J = 9.3 Hz, 2 × *C*H$_{Ar}$), 107.7 (+, dd, ^2J = 24.5, ^3J = 7.0 Hz, 2 × *C*H$_{Ar}$), 118.3 (C$_q$, 2 × *C*$_{Ar}$), 120.1–120.6 (+, m, 2 × *C*H$_{Ar}$), 120.9 (+, *C*H$_{Ar}$), 123.9 (C$_q$, *C*$_{Ar}$), 124.3 (+, *C*H$_{Ar}$), 124.7 (C$_q$, *C*$_{Ar}$), 124.8 (C$_q$, *C*$_{Ar}$), 128.7 (+, 2 × *C*H$_{Ar}$), 129.5 (+, 2 × *C*H$_{Ar}$), 130.5 (C$_q$, *C*$_{Ar}$), 137.6 (C$_q$, dd, ^3J = 17.5, ^3J = 12.6 Hz, *C*$_q$CHCHF), 150.8 (C$_q$, *C*$_{Ar}$), 159.23 (C$_q$, d, ^1J = 235.2 Hz, *C*F), 161.6 (C$_q$, d, ^1J = 235.6 Hz, *C*F), 172.7 (C$_q$, *C*O$_2$Et) ppm; ^{19}F NMR (376 MHz, acetone-d$_6$, 25 °C): δ = –128.1, –128.3 ppm; IR (ATR): $\tilde{\nu}$ = 3370, 2923, 2852, 1722, 1696, 1626, 1591, 1553, 1489, 1455, 1405, 1371, 1342, 1248, 1221, 1178, 1137, 1090, 1024, 951, 828, 799, 755, 720, 670, 569, 476, 432 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 534 (9) [*M*]$^+$, 132 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}ClF_2$ [*M*+H]$^+$: 534.1754; found: 534.1755.

*Ethyl (2S,4S,6S)-4,6-bis(5-chloro-1H-indol-3-yl)-1phenylpiperidin e-2-carboxylate (**5ga**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5ga** as a brown oil (cat-(*R*): 17.0 mg, 32.0 µmol, 32%; cat-(*S*): 35.5 mg, 66.7 µmol, 67%).

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 39.0 mg, 0.200 mmol, 1.80 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 21.4 mg, 0.121 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The

product **5ga** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a brown oil (16.3 mg, 30.6 µmol, 28%).

R_f = 0.35 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.10 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.06 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.26–2.36 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.50 (dq, ^3J = 13.2, ^4J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.19 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 3.88–3.98 (m, 1H, C*H*HCH$_3$), 4.04–4.11 (m, 1H, CH*H*CH$_3$), 4.68 (dd, ^3J = 5.5, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.47 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.55 (t, ^3J = 7.3 Hz, 1H, C*H*$_{Ar}$), 6.78–6.87 (m, 3H, C*H*$_{Ar}$), 6.95 (dd, ^3J = 8.6, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.06–7.14 (m, 4H, C*H*$_{Ar}$), 7.16 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.26 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.48 (d, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.81 (d, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 9.93 (sbr, 1H, N*H*), 10.09 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.6 (–, $CHCH_2$), 43.0 (–, $CHCH_2$), 52.8 (+, NCHC$_{Ind}$), 60.7 (–, CH_2CH_3), 65.7 (+, NCHCO$_2$Et), 113.3 (+, *C*H$_{Ar}$), 113.7 (+, *C*H$_{Ar}$), 118.6 (+, *C*H$_{Ar}$), 119.6 (C$_q$, *C*$_{Ar}$), 120.2 (C$_q$, *C*$_{Ar}$), 120.3 (+, *C*H$_{Ar}$), 121.9 (+, *C*H$_{Ar}$), 122.2 (+, *C*H$_{Ar}$), 122.5 (+, *C*H$_{Ar}$), 123.1 (+, *C*H$_{Ar}$), 124.5 (C$_q$, *C*$_{Ar}$), 124.7 (C$_q$, *C*$_{Ar}$), 125.5 (+, 2 × *C*H$_{Ar}$), 125.7 (+, *C*H$_{Ar}$), 127.8 (C$_q$, *C*$_{Ar}$), 128.3 (+, 2 × *C*H$_{Ar}$), 128.7 (C$_q$, *C*$_{Ar}$), 136.1 (C$_q$, *C*$_{Ar}$), 136.2 (C$_q$, *C*$_{Ar}$), 151.7 (C$_q$, *C*$_{Ar}$), 173.5 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3412, 2927, 1721, 1694, 1596, 1492, 1461, 1370 1340, 1246, 1220, 1175, 1097, 1023, 955, 933, 892, 861, 794, 753, 696, 587, 568, 476, 422 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 532 (9) [*M*+H]$^+$, 178 (46), 133 (100), 109 (40), 107 (40), 105 (46), 104 (33), 97 (40), 95 (72), 93 (44), 91 (74), 83 (58), 81 (88); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3{}^{35}Cl_2$ [*M*+H]$^+$: 532.1553; found: 532.1552.

*Ethyl (2S,4S,6S)-4,6-bis(5-chloro-1H-indol-3-yl)-1-(4-tolyl)piperidine-2-carboxylate (**5gb**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(4-tolylimino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5gb** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 36.4 mg, 66.6 µmol, 67%; cat-(*S*): 22.8 mg, 41.8 µmol, 42%)

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(4-tolylimino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5gb** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (22.5 mg, 41.2 µmol, 41%).

R_f = 0.50 (cyclohexane/EtOAc 2:1); ^{1}H NMR (500 MHz, acetone-d_6, 25 °C, TMS): δ = 1.24 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 1.96 (s, 3H, C$_{Ar}$CH_3), 2.15–2.26 (m, 1H, NCHC*H*H), 2.34–2.49 (m, 2H, CH_2CHCO$_2$Et), 2.61 (dq, ^2J = 13.1, ^3J = 2.4 Hz, 1H, NCHCH*H*), 3.32 (tt, ^2J = 12.3, ^3J = 3.1 Hz, 1H, CH_2CHCH_2), 4.01–4.11 (m, 1H, C*H*HCH$_3$), 4.13–4.26 (m, 1H, CH*H*CH$_3$), 4.73 (dd, ^3J = 5.5, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.60 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.77 (d, ^3J = 8.1 Hz, 2H, C*H*$_{Ar}$), 6.90–6.99 (m, 1H, C*H*$_{Ar}$), 7.05–7.13 (m, 3H, C*H*$_{Ar}$), 7.20–7.30 (m, 3H, C*H*$_{Ar}$), 7.39 (d, ^3J = 8.7 Hz, 1H, C*H*$_{Ar}$), 7.61 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.95 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 10.03 (sbr, 1H, N*H*), 10.21 (sbr, 1H, N*H*) ppm; ^{13}C NMR (125 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 20.6 (+, C$_{Ar}$CH_3), 33.6 (–, $CHCH_2$), 35.0 (+, CH_2CHCH_2), 43.0 (–, $CHCH_2$), 52.8 (+, NCHC$_{Ind}$), 60.6 (–, CH_2CH_3), 65.8 (+, NCHCO$_2$Et), 113.4 (C$_q$, *C*$_{Ar}$), 113.7 (+, *C*H$_{Ar}$), 115.5 (C$_q$, *C*$_{Ar}$), 118.6 (+, *C*H$_{Ar}$), 119.4 (+, *C*H$_{Ar}$), 119.7 (C$_q$, *C*$_{Ar}$), 120.4 (+, *C*H$_{Ar}$), 121.8 (+, *C*H$_{Ar}$), 122.1 (+, *C*H$_{Ar}$), 122.2 (+, *C*H$_{Ar}$), 123.1 (C$_q$, *C*$_{Ar}$), 124.7 (C$_q$, *C*$_{Ar}$), 125.5 (2 × *C*H$_{Ar}$), 126.5 (C$_q$, *C*$_{Ar}$), 127.9 (C$_q$, *C*$_{Ar}$), 128.5 (+, *C*H$_{Ar}$), 128.9 (2 × *C*H$_{Ar}$), 130.1 (C$_q$, *C*$_{Ar}$), 131.6 (C$_q$, *C*$_{Ar}$), 149.2 (C$_q$, *C*$_{Ar}$), 173.6 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3386, 2923, 1720, 1617, 1509, 1461, 1370, 1210, 1177, 1098, 1020, 892, 859, 794, 690, 586, 468, 425, 399 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 547/546/545 (42/25/100) [*M*]$^+$, 394 (41), 368 (87), 366 (14), 364 (52), 292 (12), 151 (37); HRMS (EI): calcd for $C_{31}H_{29}O_2N_3{}^{35}Cl_2$ [*M*]$^+$: 545.1631; found: 545.1629.

*Ethyl (2S,4S,6S)-4,6-bis(5-chloro-1H-indol-3-yl)-1-(4-methoxyphenyl)-piperidine-2-carboxylate (**5ge**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ge** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 35.9 mg, 63.8 µmol, 64%; cat-(*S*): 20.2 mg, 36.0 µmol, 36%)

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5ge** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (4.69 mg, 8.35 µmol, 8.4%).

R_f = 0.41 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.13–2.26 (m, 1H, NCHC*H*H), 2.35–2.49 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.55–2.63 (m, 1H, CH*H*CHCO$_2$Et), 3.35 (tt, ^2J = 12.5, ^3J = 3.1 Hz, 1H, CH_2CHCH_2), 3.58 (s, 3H, OCH_3), 4.03–4.09 (m, 1H, C*H*HCH$_3$), 4.18–4.25 (m, 1H, CH*H*CH$_3$), 4.62 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.54–6.57 (m, 2H, C*H*$_{Ar}$), 6.95 (dd, ^3J = 8.6, ^4J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.08 (dd, ^3J = 8.6, ^4J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.15–7.18 (m, 2H, C*H*$_{Ar}$), 7.22 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.27 (dd, ^3J = 6.6, ^4J = 2.0 Hz, 2H, C*H*$_{Ar}$), 7.39 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.61 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.96 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 10.01 (sbr, 1H, N*H*), 10.21 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.8 (–, $CHCH_2$), 43.1 (–, $CHCH_2$), 53.0 (+, NCHC$_{Ind}$), 55.2 (+, OCH_3), 60.6 (–, CH_2CH_3), 66.0 (+, NCHCO$_2$Et), 113.3 (+, *C*H$_{Ar}$), 113.6 (+, 2 × *C*H$_{Ar}$), 113.7 (+, *C*H$_{Ar}$), 118.6 (+, *C*H$_{Ar}$), 119.6 (C$_q$, *C*$_{Ar}$), 120.3 (C$_q$, *C*$_{Ar}$), 120.4 (+, *C*H$_{Ar}$), 121.8 (+, *C*H$_{Ar}$), 122.2 (+, *C*H$_{Ar}$), 123.1 (+, *C*H$_{Ar}$), 124.4 (C$_q$, *C*$_{Ar}$), 124.7 (C$_q$, *C*$_{Ar}$), 125.8 (+, *C*H$_{Ar}$), 127.0 (+, 2 × *C*H$_{Ar}$), 127.9 (C$_q$, *C*$_{Ar}$), 128.7 (C$_q$, *C*$_{Ar}$), 136.1 (C$_q$, *C*$_{Ar}$), 136.2 (C$_q$, *C*$_{Ar}$), 144.7 (C$_q$, *C*$_{Ar}$), 155.8 (C$_q$, *C*$_{Ar}$), 173.8 (C$_q$, *C*O$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3414, 2931, 1716, 1506, 1461, 1371, 1239, 1176, 1097, 1032, 934, 891, 860, 828, 793, 752, 690, 586, 479, 422 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 563/562/561 (34/38/44) [*M*]$^+$, 341/339 (65/100), 208 (82), 154 (36), 136 (43), 134 (90), 107 (43), 97 (47), 95 (65),

81 (68); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{29}O_3N_3{}^{35}Cl_2$ [*M*]$^+$: 561.1580; found: 561.1581.

*Ethyl 4,6-bis(5-chloro-1H-indol-3-yl)-1-(4-fluorophenyl)-piperidine-2-carboxylate (**5gg**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-fluorophenyl)imino)acetate (**4g**, 19.5 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5gg** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (cat-(*R*): F1: 36.7 mg, 66.7 µmol, 67%, F2: 17.7 mg, 32.2 µmol, 32%; cat-(*S*): 31.3 mg, 56.9 µmol, 57%, F2: 12.4 mg, 22.5 µmol, 23%).

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 37.3 mg, 0.210 mmol, 1.78 Equiv.) and ethyl 2-((4-fluorophenyl)imino)acetate (**4g**, 23.0 mg, 0.118 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5gg** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 30.7 mg, 55.7 µmol, 53%; F2: 23.9 mg, 43.3 µmol, 41%).

fraction 1 (F1): R_f = 0.32 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.21 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.37–2.50 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.64 (dq, ^3J = 13.2, ^3J = 2.4 Hz, 1H, CH*H*CHCO$_2$Et), 3.32 (tt, ^3J = 12.5, ^3J = 2.9 Hz, 1H, CH_2CHCH_2), 4.02–4.13 (m, 1H, C*H*HCH$_3$), 4.18–4.28 (m, 1H, CH*H*CH$_3$), 4.73 (dd, ^3J = 5.5, ^3J = 2.2 Hz, 1H, NC*H*CO$_2$Et), 5.57 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.74 (t, ^3J = 8.8 Hz, 2H, C*H*$_{Ar}$), 6.96 (dd, ^3J = 8.6, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.09 (dd, ^3J = 8.6, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.22–7.28 (m, 4H, C*H*$_{Ar}$), 7.32 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.40 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.62 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.94 (d, ^4J = 2.0 Hz, 1H, C*H*$_{Ar}$), 10.10 (sbr, 1H, N*H*), 10.24 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.7 (–, $CHCH_2$), 42.9 (–, $CHCH_2$), 53.0 (+, NCHC$_{Ind}$), 60.8 (–, CH_2CH_3), 65.8 (+, NCHCO$_2$Et), 113.4 (+, C*H*$_{Ar}$), 113.7 (+, C*H*$_{Ar}$), 114.5 (+, C*H*$_{Ar}$), 114.8 (+, C*H*$_{Ar}$), 118.6 (+, C*H*$_{Ar}$), 119.2 (C$_q$, *C*$_{Ar}$), 120.0 (C$_q$, *C*$_{Ar}$), 120.3 (+, C*H*$_{Ar}$), 121.9 (+, C*H*$_{Ar}$), 122.2 (+, C*H*$_{Ar}$), 123.1 (+, C*H*$_{Ar}$), 124.6 (C$_q$, *C*$_{Ar}$), 124.7 (C$_q$, *C*$_{Ar}$), 125.9 (+, C*H*$_{Ar}$), 127.3 (+, C*H*$_{Ar}$), 127.4 (+, C*H*$_{Ar}$), 127.7 (C$_q$, *C*$_{Ar}$), 128.7 (C$_q$, *C*$_{Ar}$), 136.1 (C$_q$, *C*$_{Ar}$), 136.2 (C$_q$, *C*$_{Ar}$), 147.9 (C$_q$, *C*$_{Ar}$), 158.8 (C$_q$, d, ^1J = 238.9 Hz, *C*F), 173.4 (C$_q$, *C*O$_2$Et) ppm; ^{19}F NMR (376 MHz, acetone-d$_6$, 25 °C): δ = –127.4 ppm; IR (ATR): $\tilde{\nu}$ = 3369, 2929, 1696, 1549, 1504, 1461, 1368, 1248, 1210, 1175, 1097, 1022, 934, 892, 862, 833, 795, 754, 690, 588, 478, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 550 (22) [*M*+H]$^+$, 155 (41), 154 (92), 138 (41), 137 (69), 136 (81), 133 (55), 123 (37), 121 (32), 119 (34), 111 (35), 109 (55), 107 (56), 105 (41), 97 (68), 95 (89), 93 (47), 91 (64), 85 (35), 83 (76), 81 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}Cl_2F$ [*M*+H]$^+$: 550.1459; found: 550.1461.

fraction 2 (F2): R_f = 0.13 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 0.97 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.18–2.29 (m, 1H, NCHC*H*H), 2.30–2.39 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.40–2.50 (m, 1H, CH*H*CHCO$_2$Et), 3.45 (tt, ^3J = 12.2, ^3J = 3.6 Hz, 1H, CH_2CHCH_2), 3.88 (q, ^3J = 7.1 Hz, 2H, CH_2CH_3), 4.07 (dd, ^3J = 11.3, ^3J = 2.6 Hz, 1H, NC*H*CO$_2$Et), 4.60 (dd, ^3J = 11.1, ^3J = 2.9 Hz, 1H, NC*H*C$_{Ind}$), 6.72–6.81 (m, 2H, C*H*$_{Ar}$), 6.99 (dd, ^3J = 8.6, ^3J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.08 (dd, ^3J = 8.6, ^3J = 2.1 Hz, 1H, C*H*$_{Ar}$), 7.16 (d, ^3J = 2.5 Hz, 1H, C*H*$_{Ar}$), 7.22–7.29 (m, 3H, C*H*$_{Ar}$), 7.35 (d, ^3J = 2.3 Hz, 1H, C*H*$_{Ar}$), 7.40 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.73 (d, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 8.00 (d, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 10.03 (sbr, 1H, N*H*), 10.27 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.3 (+, CH_2CH_3), 33.8 (+, CH_2CHCH_2), 38.1 (–, $CHCH_2$), 42.4 (–, $CHCH_2$), 60.6 (–, CH_2CH_3), 61.4 (+, NCHC$_{Ind}$), 69.6 (+, NCHCO$_2$Et), 113.5 (+, C*H*$_{Ar}$), 113.7 (+, C*H*$_{Ar}$), 115.0 (+, C*H*$_{Ar}$), 115.2 (+, C*H*$_{Ar}$), 118.2 (C$_q$, *C*$_{Ar}$), 118.8 (+, C*H*$_{Ar}$), 120.2 (C$_q$, *C*$_{Ar}$), 120.3 (+, C*H*$_{Ar}$), 122.0 (+, C*H*$_{Ar}$), 122.2 (+, C*H*$_{Ar}$), 123.3 (+, C*H*$_{Ar}$), 124.6 (C$_q$, *C*$_{Ar}$), 124.8 (C$_q$, *C*$_{Ar}$), 126.0 (+, C*H*$_{Ar}$), 128.4 (C$_q$, *C*$_{Ar}$), 128.7 (C$_q$, *C*$_{Ar}$), 129.9 (+, C*H*$_{Ar}$), 130.0 (+, C*H*$_{Ar}$), 136.1 (C$_q$, *C*$_{Ar}$), 136.2 (C$_q$, *C*$_{Ar}$), 148.0 (C$_q$, *C*$_{Ar}$), 160.8 (C$_q$, d, ^1J = 238.9 Hz, *C*F), 172.6 (C$_q$, *C*O$_2$Et) ppm; ^{19}F NMR (376 MHz, acetone-d$_6$, 25 °C): δ = –123.1 ppm; IR (ATR): $\tilde{\nu}$ = 3352, 2923, 1724, 1695, 1504, 1462, 1380, 1247, 1210, 1177, 1095, 1029, 893, 858, 832, 796, 754, 671, 588, 541, 477, 424 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 550 (31) [*M*+H]$^+$, 341 (30), 339 (46), 221 (36), 207 (36), 196 (65), 154 (37), 149 (64), 147 (94), 137 (31), 136 (38), 133 (80), 123 (30), 122 (43), 119 (37), 109 (45), 107 (40), 105 (40), 97 (54), 95 (81), 93 (57), 91 (67), 85 (57), 83 (89), 80 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}Cl_2F$ [*M*+H]$^+$: 550.1459; found: 550.1458.

*Ethyl 4,6-bis(5-chloro-1H-indol-3-yl)-1-(4-chlorophenyl)-piperidine-2-carboxylate (**5gh**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 21.2 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5gh** as a yellow oil (cat-(*R*): 16.5 mg, 29.0 µmol, 29%; cat-(*S*): 52.2 mg, 92.1 µmol, 92%).

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 36.4 mg, 0.205 mmol, 2.00 Equiv.) and ethyl 2-((4-chlorophenyl)imino)acetate (**4h**, 29.2 mg, 0.138 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5gh** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 34.6 mg, 61.0 µmol, 44%; F2: 33.9 mg, 59.8 µmol, 43%).

fraction 1 (F1): R_f = 0.38 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.27 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.20 (q, ^2J = 12.5 Hz, 1H, NCHC*H*H), 2.38–2.49 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.67 (dq, ^2J = 13.2, ^3J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.28 (tt, ^2J = 12.5, ^3J = 2.9 Hz, 1H, CH_2CHCH_2), 4.05–4.15 (m, 1H, C*H*HCH$_3$), 4.18–4.35 (m, 1H, CH*H*CH$_3$), 4.83 (dd, ^3J = 5.5, ^3J = 2.6 Hz, 1H, NC*H*CO$_2$Et), 5.54 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NC*H*C$_{Ind}$), 6.63–6.69 (m, 1H, C*H*$_{Ar}$), 6.93–7.00 (m, 2H, C*H*$_{Ar}$), 7.01–7.05 (m, 1H, C*H*$_{Ar}$), 7.08 (dd, ^3J = 8.6, ^3J = 2.0 Hz, 1H, C*H*$_{Ar}$), 7.20–7.28 (m, 3H, C*H*$_{Ar}$), 7.33 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.40 (d, ^3J = 8.6 Hz, 1H, C*H*$_{Ar}$), 7.61 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 7.91 (d, ^3J = 2.4 Hz, 1H, C*H*$_{Ar}$), 10.13 (sbr, 1H, N*H*), 10.24 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.6 (–, $CHCH_2$), 42.8

(–, CHCH$_2$), 53.0 (+, NCHC$_{Ind}$), 60.9 (–, CH$_2$CH$_3$), 65.5 (+, NCHCO$_2$Et), 113.5 (+, CH$_{Ar}$), 113.7 (+, CH$_{Ar}$), 116.4 (+, CH$_{Ar}$), 118.6 (+, CH$_{Ar}$), 119.1 (C$_q$, C$_{Ar}$), 120.0 (C$_q$, C$_{Ar}$), 120.2 (+, CH$_{Ar}$), 122.0 (+, CH$_{Ar}$), 122.2 (+, CH$_{Ar}$), 123.1 (+, CH$_{Ar}$), 124.6 (C$_q$, C$_{Ar}$), 124.7 (C$_q$, C$_{Ar}$), 125.9 (+, CH$_{Ar}$), 126.9 (C$_q$, C$_{Ar}$), 127.0 (+, CH$_{Ar}$), 127.7 (C$_q$, C$_{Ar}$), 128.2 (+, CH$_{Ar}$), 128.7 (C$_q$, C$_{Ar}$), 129.5 (+, CH$_{Ar}$), 136.1 (C$_q$, C$_{Ar}$), 136.2 (C$_q$, C$_{Ar}$), 150.7 (C$_q$, C$_{Ar}$), 173.3 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3367, 2926, 1723, 1695, 1592, 1568, 1489, 1461, 1370, 1340, 1246, 1220, 1176, 1093, 1022, 956, 934, 892, 861, 827, 795, 754, 717, 665, 587, 565, 476, 422 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 566 (13) [*M*]$^+$, 339 (38), 135 (85); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}Cl_3$ [*M*+H]$^+$: 566.1163; found: 566.1163.

fraction 2 (F2): R_f = 0.18 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 0.83 (t, ^3J = 7.1 Hz, 3H, CH$_2$CH$_3$), 2.17–2.51 (m, 4H, NCHCH$_2$, CH$_2$CHCO$_2$Et), 3.45 (tt, ^3J = 12.2, ^3J = 3.5 Hz, 1H, CH$_2$CHCH$_2$), 3.90 (q, ^3J = 7.1 Hz, 2H, CH$_2$CH$_3$), 4.09 (dd, ^3J = 11.1, ^3J = 2.6 Hz, 1H, NCHCO$_2$Et), 4.64 (dd, ^3J = 11.0, ^3J = 2.4 Hz, 1H, NCHC$_{Ind}$), 6.96–7.11 (m, 4H, CH$_{Ar}$), 7.20–7.24 (m, 2H, CH$_{Ar}$), 7.34 (s, 1H, CH$_{Ar}$), 7.40 (d, ^3J = 8.6 Hz, 1H, CH$_{Ar}$), 7.72 (s, 1H, CH$_{Ar}$), 7.98 (d, ^3J = 10.3 Hz, 3H, CH$_{Ar}$), 10.08 (sbr, 1H, NH), 10.30 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.3 (+, CH$_2$CH$_3$), 33.7 (+, CH$_2$CHCH$_2$), 38.0 (–, CHCH$_2$), 42.2 (–, CHCH$_2$), 60.8 (–, CH$_2$CH$_3$), 61.0 (+, NCHC$_{Ind}$), 69.1 (+, NCHCO$_2$Et), 113.6 (+, CH$_{Ar}$), 113.8 (+, CH$_{Ar}$), 118.1 (C$_q$, 2 × C$_{Ar}$), 118.9 (+, CH$_{Ar}$), 120.3 (+, CH$_{Ar}$), 122.1 (+, CH$_{Ar}$), 122.3 (+, CH$_{Ar}$), 123.4 (+, CH$_{Ar}$), 124.7 (C$_q$, C$_{Ar}$), 124.8 (C$_q$, C$_{Ar}$), 126.2 (+, CH$_{Ar}$), 128.4 (C$_q$, C$_{Ar}$), 128.8 (+, 2 × CH$_{Ar}$), 128.8 (C$_q$, C$_{Ar}$), 129.6 (+, 2 × CH$_{Ar}$), 130.7 (C$_q$, C$_{Ar}$), 136.2 (C$_q$, C$_{Ar}$), 136.3 (C$_q$, C$_{Ar}$), 150.9 (C$_q$, C$_{Ar}$), 172.8 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3292, 2925, 1727, 1662, 1459, 1381, 1222, 1144, 1093, 1011, 981, 893, 851, 796, 757, 671, 625, 425 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 566 (9) [*M*+H]$^+$, 133 (100), 109 (29), 107 (25), 105 (27), 97 (32), 95 (50), 93 (27), 91 (41), 83 (46), 81 (55); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{35}Cl_3$ [*M*+H]$^+$: 566.1163; found: 566.1162.

*Ethyl 4,6-bis(5-chloro-1H-indol-3-yl)-1-(4-bromophenyl)-piperidine-2-carboxylate (**5gi**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-bromophenyl)imino)acetate (**4i**, 25.6 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5gi** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions cat-(*R*): F1: 28.5 mg, 46.6 µmol, 47%, F2: 9.40 mg, 15.4 µmol, 15%; cat-(*S*): F1: 21.4 mg, 35.0 µmol, 35%, F2: 25.2 mg, 41.2 µmol, 41%).

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 39.0 mg, 0.219 mmol, 1.80 Equiv.) and ethyl 2-((4-bromophenyl)imino)acetate (**4i**, 21.4 mg, 0.121 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5gi** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil in two fractions (F1: 26.3 mg, 43.0 µmol, 41%; F2: 14.7 mg, 24.0 µmol, 23%).

fraction 1 (F1): R_f = 0.39 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.27 (t, ^3J = 7.0 Hz, 3H, CH$_2$CH$_3$), 2.19 (q, ^3J = 12.5 Hz, 1H, NCHCHH), 2.39–2.49 (m, 2H, CHHCHCO$_2$Et, NCHCHH), 2.67 (dq, ^3J =13.2, ^4J = 2.5 Hz, 1H, CHHCHCO$_2$Et), 3.28 (tt, ^3J = 12.6, ^3J = 3.0 Hz, 1H, CH$_2$CHCH$_2$), 4.04–4.16 (m, 1H, CHHCH$_3$), 4.19–4.29 (m, 1H, CHHCH$_3$), 4.84 (dd, ^3J = 5.5, ^3J = 2.3 Hz, 1H, NCHCO$_2$Et), 5.53 (dd, ^3J = 11.3, ^3J = 3.6 Hz, 1H, NCHC$_{Ind}$), 6.96 (dd, ^3J = 8.6, ^3J = 2.1 Hz, 1H, CH$_{Ar}$), 7.05–7.20 (m, 5H, CH$_{Ar}$), 7.25 (d, ^3J = 8.8 Hz, 2H, CH$_{Ar}$), 7.33 (d, ^3J = 2.4 Hz, 1H, CH$_{Ar}$), 7.40 (d, ^3J = 8.6 Hz, 1H, CH$_{Ar}$), 7.61 (d, ^3J = 1.9 Hz, 1H, CH$_{Ar}$), 7.91 (d, ^3J = 2.4 Hz, 1H, CH$_{Ar}$), 10.13 (sbr, 1H, NH), 10.24 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.7 (+, CH$_2$CH$_3$), 27.5 (+, CH$_2$CHCH$_2$), 36.6 (–, CHCH$_2$), 42.8 (–, CHCH$_2$), 52.9 (+, NCHC$_{Ind}$), 60.9 (–, CH$_2$CH$_3$), 65.4 (+, NCHCO$_2$Et), 113.5 (+, CH$_{Ar}$), 113.7 (+, CH$_{Ar}$), 114.6 (C$_q$, C$_{Ar}$), 118.6 (+, CH$_{Ar}$), 119.1 (C$_q$, C$_{Ar}$), 120.0 (C$_q$, C$_{Ar}$), 120.2 (+, CH$_{Ar}$), 122.0 (+, CH$_{Ar}$), 122.2 (+, CH$_{Ar}$), 123.1 (+, CH$_{Ar}$), 124.6 (C$_q$, C$_{Ar}$), 124.7 (C$_q$, C$_{Ar}$), 125.9 (+, CH$_{Ar}$), 127.4 (+, 2 × CH$_{Ar}$), 127.6 (C$_q$, C$_{Ar}$), 128.7 (C$_q$, C$_{Ar}$), 131.1 (+, 2 × CH$_{Ar}$), 136.1 (C$_q$, C$_{Ar}$), 136.2 (C$_q$, C$_{Ar}$), 151.1 (C$_q$, C$_{Ar}$), 173.2 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3360, 2926, 1695, 1586, 1487, 1461, 1369, 1247, 1177, 1098, 1023, 892, 862, 823, 795, 754, 651, 587, 564, 477, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 610 (5) [*M*+H]$^+$, 133 (67), 123 (32), 119 (32), 111 (30), 109 (55), 107 (37), 105 (41), 97 (61), 95 (91), 93 (44), 91 (51), 85 (38), 83 (83), 81 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{79}Br^{35}Cl_2$ [*M*+H]$^+$: 610.0658; found: 610.0660.

fraction 2 (F2): R_f = 0.22 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d$_6$, 25 °C, TMS): δ = 1.00 (t, ^3J = 7.1 Hz, 3H, CH$_2$CH$_3$), 2.17–2.50 (m, 4H, NCHCH$_2$, CH$_2$CHCO$_2$Et), 3.46 (tt, ^3J = 11.9, ^3J = 3.6 Hz, 1H, CH$_2$CHCH$_2$), 3.91 (q, ^3J = 7.1 Hz, 2H, CH$_2$CH$_3$), 4.11 (dd, ^3J = 11.0, ^3J = 2.9 Hz, 1H, NCHCO$_2$Et), 4.66 (dd, ^3J = 10.8, ^3J = 3.1 Hz, 1H, NCHC$_{Ind}$), 7.00 (dd, ^3J = 8.6, ^3J = 2.0 Hz, 1H, CH$_{Ar}$), 7.08 (dd, ^3J = 8.6, ^3J = 2.0 Hz, 1H, CH$_{Ar}$), 7.13–7.28 (m, 6H, CH$_{Ar}$), 7.34 (d, ^3J = 2.2 Hz, 1H, CH$_{Ar}$), 7.40 (d, ^3J = 8.7 Hz, 1H, CH$_{Ar}$), 7.72 (d, ^3J = 1.9 Hz, 1H, CH$_{Ar}$), 7.99 (d, ^3J = 1.9 Hz, 1H, CH$_{Ar}$), 10.06 (sbr, 1H, NH), 10.27 (sbr, 1H, NH) ppm; ^{13}C NMR (100 MHz, acetone-d$_6$, 25 °C, TMS): δ = 14.2 (+, CH$_2$CH$_3$), 27.4 (+, CH$_2$CHCH$_2$), 33.5 (–, CHCH$_2$), 37.7 (–, CHCH$_2$), 42.2 (+, NCHC$_{Ind}$), 60.8 (–, CH$_2$CH$_3$), 68.9 (+, NCHCO$_2$Et), 113.5 (+, CH$_{Ar}$), 113.7 (+, CH$_{Ar}$), 118.0 (C$_q$, C$_{Ar}$), 118.5 (C$_q$, C$_{Ar}$), 118.8 (+, CH$_{Ar}$), 120.1 (C$_q$, C$_{Ar}$), 120.2 (+, CH$_{Ar}$), 122.0 (+, CH$_{Ar}$), 122.2 (+, CH$_{Ar}$), 123.3 (+, CH$_{Ar}$), 124.6 (C$_q$, C$_{Ar}$), 124.8 (C$_q$, C$_{Ar}$), 126.1 (+, CH$_{Ar}$), 128.3 (C$_q$, C$_{Ar}$), 128.7 (C$_q$, C$_{Ar}$), 129.8 (+, 2 × CH$_{Ar}$), 131.8 (+, 2 × CH$_{Ar}$), 136.0 (C$_q$, C$_{Ar}$), 136.2 (C$_q$, C$_{Ar}$), 151.3 (C$_q$, C$_{Ar}$), 172.7 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3292, 2924, 1725, 1697, 1661, 1484, 1461, 1384, 1245, 1176, 1095, 1031, 1008, 893, 858, 795, 755, 718, 658, 621, 539, 476, 423 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 610 (8) [*M*+H]$^+$, 154 (37), 147 (52), 137 (34), 136 (41), 133 (43), 123 (34), 121 (30), 119 (30), 111 (34), 109 (59), 107 (43), 105 (37), 97 (73), 95 (96), 93 (43), 91 (50), 85 (51), 83 (93), 81 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{27}O_2N_3{}^{79}Br^{35}Cl_2$ [*M*+H]$^+$: 610.0658; found: 610.0658.

*Ethyl (2S,4S,6S)-4,6-bis(5-chloro-1H-indol-3-yl)-1-(3,5-dichloro-4-hydroxyphenyl)–piperidine-2-carboxylate (**5gk**):* This compound was synthesized following the **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((3,5-dichloro-4-hydroxyphenyl)imino)acetate (**4k**, 26.2 mg, 0.100 mmol,

1.00 Equiv.) in 3.0 mL dichloromethane. The product **5gk** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 24.1 mg, 39.0 µmol, 39%; cat-(*S*): 28.9 mg, 46.8 µmol, 47%)

The racemic compound was obtained following **GP C** with 5-chloro-3-vinylindole (**3g**, 35.5 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((3,5-dichloro-4-hydroxyphenyl)imino)acetate (**4k**, 26.2 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5gk** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (32.3 mg, 52.4 µmol, 48%).

R_f = 0.28 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.30 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.23 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.33–2.52 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.67 (dq, ^3J = 13.1, ^3J = 2.5 Hz, 1H, CH*H*CHCO$_2$Et), 3.27 (tt, ^3J = 12.5, ^3J = 2.9 Hz, 1H, CH_2CHCH_2), 4.07–4.18 (m, 1H, C*H*HCH$_3$), 4.22–4.33 (m, 1H, CH*H*CH$_3$), 4.76 (d, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.48 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.97 (dd, ^3J = 8.6, ^3J = 2.1 Hz, 1H, CH_{Ar}), 7.08 (dd, ^3J = 8.6, ^3J = 2.1 Hz, 1H, CH_{Ar}), 7.23–7.28 (m, 4H, CH_{Ar}), 7.40 (d, ^3J = 8.6 Hz, 1H, CH_{Ar}), 7.43 (d, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.61 (d, ^3J = 1.9 Hz, 1H, CH_{Ar}), 7.94 (d, ^3J = 1.9 Hz, 1H, CH_{Ar}), 8.13 (sbr, 1H, O*H*), 10.16 (sbr, 1H, N*H*), 10.24 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.6 (–, $CHCH_2$), 42.6 (–, $CHCH_2$), 53.3 (+, NCHC$_{Ind}$), 61.0 (–, CH_2CH_3), 65.6 (+, NCHCO$_2$Et), 113.5 (+, CH_{Ar}), 113.7 (+, CH_{Ar}), 118.6 (+, CH_{Ar}), 118.8 (C$_q$, C$_{Ar}$), 120.0 (C$_q$, C$_{Ar}$), 120.3 (+, CH_{Ar}), 121.3 (C$_q$, C$_{Ar}$), 122.1 (+, CH_{Ar}), 122.2 (+, CH_{Ar}), 123.1 (+, CH_{Ar}), 124.7 (C$_q$, C$_{Ar}$), 124.8 (C$_q$, C$_{Ar}$), 126.1 (+, CH_{Ar}), 126.3 (+, 2 × CH_{Ar}), 127.6 (C$_q$, C$_{Ar}$), 128.7 (C$_q$, C$_{Ar}$), 136.2 (C$_q$, C$_{Ar}$), 136.3 (C$_q$, C$_{Ar}$), 144.8 (C$_q$, C$_{Ar}$), 145.0 (C$_q$, 2 × C$_{Ar}$), 173.3 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3389, 2926, 1693, 1565, 1481, 1461, 1249, 1176, 1098, 1022, 939, 893, 859, 795, 750, 692, 587, 477, 422 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 616 (4) [*M*+H]$^+$, 165 (23), 154 (21), 136 (25), 133 (100), 109 (29), 107 (28), 105 (26), 97 (33), 95 (49), 93 (26), 91 (37), 85 (20), 83 (43), 81 (54); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{26}O_3N_3{}^{35}Cl_4$ [*M*+H]$^+$: 616.0723; found: 616.0721.

*Ethyl (2S,4S,6S)-4,6-bis(5-bromo-1H-indol-3-yl)-1-phenylpiperidine-2-carboxylate (**5ha**):* This compound was synthesized following the **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5ha** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (cat-(*R*): 4.62 mg, 7.43 µmol, 7.9%; cat-(*S*): 25.9 mg, 41.8 µmol, 42%).

The racemic compound was obtained following **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-(phenylimino)acetate (**4a**, 17.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5ha** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (41.4 mg, 66.6 µmol, 67%).

R_f = 0.45 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.25 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.19 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.38–2.48 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.64 (dd, ^3J = 13.2, ^4J = 2.6 Hz, 1H, CH*H*CHCO$_2$Et), 3.32 (tt, ^2J = 12.5, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 4.04–4.10 (m, 1H, C*H*HCH$_3$), 4.17–4.25 (m, 1H, CH*H*CH$_3$), 4.82 (dd, ^3J = 5.5, ^3J = 2.2 Hz, 1H, NC*H*CO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.69 (t, ^3J = 7.3 Hz, 1H, CH_{Ar}), 6.98 (t, ^3J = 7.9 Hz, 2H, CH_{Ar}), 7.07 (dd, ^3J = 7.9, ^4J = 1.8 Hz, 1H, CH_{Ar}), 7.16–7.23 (m, 4H, CH_{Ar}), 7.25 (d, ^4J = 2.1 Hz, 1H, CH_{Ar}), 7.28 (d, ^4J = 2.1 Hz, 1H, CH_{Ar}), 7.36 (d, ^3J = 8.6 Hz, 1H, CH_{Ar}), 7.77 (d, ^4J = 2.1 Hz, 1H, CH_{Ar}), 8.10 (d, ^4J = 2.1 Hz, 1H, CH_{Ar}), 10.08 (sbr, 1H, N*H*), 10.25 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.7 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.7 (–, $CHCH_2$), 43.0 (–, $CHCH_2$), 52.7 (+, NCHC$_{Ind}$), 60.7 (–, CH_2CH_3), 65.6 (+, NCHCO$_2$Et), 112.2 (C$_q$, *C*Br), 112.3 (C$_q$, *C*Br), 113.9 (+, CH_{Ar}), 114.2 (+, CH_{Ar}), 119.5 (C$_q$, C$_{Ar}$), 120.1 (C$_q$, C$_{Ar}$), 121.8 (+, CH_{Ar}), 122.5 (+, CH_{Ar}), 123.0 (+, CH_{Ar}), 123.4 (+, CH_{Ar}), 124.5 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 125.5 (+, 2 × CH_{Ar}), 125.6 (+, CH_{Ar}), 128.3 (+, 2 × CH_{Ar}), 128.5 (C$_q$, C$_{Ar}$), 129.4 (C$_q$, C$_{Ar}$), 136.4 (C$_q$, C$_{Ar}$), 136.5 (C$_q$, C$_{Ar}$), 151.7 (C$_q$, C$_{Ar}$), 173.5 (C$_q$, CO$_2$Et) ppm; IR (ATR): $\tilde{\nu}$ = 3413, 2923, 2852, 1720, 1596, 1492, 1457, 1370, 1245, 1219, 1176, 1094, 1021, 954, 933, 882, 793, 750, 695, 583, 563, 477, 420 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 623/622/621 (46/64/57) [*M*+H]$^+$, 594 (100); HRMS (FAB, 3-NBA): calcd for $C_{30}H_{28}O_2N_3{}^{79}Br_2$ [*M*+H]$^+$: 620.0543; found: 620.0543.

*Ethyl (2S,4S,6S)-4,6-bis(5-bromo-1H-indol-3-yl)-1-(4-tolyl)piperidine-2-carboxylate (**5hb**):* This compound was synthesized following the **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5hb** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 21.7 mg, 34.2 µmol, 34%; cat-(*S*): 15.2 mg, 24.0 µmol, 24%).

The racemic compound was obtained following **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-tolyl)imino)acetate (**4b**, 19.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5hb** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (17.4 mg, 27.5 µmol, 28%).

R_f = 0.35 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.26 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.06 (s, 3H, CH_3), 2.10–2.22 (m, 1H, NCHC*H*H), 2.38–2.48 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.62 (dq, ^3J = 13.2, ^3J = 2.5 Hz, 1H, CH*H*CHCO$_2$Et), 3.32 (tt, ^3J = 12.5, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 4.03–4.11 (m, 1H, C*H*HCH$_3$), 4.16–4.28 (m, 1H, CH*H*CH$_3$), 4.73 (dd, ^3J = 5.6, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.5 Hz, 1H, NC*H*C$_{Ind}$), 6.79 (d, ^3J = 8.2 Hz, 2H, CH_{Ar}), 7.06–7.13 (m, 3H, CH_{Ar}), 7.18–7.23 (m, 2H, CH_{Ar}), 7.25 (d, ^3J = 2.2 Hz, 1H, CH_{Ar}), 7.28 (d, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.36 (d, ^3J = 8.6 Hz, 1H, CH_{Ar}), 7.77 (d, ^3J = 1.8 Hz, 1H, CH_{Ar}), 8.12 (d, ^3J = 1.8 Hz, 1H, CH_{Ar}), 10.07 (sbr, 1H, N*H*), 10.25 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.8 (+, CH_2CH_3), 20.6 (+, CH_3), 27.5 (+, CH_2CHCH_2), 36.7 (–, $CHCH_2$), 43.1 (–, $CHCH_2$), 52.8 (+, NCHC$_{Ind}$), 60.6 (–, CH_2CH_3), 65.8 (+, NCHCO$_2$Et), 112.2 (C$_q$, C$_{Ar}$), 112.3 (C$_q$, C$_{Ar}$), 113.8 (+, CH_{Ar}), 114.2 (+, CH_{Ar}), 119.6 (C$_q$, C$_{Ar}$), 120.1 (C$_q$, C$_{Ar}$), 121.7 (+, CH_{Ar}), 122.9 (+, CH_{Ar}), 123.5 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 125.5 (+, 3 × CH_{Ar}),

128.6 (C_q, C_{Ar}), 129.0 (+, 2 × CH_{Ar}), 129.4 (C_q, C_{Ar}), 131.6 (C_q, C_{Ar}), 136.4 (C_q, C_{Ar}), 136.5 (C_q, C_{Ar}), 149.2 (C_q, C_{Ar}), 173.6 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3416, 2921, 2851, 1719, 1694, 1611, 1565, 1509, 1457, 1369, 1337, 1246, 1219, 1175, 1094, 1020, 955, 934, 882, 818, 792, 751, 719, 671, 582, 475, 419 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 636 (43) $[M+H]^+$, 429 (45), 192 (69), 133 (63), 118 (46), 95 (73), 89 (100); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{32}O_2N_3{}^{79}Br_2$ $[M+H]^+$: 636.0856; found: 636.0857.

*Ethyl (2S,4S,6S)-4,6-bis(5-bromo-1H-indol-3-yl)-1-(4-ethynylphenyl)piperidine-2-carboxylate (**5hc**):* This compound was synthesized following the **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-ethynylphenyl)imino)acetate (**4c**, 20.1 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5hc** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 36.5 mg, 56.6 µmol, 57%; cat-(*S*): 19.2 mg, 29.7 µmol, 30%).
The racemic compound was obtained following **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-ethynylphenyl)imino)acetate (**4c**, 20.1 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The crude product was purified by preparative TLC (cyclohexane/ethyl acetate = 3:1) to give **5hc** as a yellow oil (6.18 mg, 10.0 µmol, 10%).
R_f = 0.31 (cyclohexane/EtOAc 3:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.14 (t, ^3J = 7.0 Hz, 3H, CH_2CH_3), 2.05 (q, ^3J = 12.4 Hz, 1H, NCHC*H*H), 2.23–2.38 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.55 (dd, ^3J =13.3, ^4J = 2.7 Hz, 1H, CH*H*CHCO$_2$Et), 3.15 (tt, ^3J = 12.4, ^3J = 2.8 Hz, 1H, CH_2CHCH_2), 3.25 (s, 1H, C*H*), 3.94–3.99 (m, 1H, C*H*HCH$_3$), 4.08–4.14 (m, 1H, CH*H*CH$_3$), 4.80 (dd, ^3J = 5.5, ^3J = 2.3 Hz, 1H, NC*H*CO$_2$Et), 5.41 (dd, ^3J = 11.3, ^3J = 3.7 Hz, 1H, NC*H*C$_{Ind}$), 6.95–7.00 (m, 2H, CH_{Ar}), 7.02–7.12 (m, 6H, CH_{Ar}), 7.18 (d, ^3J = 2.4 Hz, 1H, CH_{Ar}), 7.23 (d, ^3J = 8.6 Hz, 1H, CH_{Ar}), 7.64 (d, ^3J = 1.8 Hz, 1H, CH_{Ar}), 7.92 (d, ^3J = 1.9 Hz, 1H, CH_{Ar}), 10.01 (sbr, 1H, N*H*), 10.12 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.8 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.5 (–, $CHCH_2$), 42.7 (–, $CHCH_2$), 52.9 (+, NCHC$_{Ind}$), 61.0 (–, CH_2CH_3), 65.1 (+, NCHCO$_2$Et), 77.5 (+, C*H*), 84.7 (C_q, *C*CH), 112.3 (C_q, C_{Ar}), 112.4 (C_q, C_{Ar}), 113.9 (+, CH_{Ar}), 114.2 (+, CH_{Ar}), 115.4 (+, CH_{Ar}), 119.1 (C_q, C_{Ar}), 119.9 (C_q, C_{Ar}), 121.7 (+, CH_{Ar}), 123.0 (+, CH_{Ar}), 123.2 (+, CH_{Ar}), 124.6 (+, CH_{Ar}), 124.7 (+, 2 × CH_{Ar}), 124.8 (C_q, C_{Ar}), 125.6 (+, CH_{Ar}), 128.3 (C_q, C_{Ar}), 129.4 (C_q, C_{Ar}), 132.1 (+, 2 × CH_{Ar}), 136.4 (C_q, C_{Ar}), 136.5 (C_q, C_{Ar}), 152.5 (C_q, C_{Ar}), 173.2 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3282, 2924, 2851, 2100, 1721, 1693, 1601, 1564, 1503, 1457, 1368, 1247, 1220, 1176, 1094, 1021, 933, 883, 835, 793, 752, 664, 582, 535, 476, 420 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 646 (15) $[M+H]^+$, 429 (17), 202 (39), 132 (100); HRMS (FAB, 3-NBA): calcd for $C_{32}H_{30}O_2N_3{}^{79}Br_2$ $[M+H]^+$: 646.0699; found: 646.0699.

*Ethyl (2S,4S,6S)-4,6-bis(5-bromo-1H-indol-3-yl)-1-(4-methoxyphenyl)piperidine-2-carboxylate (**5he**):* This compound was synthesized following the **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) in 3.0 mL dichloromethane. The product **5he** was obtained after column chromatography (cyclohexane/ethyl acetate = 2:1) as a yellow oil (cat-(*R*): 23.7 mg, 36.4 µmol, 36%; cat-(*S*): 18.4 mg, 28.3 µmol, 28%).
The racemic compound was obtained following **GP C** with 5-bromo-3-vinylindole (**3h**, 44.4 mg, 0.200 mmol, 2.00 Equiv.) and ethyl 2-((4-methoxyphenyl)imino)acetate (**4e**, 20.7 mg, 0.100 mmol, 1.00 Equiv.) without a catalyst in 3.0 mL dichloromethane. The product **5he** was obtained after column chromatography (cyclohexane/ethyl acetate = 3:1) as a yellow oil (14.9 mg, 22.9 µmol, 23%).
R_f = 0.33 (cyclohexane/EtOAc 2:1); ^{1}H NMR (400 MHz, acetone-d_6, 25 °C, TMS): δ = 1.26 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.18 (q, ^3J = 12.5 Hz, 1H, NCHC*H*H), 2.34–2.49 (m, 2H, C*H*HCHCO$_2$Et, NCHCH*H*), 2.59 (dq, ^3J = 13.1, ^3J = 2.5 Hz, 1H, CH*H*CHCO$_2$Et), 3.34 (tt, ^3J = 12.4, ^3J = 3.0 Hz, 1H, CH_2CHCH_2), 3.58 (s, 3H, OCH_3), 4.00–4.10 (m, 1H, C*H*HCH$_3$), 4.16–4.27 (m, 1H, CH*H*CH$_3$), 4.62 (dd, ^3J = 5.5, ^3J = 2.2 Hz, 1H, NC*H*CO$_2$Et), 5.61 (dd, ^3J = 11.3, ^3J = 3.4 Hz, 1H, NC*H*C$_{Ind}$), 6.51–6.58 (m, 2H, CH_{Ar}), 7.07 (dd, ^3J = 8.6, ^3J = 1.9 Hz, 1H, CH_{Ar}), 7.13–7.22 (m, 4H, CH_{Ar}), 7.26 (dd, ^3J = 6.5, ^3J = 2.2 Hz, 2H, CH_{Ar}), 7.36 (d, ^3J = 8.6 Hz, 1H, CH_{Ar}), 7.76 (d, ^3J = 1.8 Hz, 1H, CH_{Ar}), 8.12 (d, ^3J = 1.8 Hz, 1H, CH_{Ar}), 10.06 (sbr, 1H, N*H*), 10.25 (sbr, 1H, N*H*) ppm; ^{13}C NMR (100 MHz, acetone-d_6, 25 °C, TMS): δ = 14.8 (+, CH_2CH_3), 27.5 (+, CH_2CHCH_2), 36.8 (–, $CHCH_2$), 43.1 (–, $CHCH_2$), 53.0 (+, NCHC$_{Ind}$), 55.2 (+, OCH_3), 60.6 (–, CH_2CH_3), 66.0 (+, NCHCO$_2$Et), 112.2 (C_q, C_{Ar}), 112.3 (C_q, C_{Ar}), 113.6 (+, 2 × CH_{Ar}), 113.8 (+, CH_{Ar}), 114.2 (+, CH_{Ar}), 119.6 (C_q, C_{Ar}), 120.2 (C_q, C_{Ar}), 121.7 (+, CH_{Ar}), 122.9 (+, CH_{Ar}), 123.5 (+, CH_{Ar}), 124.4 (+, CH_{Ar}), 124.8 (+, CH_{Ar}), 125.6 (+, CH_{Ar}), 127.0 (+, 2 × CH_{Ar}), 128.6 (C_q, C_{Ar}), 129.4 (C_q, C_{Ar}), 136.4 (C_q, C_{Ar}), 136.5 (C_q, C_{Ar}), 144.7 (C_q, C_{Ar}), 155.8 (C_q, C_{Ar}), 173.7 (C_q, CO_2Et) ppm; IR (ATR): $\tilde{\nu}$ = 3413, 2923, 2851, 2549, 1703, 1506, 1457, 1370, 1337, 1239, 1175, 1095, 1032, 934, 883, 860, 828, 793, 752, 709, 671, 582, 481, 420 cm^{-1}; MS (FAB, 3-NBA): *m/z* (%): 651 (55), $[M]^+$, 429 (54), 208 (100); HRMS (FAB, 3-NBA): calcd for $C_{31}H_{29}O_3N_3{}^{79}Br_2$ $[M]^+$: 651.0555; found: 651.0553.

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Keywords: Bisindole • Heterocycles • Asymmetric • Organocatalytic • Cross Coupling • Click-reaction • Reduction

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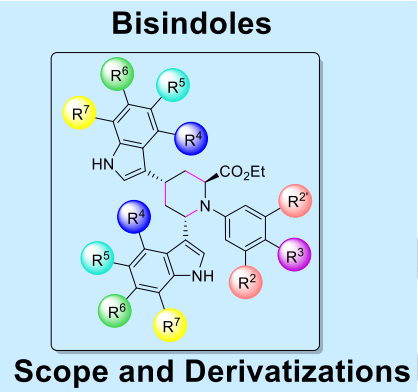
FULL PAPER

Various novel bisindole derivatives with different substitution patterns providing an easy access to a library of biological active compounds were synthesized. Electron withdrawing groups on the starting material led to the formation of Povarov-type structures. Furthermore we could successfully demonstrate that consecutive reactions like cross couplings, reductions or even click reactions on bisindoles are feasible.



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Asymmetric organocatalytic synthesis of Bisindoles – Scope and Derivatizations