JOC The Journal of Organic Chemistry

Article

Synthesis of Chiral Bis(3-indolyl)methanes Bearing a Trifluoromethylated All-Carbon Quaternary Stereocenter via Nickel-catalyzed Asymmetric Friedel-Crafts Alkylation Reaction

Wen-Jing Zhu, Jun-Fang Gong, and Mao-Ping Song

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00336 • Publication Date (Web): 06 Jul 2020

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Synthesis of Chiral Bis(3-indolyl)methanes Bearing a Trifluoromethylated All-Carbon Quaternary Stereocenter via Nickel-catalyzed Asymmetric Friedel-Crafts Alkylation Reaction

Wen-Jing Zhu, Jun-Fang Gong,* and Mao-Ping Song*

College of Chemistry, Henan Key Laboratory of Chemical Biology and Organic Chemistry, Green Catalysis Center, Zhengzhou University, Zhengzhou 450001, People's Republic of China

ABSTRACT: Bis(3-indolyl)methanes are well known natural products with a broad range of important biological functions including cancer cell growth inhibition and anti-microbial activity. Incorporation of a trifluoromethyl group is known to have a profound effect on the parent compound's biological activities. Here an efficient method for the synthesis of chiral trifluoromethylated bis(3-indolyl)methanes via a catalytic asymmetric Friedel-Crafts (F-C) alkylation reaction has been established. Both enantiomers of the catalysis products can be obtained by tuning the chiral substituents of the catalyst. With 5 mol% of the Ni(II)/(imidazoline-oxazoline) complex as the catalyst, the F-C reaction of indoles with *β*-CF_3-*β*-(3-indolyl)nitroalkenes proceeded well to afford a series of chiral bis(3-indolyl)methanes bearing a trifluoromethylated all-carbon quaternary stereocenter in generally good yields with excellent enantioselectivities (up to 98% yield and 94% *ee*). Furthermore, through interchanging the indole moieties of the two reactants, indole vs *β*-CF_3-*β*-(3-indolyl)nitroalkene in the F-C reaction, both enantiomers of a given

* Tel./Fax: (+86)-371-6776-3869. E-mail: gongjf@zzu.edu.cn (J.-F. Gong) or mpsong@zzu.edu.cn (M.-P. Song).

trifluoromethylated bis(3-indolyl)methane were obtained with high enantioselectivities (89-94% *ee*) upon removal of the indole *N*-protecting group in the F-C products. The current work represents the first general catalytic enantioselective approach to the important class of trifluoromethylated bis(3-indolyl)methanes.

INTRODUCTION

The heterocyclic bis(3-indolyl)methane (3,3′-BIM) compounds, in which two 3-indolyl units are joined together by a simple or a substituted methylene bridge, have been increasingly gaining research interests.[1] This is largely due to a number of studies reporting a broad range of biological functions for BIMs, including cancer cell growth inhibition,[2] anti-inflammation,[3] anti-fungal activity,[4] and regulation of cell differentiation.[5] BIMs have also been found able to act as colorimetric sensors.[6] These reported various biological activities apparently aroused from the differences in the structures of those functionally tested BIMs. Thus, design and synthesis of new BIM compounds particularly the new chiral BIMs are then imperative to understand and expand structural basis for the therapeutically important BIMs.

A number of strategies have been successfully developed for the synthesis of bis(3-indolyl)methanes.[1,7] Nonetheless, enantioselective approaches to the chiral BIMs are rather limited.[8,9] Among these reports, the catalytic asymmetric Friedel-Crafts (F-C) alkylation reaction[10] especially organo-catalyzed F-C reaction accounts for the dominant approach. Thus, in the presence of chiral phosphoric acids[8a,d,f] or chiral imidodiphosphoric acids[8b,c,e] as the catalysts, several indole-containing electrophiles including (3-indolyl)methanamines,[8a] trimethylsilyl-protected 3-arylindolylmethanols,[8b]

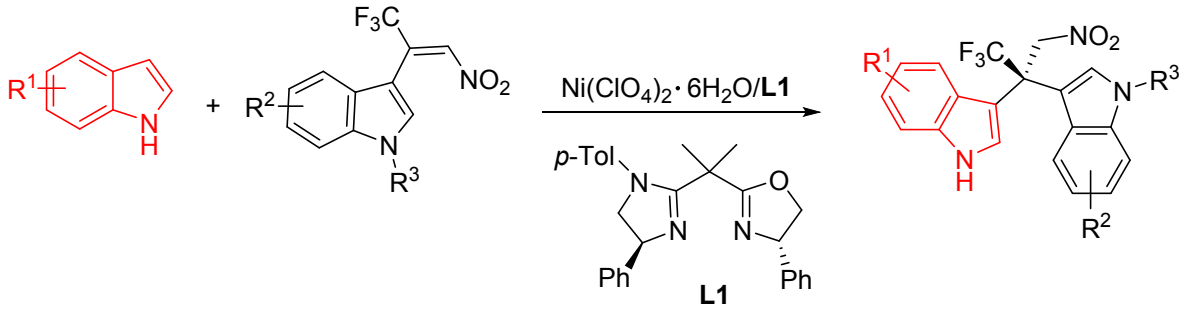
3-hydroxy-indolyloxindoles,[8c] 3-vinylindoles[8d,e] as well as 3-indolylsulfamidates[8f] reacted smoothly with indoles to give structurally diverse chiral BIMs in generally high yields with good to excellent enantioselectivities.

On the other hand, it has been reported that organic compounds bearing a trifluoromethylated tertiary or quaternary stereogenic carbon center play a unique and significant role in pharmaceutical, agochemical and materials sciences.[11] In particular, introduction of a trifluoromethylated stereogenic carbon center has a profound effect on the biological activities of the parent compounds. Therefore, chiral trifluoromethylated bis(3-indolyl)methanes[12] containing a trifluoromethylated carbon stereocenter may have novel and interesting biological functions, and it is highly desirable to develop efficient methods for the synthesis of these compounds.

We have previously demonstrated that Co(II), complexed with chiral hybrid (imidazoline-oxazoline) ligand derived from 2,2-dimethylmalonic acid, was an effective and highly stereoselective catalyst for enantioselective Michael addition of 2-acetyl azaarenes to β-CF_3-β-aryl(indole) nitroalkenes.[13] In view of the high efficiency of the (imidazoline-oxazoline) ligand in the above Co-catalyzed enantioselective transformations, we expected that this type of ligand could also perform well in asymmetric Friedel-Crafts alkylation reaction involving β-CF_3-β-disubstituted nitroalkenes. In the current report, we extended our previous work by using chiral Ni(II)/(imidazoline–oxazoline) complex to catalyze asymmetric F-C reaction of indoles with β-CF_3-β-(3-indolyl)nitroalkenes (Scheme 1).[14] A variety of chiral trifluoromethylated bis(3-indolyl)methanes bearing a trifluoromethylated all-carbon quaternary stereocenter were thus obtained in high yields

and enantioselectivities. The current work represents the first example of synthesis of biologically relevant chiral trifluoromethylated BIMs. In addition, we found that upon removal of the indole *N*-protecting group (R^3) in the F-C products, both enantiomers of a given trifluoromethylated bis(3-indolyl)methane could be generated with high enantioselectivities.

Scheme 1. Ni-catalyzed Asymmetric Friedel-Crafts Alkylation Reaction of Indoles with *β*-CF_3-*β*-(3-indolyl)nitroalkenes



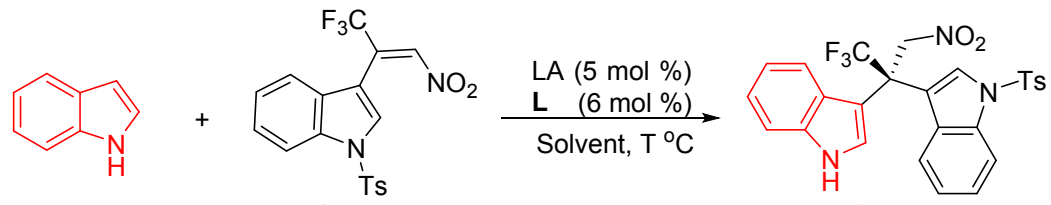
RESULTS AND DISCUSSION

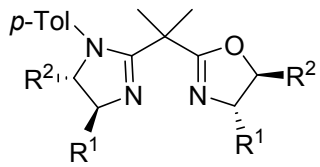
We began our investigations by choosing indole **1a** and the *N*-Ts-protected *β*-CF_3-*β*-(3-indolyl)nitroalkene **2a** as reactants for the F-C reaction (Table 1). The reaction of **2a** with 1.5 equivalent of **1a** was first carried out in the presence of 5 mol% of $Ni(ClO_4)_2·6H_2O$ and 6 mol% of chiral imidazoline-oxazoline ligand **L1** in toluene at 80 °C for 12 h. Under the above stated conditions the reaction proceeded efficiently to produce the expected trifluoromethylated bis(3-indolyl)methane **3aa** in a 97% yield with 90% *ee* (entry 1). In the absence of ligand **L1** the product **3aa** was not detected which suggested the crucial role of the ligand for the reaction (entry 2). Then potential of the other three Lewis acids was examined. It was found that the use of $Ni(OTf)_2$, $Zn(OTf)_2$ or $Zn(ClO_4)_2·6H_2O$ as Lewis acid resulted in marked decrease in both yield and enantioselectivity of **3aa** (8–34

yields with 48–77% *ee*, entries 3–5). Subsequently, the reaction temperature was optimized. Elevating temperature to 90 °C was detrimental to the enantioselectivity though an excellent yield could still be achieved (entry 6). In contrast, lowering temperature to 70 °C was beneficial for the enantioselectivity which improved from 90% *ee* to 92% *ee* while the yield dropped noticeably from 97% to 70% (entry 7). Further lowering the temperature to 60 °C did not lead to a further improvement in enantioselectivity and the yield decreased drastically to 28% (entry 8). Therefore, 70 °C was considered to be an appropriate reaction temperature. At the temperature of 70 °C, a yield of 90% or above could be obtained when the concentration of substrate **2a** was changed from 0.1 M (mol/L) to 0.2 M (entry 9) or 0.13 M (entry 10). Unfortunately, the enantioselectivity reduced to 88% *ee*. We also tested reactions in different solvents and found toluene to be an optimal solvent and superior to at least DCE and CH_3CN (entries 11 and 12). Changing the ratio of **1a** and **2a** from 1.5:1 to 1:1 did not give better results, either (entry 13). Gratifyingly, a length of 24 hours appeared to be sufficient to provide the optimal yield and enantioselectivity (93% yield with 92% *ee*, entry 14 vs 7). Thus, under the conditions as shown in entry 14 the performance of the other chiral ligands **L2–L9** was investigated and compared. The ligands **L2-L4**, which are the same type as ligand **L1**, gave **3aa** in much lower yields and/or enantioselectivity (entries 15-17). Interestingly, in the presence of the ligands **L2** and **L3** the major enantiomer of the product **3aa** possesses the *opposite* absolute configuration to that obtained with ligand **L1**. In particular, the ligand **L2** containing additional phenyl groups afforded a promising enantioselectivity of 82% though the yield was somewhat moderate (entry 15). The structurally very related four bis(oxazoline) ligands **L5-L8** also showed

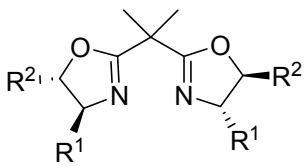
inferior stereocontrol compared with ligand **L1** (entries 18-21). Among them, good enantioselectivity could be achieved with ligands **L5** and **L6**. Ligands **L5**, **L7** and **L8** behaved similarly to their corresponding analogues **L1**, **L3** and **L4**. By contrast, ligand **L6** performed very differently from its analogue **L2** (entry 19 vs 15). In the presence of ligand **L6** the major enantiomer of **3aa** has the *opposite* absolute configuration to that obtained with ligand **L2**. In addition, in the presence of the bis(imidazoline) ligand **L9** the reaction did not occur (entry 22). Therefore, the ligand **L1** was ideal for the catalysis. Importantly, when the reaction was conducted under air, **3aa** was produced without any loss of enantioselectivity though the yield showed somewhat decrease (entry 23 vs 14). This result indicates that the synthesis of chiral trifluoromethylated bis(3-indoyl)methanes via Ni(II)-(imidazoline-oxazoline) complex-catalyzed Friedel-Crafts reaction can be carried out without the need for strictly exclusion of air.

Table 1. Optimization of Reaction Conditions[a]

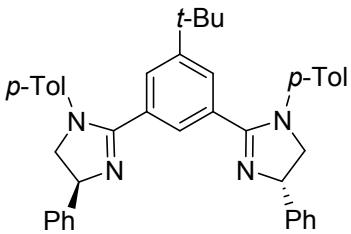




L1 R^1 = Ph, R^2 = H
L2 R^1 = R^2 = Ph
L3 R^1 = Bn, R^2 = H
L4 R^1 = *t*-Bu, R^2 = H



L5 R^1 = Ph, R^2 = H
L6 R^1 = R^2 = Ph
L7 R^1 = Bn, R^2 = H
L8 R^1 = *t*-Bu, R^2 = H



L9

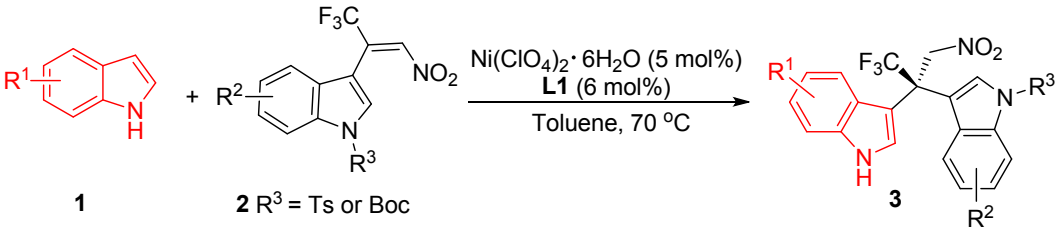
entry	**L**	LA	solvent	*T* (°C)	time (h)	yield[b] (%)	*ee*[c,d] (%)
1	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	80	12	97	90
2	/	$Ni(ClO_4)_2·6H_2O$	Toluene	80	12	n.d.	--
3	**L1**	$Ni(OTf)_2$	Toluene	80	12	17	60
4	**L1**	$Zn(OTf)_2$	Toluene	80	12	8	48
5	**L1**	$Zn(ClO_4)_2·6H_2O$	Toluene	80	12	34	77
6	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	90	12	98	88
7	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	12	70	92
8	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	60	12	28	87
9[e]	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	12	90	88
10[f]	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	12	92	88
11	**L1**	$Ni(ClO_4)_2·6H_2O$	DCE	70	12	13	76
12	**L1**	$Ni(ClO_4)_2·6H_2O$	CH_3CN	70	12	trace	--
13[g]	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	12	53	90
14	**L1**	**$Ni(ClO_4)_2·6H_2O$**	**Toluene**	**70**	**24**	**93**	**92**
15	**L2**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	48	-82
16	**L3**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	63	-22
17	**L4**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	trace	8
18	**L5**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	96	89
19	**L6**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	69	85
20	**L7**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	61	-18
21	**L8**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	15	6
22	**L9**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	n.d.	--
23[h]	**L1**	$Ni(ClO_4)_2·6H_2O$	Toluene	70	24	81	92

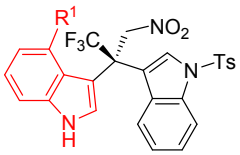
[a]Reaction conditions unless noted otherwise: **1a** (0.3 mmol), **2a** (0.2 mmol), Lewis acid (LA) (5 mol%), **L** (6 mol%), solvent (2.0 mL), T °C, Ar. [b]Isolated yield. n.d.: Not detected. [c]Determined by chiral HPLC. [d]The absolute configuration of **3ja** was determined to be *R* according to the X-ray crystal diffraction analysis (vide infra). That of **3aa** was assigned to be *R* by analogy. [e]Toluene (1.0 mL). [f]Toluene (1.5 mL). [g]**1a**:**2a** = 1:1. [h]Under air.

Upon the optimized reaction conditions being determined as described above (Table 1, entry 14), we next investigated the scope of indole and nitroalkene substrates. As shown in Scheme 2, a list of substituted indoles **1b-1l** were used in the F-C reaction to react with the *N*-Ts-protected nitroalkene **2a**, resulting in chiral trifluoromethylated BIM derivatives **3ba-3la** with diverse structures in generally good yields with good to excellent enantioselectivities (81-93% *ee*). It appears that both the reactivity (yield) and the enantioselectivity are affected by the position and electronic property of the substituent on the indole. In the case of 4-F substituted indole **1b**, the reactivity and stereoselectivity reduced apparently which might be likely due to the strong electron-withdrawing property of the fluorine and steric hindrance at the 4-position. In other cases, a reaction time longer than 24 h was usually necessary to ensure good yields, indicating that the reactivity of **1c-1l** was also lower than indole **1a**. In comparison with indoles containing an electron-withdrawing group such as F, Cl and Br, indoles with electron-donating group such as Me and OMe exhibited obviously higher reactivity. On the other hand, a clear trend for the effect of the substituent on the reaction enantioselectivities could not be obtained. Besides the *N*-Ts-protected nitroalkene **2a**, the *N*-Boc-protected nitroalkene **2a′** was also a suitable reactant for the current F-C reaction though it was unreactive in the related

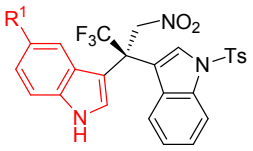
Co(II)-catalyzed Michael addition.[13b] The reactions of **2a′** with indole **1a** and indoles containing electron-donating group at 5-, 6- and 7-positions proceeded equally well to afford the corresponding chiral BIMs (**3aa′-3la′**) with a C-CF_3 stereogenic center in good yields with high enantioselectivities (84-94% *ee*). Roughly, the reaction yields were lower than those with the *N*-Ts-protected nitroalkene **2a** while the enantioselectivities were slightly higher instead. Unfortunately, the indole with electron-withdrawing group such as 5-F reacted poorly with *N*-Boc-protected nitroalkene **2a′** and only trace amount of the product **3ca′** was formed.

Scheme 2. Substrate Scope of the Reaction[a]

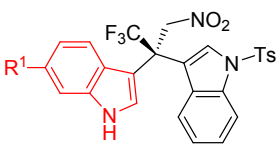




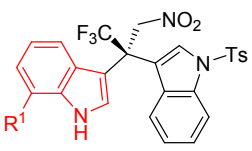
3aa R^1 = H, 93%, 92% *ee*[b]
3ba R^1 = F, 69%, 88% *ee*[c]



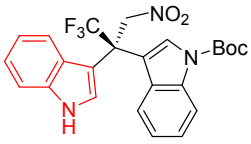
3ca R^1 = F, 69%, 91% *ee*[c]
3da R^1 = Cl, 87%, 93% *ee*[c]
3ea R^1 = Br, 75%, 92% *ee*
3fa R^1 = Me, 95%, 90% *ee*
3ga R^1 = OMe, 94%, 89% *ee*



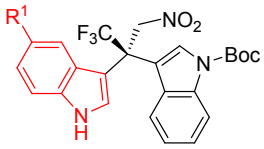
3ha R^1 = Cl, 58%, 83% *ee*
3ia R^1 = Me, 91%, 90% *ee*
3ja R^1 = OMe, 90%, 88% *ee*[b]



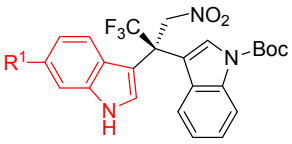
3ka R^1 = Me, 85%, 81% *ee*
3la R^1 = OMe, 63%, 93% *ee*



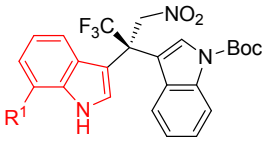
3aa' 74%, 91% *ee*[b]



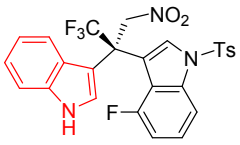
3ca' R^1 = F, trace[d]
3fa' R^1 = Me, 88%, 94% *ee*[b]
3ga' R^1 = OMe, 86%, 93% *ee*



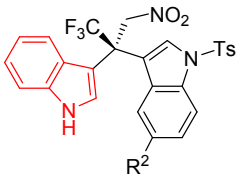
3ia' R^1 = Me, 80%, 93% *ee*
3ja' R^1 = OMe, 82%, 91% *ee*[b]



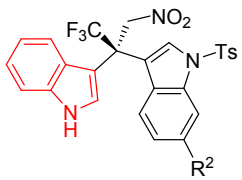
3ka' R^1 = Me, 75%, 84% *ee*
3la' R^1 = OMe, 41%, 93% *ee*



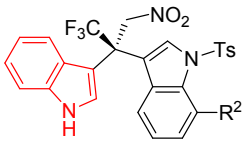
3ab 66%, 93% *ee*[e]



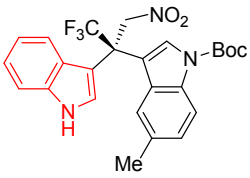
3ac R^2 = F, 68%, 89% *ee*[e]
3ae R^2 = Br, 74%, 87% *ee*[c]
3af R^2 = Me, 89%, 86% *ee*[c]
3ag R^2 = OMe, 91%, 92% *ee*[c]
3am R^2 = CO_2Me, 98%, 92% *ee*[e]



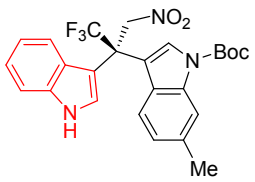
3ai R^2 = Me, 96%, 94% *ee*[e]
3ai R^2 = Me, 84%, 94% *ee*[f]



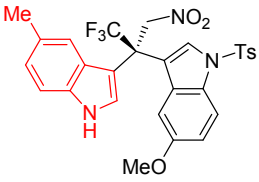
3ak R^2 = Me, 93%, 93% *ee*[e]
3al R^2 = OMe, 87%, 93% *ee*[e]



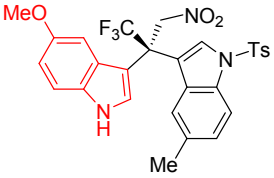
3af' 14%, 90% *ee*[e]



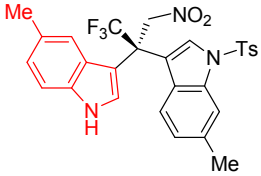
3ai' 20%, 82% *ee*[e]



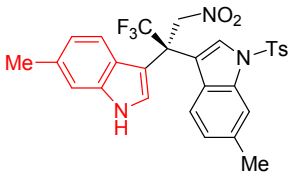
3fg 92%, 90% *ee*[e]



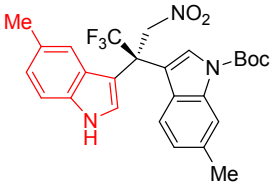
3gf 68%, 85% *ee*[e]



3fi 97%, 91% *ee*[c]



3ii 93%, 92% *ee*[c]



3fi' 40%, 90% *ee*[e]

[a]Reaction conditions: **1** (0.3 mmol), **2** (0.2 mmol), $Ni(ClO_4)_2·6H_2O$ (5 mol%), **L1** (6 mol%), toluene (2.0 mL), Ar, 70 °C for 36 h. Yields are of the isolated products. The *ee* values were determined by chiral HPLC. The absolute configurations of the products **3** were assigned to be *R* by analogy based on the X-ray crystal diffraction analysis of **3ja**. [b]For 24 h. [c]For 48 h. [d]For 72 h. [e]For 60 h. [f]**1a** (6.0 mmol), **2i** (4.0 mmol), $Ni(ClO_4)_2·6H_2O$ (5 mol%), **L1** (6 mol%), toluene (40.0 mL), Ar, 70 °C for 84 h.

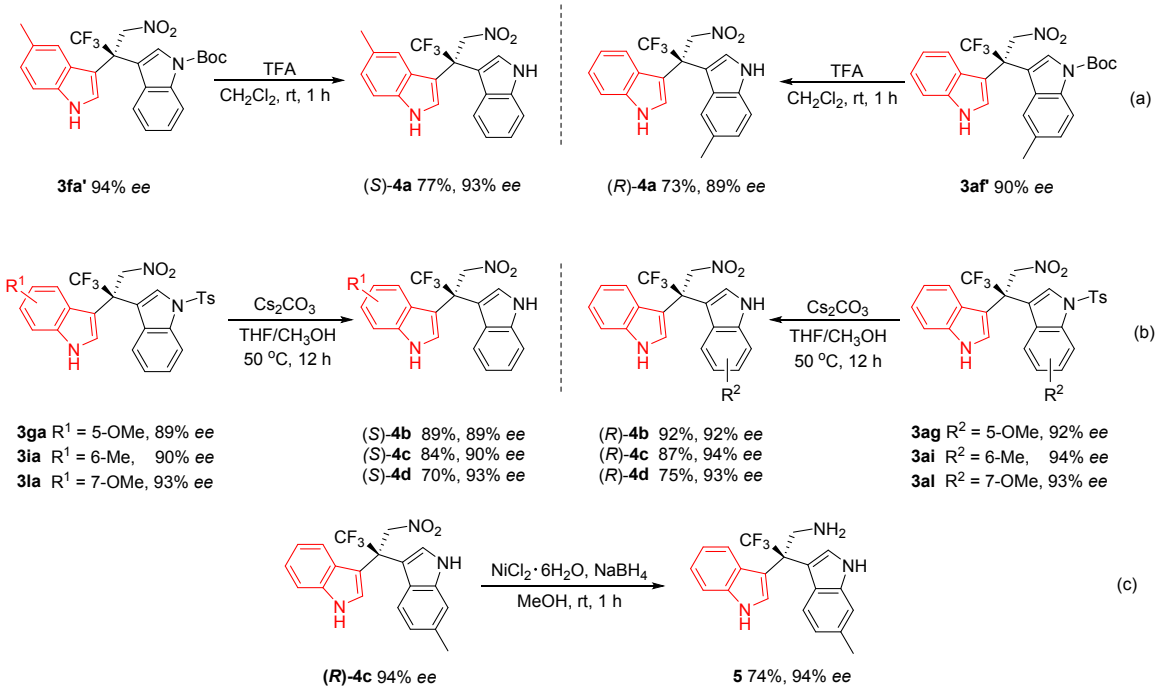
A wide range of substituted nitroalkenes were also tested under the optimal reaction conditions (Scheme 2). The *N*-Ts-protected nitroalkenes **2b-2l** with various substituents on the indole ring were well tolerated, giving the desired chiral trifluoromethylated BIMs **3ab-3al** in 66-98% yields with 86-94% *ee*. The substituents include electron-withdrawing groups (F, Br and COOMe) and electron-donating group (Me and OMe) at 4-, 5-, 6- or 7-position of indole ring. For the reactions of *N*-Boc-protected nitroalkenes **2f′** and **2i′** bearing 5- or 6-Me on the indole ring with indole **1a**, good to excellent enantioselectivities (**3af′** and **3ai′**, 90% and 82% *ee*, respectively) were obtained. However, the yields were rather low (< 20%). Notably, good results could still be achieved when both indole and the *N*-Ts-protected nitroalkene were substituted with electron-donating group such as Me and OMe (**3fg**, **3gf**, **3fi** and **3ii**, 68-97% yields with 85-92% *ee*). Lastly, 5-Me indole **1f** was subjected to the reaction with *N*-Boc-protected nitroalkene **2i′**, which afforded the product **3fi′** in 40% yield with 90% *ee*. Overall, the *N*-Boc-protected nitroalkenes exhibited lower reactivity than the corresponding *N*-Ts-protected nitroalkenes especially when they contained substituent on the indole ring.

From the above investigations it can be seen that the current method tolerates various substituents which are located at 4-, 5-, 6- or 7-position of indole ring in both the indole and the nitroalkene, providing a series of chiral trifluoromethylated BIMs with structural diversity. In particular, some substituents such as F, Cl, Br and COOMe in the obtained BIM compounds can be easily utilized for further transformations to produce more new trifluoromethylated BIMs.

To further explore the practical potential of the method established above, the synthesis reaction for the chiral CF_3-containing BIM **3ai** from indole **1a** and the nitroalkene **2i** was carried out at a gram-scale level under the optimal conditions with a reaction time of 84 h (Scheme 2). The target product **3ai** was isolated in a yield of 84% (1.81g) without any loss of enantioselectivity (94% *ee*).

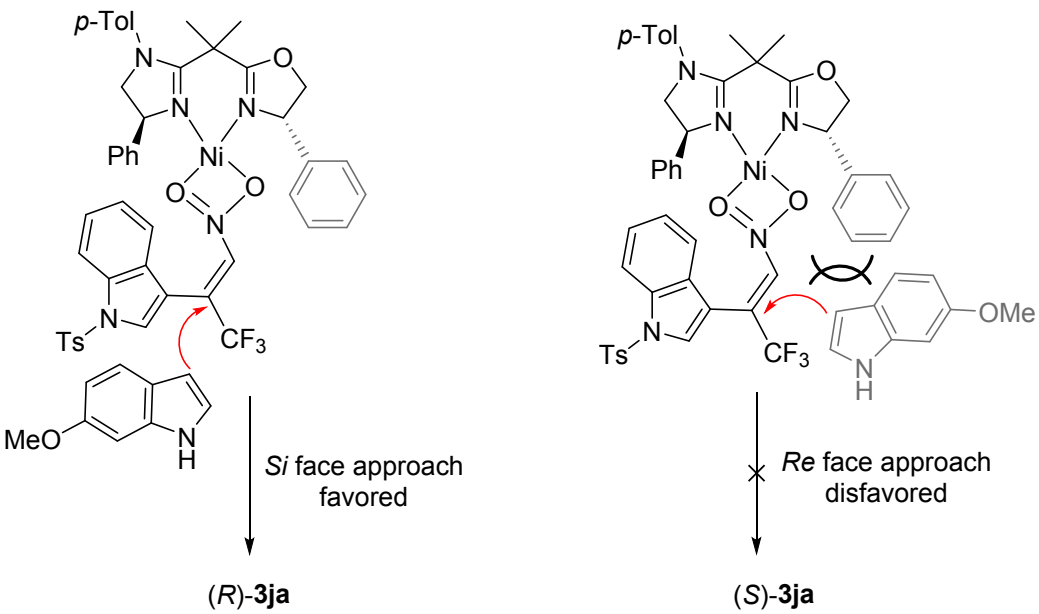
Besides the gram scale synthesis, we next conducted a series of transformation reactions of the F-C products (Scheme 3). First, under a strong acidic condition, the *N*-Boc protecting group in the product **3fa′** was successfully removed according to previously reported method,[15] giving the corresponding product **(*S*)-4a** in 77% yield with 93% *ee* (Scheme 3a). Similarly, removal of the Boc group in the product **3af′** afforded **(*R*)-4a**, the enantiomer of **(*S*)-4a** (Scheme 3a). Subsequently, three additional pairs of enantiomeric trifluoromethylated BIMs **4b-4d** were obtained by removing the *N*-Ts protecting group in the products **3** in the presence of cesium carbonate as previously reported (Scheme 3b).[13b,16] In all cases, the corresponding enantiomers **4** were prepared in good yields without loss of enantioselectivity. Furthermore, as shown in Scheme 3c, the NO_2 group of **(*R*)-4c** was readily reduced to NH_2 by $NaBH_4/NiCl_2{\cdot}6H_2O$ in methanol at room temperature. The expected tryptamine derivative **5** was obtained in a yield of 74% with an enantioselectivity of 94% *ee*.

Scheme 3. Transformations of the Products 3



The absolute configurations of the F-C reaction product **3ja** and the transformed product **4a** from **3fa'** were determined by X-ray crystallographic analysis to be *R* and *S*, respectively (see Figures S1 and S2 in the Supporting Information). Based on the stereochemical outcomes and the previously reported studies,[14a] one possible pathway for the formation of (*R*)-**3** was then proposed accordingly. As depicted in Scheme 4, the imidazoline-oxazoline ligand **L1** first coordinates to the Ni(II) center in a *N*,*N*-bidentate fashion, thereby generating a chiral Ni(II) complex that in turn acts as an efficient Lewis acid catalyst. Next, 1,3-binding of the nitroalkene **2a** to the Ni(II) catalyst through NO_2 group results in activation of the nitroalkene. To avoid unfavorable steric repulsions between the indole **1j** and the phenyl group of chiral ligand **L1**, the *Si*-face attacking of the indole **1j** at the *β*-position of the nitroalkene occurs preferentially, whereby the (*R*)-isomer of **3ja** is formed.

Scheme 4. Possible Stereochemical Pathway



CONCLUSION

In summary, we have developed a highly enantioselective Friedel-Crafts alkylation reaction of indoles with β-CF_3-β-(3-indolyl)nitroalkenes catalyzed by a Ni(II)/(imidazoline-oxazoline) complex. A series of bis(3-indolyl)methane derivatives containing a trifluoromethylated all-carbon quaternary stereocenter have been prepared in high yields with excellent enantioselectivities. Our work established for the first time an enantioselective synthesis method for chiral trifluoromethylated BIMs with a feasible way to obtain both enantiomers.

EXPERIMENTAL SECTION

General Procedures. Solvents were dried with standard methods and freshly distilled prior to use if needed. The imidazoline-oxazoline ligands **L1**–**L4**,[13] the bis(oxazoline) ligands **L5** and **L7**,[17] the bis(oxazoline) ligand **L6**,[18] the bis(imidazoline) ligand **L9**,[19] as well as β-CF_3-β-(3-indolyl)nitroalkenes **2**[20] were prepared according to the literature methods. All other chemicals including the bis(oxazoline) ligand **L8** were used as purchased. All reactions that required heating were heated using an oil bath. ^1H, $^{13}C\{^1H\}$,

and ^{19}F NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ or DMSO-d_6 as the solvent and TMS as an internal standard. HRMS were determined on a Waters Q-Tof Micro MS/MS System ESI spectrometer. The enantiomeric excesses of (*R*)- and (*S*)-enantiomers were determined by HPLC analysis over a chiral column with a UV detector. The absolute configuration of the major enantiomer was assigned by X-ray diffraction analysis. Melting points were measured on a WC-1 instrument and uncorrected. Optical rotations were recorded on a PerkinElmer 341 polarimeter.

Synthesis of *β*-CF_3-*β*-(3-indolyl)nitroalkenes. The nitroalkenes **2** were synthesized according to the procedure reported by Kang, He, and Liu.[20] The analytical data of the new nitroalkenes are given as follows.

(E)-Tert-butyl 5-methyl-3-(3,3,3-trifluoro-1-nitroprop-1-en-2-yl)-1H-indole-1-carboxylate ***(2f')***. With petroleum ether/EtOAc (50/1) as eluent; yellow solid (1.50 g, 81%); mp: 106.2–108.1 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.5 Hz, 1H), 7.79 (s, 1H), 7.66 (d, J = 1.2 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.01 (s, 1H), 2.42 (s, 3H), 1.68 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.9, 140.2 (q, J_{C-F} = 6.2 Hz), 133.4, 133.2, 129.8 (q, J_{C-F} = 32.7 Hz), 127.8, 127.02, 126.98, 122.1 (q, J_{C-F} = 274.2 Hz), 118.9, 115.4, 106.9, 85.0, 28.1, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -66.8; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}F_3N_2O_4Na$ 393.1038; Found 393.1038.

(E)-Tert-butyl 6-methyl-3-(3,3,3-trifluoro-1-nitroprop-1-en-2-yl)-1H-indole-1-carboxylate ***(2i')***. With petroleum ether/EtOAc (50/1) as eluent; yellow solid (1.55 g, 84%); mp: 109.2–111.5 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.75 (s, 1H), 7.66 (s, 1H), 7.11 (s, 2H), 2.49 (s, 3H), 1.69 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.0, 140.1

(q, J_{C-F} = 6.3 Hz), 135.8, 135.4, 129.8 (q, J_{C-F} = 32.7 Hz), 126.5, 125.2, 122.1 (q, J_{C-F} = 274.3 Hz), 118.6, 116.0, 107.1, 85.0, 28.1, 21.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ -66.7; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}F_3N_2O_4Na$ 393.1038; Found 393.1039.

General Procedure for the Catalytic Friedel-Crafts alkylation Reaction. To a Schlenk tube were added $Ni(ClO_4)_2 \cdot 6H_2O$ (3.7 mg, 0.010 mmol) and the ligand **L1** (5.1 mg, 0.012 mmol) under argon atmosphere. Toluene (2.0 mL) was then added through a syringe. The resulting mixture was stirred at 70 °C for 1 h, after which the indole **1** (0.3 mmol) and the nitroalkene **2** (0.2 mmol) were added successively. The mixture was stirred at 70 °C until the reaction was completed (monitored by TLC). The solvent was evaporated under vacuum and the residue was purified by chromatography on silica gel plates to afford the product **3**. The corresponding racemic products were prepared by the reaction of indole (0.15 mmol) and nitroalkene (0.10 mmol) in the presence of 20 mol% of $Cu(OAc)_2$ and 10 mol% Cs_2CO_3 in toluene (1.0 mL) at 100 °C for 12 h.

Procedure for the Gram-Scale Experiment. To a Schlenk tube were added $Ni(ClO_4)_2 \cdot 6H_2O$ (73.1 mg, 0.20 mmol) and the ligand **L1** (101.6 mg, 0.24 mmol) under argon atmosphere. Toluene (40 mL) was then added through a syringe. The resulting mixture was stirred at 70 °C for 1 h, after which indole **1a** (702.9 mg, 6.0 mmol) and the nitroalkene **2i** (1697.6 mg, 4.0 mmol) were added successively. The mixture was stirred at 70 °C for 84 h. The solvent was evaporated under vacuum and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 20/1) to afford the product **3ai** (1.81 g, 84% yield, 94% *ee*).

(R)-1-Tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3aa)***. With petroleum ether/EtOAc (3/1) as eluent; white solid (97.6 mg, 93%); mp: 110.1–111.7 ^{o}C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 12.6 min (major), 14.2 min (minor), 92% *ee*. $[\alpha]_D^{20}$ = -5 (*c* 0.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.87 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.29–7.27 (m, 3H), 7.21–7.17 (m, 1H), 7.10–7.06 (m, 1H), 6.88–6.85 (m, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.68–6.62 (m, 2H), 5.55 (d, *J* = 11.4 Hz, 1H), 5.40 (d, *J* = 11.4 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.5, 136.2, 135.1, 134.8, 130.1, 128.9, 126.9, 126.5, 125.9 (q, J_{C-F} = 283.7 Hz), 125.4, 125.1, 124.1, 123.5, 122.7, 120.9, 120.3, 119.9, 116.0, 113.8, 111.7, 107.8, 77.3, 51.0 (q, J_{C-F} = 28.2 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{20}F_3N_3O_4NaS$ 550.1024; Found 550.1024.

(R)-4-Fluoro-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ba)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (74.8 mg, 69%); mp: 113.0–114.6 ^{o}C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 6.6 min (major), 7.5 min (minor), 88% *ee*. $[\alpha]_D^{20}$ = +28 (*c* 0.24, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.29–7.27 (m, 3H), 7.24–7.17 (m, 2H), 7.01 (dd, *J* = 1.8, 8.7 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.74 (s, 1H), 5.49 (d, *J* = 11.4 Hz, 1H), 5.42 (d, *J* = 11.4 Hz, 1H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ

155.3 (d, $J_{C–F}$ = 244.0 Hz), 145.4, 139.0 (d, $J_{C–F}$ = 10.6 Hz), 135.1, 134.6, 130.0, 128.5, 126.9, 126.5, 126.1 (q, $J_{C–F}$ = 284.3 Hz), 125.4, 124.9, 123.6 (d, $J_{C–F}$ = 8.4 Hz), 123.5, 121.2, 117.6, 114.4 (d, $J_{C–F}$ = 19.2 Hz), 113.6, 108.2 (d, $J_{C–F}$ = 3.5 Hz), 106.8 (d, $J_{C–F}$ = 3.4 Hz), 106.1 (d, $J_{C–F}$ = 22.1 Hz), 78.3 (d, $J_{C–F}$ = 10.2 Hz), 51.2 (q, $J_{C–F}$ = 28.1 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.6, -114.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}F_4N_3O_4NaS$ 568.0930; Found 568.0928.

(R)-5-Fluoro-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ca)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (75.7 mg, 69%); mp: 103.6–105.8 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 6.9 min (major), 7.9 min (minor), 91% *ee*. $[\alpha]_D^{20}$ = +4 (*c* 0.35, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 2.5 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.24–7.17 (m, 2H), 6.89–6.85 (m, 1H), 6.82–6.75 (m, 2H), 6.24 (dd, *J* = 2.1, 10.1 Hz, 1H), 5.47 (d, *J* = 11.4 Hz, 1H), 5.39 (d, *J* = 11.4 Hz, 1H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.6 (d, $J_{C–F}$ = 234.5 Hz), 145.9, 135.1, 134.5, 132.7, 130.3, 128.7, 126.7, 126.6, 125.9 (d, $J_{C–F}$ = 10.2 Hz), 125.8 (q, $J_{C–F}$ = 283.9 Hz), 125.6, 125.2, 123.5, 120.8, 115.3, 113.9, 112.5 (d, $J_{C–F}$ = 9.7 Hz), 111.5 (d, $J_{C–F}$ = 26.3 Hz), 107.9 (d, $J_{C–F}$ = 4.7 Hz), 104.9 (d, $J_{C–F}$ = 24.9 Hz), 77.2, 50.9 (q, $J_{C–F}$ = 28.3 Hz), 21.6; ^{19}F NMR (376 MHz, CDCl3): δ -69.4, -122.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}F_4N_3O_4NaS$ 568.0930; Found 568.0929.

(R)-5-Chloro-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3da)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (98.2 mg, 87%); mp: 107.6–108.4 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 30.3 min (major), 35.9 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = +105 (*c* 0.32, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.55 (s, 1H), 7.27–7.17 (m, 4H), 7.11 (d, J = 8.1 Hz, 1H), 7.07–7.02 (m, 1H), 6.97–6.92 (m, 2H), 6.52 (dd, J = 7.6, 12.1 Hz, 1H), 5.71–5.62 (m, 2H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.7, 135.0, 134.62, 134.56, 130.4, 128.5, 126.8, 126.4, 126.0, 125.8 (q, J_{C-F} = 284.0 Hz), 125.7, 125.2, 123.5, 123.3, 120.9, 119.3, 115.1, 113.7, 112.9, 107.6, 77.2, 51.0 (q, J_{C-F} = 28.3 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}ClF_3N_3O_4NaS$ 584.0635; Found 584.0634.

(R)-5-Bromo-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ea)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (90.7 mg, 75%); mp: 106.7–108.2 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 10.4 min (major), 12.9 min (minor), 92% *ee*. $[\alpha]_D^{20}$ = +26 (*c* 0.28, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.83 (s, 1H), 7.78 (d, J = 8.4 Hz, 2H), 7.31–7.29 (m, 3H), 7.23–7.16 (m, 3H), 6.98 (s, 1H), 6.93–6.89 (m, 1H), 6.81 (d, J = 8.1 Hz, 1H), 5.51 (d, J = 11.5 Hz, 1H), 5.43 (d, J = 11.5 Hz, 1H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.6, 134.94, 134.89,

134.6, 130.4, 128.4, 127.0, 126.8, 126.5, 125.9, 125.74 (q, J_{C-F} = 284.0 Hz), 125.69, 125.2, 123.4, 122.4, 120.9, 115.0, 113.8, 113.7, 113.2, 107.6, 77.1, 51.0 (q, J_{C-F} = 28.1 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}BrF_3N_3O_4NaS$ 628.0129; Found 628.0128.

(R)-5-Methyl-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3fa)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (103.2 mg, 95%); mp: 112.2–113.6 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (92/8) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 15.4 min (major), 19.4 min (minor), 90% *ee*. $[\alpha]_D^{20}$ = +28 (*c* 0.21, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.27–7.24 (m, 2H), 7.21–7.12 (m, 3H), 6.92–6.85 (m, 2H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.65 (s, 1H), 5.59 (d, *J* = 11.5 Hz, 1H), 5.39 (d, *J* = 11.4 Hz, 1H), 2.33 (s, 3H), 2.07 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.5, 135.0, 134.9, 134.6, 130.1, 129.6, 128.8, 126.9, 126.3, 125.9 (q, J_{C-F} = 284.0 Hz), 125.5, 125.0, 124.6, 124.5, 123.4, 121.1, 119.5, 115.8, 113.7, 111.3, 107.3, 77.2, 51.2 (q, J_{C-F} = 28.3 Hz), 21.6, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1181.

(R)-5-Methoxy-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ga)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (104.8 mg, 94%); mp: 106.1–108.2 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (88/12) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 11.1 min (major), 12.8 min (minor), 89% *ee*. $[\alpha]_D^{20}$

= +45 (*c* 0.28, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.90 (s, 1H), 7.79 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 7.21–7.16 (m, 3H), 6.88–6.84 (m, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.72 (dd, J = 2.4, 8.9 Hz, 1H), 6.19 (s, 1H), 5.52 (d, J = 11.4 Hz, 1H), 5.37 (d, J = 11.4 Hz, 1H), 3.25 (s, 3H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.1, 145.5, 134.9, 134.8, 131.3, 130.2, 128.8, 127.0, 126.3, 126.0, 125.9 (q, J_{C-F} = 283.8 Hz), 125.1, 124.6, 123.4, 121.1, 115.4, 113.5, 113.0, 112.3, 107.4, 102.0, 77.3, 55.3, 51.0 (q, J_{C-F} = 28.3 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_5NaS$ 580.1130; Found 580.1130.

(R)-6-Chloro-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ha)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (65.2 mg, 58%); mp: 111.5–113.4 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 6.7 min (major), 7.6 min (minor), 83% *ee*. $[\alpha]_D^{20}$ = -4 (*c* 0.23, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.87 (s, 1H), 7.78 (d, J = 8.1 Hz, 2H), 7.32–7.25 (m, 4H), 7.20 (t, J = 7.8 Hz, 1H), 6.86 (t, J = 7.7 Hz, 1H), 6.71 (d, J = 8.1 Hz, 1H), 6.48 (d, J = 8.9 Hz, 1H), 6.40 (d, J = 8.7 Hz, 1H), 5.48 (d, J = 11.4 Hz, 1H), 5.37 (d, J = 11.4 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.6, 136.5, 135.1, 134.7, 130.1, 128.8, 128.6, 126.9, 126.5, 125.7 (q, J_{C-F} = 284.0 Hz), 125.3, 124.5, 124.1, 123.6, 121.2, 120.8, 120.7, 115.7, 113.9, 111.5, 108.2, 77.4, 50.8 (q, J_{C-F} = 28.3 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.6; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}ClF_3N_3O_4NaS$ 584.0635; Found 584.0634.

(R)-6-Methyl-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ia)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (99.0 mg, 91%); mp: 113.2–114.5 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (87/13) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 9.6 min (major), 11.5 min (minor), 90% *ee*. $[\alpha]_D^{20}$ = -6 (*c* 0.32, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.21–7.17 (m, 2H), 7.11 (s, 1H), 6.89–6.85 (m, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.46 (d, *J* = 8.4 Hz, 1H), 5.53 (d, *J* = 11.4 Hz, 1H), 5.38 (d, *J* = 11.4 Hz, 1H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.3, 136.6, 135.1, 134.8, 132.6, 130.1, 128.9, 126.9, 126.5, 125.8 (q, J_{C-F} = 283.8 Hz), 125.0, 123.4, 123.2, 122.3, 120.9, 119.6, 116.0, 113.9, 111.4, 107.8, 77.3, 51.0 (q, J_{C-F} = 28.1 Hz), 21.6, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1179.

(R)-6-Methoxy-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ja)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (100.2 mg, 90%); mp: 236.4–238.6 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 10.0 min (major), 12.0 min (minor), 88% *ee*. $[\alpha]_D^{20}$ = -12 (*c* 0.82, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.28 (s, 1H), 7.95–7.92 (m, 4H), 7.53 (s, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 2.2 Hz, 1H), 6.71 (d, *J* = 8.1 Hz, 1H), 6.15 (d, *J* = 8.8 Hz, 1H), 5.96 (dd, *J* = 2.2, 8.8 Hz, 1H), 5.86 (d, *J* = 12.3 Hz, 1H), 5.79 (d, *J* = 12.3 Hz, 1H), 3.64 (s, 3H), 2.39 (s, 3H);

$^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ 155.1, 145.7, 137.0, 134.3, 133.8, 130.3, 128.8, 126.8 126.0 (q, J_{C-F} = 283.5 Hz), 125.4, 125.0, 123.5, 123.3, 120.8, 119.4, 116.7, 113.3, 109.3, 105.8, 94.4, 77.2, 54.9, 49.8 (q, J_{C-F} = 27.6 Hz), 21.0; ^{19}F NMR (376 MHz, DMSO-d_6): δ -68.9; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_5NaS$ 580.1130; Found 580.1131.

(R)-7-Methyl-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3ka)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (92.2 mg, 85%); mp: 113.6–115.3 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 12.6 min (major), 14.6 min (minor), 81% *ee*. $[\alpha]_D^{20}$ = -1 (*c* 0.31, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.28–7.16 (m, 4H), 6.88–6.85 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.59–6.53 (m, 2H), 5.55 (d, *J* = 11.4 Hz, 1H), 5.40 (d, *J* = 11.4 Hz, 1H), 2.41 (s, 3H), 2.37 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 145.4, 135.8, 135.1, 134.8, 130.1, 128.9, 126.9, 126.5, 125.9 (q, J_{C-F} = 283.8 Hz), 125.1, 124.9, 123.9, 123.5, 123.2, 121.0, 120.7, 120.5, 117.7, 116.0, 113.8, 108.3, 77.2, 51.1 (q, J_{C-F} = 28.1 Hz), 21.6, 16.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1180.

(R)-7-Methoxy-3-(1,1,1-trifluoro-3-nitro-2-(1-tosyl-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3la)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (70.3 mg, 63%); mp: 109.9–111.9 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (92/8) and flow rate 1.0 mL/min and detected at a UV

wavelength of 254 nm. Retention times: 26.1 min (major), 29.8 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = +6 (*c* 0.20, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.61 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.21–7.16 (m, 2H), 6.88–6.85 (m, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.57 (t, *J* = 7.8 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1H), 6.27 (d, *J* = 8.0 Hz, 1H), 5.54 (d, *J* = 11.4 Hz, 1H), 5.38 (d, *J* = 11.4 Hz, 1H), 3.89 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 146.1, 145.3, 135.1, 134.8, 130.0, 128.9, 127.0, 126.9, 126.6, 126.5, 125.9 (q, J_{C-F} = 283.9 Hz), 125.0, 123.6, 123.4, 121.0, 120.8, 116.0, 113.8, 112.5, 108.4, 102.3, 77.2, 55.3, 51.0 (q, J_{C-F} = 28.3 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_5NaS$ 580.1130; Found 580.1128.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3aa'**)*. With petroleum ether/EtOAc (3/1) as eluent; white solid (69.7 mg, 74%); mp: 95.6–96.9 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (96/4) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 10.8 min (major), 12.1 min (minor), 91% *ee*. $[\alpha]_D^{20}$ = -9 (*c* 0.33, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.87 (s, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.25–7.24 (m, 1H), 7.21–7.17 (m, 1H), 7.13–7.09 (m, 1H), 7.05 (d, *J* = 8.2 Hz, 1H), 6.89–6.84 (m, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.58 (d, *J* = 11.3 Hz, 1H), 5.48 (d, *J* = 11.3 Hz, 1H), 1.71 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.4, 136.3, 135.3, 128.5, 126.0 (q, J_{C-F} = 285.6 Hz), 125.5, 125.4, 124.7, 124.6, 122.72, 122.68, 120.7, 120.5, 120.1, 115.3, 113.9, 111.6, 108.2, 84.8, 77.4, 51.1 (q, J_{C-F} = 28.2 Hz), 28.2;

^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{24}H_{22}F_3N_3O_4Na$ 496.1460; Found 496.1458.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(5-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3fa'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (85.9 mg, 88%); mp: 96.1–98.6 °C. The enantiomeric excess was determined on a Daicel Chiralcel OD-H column with *n*-hexane/2-propanol (96/4) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 32.6 min (major), 39.5 min (minor), 94% *ee*. $[\alpha]_D^{20}$ = +3 (*c* 0.27, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.84 (s, 1H), 7.23–7.19 (m, 2H), 7.10 (s, 1H), 6.97–6.85 (m, 4H), 5.65 (d, *J* = 11.4 Hz, 1H), 5.48 (d, *J* = 11.4 Hz, 1H), 2.25 (s, 3H), 1.71 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.5, 135.4, 134.7, 129.7, 128.5, 126.1 (q, J_{C-F} = 283.8 Hz), 125.6, 125.3, 124.7, 124.4, 122.7, 120.9, 119.7, 115.3, 114.0, 111.4, 107.6, 84.8, 77.2, 51.3 (q, J_{C-F} = 28.1 Hz), 28.2, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_4Na$ 510.1617; Found 510.1616.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(5-methoxy-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3ga'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (86.5 mg, 86%); mp: 95.8–97.6 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 13.7 min (major), 16.3 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = -14 (*c* 0.27, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.88 (s, 1H), 7.23–7.17 (m, 3H), 6.89–6.81 (m, 2H), 6.76 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.43 (d, *J* = 2.0 Hz, 1H), 5.55 (d, *J* = 11.3 Hz, 1H), 5.46 (d, *J* = 11.3 Hz,

1H), 3.50 (s, 3H), 1.70 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 154.1, 149.4, 135.4, 131.5, 128.6, 126.2, 126.1 (q, J_{C-F} = 283.6 Hz), 125.5, 125.2, 124.8, 122.8, 120.7, 115.3, 113.8, 112.4, 112.2, 107.7, 102.8, 84.8, 77.3, 55.7, 51.0 (q, J_{C-F} = 28.3 Hz), 28.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_5Na$ 526.1566; Found 526.1564.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(6-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3ia'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (77.9 mg, 80%); mp: 108.3–109.8 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (96/4) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 11.0 min (major), 12.9 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = -8 (*c* 0.26, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.86 (s, 1H), 7.23–7.10 (m, 3H), 6.93 (d, *J* = 8.3 Hz, 1H), 6.89–6.85 (m, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 9.3 Hz, 1H), 5.57 (d, *J* = 11.3 Hz, 1H), 5.46 (d, *J* = 11.3 Hz, 1H), 2.34 (s, 3H), 1.71 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 149.5, 136.7, 135.3, 132.6, 128.6, 126.0 (q, J_{C-F} = 283.4 Hz), 125.3, 124.7, 123.9, 123.4, 122.7, 122.3, 120.7, 119.7, 115.3, 114.0, 111.5, 108.1, 84.8, 77.4, 51.1 (q, J_{C-F} = 28.2 Hz), 28.2, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_4Na$ 510.1617; Found 510.1617.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(6-methoxy-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3ja'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (82.4 mg, 82%); mp: 106.1–108.5 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (94/6) and flow rate 1.0 mL/min and

detected at a UV wavelength of 254 nm. Retention times: 12.8 min (major), 14.3 min (minor), 91% *ee*. $[\alpha]_D^{20}$ = -20 (*c* 0.27, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.15(d, *J* = 8.1 Hz, 1H), 7.86 (s, 1H), 7.20 (t, *J* = 8.2 Hz, 1H), 7.15 (d, *J* = 2.2 Hz, 1H), 6.89–6.85 (m, 2H), 6.82–6.78 (m, 2H), 6.52 (dd, *J* = 2.3, 8.9 Hz, 1H), 5.53 (d, *J* = 11.3 Hz, 1H), 5.46 (d, *J* = 11.3 Hz, 1H), 3.73 (s, 3H), 1.72 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.5, 149.4, 137.1, 135.3, 128.6, 126.0 (q, J_{C-F} = 283.5 Hz), 125.3, 124.7, 123.1, 122.7, 120.8, 120.7, 119.9, 115.3, 113.9, 110.6, 108.3, 94.6, 84.8, 77.5, 55.4, 51.0 (q, J_{C-F} = 28.2 Hz), 28.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_5Na$ 526.1566; Found 526.1566.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(7-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3ka'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (73.5 mg, 75%); mp: 110.7–112.0 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 7.7 min (major), 8.9 min (minor), 84% *ee*. $[\alpha]_D^{20}$ = -3 (*c* 0.36, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.86 (s, 1H), 7.25–7.18 (m, 2H), 6.93–6.86 (m, 3H), 6.82–6.79 (m, 2H), 5.60 (d, *J* = 11.3 Hz, 1H), 5.49 (d, *J* = 11.3 Hz, 1H), 2.45 (s, 3H), 1.72 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.4, 135.8, 135.3, 128.5, 126.0 (q, J_{C-F} = 283.6 Hz), 125.3, 125.0, 124.6, 124.3, 123.2, 122.7, 120.7, 120.6, 117.9, 115.3, 113.9, 108.7, 84.7, 77.3, 51.1 (q, J_{C-F} = 28.1 Hz), 28.2, 16.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_4Na$ 510.1617; Found 510.1616.

*(R)-Tert-butyl 3-(1,1,1-trifluoro-2-(7-methoxy-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3la'**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (40.9 mg, 41%); mp: 107.6–109.4 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (97/3) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 38.2 min (minor), 40.4 min (major), 93% *ee*. $[\alpha]_D^{20}$ = -1 (*c* 0.25, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.85 (s, 1H), 7.25–7.18 (m, 2H), 6.90–6.86 (m, 1H), 6.82–6.78 (m, 2H), 6.65 (d, *J* = 8.2 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 1H), 5.59 (d, *J* = 11.3 Hz, 1H), 5.48 (d, *J* = 11.3 Hz, 1H), 3.91 (s, 3H), 1.72 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.4, 146.1, 135.3, 128.5, 127.1, 126.7, 126.0 (q, J_{C-F} = 283.5 Hz), 125.3, 124.7, 124.1, 122.7, 120.9, 120.8, 115.3, 113.9, 112.7, 108.8, 102.3, 84.7, 77.4, 55.3, 51.1 (q, J_{C-F} = 28.2 Hz), 28.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_5Na$ 526.1566; Found 526.1567.

*(R)-4-Fluoro-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**3ab**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (72.5 mg, 66%); mp: 207.5–209.8 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 15.0 min (major), 17.4 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = -180 (*c* 0.76, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.86–8.81 (m, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.32–7.28 (m, 3H), 7.21–7.15 (m, 1H), 7.11–7.07 (m, 1H), 7.01 (d, *J* = 2.2 Hz, 1H), 6.81–6.64 (m, 3H), 5.71 (d, *J* = 12.0 Hz, 1H), 5.50 (dd, *J* = 4.4, 12.0 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.0 (d, J_{C-F} = 246.7 Hz), 145.7,

137.2 (d, $J_{C–F}$ = 9.1 Hz), 136.2, 134.5, 130.2, 127.1 (d, $J_{C–F}$ = 3.2 Hz), 127.0, 126.23 (d, $J_{C–F}$ = 8.3 Hz), 126.15 (q, $J_{C–F}$ = 284.0 Hz), 125.0, 123.9, 122.5, 120.4, 119.9, 117.7 (d, $J_{C–F}$ = 18.9 Hz), 114.8 (d, $J_{C–F}$ = 4.2 Hz), 111.7, 110.2, 110.0 (d, $J_{C–F}$ = 17.6 Hz), 109.5, 77.8 (d, $J_{C–F}$ = 10.3 Hz), 51.0 (q, $J_{C–F}$ = 28.1 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.1, -112.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}F_4N_3O_4NaS$ 568.0930; Found 568.0929.

(R)-5-Fluoro-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3ac)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (73.7 mg, 68%); mp: 101.5–103.7 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (87/13) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 25.8 min (minor), 28.3 min (major), 89% *ee*. $[\alpha]_D^{20}$ = +12 (*c* 0.74, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.93–7.90 (m, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.32–7.28 (m, 4H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.90 (dt, *J* = 2.5, 8.9 Hz, 1H), 6.61–6.55 (m, 2H), 6.35 (dd, *J* = 2.2, 9.5 Hz, 1H), 5.50 (d, *J* = 11.4 Hz, 1H), 5.32 (d, *J* = 11.3 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.2 (d, $J_{C–F}$ = 239.0 Hz), 145.7, 136.2, 134.5, 131.5, 130.2, 130.1 (d, $J_{C–F}$ = 10.2 Hz), 128.0, 126.9, 125.8 (q, $J_{C–F}$ = 283.9 Hz), 125.3, 123.9, 122.8, 120.4, 119.7, 115.9, 114.9 (d, $J_{C–F}$ = 9.5 Hz), 113.5 (d, $J_{C–F}$ = 25.6 Hz), 111.8, 107.3, 106.7 (d, $J_{C–F}$ = 25.2 Hz), 77.2, 50.8 (q, $J_{C–F}$ = 28.3 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.6, -118.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}F_4N_3O_4NaS$ 568.0930; Found 568.0932.

(R)-5-Bromo-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3ae)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (89.9 mg, 74%); mp:

110.7–112.9 °C. The enantiomeric excess was determined on a Daicel Chiralcel OD-H column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 22.1 min (minor), 27.1 min (major), 87% *ee*. $[\alpha]_D^{20}$ = +3 (*c* 0.30, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.88–7.84 (m, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.34–7.24 (m, 5H), 7.11–7.06 (m, 1H), 6.86 (d, J = 1.6 Hz, 1H), 6.65–6.64 (m, 2H), 5.53 (d, J = 11.4 Hz, 1H), 5.34 (d, J = 11.5 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.8, 136.2, 134.5, 133.9, 130.6, 130.2, 128.2, 127.7, 126.9, 125.7 (q, J_{C-F} = 283.7 Hz), 125.2, 124.0, 123.5, 122.9 120.5, 119.8, 117.1, 115.3, 111.8, 107.5, 77.1, 50.9 (q, J_{C-F} = 28.4 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{19}BrF_3N_3O_4NaS$ 628.0129; Found 628.0129.

(R)-5-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3af)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (96.3 mg, 89%); mp: 111.5–113.3 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 28.5 min (major), 33.0 min (minor), 86% *ee*. $[\alpha]_D^{20}$ = -20 (*c* 0.34, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.85 (d, J = 8.5 Hz, 1H), 7.79 (s, 1H), 7.75 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 1H), 7.25 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 2.3 Hz, 1H), 7.09–7.05 (m, 1H), 7.00 (dd, J = 0.9, 8.6 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 6.66 (t, J = 7.6 Hz, 1H), 6.58 (s, 1H), 5.55 (d, J = 11.5 Hz, 1H), 5.41 (d, J = 11.4 Hz, 1H), 2.35 (s, 3H), 2.06 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.4, 136.3, 134.8, 133.4, 133.1, 130.1, 129.1, 126.9, 126.7, 125.9 (q, J_{C-F} = 283.9 Hz), 125.3, 124.3, 122.7, 120.7, 120.3, 120.0, 115.8, 113.5, 111.7, 107.8, 77.1, 51.1 (q, J_{C-F} = 28.4 Hz), 21.6,

21.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1180.

*(R)-5-Methoxy-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**3ag**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (101.5 mg, 91%); mp: 97.5–100.2 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 21.7 min (minor), 25.5 min (major), 92% *ee*. $[\alpha]_D^{20}$ = +6 (*c* 0.35, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.87–7.83(m, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.29–7.24 (m, 4H), 7.06–7.02 (m, 1H), 6.78 (dd, *J* = 2.4, 9.1 Hz, 1H), 6.62–6.57 (m, 2H), 6.11 (d, *J* = 2.4 Hz, 1H), 5.49 (d, *J* = 11.3 Hz, 1H), 5.36 (d, *J* = 11.3 Hz, 1H), 3.35 (s, 3H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.0, 145.4, 136.2, 134.7, 130.1, 129.9, 127.1, 126.9, 125.9 (q, J_{C-F} = 283.9 Hz), 125.4, 124.0, 122.8, 120.3, 119.9, 116.0, 114.6, 113.6, 111.6, 107.6, 104.1, 77.2, 55.2, 50.9 (q, J_{C-F} = 28.3 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_5NaS$ 580.1130; Found 580.1128.

*(R)-Methyl 1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-5-carboxylate (**3am**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (114.4 mg, 98%); mp: 101.9–103.2 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (70/30) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 9.4 min (minor), 17.8 min (major), 92% *ee*. $[\alpha]_D^{20}$ = -8 (*c* 0.82, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 7.95 (s, 1 H), 7.88 (dd, *J* = 1.5, 8.8 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H),

7.31–7.28 (m, 4H), 7.07–7.03 (m, 1H), 6.65–6.60 (m, 2H), 5.57 (d, J = 11.5 Hz, 1H), 5.41 (d, J = 11.5 Hz, 1H), 3.69 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 145.8, 137.7, 136.3, 134.5, 130.2, 128.8, 127.7, 127.0, 126.2, 125.8 (q, $J_{C–F}$ = 283.9 Hz), 125.4, 125.2, 124.0, 123.1, 122.7, 120.3, 119.8, 116.4, 113.6, 111.8, 107.6, 77.2, 52.1, 50.9 (q, $J_{C–F}$ = 28.4 Hz), 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{22}F_3N_3O_6NaS$ 608.1079; Found 608.1080.

(R)-6-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3ai)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (104.0 mg, 96%); mp: 115.2–117.9 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 26.6 min (major), 30.8 min (minor), 94% *ee*. $[\alpha]_D^{20}$ = -3 (*c* 0.67, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.79–7.76 (m, 4H), 7.32–7.24 (m, 4H), 7.06 (t, J = 7.9 Hz, 1H), 6.70–6.61 (m, 4H), 5.52 (d, J = 11.4 Hz, 1H), 5.38 (d, J = 11.3 Hz, 1H), 2.38 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.3, 136.2, 135.5, 135.4, 134.9, 130.1, 126.9, 126.6, 125.9 (q, $J_{C–F}$ = 283.9 Hz), 125.8, 125.4, 125.1, 124.1, 122.7, 120.4, 120.3, 120.0, 116.0, 113.9, 111.6, 108.0, 77.3, 51.0 (q, $J_{C–F}$ = 28.3 Hz), 21.74, 21.65; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1179.

(R)-7-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3ak)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (101.0 mg, 93%); mp: 104.7–106.3 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV

wavelength of 254 nm. Retention times: 18.1 min (minor), 23.8 min (major), 93% *ee*. $[\alpha]_D^{20}$ = -31 (*c* 0.60, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 8.11 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.16 (s, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.94–6.88 (m, 2H), 6.79 (t, *J* = 7.6 Hz, 1H), 6.75–6.71 (m, 1H), 6.62 (d, *J* = 8.0 Hz, 1H), 5.62 (d, *J* = 11.4 Hz, 1H), 5.43 (d, *J* = 11.4 Hz, 1H), 2.55 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.2, 136.5, 136.2, 135.1, 130.8, 130.2, 129.7, 128.8, 126.6, 125.9 (q, J_{C-F} = 283.9 Hz), 125.4, 125.2, 124.4, 123.7, 122.8, 120.5, 120.1, 118.6, 114.7, 111.7, 108.0, 77.2, 51.0 (q, J_{C-F} = 28.2 Hz), 22.0, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_4NaS$ 564.1181; Found 564.1180.

(R)-7-Methoxy-1-tosyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***(3al)***. With petroleum ether/EtOAc (2/1) as eluent; white solid (96.8 mg, 87%); mp: 127.4–129.7 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 22.9 min (major), 28.3 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = -11 (*c* 0.64, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 1H), 8.13 (s, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.30–7.27 (m, 3H), 7.13–7.03 (m, 3H), 6.84 (t, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.58 (d, *J* = 11.4 Hz, 1H), 5.41 (d, *J* = 11.4 Hz, 1H), 3.60 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 147.3, 144.7, 136.8, 136.3, 131.5, 129.6, 128.4, 127.3, 126.0 (q, J_{C-F} = 283.7 Hz), 125.5, 125.0, 124.4, 124.2, 122.7, 120.4, 120.1, 113.5, 113.2, 111.7, 108.0, 106.9, 77.2, 55.2, 51.0

(q, J_{C-F} = 28.4 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{27}H_{22}F_3N_3O_5NaS$ 580.1130; Found 580.1131.

*(R)-Tert-butyl 5-methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3af'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (13.6 mg, 14%); mp: 98.9–100.1 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 8.4 min (major), 9.5 min (minor), 90% *ee*. $[\alpha]_D^{20}$ = -26 (*c* 0.13, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.79 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 2.4 Hz, 1H), 7.17–7.14 (m, 2H), 7.03 (d, *J* = 8.6 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 5.63 (d, *J* = 11.4 Hz, 1H), 5.51 (d, *J* = 11.4 Hz, 1H), 2.13 (s, 3H), 1.70 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.4, 136.3, 133.6, 132.0, 128.6, 126.2, 126.0 (q, J_{C-F} = 284.0 Hz), 125.6, 125.5, 124.9, 122.7, 120.5, 120.3, 114.9, 113.5, 111.6, 108.4, 84.5, 77.2, 51.2 (q, J_{C-F} = 28.3 Hz), 28.2, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_4Na$ 510.1617; Found 510.1616.

*(R)-Tert-butyl 6-methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole-1-carboxylate (**3ai'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (19.1 mg, 20%); mp: 108.3–109.6 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (97/3) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 13.0 min (major), 15.4 min (minor), 82% *ee*. $[\alpha]_D^{20}$ = -15 (*c* 0.18, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.01 (s, 1H), 7.76 (s, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.15–7.07 (m,

2H), 6.91–6.87 (m, 1H), 6.71–6.65 (m, 2H), 5.58 (d, J = 11.3 Hz, 1H), 5.48 (d, J = 11.3 Hz, 1H), 2.35 (s, 3H), 1.71 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 149.5, 136.2, 135.8, 134.8, 126.2, 126.0 (q, $J_{C–F}$ = 283.5 Hz), 125.6, 124.6, 124.2, 122.7, 120.5, 120.2, 115.5, 113.9, 111.6, 108.4, 84.5, 77.4, 51.1 (q, $J_{C–F}$ = 28.3 Hz), 28.2, 21.8; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{25}H_{24}F_3N_3O_4Na$ 510.1617; Found 510.1615.

*(R)-5-Methoxy-1-tosyl-3-(1,1,1-trifluoro-2-(5-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**3fg**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (105.1 mg, 92%); mp: 105.9–107.8 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (95/5) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 36.2 min (major), 41.6 min (minor), 90% *ee*. $[\alpha]_D^{20}$ = +46 (*c* 0.51, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.85–7.83 (m, 2H), 7.77 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.2 Hz, 1H), 6.79 (dd, J = 2.3, 9.1 Hz, 1H), 6.62 (s, 1H), 6.15 (d, J = 2.2 Hz, 1H), 5.54 (d, J = 11.4 Hz, 1H), 5.37 (d, J = 11.4 Hz, 1H), 3.37 (s, 3H), 2.34 (s, 3H), 2.05 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 155.9, 145.4, 134.8, 134.6, 130.1, 130.0, 129.7, 129.6, 126.8, 125.9 (q, $J_{C–F}$ = 284.0 Hz), 125.6, 124.6, 124.4, 119.5, 115.7, 114.4, 113.6, 111.2, 107.1, 104.2, 77.1, 55.2, 51.0 (q, $J_{C–F}$ = 28.3 Hz), 21.6, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{24}F_3N_3O_5NaS$ 594.1286; Found 594.1286.

*(R)-5-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(5-methoxy-1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**3gf**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (78.1 mg, 68%); mp: 94.7–96.4 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC

column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 13.1 min (major), 15.4 min (minor), 85% *ee*. $[\alpha]_D^{20}$ = +4 (*c* 0.28, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.83–7.81 (m, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.26–7.19 (m, 4H), 7.02 (d, *J* = 8.6 Hz, 1H), 6.76 (dd, *J* = 2.3, 8.8 Hz, 1H), 6.61 (s, 1H), 6.30 (s, 1H), 5.54 (d, *J* = 11.5 Hz, 1H), 5.40 (d, *J* = 11.5 Hz, 1H), 3.34 (s, 3H), 2.35 (s, 3H), 2.09 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.2, 145.3, 134.8, 133.2, 133.0, 131.3, 130.1, 129.0, 126.9, 126.6, 125.98, 125.95 (q, J_{C-F} = 283.9 Hz), 124.8, 120.8, 115.2, 113.3, 112.9, 112.2, 107.6, 102.1, 77.0, 55.3, 51.1 (q, J_{C-F} = 28.2 Hz), 21.6, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{24}F_3N_3O_5NaS$ 594.1286; Found 594.1287.

*(R)-6-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(5-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1 H-indole (**3fi**)*. With petroleum ether/EtOAc (2/1) as eluent; white solid (107.3 mg, 97%); mp: 116.2–118.1 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 6.9 min (major), 8.2 min (minor), 91% *ee*. $[\alpha]_D^{20}$ = -1 (*c* 0.63, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.78–7.76 (m, 4H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 2.0 Hz, 1H), 7.08 (s, 1H), 6.69–6.63 (m, 2H), 6.56 (d, *J* = 8.3 Hz, 1H), 6.46 (d, *J* = 8.3 Hz, 1H), 5.51 (d, *J* = 11.4 Hz, 1H), 5.36 (d, *J* = 11.4 Hz, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.30 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.3, 136.7, 135.5, 135.3, 134.9, 132.5, 130.1, 126.9, 126.7, 125.9 (q, J_{C-F} = 283.9 Hz), 125.7, 125.1, 123.4, 123.3, 122.2, 120.5, 119.6, 116.1, 113.9, 111.5, 107.8, 77.3, 51.0 (q, J_{C-F} = 28.2 Hz),

21.7, 21.6, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{24}F_3N_3O_4NaS$ 578.1337; Found 578.1336.

*(R)-6-Methyl-1-tosyl-3-(1,1,1-trifluoro-2-(6-methyl-1H-indol-3-yl)-3-nitropropan-2-yl)-1 H-indole (**3ii**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (103.8 mg, 93%); mp: 113.1–114.4 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (85/15) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 20.2 min (minor), 29.0 min (major), 92% *ee*. $[\alpha]_D^{20}$ = +45 (*c* 0.48, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.78–7.75 (m, 4H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 1H), 7.10 (s, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.70–6.64 (m, 3H), 5.56 (d, *J* = 11.4 Hz, 1H), 5.38 (d, *J* = 11.4 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H), 2.07 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.4, 135.4, 135.3, 135.0, 134.6, 130.2, 129.5, 126.9, 126.6, 125.9 (q, J_{C-F} = 283.8 Hz), 125.6, 125.1, 124.6, 124.5, 120.6, 119.5, 115.8, 113.7, 111.4, 107.3, 77.2, 51.1 (q, J_{C-F} = 28.2 Hz), 21.7, 21.59, 21.55; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{24}F_3N_3O_4NaS$ 578.1337; Found 578.1337.

*(R)-Tert-butyl 6-methyl-3-(1,1,1-trifluoro-2-(5-methyl-1H-indol-3-yl)-3-nitropropan-2-yl) -1H-indole-1-carboxylat (**3fi'**).* With petroleum ether/EtOAc (2/1) as eluent; white solid (40.5 mg, 40%); mp: 103.1–104.9 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 7.8 min (major), 9.3 min (minor), 90% *ee*. $[\alpha]_D^{20}$ = -5 (*c* 0.38, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.02 (s, 1H), 7.74 (s, 1H), 7.24–7.22 (m, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 6.98–6.96 (m, 2H),

6.76–6.71 (m, 2H), 5.64 (d, J = 11.4 Hz, 1H), 5.48 (d, J = 11.4 Hz, 1H), 2.37 (s, 3H), 2.27 (s, 3H), 1.70 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.5, 135.9, 134.74, 134.70, 129.7, 126.2, 126.1 (q, J_{C-F} = 283.8 Hz), 125.6, 125.3, 124.9, 124.4, 124.2, 120.4, 119.7, 115.6, 113.9, 111.3, 107.7, 84.5, 77.2, 51.3 (q, J_{C-F} = 28.2 Hz), 28.2, 21.8, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{26}H_{26}F_3N_3O_4Na$ 524.1773; Found 524.1771.

General Procedure for Removal of the *N*-Boc Group: To a tube were added the F-C reaction product **3** (0.10 mmol), TFA (0.5 mL) and CH_2Cl_2 (1.5 mL). Then the reaction mixture was stirred at room temperature for 1 h. After which, the mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated under vacuum and the residue was purified by chromatography on silica gel plates (petroleum ether/EtOAc, 3/1) to give the target compound.

(S)-5-Methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((S)-4a)***. According to the general procedure, the title compound **(*S*)-4a** was obtained from **3fa′** (61.4 mg, 0.126 mmol, 94% *ee*) as a white solid (37.7 mg, 77%); mp: 183.1–184.3 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (93/7) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 9.4 min (minor), 10.7 min (major), 93% *ee*. $[\alpha]_D^{20}$ = +6 (*c* 0.24, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 8.07 (s, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.20–7.06 (m, 5H), 6.96–6.93 (m, 1H), 6.90–6.85 (m, 2H), 5.61 (d, J =11.4 Hz, 1H), 5.58 (d, J =11.5 Hz, 1H), 2.21 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.4, 134.7, 129.4,

126.5 (q, J_{C-F} = 283.6 Hz), 125.8, 125.7, 125.2, 125.0, 124.2, 122.4, 120.6, 120.2, 120.1, 111.6, 111.2, 109.4, 108.8, 77.6, 51.7 (q, J_{C-F} = 28.2 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{16}F_3N_3O_2Na$ 410.1092; Found 410.1092.

*(R)-5-Methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**(R)-4a**).* According to the general procedure, the title compound **(*R*)-4a** was obtained from **3af′** (89.6 mg, 0.184 mmol, 90% *ee*) as a white solid (51.8 mg, 73%). The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (93/7) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 9.0 min (major), 10.3 min (minor), 89% *ee*. $[\alpha]_D^{20}$ = -6 (*c* 0.24, CH_2Cl_2).

General Procedure for Removal of the *N*-Ts Group. To a Schlenk tube were added the product **3** (0.10 mmol), THF–MeOH (1.5 mL, v/v = 2/1) and Cs_2CO_3 (97.7 mg, 0.30 mmol, 3.0 equiv) sequentially at room temperature under Ar atmosphere. Then the reaction mixture was stirred at 50 °C. After the reaction was completed (monitored by TLC), the mixture was filtrated through Celite and washed with ethyl acetate (20 mL). The organic solvent was evaporated under vacuum and the residue was purified by chromatography on silica gel plates (petroleum ether/EtOAc, 2/1) to give the target compound.

*(S)-5-Methoxy-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole (**(S)-4b**).* According to the general procedure, the title compound **(*S*)-4b** was obtained from **3ga** (74.2 mg, 0.13 mmol, 89% *ee*) as a white solid (46.5 mg, 89%). The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (90/10)

and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 32.2 min (major), 36.4 min (minor), 89% *ee*. $[\alpha]_D^{20} = +1$ (*c* 0.31, CH_2Cl_2).

(R)-5-Methoxy-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((R)-4b)***. According to the general procedure, the title compound **(*R*)-4b** was obtained from **3ag** (55.8 mg, 0.10 mmol, 92% *ee*) as a white solid (37.1 mg, 92%); mp: 91.3–92.9 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (90/10) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 32.5 min (minor), 35.4 min (major), 92% *ee*. $[\alpha]_D^{20} = -1$ (*c* 0.21, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.22 (s, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.24–7.22 (m, 2H), 7.17 (d, J = 8.8 Hz, 1H), 7.11–7.07 (m, 1H), 6.97 (d, J =8.2 Hz, 1H), 6.83 (t, J =7.6 Hz, 1H), 6.75 (dd, J = 2.3, 8.8 Hz, 1H), 6.32 (s, 1H), 5.52 (s, 2H), 3.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.8, 136.3, 131.5, 126.5 (q, J_{C-F} = 280.3 Hz), 126.4, 125.8, 125.1, 124.6, 122.5, 120.4, 120.1, 112.2, 112.1, 111.6, 109.0, 108.8, 103.1, 77.8, 55.6, 51.4 (q, J_{C-F} = 27.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{16}F_3N_3O_3Na$ 426.1041; Found 426.1039.

(S)-6-Methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((S)-4c)***. According to the general procedure, the title compound **(*S*)-4c** was obtained from **3ia** (54.2 mg, 0.10 mmol, 90% *ee*) as a white solid (32.4 mg, 84%). The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (91/9) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 45.3 min (major), 49.7 min (minor), 90% *ee*. $[\alpha]_D^{20} = +4$ (*c* 0.26, CH_2Cl_2).

(R)-6-Methyl-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((R)-4c)***. According to the general procedure, the title compound **(*R*)-4c** was obtained from **3ai** (54.2 mg, 0.10 mmol, 94% *ee*) as a white solid (33.8 mg, 87%); mp: 101.2–102.6 °C. The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (91/9) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 46.1 min (minor), 50.2 min (major), 94% *ee*. $[\alpha]_D^{20}$ = -4 (*c* 0.27, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.11 (s, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 1.6 Hz 1H), 7.18 (d, *J* = 1.6 Hz 1H), 7.14–7.10 (m, 2H), 7.02 (d, *J* =8.2 Hz, 1H), 6.88–6.85 (m, 2H), 6.69 (d, *J* = 8.4 Hz 1H), 5.56 (s, 2H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.7, 136.3, 132.4, 126.5 (q, J_{C-F} = 283.7 Hz), 125.8, 124.7, 124.1, 123.6, 122.5, 122.0, 120.5, 120.2, 120.1, 111.6, 111.5, 109.4, 109.2, 77.8, 51.5 (q, J_{C-F} = 28.0 Hz), 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{16}F_3N_3O_2Na$ 410.1092; Found 410.1093.

(S)-7-Methoxy-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((S)-4d)***. According to the general procedure, the title compound **(*S*)-4d** was obtained from **3la** (55.8 mg, 0.10 mmol, 93% *ee*) as a white solid (28.2 mg, 70%). The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (92/8) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 48.0 min (minor), 50.0 min (major), 93% *ee*. $[\alpha]_D^{20}$ = +13 (*c* 0.28, CH_2Cl_2).

(R)-7-Methoxy-3-(1,1,1-trifluoro-2-(1H-indol-3-yl)-3-nitropropan-2-yl)-1H-indole ***((R)-4d)***. According to the general procedure, the title compound **(*R*)-4d** was obtained from **3al** (55.8 mg, 0.10 mmol, 93% *ee*) as a white solid (30.3 mg, 75%); mp: 101.8–102.8 °C.

The enantiomeric excess was determined on a Daicel Chiralpak IA column with *n*-hexane/2-propanol (92/8) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 46.7 min (major), 51.1 min (minor), 93% *ee*. $[\alpha]_D^{20}$ = -15 (*c* 0.29, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.24 (s, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.23–7.21 (m, 2H), 7.10 (t, *J* = 7.9 Hz 1H), 7.00 (d, *J* = 8.2 Hz 1H), 6.85 (t, *J* =8.0 Hz, 1H), 6.77 (t, *J* =8.0 Hz, 1H), 6.59 (d, *J* =8.2 Hz, 1H), 6.55 (d, *J* = 7.7 Hz 1H), 5.56 (s, 2H), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 146.1, 136.3, 127.1, 127.0, 126.5 (q, J_{C-F} = 283.6 Hz), 125.8, 124.7, 124.3, 122.4, 120.6, 120.5, 120.1, 113.1, 111.6, 109.8, 109.4, 102.1, 77.8, 55.3, 51.6 (q, J_{C-F} = 28.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -69.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{16}F_3N_3O_3Na$ 426.1041; Found 426.1042.

*(R)-3,3,3-Trifluoro-2-(1H-indol-3-yl)-2-(6-methyl-1H-indol-3-yl)propan-1-amine (**5**).* To a suspension of **(*R*)-4c** (89.7 mg, 0.232 mmol, 94% ee) and $NiCl_2{\cdot}6H_2O$ (55.0 mg, 0.232 mmol) in methanol (2.0 mL) was added $NaBH_4$ (43.9 mg, 1.16 mmol) at 0 °C and the mixture was stirred at room temperature for 1 h. After which, the mixture was quenched with sat. NH_4Cl at 0 °C, and then extracted with CH_2Cl_2. The organic layer was washed with brine and dried over $MgSO_4$. After filtered and concentrated under vacuum, the crude product was purified by chromatography on silica gel plates, eluting with petroleum ether/ EtOAc (1/2) to afford the amine **5** as a white solid (61.0 mg, 74%); mp: 105.9–106.7 °C. The enantiomeric excess was determined on a Daicel Chiralpak IC column with *n*-hexane/2-propanol (87/13) and flow rate 1.0 mL/min and detected at a UV wavelength of 254 nm. Retention times: 12.3 min (minor), 14.0 min (major), 94% *ee*. $[\alpha]_D^{20}$ = -5 (*c* 0.20, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.44 (s, 1H), 7.22 (d, *J* = 8.1 Hz, 1H),

7.11 (s, 1H), 7.08–7.02 (m, 4H), 6.92 (d, J =8.2 Hz, 1H), 6.79 (t, J = 7.5 Hz, 1H), 6.62 (d, J = 8.3 Hz 1H), 3.89 (s, 2H), 2.31 (s, 3H), 1.65 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.9, 136.4, 131.9, 128.5 (q, $J_{C–F}$ = 283.8 Hz), 126.3, 124.6, 124.1, 124.0, 122.0, 121.6, 121.1, 120.7, 119.7, 111.7, 111.5, 111.4, 111.3, 52.3 (q, $J_{C–F}$ = 23.6 Hz), 46.2, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -68.8; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{19}F_3N_3$: 358.1531; Found 358.1530.

Supporting Information

Crystallographic details for **3ja** and (***S***)-**4a**. Nickel-catalyzed asymmetric F-C alkylation reaction of indoles with β-CF_3-β-arylnitroalkene and β-CF_3-β-alkylnitroalkene including the results shown in Table S2 and Scheme S1, characterization data, ^1H NMR spectra and chiral HPLC spectra of the products **7a-f**. NMR spectra of the new nitroalkenes **2**, NMR spectra of the products **3** and the transformed products **4**–**5** as well as their chiral HPLC spectra and CIF files for **3ja** and **(*S*)-4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (21472176 and 21672192) for the financial support of this work.

REFERENCES

(1) For reviews, see: (a) Shiri, M.; Zolfigol, M. A.; Kruger, H. G.; Tanbakouchian, Z. Bis- and trisindolylmethanes (BIMs and TIMs). *Chem. Rev.* **2010**, *110*, 2250–2293. (b) Palmieri, A.; Petrini, M. Recent Advances in the Synthesis of Unsymmetrical Bisindolylmethane Derivatives. *Synthesis* **2019**, *51*, 829–841.

(2) (a) Marrelli, M.; Cachet, X.; Conforti, F.; Sirianni, R.; Chimento, A.; Pezzi, V.; Michel, S.; Statti, G. A.; Menichini, F. Synthesis of a new bis(indolyl)methane that inhibits growth and induces apoptosis in human prostate cancer cells. *Nat. Prod. Res*. **2013**, *27*, 2039–2045. (b) Lee, J. 3,3′-Diindolylmethane Inhibits TNF-*α*- and TGF-*β*- Induced Epithelial-Mesenchymal Transition in Breast Cancer Cells. *Nutr. Cancer* **2019**, *71*, 992–1006.

(3) (a) Cho, H. J.; Seon, M. R.; Lee, Y. M.; Kim, J.; Kim, J.-K.; Kim, S. G.; Park, J. H. Y. 3,3′-Diindolylmethane Suppresses the Inflammatory Response to Lipopolysaccharide in Murine Macrophages[1-3]. *J. Nutr*. **2008**, *138*, 17–23. (b) Luo, Q.; Yang, A.; Cao, Q.; Guan, H. 3,3′-Diindolylmethane protects cardiomyocytes from LPS-induced inflammatory response and apoptosis. *BMC Pharmacol. Toxico.* **2018**, *19*, 71.

(4) Sivaprasad, G.; Perumal, P. T.; Prabavathy, V. R.; Mathivanan, N. Synthesis and anti-microbial activity of pyrazolylbisindoles-Promising anti-fungal compounds. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 6302–6305.

(5) (a) Jayakumar, P.; Pugalendi, V. K.; Sankaran, M. Attenuation of hyperglycemia-mediated oxidative stress by indole-3-carbinol and its metabolite 3,3'-diindolylmethane in C57BL/6J mice. *J. Physiol. Biochem*. **2014**, *70*, 525–534. (b) Zong, J.; Wu, Q.-Q.; Zhou, H.; Zhang, J.-Y.; Yuan, Y.; Bian, Z.-Y.; Deng, W.; Dai, J.; Li, F.-F.; Xu, M.; Fang, Y.; Tang, Q.-Z. 3,3′-Diindolylmethane attenuates cardiac H9c2 cell hypertrophy through 5′-adenosine monophosphate-activated protein kinase-*α*. *Mol. Med. Rep*. **2015**, *12*, 1247–1252. (c) He, J.; Huang, T.; Zhao, L. 3,3'-Diindolylmethane mitigates lipopolysaccharide-induced acute kidney injury in mice by inhibiting NOX-mediated oxidative stress and the apoptosis of renal tubular epithelial cells. *Mol. Med. Rep*. **2019**, *19*, 5115–5122.

(6) He, X.; Hu, S.; Liu, K.; Guo, Y.; Xu, J.; Shao, S. Oxidized Bis(indolyl)methane: A Simple and Efficient Chromogenic-Sensing Molecule Based on the Proton Transfer Signaling Mode. *Org. Lett.* **2006**, *8*, 333–336.

(7) For some examples on the synthesis of achiral BIMs, see: (a) Pathak, T. P.; Osiak. J. G; Vaden, R. M.; Welm, B. E.; Sigman, M. S. Synthesis and preliminary biological study of bisindolylmethanes accessed by an acid-catalyzed hydroarylation of vinyl indoles. *Tetrahedron* **2012**, *68*, 5203–5208. (b) Xiao, J.; Wen, H.; Wang, L.; Xu, L.; Hao, Z.; Shao, C.-L.; Wang, C.-Y. Catalyst-free dehydrative S_N1-type reaction of indolyl alcohols with diverse nucleophiles "on water". *Green Chem*. **2016**, *18*, 1032–1037. (c) Pillaiyar, T.; Gorska, E.; Schnakenburg, G.; Müller, C. E. General Synthesis of Unsymmetrical 3,3′-(Aza)diindolylmethane Derivatives. *J. Org. Chem.* **2018**, *83*, 9902–9913. (d) Qiao, C.; Liu, X.-F.; Fu, H.-C.; Yang, H.-P.; Zhang, Z.-B.; He, L.-N. Directly Bridging Indoles to 3,3′-Bisindolylmethanes by Using Carboxylic Acids and Hydrosilanes under Mild Conditions. *Chem. Asian J.* **2018**, *13*, 2664–2670. (e) Yang, T.; Lu, H.; Shu, Y.; Ou, Y.; Hong, L.; Au, C.-T.; Qiu, R. CF_3SO_2Na-Mediated, UV-Light-Induced Friedel-Crafts Alkylation of Indoles with Ketones/Aldehydes and Bioactivities of Products. *Org. Lett*. **2020**, *22*, 827–831.

(8) (a) Sun, F.-L.; Zheng, X.-J.; Gu, Q.; He, Q.-L.; You, S.-L. Enantioselective Synthesis of Unsymmetrical Triarylmethanes by Chiral Brønsted Acids. *Eur. J. Org. Chem.* **2010**, *2010*, 47–50. (b) Zhuo, M.-H.; Jiang, Y.-J.; Fan, Y.-S.; Gao, Y.; Liu, S.; Zhang, S. Enantioselective Synthesis of Triarylmethanes by Chiral Imidodiphosphoric Acids Catalyzed Friedel-Crafts Reactions. *Org. Lett.* **2014**, *16*, 1096–1099. (c) Zhuo, M.-H; Liu,

G.-F.; Song, S.-L.; An, D.; Gao, J.; Zheng, L.; Zhang, S. Chiral Imidodiphosphoric Acids-Catalyzed Friedel-Crafts Reactions of Indoles/Pyrroles with 3-Hydroxy-indolyloxindoles: Enantioselective Synthesis of 3,3-Diaryloxindoles. *Adv. Synth. Catal.* **2016**, *358*, 808–815. (d) Zhang,Y.; Zhang, S.-X.; Fu, L.-N.; Guo, Q.-X. Highly Efficient Atom-Economic Synthesis of Chiral Bis(indolyl)methanes Bearing Quaternary Stereogenic Carbon Centers. *ChemCatChem* **2017**, *9*, 3107–3110. (e) Guan, X.-K.; Zhang, H.; Gao, J.-G.; Sun, D.-Y.; Qin, X.-S.; Jiang, G.-F.; Zhang, G.-L.; Zhang, S. Asymmetric Synthesis of 1,1,1-Triarylethanes by Chiral Imidodiphosphoric Acid Catalyzed Nucleophilic Addition of Pyrrole and Indoles to 3-Vinylindoles. *J. Org. Chem*. **2019**, *84*, 12562–12572. (f) Kim, Y.; Lee, J.; Jung, J.; Kim, S.-G. Chiral Brønsted Acid-Catalyzed Friedel-Crafts Reaction of 3-Indolylsulfamidates with Indoles: Synthesis of Enantioenriched Bisindolylmethane Sulfamates. *Tetrahedron Lett.* **2019**, *60*, 1625–1630.

(9) For synthesis of the related chiral BIM compounds which have differently oxidized indole units, see: (a) Ren, C.-L.; Zhang, T.; Wang, X.-Y.; Wu, T.; Ma, J.; Xuan, Q.-Q.; Wei, F.; Huang, H.-Y.; Wang, D.; Liu, L. Highly enantioselective reaction of 2-oxindoles with (3-indolyl)methanols by cooperative catalysis of a Lewis acid and organocatalyst. *Org. Biomol. Chem.* **2014**, *12*, 9881–9886. (b) Huang, J.-Z.; Zhang, C.-L.; Zhu, Y.-F.; Li, L.-L.; Chen, D.-F.; Han, Z.-Y.; Gong, L.-Z. Organocatalytic Highly Enantioselective Substitution of 3-(1-Tosylalkyl)indoles with Oxindoles Enables the First Total Synthesis of (+)-Trigolutes B. *Chem.-Eur. J.* **2015**, *21*, 8389–8393. (c) Sato, R.; Tosaka, T.; Masu, H.; Arai, T. Catalytic Asymmetric Synthesis of Chiral Bis(indolyl)methanes Using a Ts-PyBidine-Nickel Complex. *J. Org. Chem.* **2019**, *84*, 14248–14257.

(10) For some reviews on catalytic asymmetric Friedel-Crafts alkylation reactions, see: (a) Poulsen, T. B.; Jørgensen, K. A. Catalytic Asymmetric Friedel-Crafts Alkylation Reactions-Copper Showed the Way. *Chem. Rev.* **2008**, *108*, 2903–2915. (b) You, S.-L.; Cai, Q.; Zeng, M. Chiral Brønsted acid catalyzed Friedel-Crafts alkylation reactions. *Chem. Soc. Rev.* **2009**, *38*, 2190–2201. (c) Zeng, M.; You, S.-L. Asymmetric Friedel-Crafts Alkylation of Indoles: The Control of Enantio- and Regioselectivity. *Synlett* **2010**, *2010*, 1289–1301. (d) Terrasson, V.; de Figueiredo, R. M.; Campagne, J. M. Organocatalyzed Asymmetric Friedel-Crafts Reactions. *Eur. J. Org. Chem.* **2010**, *2010*, 2635–2655. (e) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. Organocatalytic strategies for the asymmetric functionalization of indoles. *Chem. Soc. Rev.* **2010**, *39*, 4449–4465. (f) Dalpozzo, R. Strategies for the asymmetric functionalization of indoles: an update. *Chem. Soc. Rev.* **2015**, *44*, 742–778. (g) Chen J.-B.; Jia Y.-X. Recent progress in transition-metal-catalyzed enantioselective indole functionalizations. *Org. Biomol. Chem.* **2017**, *15*, 3550–3567. (h) Heravi, M. M.; Zadsirjan, V.; Heydari, M.; Masoumi, B. Organocatalyzed Asymmetric Friedel-Crafts Reactions: An Update. *Chem. Rec*. **2019**, *19*, 2236–2340. (i) Heravi, M. M.; Zadsirjan, V.; Masoumi, B.; Heydari, M. Organometal-catalyzed asymmetric Friedel-Crafts reactions. *J. Organomet. Chem.* **2019**, *879*, 78–138.

(11) For some reviews, see: (a) Nie, J.; Guo, H.-C.; Cahard, D.; Ma, J.-A. Asymmetric Construction of Stereogenic Carbon Centers Featuring a Trifluoromethyl Group from Prochiral Trifluoromethylated Substrates. *Chem. Rev.* **2011**, *111*, 455–529. (b) Yang, X.; Wu, T.; Phipps, R. J.; Toste, F. D. Advances in Catalytic Enantioselective Fluorination, Mono-, Di-, and Trifluoromethylation, and Trifluoromethylthiolation Reactions. *Chem. Rev.*

2015, *115*, 826–870. (c) Huang, Y.-Y.; Yang, X.; Chen, Z.; Verpoort, F.; Shibata, N. Catalytic Asymmetric Synthesis of Enantioenriched Heterocycles Bearing a C-CF_3 Stereogenic Center. *Chem.-Eur. J.* **2015**, *21*, 8664–8684. (d) Shibatomi, K. Catalytic Enantioselective Constructions of Trifluoromethylated Chiral Stereogenic Centers *via* the Conjugate Addition to CF_3-Alkenes: Overview of Current Progress. *Curr. Org. Chem.* **2015**, *19*, 1619–1637. (e) Meyer, F. Trifluoromethyl nitrogen heterocycles: synthetic aspects and potential biological targets. *Chem. Commun.* **2016**, *52*, 3077–3094. (f) Mei, H.; Xie, C.; Han, J.; Soloshonok, V. A. *N-tert*-Butylsulfinyl-3,3,3-trifluoroacetaldimine: Versatile Reagent for Asymmetric Synthesis of Trifluoromethyl-Containing Amines and Amino Acids of Pharmaceutical Importance. *Eur. J. Org. Chem.* **2016**, *2016*, 5917–5932. (g) Noda, H.; Kumagai, N.; Shibasaki, M. Catalytic Asymmetric Synthesis of α-Trifluoromethylated Carbinols: A Case Study of Tertiary Propargylic Alcohols. *Asian J. Org. Chem.* **2018**, *7*, 599–612.

(12) For synthesis of the achiral trifluoromethylated BIMs, see: (a) Wang, Y.; Yuan, Y.; Xing, C.-H.; Lu, L. Trifluoromethanesulfonic acid-catalyzed solvent-free bisindolylation of trifluoromethyl ketones. *Tetrahedron Lett.* **2014**, *55*, 1045–1048. (b) Pandey, V. K.; Anbarasan, P. One-Pot Trifluoromethylative Functionalization of Amides: Synthesis of Trifluoromethylated Bis(indolyl)arylmethanes and Triarylmethanes. *J. Org. Chem.* **2017**, *82*, 12328−12336. (c) Ling, Y.; An, D.; Zhou, Y.; Rao, W. $Ga(OTf)_3$-Catalyzed Temperature-Controlled Regioselective Friedel-Crafts Alkylation of Trifluoromethylated 3-Indolylmethanols with 2-Substituted Indoles: Divergent Synthesis of Trifluoromethylated Unsymmetrical 3,3′-and 3,6′-Bis(indolyl)methanes. *Org. Lett.* **2019**, *21*,

3396−3401. (d) Yuan, X.; Wu, L.; Xu, C.; Pan, Z.; Shi, L.; Yang, G.; Wang, C.; Fan, S. A consecutive one-pot two-step approach to novel trifluoromethylsubstituted bis(indolyl)methane derivatives promoted by $Sc(OTf)_3$ and *p*-TSA. *Tetrahedron Lett.* **2019**, *60*, 151329–151333.

(13) (a) Hao, X.-Q.; Wang, C.; Liu, S.-L.; Wang, X.; Wang, L.; Gong, J.-F.; Song, M.-P. Cobalt(II)/(imidazoline-oxazoline)-catalyzed enantioselective Michael addition of 2-acetyl azaarenes to *β*-CF_3-*β*-disubstituted nitroalkenes. *Org. Chem. Front.* **2017**, *4*, 308–312. (b) Wang, C.; Li, N.; Zhu, W.-J.; Gong, J.-F.; Song, M.-P. Asymmetric Michael Addition of 2-Acetyl Azaarenes to *β*-CF_3-*β*-(3-indolyl)nitroalkenes Catalyzed by a Cobalt(II)/(imidazoline-oxazoline) Complex. *J. Org. Chem.* **2019**, *84*, 191–203.

(14) For a pioneering work on asymmetric Friedel-Crafts alkylation reaction of indoles with *β*-CF_3-*β*-aryl nitroalkenes, see: (a) Gao, J.-R.; Wu, H.; Xiang, B.; Yu, W.-B.; Han, L.; Jia, Y.-X. Highly Enantioselective Construction of Trifluoromethylated All-Carbon Quaternary Stereocenters via Nickel-Catalyzed Friedel-Crafts Alkylation Reaction. *J. Am. Chem. Soc*. **2013**, *135*, 2983–2986. For other examples, see: (b) Wu, H.; Liu, R.-R.; Jia, Y.-X. Asymmetric Friedel-Crafts Alkylation Reaction in the Construction of Trifluoromethylated All-Carbon Quaternary Stereocenters. *Synlett* **2014**, *25*, 457-460. (c) Ibáñez, I.; Kaneko, M.; Kamei, Y.; Tsutsumi, R.; Yamanaka, M.; Akiyama, T. Enantioselective Friedel-Crafts Alkylation Reaction of Indoles with *α*-Trifluoromethylated *β*-Nitrostyrenes Catalyzed by Chiral BINOL Metal Phosphate. *ACS Catal.* **2019**, *9*, 6903−6909. For asymmetric Friedel-Crafts alkylation reaction of indoles with *β*-monosubstituted *β*-CF_3 nitroalkenes, see: (d) Lin, J.-H.; Xiao, J.-C. The Asymmetric

Friedel-Crafts Reaction of Indoles with Fluoroalkylated Nitroalkenes Catalyzed by Chiral Phosphoric Acid. *Eur. J. Org. Chem.* **2011**, *2011*, 4536–4539.

(15) (a) Choy J., Jaime-Figueroa, S.; Lara-Jaime, T. A novel practical cleavage of *tert*-butyl esters and carbonates using fluorinated alcohols. *Tetrahedron Lett.* **2010**, *51*, 2244–2246. (b) Jia Z.; Hu X.; Zhao Y.; Qiu F. G.; Chan A. S. C.; Zhao J. One-Pot Enantioselective Synthesis of 2-Pyrrolidinone Derivatives Bearing a Trifluoromethylated All-Carbon Quaternary Stereocenter. *Org. Lett.* **2019**, *21*, 9584–9588. (c) Lu, N.; Li, R.; Wei, Z.; Cao, J.; Liang, D.; Lin, Y.; Duan, H. Enantio- and Diastereoselective Nitro-Mannich Reaction of *α*-Aryl Nitromethanes with Amidosulfones Catalyzed by Phase-Transfer Catalysts. *J. Org. Chem*. **2017**, *82*, 4668–4676.

(16) Bajwa, J. S.; Chen, G.-P.; Prasad, K.; Repič, O.; Blacklock, T. J. Deprotection of *N*-tosylated indoles and related structures using cesium carbonate. *Tetrahedron Lett.* **2006**, *47*, 6425–6427.

(17) (a) Mao, J.; Liu, F.; Wang, M.; Wu, L.; Zheng, B.; Liu, S.; Zhong, J.; Bian, Q.; Walsh, P. J. Cobalt-Bisoxazoline-Catalyzed Asymmetric Kumada Cross-Coupling of Racemic *α*-Bromo Esters with Aryl Grignard Reagents. *J. Am. Chem. Soc*. **2014**, *136*, 17662–17668. (b) Evans, D. A.; Fandrick, K. R.; Song, H.-J. Enantioselective Friedel-Crafts Alkylations of *α*,*β*-Unsaturated 2-Acyl Imidazoles Catalyzed by Bis(oxazolinyl)pyridine-Scandium(III) Triflate Complexes. *J. Am. Chem. Soc*. **2005**, *127*, 8942–8943. (c) Evans, D. A.; Fandrick, K. R. Catalytic Enantioselective Pyrrole Alkylations of *α*,*β*-Unsaturated 2-Acyl Imidazoles. *Org. Lett*. **2006**, *8*, 2249–2252.

(18) Desimoni, G.; Faita, G.; Mella, M. A Stereodivergent Synthesis of Chiral

4,5-Disubstituted Bis(Oxazolines). *Tetrahedron* **1996**, *52,* 13649–13654.

(19) (a) Wu, L.-Y.; Hao, X.-Q.; Xu, Y.-X.; Jia, M.-Q.; Wang, Y.-N.; Gong, J.-F.; Song, M.-P. Chiral NCN Pincer Pt(II) and Pd(II) Complexes with 1,3-Bis(2′-imidazolinyl)benzene: Synthesis via Direct Metalation, Characterization, and Catalytic Activity in the Friedel-Crafts Alkylation Reaction. *Organometallics* **2009**, *28*, 3369–3380. (b) Hao, X.-Q.; Xu, Y.-X.; Yang, M.-J.; Wang, L.; Niu, J.-L.; Gong, J.-F.; Song, M.-P. A Cationic NCN Pincer Platinum(II) Aquo Complex with a Bis(imidazolinyl)phenyl Ligand: Studies toward its Synthesis and Asymmetric Friedel-Crafts Alkylation of Indoles with Nitroalkenes. *Organometallics* **2012**, *31*, 835–846. (c) Wang, T.; Hao, X.-Q.; Huang, J.-J.; Niu, J.-L.; Gong, J.-F.; Song, M.-P. Chiral Bis(imidazolinyl)phenyl NCN Pincer Rhodium(III) Catalysts for Enantioselective Allylation of Aldehydes and Carbonyl-Ene Reaction of Trifluoropyruvates. *J. Org. Chem.* **2013**, *78*, 8712–8721. (d) Hao, X.-Q.; Zhao, Y.-W.; Yang, J.-J.; Niu, J.-L.; Gong, J.-F.; Song, M.-P. Enantioselective Hydrophosphination of Enones with Diphenylphosphine Catalyzed by Bis(imidazoline) NCN Pincer Palladium(II) Complexes. *Organometallics* **2014**, *33*, 1801–1811.

(20) Ma, C.-H.; Kang, T.-R.; He, L.; Liu, Q.-Z. Highly Enantioselective Michael Addition of Malonates to β-CF_3-β-(3-Indolyl)-nitroalkenes: Construction of Trifluoromethylated All-Carbon Quaternary Stereogenic Centres. *Eur. J. Org. Chem.* **2014**, *2014,* 3981–3985.

Graphic abstract for the table of contents