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Organocatalytic Asymmetric Michael Addition of Aliphatic Aldehydes to Indolylnitroalkenes: Access to Contiguous Stereogenic Tryptamine Precursors

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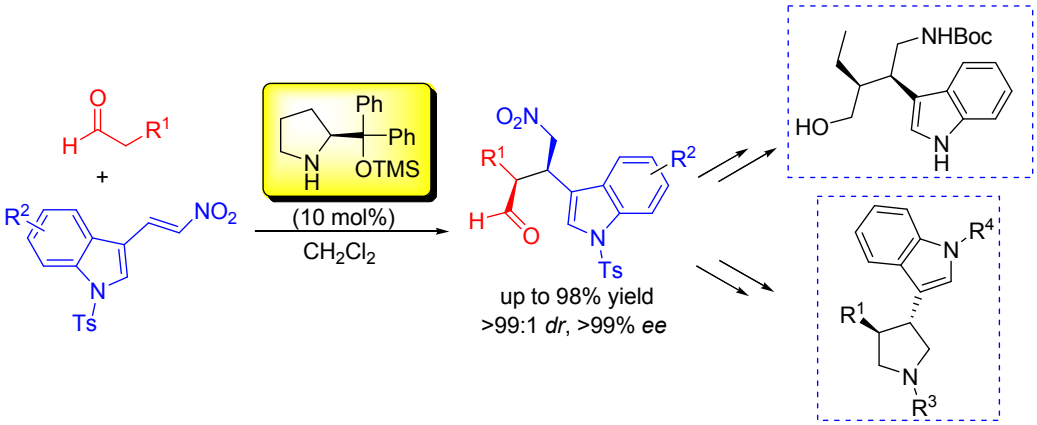


ABSTRACT: Due to the importance of indole framework and the versatile transformation of nitro- and formyl-groups, the efficient synthesis of optically pure 2-alkyl-3-(1*H*-indol-3-yl)-4-nitrobutanals, one type of tryptamine precursors, are of great interest for pharmaceutical and biological research. Herein, the Michael addition of aliphatic aldehydes to indolylnitroalkenes has been developed using (*S*)-diphenylprolinol trimethylsilyl ether as an organocatalyst, which provides the desired optically pure *syn* 2-alkyl-3-(1*H*-indol-3-yl)-4-nitrobutanal derivatives in up to 98% yield with up to >99:1 *dr* and >99% *ee*. As synthetic usefulness of this

methodology, optically active 2-alkyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butan-1-ol and tryptamine derivatives are readily obtained by stepwise systematic transformations.

INTRODUCTION

Indole derivatives bearing chiral functional groups at the 3-position have been found in a fascinating array of bioactive natural products, pharmaceutical compounds, and intermediates of complex compounds (Figure 1).[1] Tryptamine scaffolds are especially important and extensively present in many natural products and therapeutic agents.[2] For example, Hapalindol D **I**[3] is a member of the hapalindoles, which belong to a group of 20 structurally related alkaloid natural products isolated from the terrestrial blue green algae *Hapalosiphon fontinalis*, an organism found to exhibit antibacterial and antimycotic activity. Compound **II**[4] is a late stage intermediate in the synthesis of the dual action migraine drug prototype. Isatisine A **III**[5] is isolated from the leaves of Isatis indigotica Fort. (Cruciferae). Meridianin F **IV**[6] is a member of alkaloids isolated from the south Atlantic tunicate *Aplidium meridianum*. BMS-594726 **V**[7] is a highly potent and selective serotonin reuptake inhibitor. Hamacanthin B **VI**[8] reveals cytotoxic activities against a wide range of human tumor cell lines with GI_{50} values at micromolar concentration.

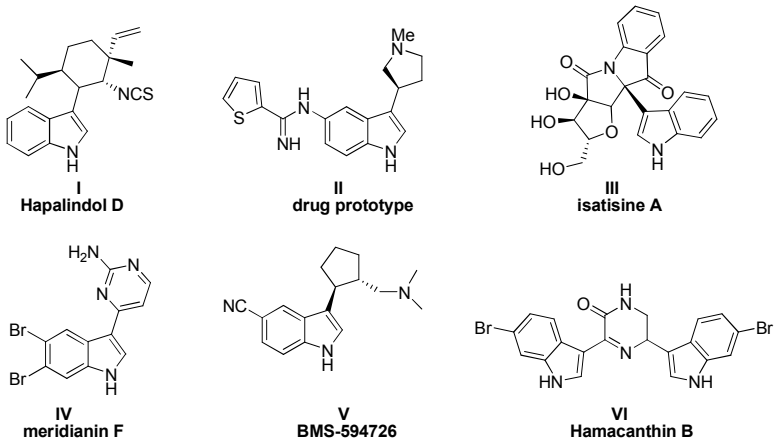


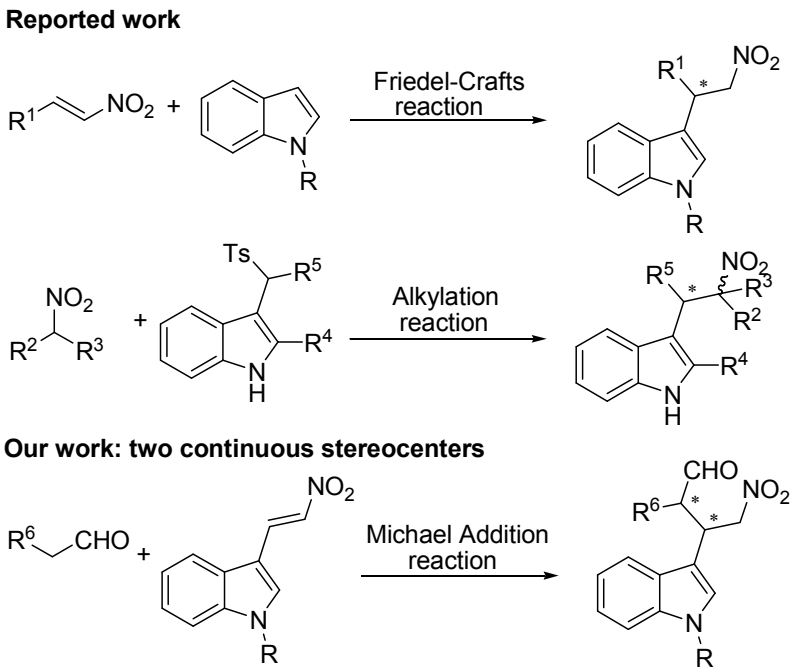
Figure 1. Tryptamine derivatives and important indol-3-yl substituted compounds.

As highly practical and atom-economic carbon-carbon bond formation reaction, the Michael additions of active methylene-containing carbonyl compounds to nitroalkenes[9] or nitroalkanes to α,β-unsaturated carbonyl compounds[10] are efficient methods for preparation of nitroalkane derivatives, which has been extensively investigated in the last decade. Among them, Michael additions of aldehydes to nitroalkenes are of great importance to furnish very useful α,β-disubstituted-γ-nitrobutanals[11b], which can be readily converted to corresponding amino acids or amino alcohols. Since List[12] and Barbas III[13] respectively reported the organocatalytic[14] asymmetric Michael addition of ketones or aldehydes to nitroalkenes in 2001, considerable efforts have subsequently been devoted to finding more effecient catalytic systems for such a transformation.[15]

Besides nitrostyrenes as being the most widely used Michael acceptors,[9,15] some functionalized nitroolefins[16] such as β-nitroacrolein dimethyl acetal[16b,c] or 3-nitroacrylate[16e] have also been recently reported as Michael acceptors. After investigating the literatures reported, we disclosed that indolylnitroalkenes were less

addressed in asymmetric transformation.[17] In addition, although construction of stereocenter on 3-position of indole scaffold mainly through Friedel-Crafts reactions has been elaborately studied in the past decade,[18] the Michael reactions of construction of two continuous stereocenters with indole motifs was seldom explored.[19] Besides Friedel-Crafts reactions, an alternative approach to tryptamine precursors involves the addtion of nitroalkanes to alkylideneindolenines.[20] Considering the importance of the tryptamine derivatives and the versatile transformation of nitro- and formyl- groups, investigating the asymmetric Michael addition between the indolylnitroalkenes and aliphatic aldehydes providing α,β-disubstituted-γ-nitrobutanals with two adjacent stereocenters is highly desirable (Scheme 1). Although Hayashi and co-workers had already reported the Michael addtion of aldehyde to nitroalkene by means of the Hayashi-Jørgensen catalyst,[21] we hoped to develop an efficient procedure for access to chiral functionalized tryptamine derivatives. Herein, optically pure *syn*-2-alkyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl) butanal derivatives, one type of tryptamine precursors, were found to be efficiently synthesized in high yields with excellent diastereo- and enantioselectivities through the Michael additions of aliphatic aldehydes to indolylnitroalkenes with (*S*)-diphenylprolinol trimethylsilyl ether as the organic catalyst.

Scheme 1. Synthetic Strategies for Tryptamine Precursors

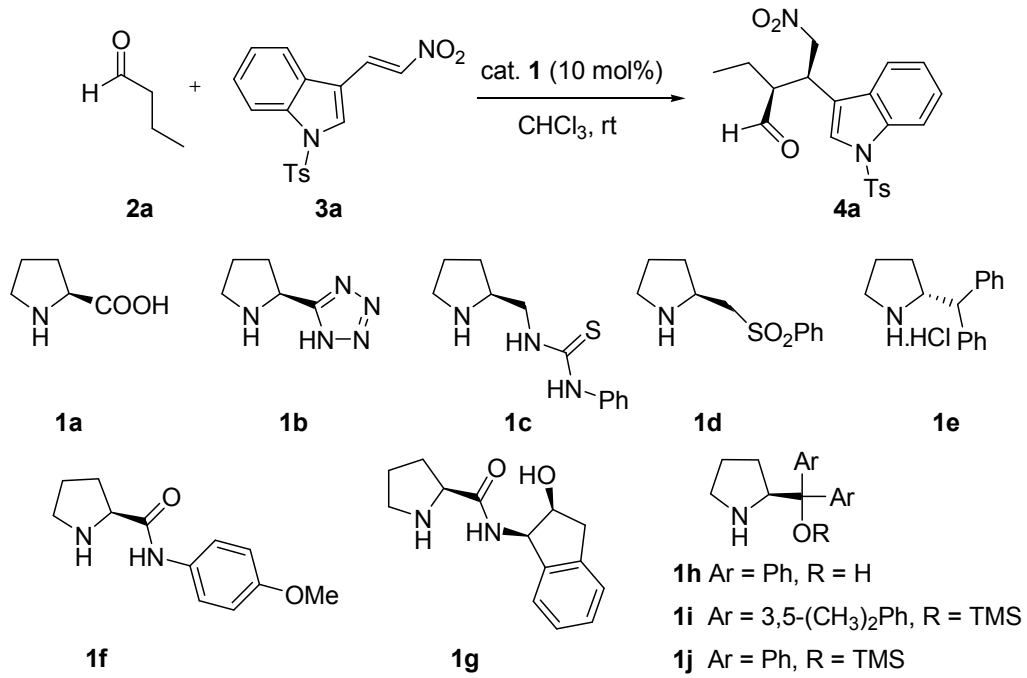


RESULTS AND DISCUSSION

In order to verify our synthetic hypothesis, the Michael addition of butyraldehyde **2a** with *trans*-3-(2-nitroethenyl)-*N*-tosylindole **3a** was chosen as a model reaction for the synthesis of desired chiral 2-ethyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butanal **4a**. Proline **1a** and proline derivatives **1b–1j** were chosen as potential catalysts, and the catalytic results are summarized in Table 1. Initially, we probed the Michael addition of butyraldehyde **2a** to *trans*-3-(2-nitroethenyl)-*N*-tosylindole **3a** using (*S*)-proline **1a** as catalyst, affording the Michael adduct **4a** in 53% yield with 80:20 *dr* and 11% *ee* within 0.5 hour (Table 1, entry 1). Organocatalysts **1c**, **1e** and **1h** were proven to be ineffective for the reaction, even prolonging the reaction time to 10 hours (Table 1, entries 3, 5 and 8). To our delight, when (*S*)-proline derived catalysts **1b**, **1d**, **1f** and **1g** were employed for this reaction, moderate yields and stereoselectivities were observed (Table 1, entries 2, 4, 6 and 7). Subsequently, two diarylprolinol silyl ether

catalysts **1i** and **1j** were used to catalyze this reaction. Fortunately, the reaction with **1j** proceeded very well to furnish the desired product **4a** in 95% yield with 92:8 *dr* and up to 99% *ee* (Table 1, entry 10). (*S*)-diphenylprolinol trimethylsilyl ether **1j** was finally confirmed to be the most effective catalyst in terms of both reactivity and stereochemistry control.

Table 1. Catalyst Screening for the Michael Addition of Butyraldehyde **2a** with *trans*-3-(2-Nitroethenyl)-*N*-tosylindole **3a**[a]



entry	cat.	time (h)	yield (%)[b]	dr (*syn*/*anti*)[c]	ee (%)[d]
1	**1a**	0.5	53	80:20	11
2	**1b**	0.5	48	86:14	60
3	**1c**	10	NR	–	–
4	**1d**	0.5	73	66:34	-12
5	**1e**	10	NR	–	–

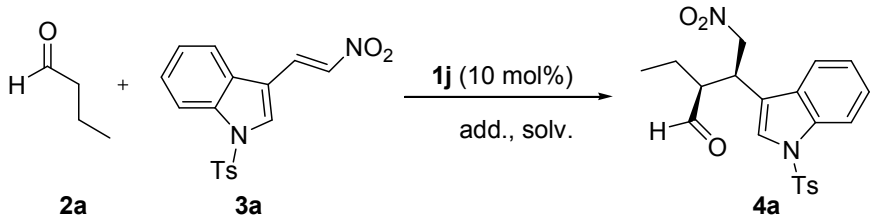
6	**1f**	0.5	15	85:15	63
7	**1g**	0.5	80	85:15	71
8	**1h**	10	NR	–	–
9	**1i**	0.5	92	87:13	96
10	**1j**	0.5	95	92:8	99

[a] Reactions were performed with **2a** (1.0 mmol), **3a** (0.2 mmol), and catalyst **1** (10 mol% with respect to **3a**) in $CHCl_3$ (1.0 mL) at room temperature. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] Determined by chiral HPLC analysis.

To further optimize the reaction conditions, some of reaction parameters including solvents, additives and temperatures, were examined in the presence of 10 mol% of catalyst **1j**, and the results are shown in Table 2. Firstly, some polar and protic solvents, such as DMF, MeOH and H_2O, were tested for the model Michael addition. All the reactions proceeded smoothly to produce the desired product **4a** in 43–81% yields with 72:28–89:11 *dr*s and 84–98% *ee*s, respectively (Table 2, entries 2–4). Subsequently, some non-polar and aprotic solvents, such as hexane, THF, toluene and CH_2Cl_2, were investigated for this reaction, CH_2Cl_2 turned out to be the best medium in terms of both yield and stereoselectivity, which furnished the expected product **4a** in 95% yield with 93:7 *dr* and 99% *ee* (Table 2, entry 8 *vs.* entries 5–7). Furthermore, a series of brønsted acids combined with **1j** as the catalysts were tested but gave inferior diastereoselectivities (87:13–92:8 *dr*s) for all cases, albeit with retained enantioselectivities (Table 2, entries 8–15). In addition, we also examined the feasibility to reduce the catalyst loading to a practical level. When the catalyst loading

of **1j** was reduced to 5 mol%, prolonged reaction time was required and decreased diastereoselectivity was exhibited (Table 2, entry 16). In order to improve the diastereoselectivity, the reaction temperature was examined for this transformation. Gratefully, by decreasing the reaction temperature from room temperature to –45 °C, the diastereoselectivity was found to be dramatically increased from 93:7 to 99:1 without sacrifice of yields and enantioselectivities (Table 2, entries 17–20). With a balance of reactivity and stereoselectivity, –30 °C turned out to be the optimal reaction temperature.

Table 2. Optimization of Catalytic Asymmetric Michael Addition of Butyraldehyde **2a** with *trans*-3-(2-Nitroethenyl)-*N*-tosylindole **3a**[a]



2a **3a** **4a**

entry	solv.	add.	temp.(°C)	time (h)	yield (%)[b]	dr (*syn*/*anti*)[c]	ee (%)[d]
1	$CHCl_3$	--	rt	0.5	95	92:8	99
2	DMF	--	rt	12	43	78:22	84
3	MeOH	--	rt	12	81	72:28	88
4	H_2O	--	rt	12	80	89:11	98
5	hexane	--	rt	12	9	93:7	>99
6	THF	--	rt	12	41	74:26	93
7	toluene	--	rt	12	89	92:8	99

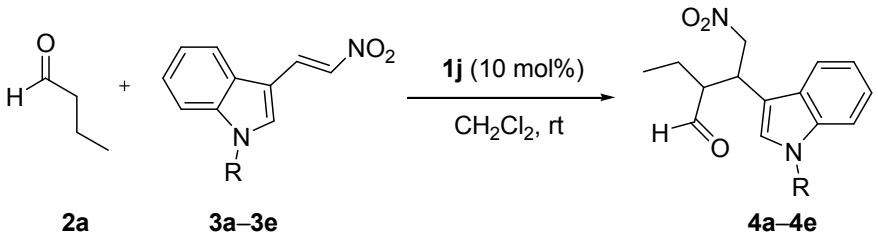
8	CH_2Cl_2	--	rt	0.5	95	93:7	99
9	CH_2Cl_2	PhCOOH	rt	0.5	98	89:11	99
10	CH_2Cl_2	4-NO_2-C_6H_4COOH	rt	3	94	88:12	99
11	CH_2Cl_2	CH_3COOH	rt	0.5	96	88:12	99
12	CH_2Cl_2	CF_3COOH	rt	3	92	90:10	99
13	CH_2Cl_2	D-CSA	rt	4	93	92:8	99
14	CH_2Cl_2	D-Mandelic acid	rt	4	97	87:13	99
15	CH_2Cl_2	L-Mandelic acid	rt	4	99	87:13	99
16[e]	CH_2Cl_2	--	rt	18	94	92:8	99
17	CH_2Cl_2	--	0	4	98	96:4	99
18	CH_2Cl_2	--	–15	12	97	97:3	>99
19	CH_2Cl_2	--	–30	20	95	98:2	>99
20	CH_2Cl_2	--	–45	84	96	99:1	>99

[a] Unless noted, reactions were performed with **2a** (1.0 mmol), **3a** (0.2 mmol), additive and **1j** (10 mol% with respect to **3a**) in solvent (1.0 mL). [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] Determined by chiral HPLC analysis. [e] 5 mol% of **1j** was used.

Besides optimization of the reaction conditions, we also tried to elucidate whether *N*-protected substituents on indole scaffold affected the catalytic results at room temperature. For non-protected 3-(2-nitrovinyl) indole **3b**, the Michael addition could produce the desired product **4b** in 96% yield with 81:19 *dr* and 98% *ee* in the presence of 10 mol% of catalyst **1j** in CH_2Cl_2 (Table 3, entry 2). For substrate **3c** bearing *N*-methyl protected group, the yield and enantioselectivity value were

somewhat dropped, albeit with diastereoselectivity retained (Table 3, entry 3 *vs.* entry 1). When substrate **3d** with benzyl protected substituent was used, even if the reaction time was prolonged to 72 hours, only trace amount of the expected product was observed (Table 3, entry 4). When indolylnitroalkene **3e** contained *N*-phenylsulfonyl group, excellent enantioselectivity of the desired product **4e** was achieved for the corresponding Michael addition, but slightly lowered yield and diastereoselectivity were observed in comparison with the outcome (95% yield, 93:7 *dr* and 99% *ee*) of *N*-tosyl protected indolylnitroalkene **3a** (Table 3, entry 5 *vs.* entry 1). Thus, it was evident that *N*-tosyl protected indolylnitroalkene **3a** was the best choice for this transformation.

Table 3. Effect of *N*-Protecting Groups of Indolylnitroalkenes **3a**–**3e** on the Michael Reaction[a]



2a **3a–3e** **4a–4e**

entry	R	product	time (h)	yield (%)[b]	dr (*syn*/*anti*)[c]	ee (%)[d]
1	Ts (**3a**)	**4a**	0.5	95	93:7	99
2	H (**3b**)	**4b**	40	96	81:19	98
3	Me (**3c**)	**4c**	72	80	93:7	96
4	Bn (**3d**)	**4d**	72	<5	–	–
5	Phenylsulfonyl (**3e**)	**4e**	0.5	92	91:9	99

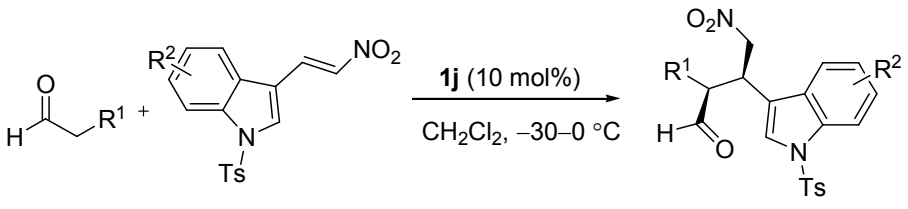
[a] Reactions were performed with **2a** (1.0 mmol), **3a–3e** (0.2 mmol), and **1j** (10 mol% with respect to **3a–3e**) in

CH_2Cl_2 (1.0 mL) at room temperature. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] Determined by chiral HPLC analysis.

With the optimized conditions in hand (dichloromethane as reaction medium, 0 °C ~ –30 °C, 10 mol% of **1j** as the catalyst), the substrate scope of the asymmetric Michael addition was then investigated by applying a range of aliphatic aldehydes and indolylnitroalkenes as donors and acceptors, and the results are summarized in Table 4. When a variety of aldehydes, including *n*-butanal **2a**, pentanal **2b**, isovaleral **2c**, heptanal **2d**, octanal **2e** and phenylpropylaldehyde **2f**, were used as Michael donor reagents to react with (*E*)-3-(2-nitrovinyl)-1-tosyl-1*H*-indole **3a**, all the reactions proceeded very well and furnished the corresponding expected products **4a** and **4f**–**4j** in 94–98% yields with 98:2–>99:1 *dr*s and >99% *ee*s (Table 4, entries 1–6). However, for this transformation, it is obvious that different Michael donors show different reactivities. For example, the Michael reactions with isovaleral **2c** and octanal **2e** as nucleophilic substrates could not complete even after 120 hours at –30 °C. When the reaction temperature were increased to 0 °C and –15 °C, the reactions were complete within 30 hours to give the desired products **4g** and **4i** in excellent yields with perfect stereoselectivities, respectively (Table 4, entries 3 and 5). Subsequently, indolylnitroalkenes **3f** and **3g** bearing -Br and -OMe substituents on 5-position of indole backbones were also respectively investigated for this transformation. All the Michael addition reactions between **2b**–**2e** and **3f**–**3g** proceeded smoothly to afford the corresponding products **4k**–**4q** in 92–97% yields with 97:3–>99:1 *dr*s and >99 *ee*s (Table 4, entries 7–13). When 6-Br substituted indolylnitroalkenes **3h**

reacted with aliphatic aldehydes **2b**–**2e**, excellent catalytic results (92–98% yields, 98:2–>99:1 *dr*s and >99% *ee*s) were achieved (Table 4, entries 14–17). More indolylnitroalkenes **3i**–**3l** bearing 2-Me, 4-Me, 6-Cl or 7-NO_2 substituents were also proven to be suitable substrates for this transformation, and the Michael addition reactions between **3i**–**3l** and **2b** proceeded smoothly to give Michael adducts **4v**–**4y** in 90–98% yields with 97:3–99:1 *dr*s and >99 *ee*s (Table 4, entries 18–21). In addition, 2-methylpropanal **2g** was also used as a substrate for access to a quaternary carbon-containing adduct **4z**, but only 26% yield and 87% *ee* of the desired product were obtained for this transformation (Scheme 2). Fortunately, single crystals of **4u** were obtained by recrystallization from hexane/ether, and its relative *syn* configuration of the nitromethyl and formyl groups was unambiguously assigned by X-ray crystallographic analysis.[22]

Table 4. Organocatalytic Asymmetric Michael Addition of Aliphatic Aldehydes **2** to Indolylnitroalkenes **3**[a]



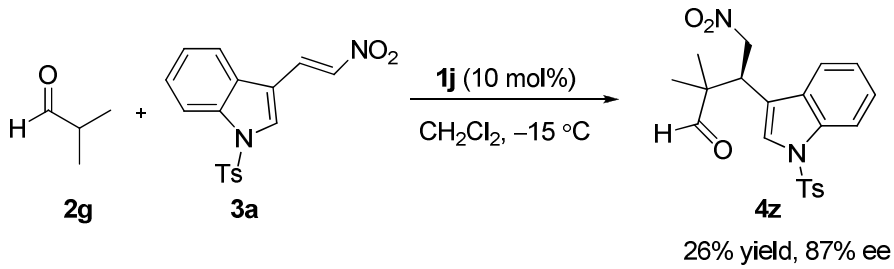
2 **3** **4**

entry	R^1	R^2	product	temp. (°C)	time (h)	yield (%)[b]	dr (*syn*/*anti*)[c]	ee (%)[d]
1	Et (**2a**)	H (**3a**)	**4a**	–30	18	95	98:2	>99
2	*n*-Pr (**2b**)	H (**3a**)	**4f**	–30	40	96	>99:1	>99

3	*i*-Pr (**2c**)	H (**3a**)	**4g**	0	30	94	>99:1	>99
4	*n*-Pentyl (**2d**)	H (**3a**)	**4h**	−30	72	95	99:1	>99
5	*n*-Hexyl (**2e**)	H (**3a**)	**4i**	−15	30	98	>99:1	>99
6	Bn (**2f**)	H (**3a**)	**4j**	−30	67	98	>99:1	>99
7	*n*-Pr (**2b**)	5-Br (**3f**)	**4k**	−30	40	97	97:3	>99
8	*i*-Pr (**2c**)	5-Br (**3f**)	**4l**	0	44	95	>99:1	>99
9	*n*-Pentyl (**2d**)	5-Br (**3f**)	**4m**	−15	40	95	97:3	>99
10	*n*-Hexyl (**2e**)	5-Br (**3f**)	**4n**	−15	40	92	97:3	>99
11	*n*-Pr (**2b**)	5-MeO (**3g**)	**4o**	−30	44	98	>99:1	>99
12	*n*-Pentyl (**2d**)	5-MeO (**3g**)	**4p**	−15	60	98	98:2	>99
13	*n*-Hexyl (**2e**)	5-MeO (**3g**)	**4q**	−15	60	97	98:2	>99
14	*n*-Pr (**2b**)	6-Br (**3h**)	**4r**	−30	38	96	99:1	>99
15	*i*-Pr (**2c**)	6-Br (**3h**)	**4s**	0	35	98	>99:1	>99
16	*n*-Pentyl (**2d**)	6-Br (**3h**)	**4t**	−15	58	93	98:2	>99
17	*n*-Hexyl (**2e**)	6-Br (**3h**)	**4u**	−15	72	92	>99:1	>99
18	*n*-Pr (**2b**)	2-CH_3 (**3i**)	**4v**	−30	48	98	97:3	>99
19	*n*-Pr (**2b**)	4-CH_3 (**3j**)	**4w**	−30	48	90	99:1	>99
20	*n*-Pr (**2b**)	6-Cl (**3k**)	**4x**	−30	48	98	99:1	>99
21	*n*-Pr (**2b**)	7-NO_2 (**3l**)	**4y**	−30	48	91	98:2	>99

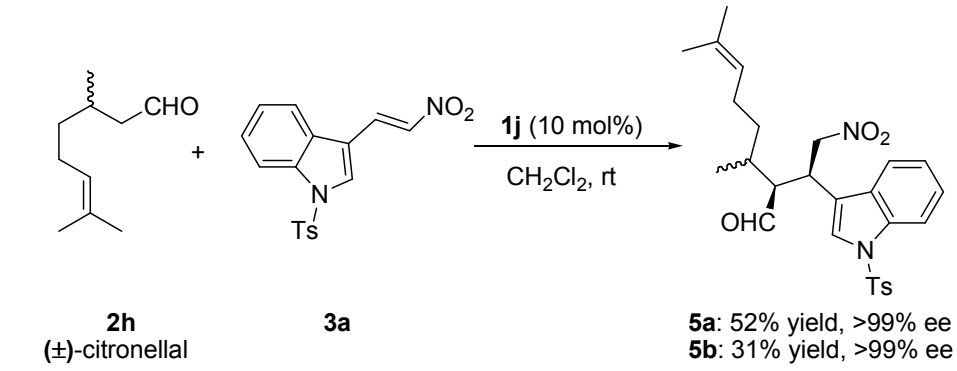
[a] Reactions were performed with **2** (1.0 mmol), **3** (0.2 mmol), and **1j** (10 mol% with respect to **3**) in CH_2Cl_2 (1.0 mL). [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] Determined by chiral HPLC analysis.

Scheme 2. Asymmetric Michael Addition of 2-Methylpropanal **2g** to **3a**

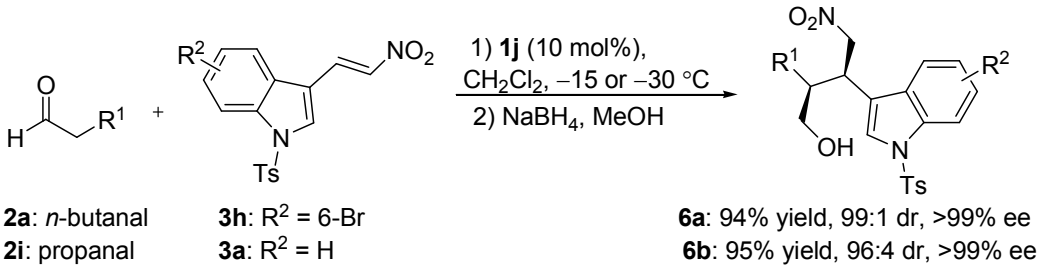


Citronellal **2h**, as a natural perfume, used to synthesize menthol with an antibacterial and antiphlogistic activity, was exploited to react with **3a** in presence of 10 mol% of **1j**, which afforded a couple of diastereomers of the desired adducts **5a** and **5b** in 52% and 31% yields with >99% *ee*s, respectively (Scheme 3). For the further application of this transformation, the direct asymmetric cascade Michael/reduction sequence was also attempted, which avoided the isolation and purification of the Michael adducts. The Michael additions between *n*-butanal **2a** with **3h** and propanal **2i** with **3a** were carried out in CH_2Cl_2 at −15 °C and −30 °C respectively until judged complete by TLC. After replacing the dichloromethane with methanol, $NaBH_4$ (3.0 eq) was added portionwise, then the reaction proceeded for another 6 hours. Pleasingly, the desired products were isolated in 94% yield with 99:1 *dr* and over 99% *ee* for **6a** and 95% yield with 96:4 *dr* and over 99% *ee* for **6b**, respectively (Scheme 4).

Scheme 3. Asymmetric Michael Addition of Racemic Citronellal **2h** to **3a**



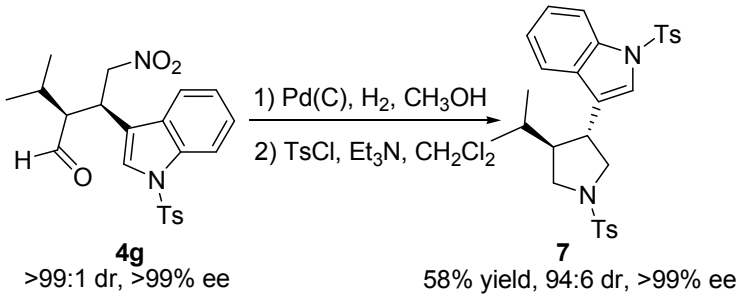
Scheme 4. Asymmetric Sequential Michael/Reduction Reaction for the Synthesis of **6a** and **6b**



In order to show the synthetic utility of the transformation, we conducted the hydrogenation of γ-formyl nitro compound **4g** with 10 mol% of Pd/C (10% w/w). The cascade reductive amination/cyclization reaction proceeded successfully to furnish the desired pyrrolidine with *trans* contiguous stereocenters. After removal of the catalyst and the solvent, the crude product was directly transferred into its *N*-tosyl protected derivative **7** in 58% yield with 94:6 *dr* and over 99% *ee* (Scheme 5). In addition, γ-formyl nitro compound **4a** was sequentially reduced by $NaBH_4$ and Pd/C (10 mol%) in anhydrous methanol to furnish 1,4-amino alcohol compound. Subsequently, the Tosyl group was removed by treatment with Mg and NH_4Cl in methanol. Finally, the resulting tryptamine product was directly transferred into its *NH*-Boc protected derivative **8** in 74% yield with 98:2 *dr* and 99% *ee* (Scheme 6). Intriguingly, it was

further disclosed that desulfonylation and nitro reduction of **4a** could be simultaneously carried out in the presence of magnesium and ammonium chloride in methanol. After reductive amination by $NaBH_4$ followed by *in situ N*-Boc protection, cyclic tryptamine derivative **9** was obtained in 13% yield with 94:6 *dr* and 82% *ee*, through a three-step, one pot operation (Scheme 6).

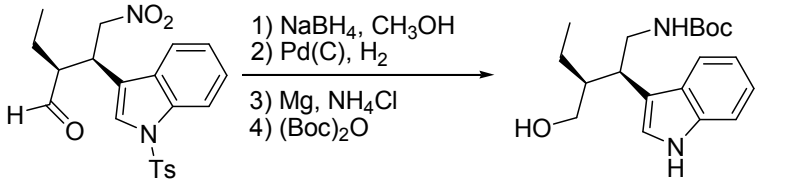
Scheme 5. Synthesis of Cyclic Tryptamine Derivative **7**



4g
>99:1 dr, >99% ee

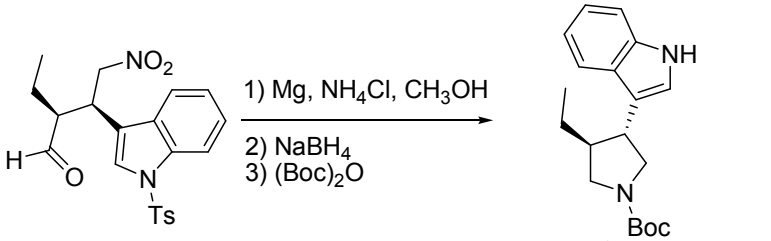
7
58% yield, 94:6 dr, >99% ee

Scheme 6. Synthesis of Tryptamine Derivative **8** and **9**



4a
98:2 dr, >99% ee

8
74% yield, 98:2 dr, 99% ee



4a
98:2 dr, >99% ee

9
13% yield, 94:6 dr, 82% ee

CONCLUSION

In summary, we have developed a direct asymmetric Michael addition of aliphatic aldehydes to indole-3-carboxaldehyde derived nitroalkenes with (*S*)-diphenylprolinol

trimethylsilyl ether as an efficient organic catalyst. The expected chiral tryptamine precursors were obtained in excellent yields with nearly optically pure form for most of cases. As instances of applications of this organocatalytic asymmetric Michael addition, 2-alkyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butan-1-ol and tryptamine derivatives were readily achieved with both good diastereoselectivities and excellent enantioselectivities. In addition, the optically pure 2-alkyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl) butanal products could be facilely converted into a wide array of useful frameworks such as 1,4-amino alcohols or γ-amino acids in a straightforword manner. The useful methodology will be expected to be further applied into the synthesis of some natural products and compounds of pharmaceutical interest.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out in air and using undistilled solvent, without any precautions to exclude air and moisture unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) on silica gel GF-254 precoated glass plates. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using silica gel. Melting points were measured on a melting point apparatus and uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or D_6-DMSO on 300 MHz or 400 MHz spectometers. Tetramethylsilane (TMS) served as internal standard for ^{1}H NMR and $CDCl_3$ or D_6-DMSO was used as internal

standard for ^{13}C NMR. IR spectra were recorded on a FT-IR spectrometer. Mass spectra were carried out using Quadrupole LC/MS system with ESI resource. HRMS was recorded on a commercial apparatus (ESI Source). HPLC analysis was conducted on a HPLC system equipped with chiral-stationary-phase columns (Φ 0.46 cm × 25 cm). Optical rotations were measured on a polarimeter and reported as follows: $[\alpha]_D$ (c in g per 100 mL, solvent).

General Procedure for the Preparation of Indolylnitroalkenes 3a–3l. Phosphorus oxychloride was added dropwise to dimethyl formamide with ice-bath cooling. The chosen indoles were added as a dimethyl formamide solution for preparation of corresponding indole carbaldehydes. Subsequently, the -NH group of indole carbaldehydes were protected with methyl, tosyl, benzyl or phenylsulfonyl by using corresponding halogenides under different basic conditions, such as sodium hydride or potassium carbonate. Then, the resulting *N*-protected or unprotected indole carbaldehydes reacted with nitromethane to furnish the desired indolylnitroalkenes in presence of ammonium acetate as the catalyst. [23]

(*E*)-3-(2-Nitrovinyl)-1-tosyl-1*H*-indole (3a): ^1H NMR (300 MHz, D_6-DMSO) δ 8.73 (s, 1H), 8.35 (d, *J* = 13.5 Hz, 1H), 8.21 (d, *J* = 13.8 Hz, 1H), 8.10–7.85 (m, 4H), 7.53–7.29 (m, 4H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 146.3, 136.8, 134.7, 133.4, 133.3, 131.0, 130.5, 127.0, 126.9, 126.01, 124.7, 121.4, 113.7, 113.4, 21.0.

(*E*)-1-Benzyl-3-(2-nitrovinyl)-1*H*-indole (3d): ^1H NMR (300 MHz, D_6-DMSO) δ 8.46–8.35 (m, 2H), 8.10–7.95 (m, 2H), 7.66–7.57 (m, 1H), 7.42–7.19 (m, 7H), 5.51 (s,

2H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 138.7, 137.5, 136.7, 134.0, 131.6, 128.7, 127.8, 127.3, 125.3, 123.6, 122.3, 120.9, 111.7, 107.8, 49.8.

(*E*)-6-Bromo-3-(2-nitrovinyl)-1-tosyl-1*H*-indole (3h): ^{1}H NMR (300 MHz, D_6-DMSO) δ 8.74 (s, 1H), 8.35–8.11 (m, 2H), 8.11–7.80 (m, 4H), 7.56–7.28 (m, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 146.6, 137.3, 135.3, 133.4, 133.2, 130.7, 130.3, 127.6, 127.0, 126.1, 123.1, 118.7, 115.8, 113.5, 21.1.

General Procedure for the Michael Addition Reaction. (*S*)-diphenylprolinol trimethylsilyl ether **1j** (6.51 mg, 0.02 mmol) and indolylnitroalkene **3** (0.20 mmol) were dissolved in DCM (1.0 mL) at rt or –30 °C. The solution was stirred for 10 min, and then aliphatic aldehyde **2** (1.00 mmol) was added. The reaction mixture was then stirred at suitable reaction temperature until complete consumption of nitroalkene (monitored by TLC). The solvent was evaporated and the residue was purified by flash column silica-gel chromatography (PE/EA = 5/1 ~ 8/1) to provide the corresponding Michael adducts.

(2*S*,3*R*)-2-Ethyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butanal (4a): Reaction at –30 °C, pale yellow oil, 95% yield (78.7 mg), >99% ee, dr = 98/2. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 41.061 min, t_{minor} = 35.479 min; $[\alpha]_D^{25}$ = +7.72 (c 0.26, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.52 (s, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.79–4.70 (m, 2H), 4.14–4.06 (m, 1H), 2.90 (q, *J* = 6.8 Hz, *J* = 13.6 Hz, 1H), 2.31 (s, 3H), 1.61–1.54 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 203.0, 145.4, 135.3, 134.6, 130.1, 129.4, 126.8, 125.5, 125.2, 123.9, 119.2, 118.4, 114.3, 77.4, 53.9, 34.3, 21.7, 20.6, 11.0; IR (KBr) ν_{max}: 3114.0, 2959.9, 2937.7, 2873.7, 2729.5, 1720.9, 1553.1, 1448.7, 1370.5, 1172.5, 1127.6, 754.6, 668.8, 575.0 cm^{-1}; MS (ESI): calcd for $C_{21}H_{22}N_2NaO_5S$ $[M+Na]^+$ 437.1, Found: 437.1; HRMS (ESI): calcd for $C_{21}H_{26}N_3O_5S$ $[M+NH_4]^+$ 432.1588, Found: 432.1575.

2-Ethyl-3-(1*H*-indol-3-yl)-4-nitrobutanal (4b): Reaction at room temperature, pale yellow oil, 96% yield (50.0 mg), 98% ee, dr = 81/19. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 25.731 min, t_{minor} = 20.987 min; $[\alpha]_D^{25}$ = –2.08 (c 2.16, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, *J* = 2.4 Hz, 1H), 8.29 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.36–7.29 (m, 1H), 7.23–7.17 (m, 1H), 7.17–7.11 (m, 1H), 6.99 (s, 1H), 4.84–4.67 (m, 2H), 4.19–4.09 (m, 1H), 2.93–2.85 (m, 1H), 1.64–1.53 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 136.5, 126.0, 123.3, 122.7, 120.2, 118.6, 111.9, 111.1, 78.1, 54.8, 35.2, 20.7, 11.2; IR (KBr) ν_{max}: 3134.5, 3057.7, 2957.0, 2877.0, 2724.3, 1717.2, 1550.8, 1448.1, 1376.2, 1094.8, 1015.6, 976.0, 747.5 cm^{-1}; MS (ESI) calcd for $C_{14}H_{16}N_2NaO_3$ $[M+Na]^+$ 283.1, Found: 283.1; HRMS (ESI) calcd for $C_{14}H_{20}N_3O_3$ $[M+NH_4]^+$ 278.1499, Found: 278.1490.

2-Ethyl-3-(1-methyl-1*H*-indol-3-yl)-4-nitrobutanal (4c): Reaction at room temperature, pale yellow oil, 80% yield (43.9 mg), 96% ee, dr = 93/7. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 27.079 min, t_{minor} = 20.001 min; $[\alpha]_D^{25}$ = –6.30 (c 1.84, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, *J* = 2.4 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.31–7.22 (m, 2H), 7.17–7.11 (m, 1H), 6.92 (s, 1H), 4.79–4.68 (m, 2H), 4.17–4.08 (m, 1H), 3.73 (s, 3H), 2.92–2.85 (m, 1H), 1.65–1.57 (m, 2H), 0.87 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 137.3, 127.8, 122.4, 122.3, 119.8, 118.7, 109.9, 109.6, 78.2, 54.9, 35.2, 33.0, 20.7, 11.3; IR (KBr) ν max: 3121.3, 3057.0, 2949.4, 2724.5, 1719.9, 1549.9, 1467.3, 1379.9, 1134.4, 969.0, 743.9 cm^{-1}; MS (ESI) calcd for $C_{15}H_{18}N_2NaO_3$ $[M+Na]^+$ 297.1, Found: 297.1; HRMS (ESI) calcd for $C_{15}H_{19}N_2O_3$ $[M+H]^+$ 275.1390,

Found: 275.1380.

2-Ethyl-4-Nitro-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl)butanal (4e): Reaction at room temperature, pale yellow oil, 92% yield (73.7 mg), 99% ee, dr = 91/9. HPLC: Chiralcel OD-H, hexane/i-PrOH (80:20) , flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 41.177 min, t_{minor} = 34.343 min; $[\alpha]_D^{25}$ = –3.52 (c 1.90, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (d, *J* = 1.6 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 2H), 7.56–7.47 (m, 3H), 7.47–7.39 (m, 3H), 7.34 (t, *J* = 7.6 Hz, 1H), 4.81–4.68 (m, 2H), 4.12–4.03 (m, 1H), 2.95–2.85 (m, 1H), 1.64–1.54 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 134.2, 129.5, 129.4, 126.8, 125.7, 125.2, 124.0, 119.3, 118.6, 114.4, 77.4, 53.8, 34.3, 20.7, 11.0; IR (KBr) ν_{max}: 3109.2, 2958.5, 2937.6, 2875.4, 2726.1, 1720.1, 1553.4, 1447.7, 1370.9, 1174.2, 1126.5, 990.6, 960.4, 750.6, 580.5 cm^{-1}; MS (ESI) calcd for $C_{20}H_{20}N_2NaO_5S$ $[M+Na]^+$ 423.1, Found: 423.1; HRMS (ESI) calcd for $C_{20}H_{24}N_3O_5S$ $[M+NH_4]^+$ 418.1431, Found: 418.1423.

(*S*)-2-((*R*)-2-Nitro-1-(1-tosyl-1*H*-indol-3-yl)ethyl)pentanal (4f): Reaction at –30 °C, pale yellow oil, 96% yield (82.3 mg), >99% ee, dr > 99/1. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 37.146 min, t_{minor} = 27.158 min; $[\alpha]_D^{25}$ = +14.29 (c 1.56, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.52 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.28–7.22 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 4.80–4.70 (m, 2H), 4.11–4.03 (m, 1H), 2.96–2.88 (m, 1H), 2.30 (s, 3H), 1.60–1.18 (m, 4H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 145.4, 135.4, 134.7, 130.1, 129.4, 126.8, 125.5, 125.1, 123.9, 119.2, 118.5, 114.3, 77.3, 52.6, 34.8, 29.7, 21.7, 20.0, 14.1; IR (KBr) ν_{max}: 3117.1, 2944.5, 2871.2, 2726.9, 1721.5, 1553.3, 1447.3, 1372.6, 1172.6, 1127.0, 751.5, 669.8, 575.9 cm^{-1}; MS (ESI): calcd for $C_{22}H_{24}N_2NaO_5S$ $[M+Na]^+$ 451.1, Found: 451.1; HRMS (ESI): calcd for $C_{22}H_{28}N_3O_5S$ $[M+NH_4]^+$ 446.1744, Found: 446.1741.

(2*S*,3*R*)-2-Isopropyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butanal (4g): Reaction at 0 °C, pale yellow solid (m.p. 51.0 °C), 94% yield (80.6 mg), >99% ee, dr > 99/1. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 22.667 min, t_{minor} = 18.604 min]; $[\alpha]_D^{25}$ = +17.14 (c 0.77, CH_3COCH_3); ^{1}H NMR (400

MHz, $CDCl_3$): δ 9.91 (d, *J* = 1.6 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.51 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.28–7.22 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.76–4.66 (m, 2H), 4.21–4.10 (m, 1H), 3.03–2.98 (m, 1H), 2.30 (s, 3H), 1.85–1.76 (m, 1H), 1.12 (d, *J* = 7.2 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 145.3, 135.5, 134.7, 130.1, 129.3, 126.8, 125.5, 125.4, 123.9, 119.1, 118.6, 114.4, 77.6, 57.7, 33.9, 28.4, 21.8, 21.7, 17.8; IR (KBr) ν_{max}: 3113.7, 2960.4, 2879.6, 2737.4, 1717.3, 1553.0, 1449.5, 1371.4, 1172.5, 1127.1, 754.3, 668.6, 575.2 cm^{-1}; MS (ESI): calcd for $C_{22}H_{24}N_2NaO_5S$ $[M+Na]^+$ 451.1, Found: 451.1; HRMS (ESI): calcd for $C_{22}H_{28}N_3O_5S$ $[M+NH_4]^+$ 446.1744, Found: 446.1734.

(*S*)-2-((*R*)-2-Nitro-1-(1-tosyl-1*H*-indol-3-yl)ethyl)heptanal (4h): Reaction at −30 °C, pale yellow oil, 95% yield (86.7 mg), >99% ee, dr = 99/1. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 $mL{\cdot}min^{-1}$, λ = 254 nm, t_{major} = 31.762 min, t_{minor} = 23.591 min; $[\alpha]_D^{25}$ = +19.29 (c 1.54, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, *J* = 1.6 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.51 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.29-7.23 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.81–4.68 (m, 2H), 4.11–4.04 (m, 1H), 2.95–2.87 (m, 1H), 2.31 (s, 3H), 1.59–1.41 (m, 2H), 1.32–1.11 (m, 6H), 0.79 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 145.4, 135.4, 134.7, 130.1, 129.4, 126.9, 125.5, 125.2, 123.9, 119.2, 118.4, 114.3, 77.3, 52.8, 34.8, 31.7, 27.6, 26.4, 22.4, 21.7, 14.0; IR (KBr) ν_{max}: 3120.3, 2932.5, 2860.2, 2726.4, 1721.0, 1630.2, 1554.3, 1449.2, 1371.1, 1173.1, 1125.9, 751.6, 673.1, 577.2 cm^{-1}; MS (ESI): calcd for $C_{24}H_{28}N_2NaO_5S$ $[M+Na]^+$ 479.2, Found: 479.2; HRMS (ESI): calcd for $C_{24}H_{32}N_3O_5S$ $[M+NH_4]^+$ 474.2057, Found: 474.2049.

(*S*)-2-((*R*)-2-Nitro-1-(1-tosyl-1*H*-indol-3-yl)ethyl)octanal (4i): Reaction at −15 °C, pale yellow oil, 98% yield (92.2 mg), >99% ee, dr > 99/1. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 $mL{\cdot}min^{-1}$, λ = 210 nm, t_{major} = 29.416 min, t_{minor} = 21.959 min; $[\alpha]_D^{25}$ = +13.85 (c 1.69, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.52 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.28-7.23 (m, 1H), 7.20 (d, *J* = 7.6

Hz, 2H), 4.82–4.68 (m, 2H), 4.12–4.03 (m, 1H), 2.96–2.87 (m, 1H), 2.31 (s, 3H), 1.59–1.41 (m, 2H), 1.30–1.10 (m, 8H), 0.80 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 145.4, 135.4, 134.7, 130.1, 129.4, 126.8, 125.5, 125.2, 123.8, 119.2, 118.4, 114.3, 77.3, 52.8, 34.8, 31.5, 29.2, 27.6, 26.6, 22.6, 21.7, 14.1； IR (KBr) ν_{max}: 3120.3, 2930.8, 2860.5, 2728.3, 1721.6, 1552.9, 1448.3, 1371.5, 1172.9, 1127.7, 972.2, 751.0, 668.7, 575.3 cm^{-1}; MS (ESI): calcd for $C_{25}H_{30}N_2NaO_5S$ $[M+Na]^+$ 493.2, Found: 493.2; HRMS (ESI): calcd for $C_{25}H_{34}N_3O_5S$ $[M+NH_4]^+$ 488.2214, Found: 488.2196.

(2*S*,3*R*)-2-Benzyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butanal (4j): Reaction at −30 °C, pale yellow solid (m.p. 48.0–49.0 °C), 98% yield (93.4 mg), >99% ee, dr > 99/1. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 44.852 min, t_{minor} = 40.961 min]; $[\alpha]_D^{25}$ = +1.57 (c 2.17, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.67 (d, J = 1.2 Hz,1H), 7.97 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.57 (s, 1H), 7.25–7.17 (m, 8H), 7.00 (d, J = 6.8 Hz, 2H), 4.88–4.81 (m, 1H), 4.76–4.70 (m, 1H), 4.09–4.00 (m, 1H), 3.25 (q, J = 7.5 Hz, 1H), 2.90–2.83 (m, 1H), 2.78–2.72 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 145.4, 137.0, 135.4, 134.6, 130.1, 129.3, 129.0, 128.97, 128.6, 127.2, 126.8, 125.6, 125.1, 123.9, 119.2, 118.6, 114.3, 76.7, 54.4, 34.7, 34.2, 21.6; IR (KBr) ν_{max}: 3030.2, 2925.4, 2863.0, 2733.0, 1717.8, 1551.7, 1444.0, 1370.6, 1171.3, 1126.3, 748.3, 681.2, 573.3 cm^{-1}; MS (ESI): calcd for $C_{26}H_{24}N_2NaO_5S$ $[M+Na]^+$ 499.1, Found: 499.1; HRMS (ESI): calcd for $C_{26}H_{28}N_3O_5S$ $[M+NH_4]^+$ 494.1744, Found: 494.1733.

(*S*)-2-((*R*)-1-(5-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)pentanal (4k): Reaction at −30 °C, pale yellow oil, 97% yield (98.4 mg), >99% ee, dr = 97/3. HPLC: Chiralcel AS-H, hexane/i-PrOH = 85:15, flow rate: 0.8 mL·min^{-1}, λ = 210 nm, t_{major} = 35.317 min, t_{minor} = 28.237 min; $[\alpha]_D^{25}$ = +11.22 (c 2.08, CH_3COCH_3); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.70 (d, J = 1.8 Hz, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 1.5 Hz, 1H), 7.54 (s, 1H), 7.42 (dd, J = 8.9 Hz, 1H), 7.22 (d, J = 8.1 Hz, 2H), 4.82–4.68 (m, 2H), 4.07–3.97 (m, 1H), 2.96–2.86 (m, 1H), 2.32 (s, 3H), 1.39–1.21 (m, 4H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 145.7, 134.3, 134.0, 131.2, 130.2, 128.5, 126.8, 126.4, 121.9, 117.9, 117.5, 115.7,

77.1, 52.5, 34.5, 29.7, 21.7, 20.0, 14.1; IR (KBr) ν_{max}: 3109.1, 2944.3, 2870.5, 2726.6, 1722.0, 1554.7, 1443.7, 1372.9, 1169.6, 804.1, 665.9, 580.9, 546.5 cm^{-1}; MS (ESI) calcd for $C_{22}H_{23}BrN_2NaO_5S$ $[M+Na]^+$ 529.0, Found: 529.0; HRMS (ESI) calcd for $C_{22}H_{27}BrN_3O_5S$ $[M+NH_4]^+$ 524.0849, Found: 524.0847.

(2*S*,3*R*)-3-(5-Bromo-1-tosyl-1*H*-indol-3-yl)-2-isopropyl-4-nitrobutanal (4l): Reaction at 0 °C, white solid (m.p. 58.0–59.0 °C), 95% yield (96.4 mg), >99% ee, dr > 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH (85:15) , flow rate: 0.8 mL·min^{-1}, λ = 254 nm, t_{major} = 26.867 min, t_{minor} = 23.952 min; $[\alpha]_D^{25}$ = +13.42 (c 0.78, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.67–7.60 (m, 3H), 7.52 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.76–4.66 (m, 2H), 4.16–4.06 (m, 1H), 3.00–2.95 (m, 1H), 2.32 (s, 3H), 1.83–1.75 (m, 1H), 1.15 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 145.7, 134.3, 134.1, 131.1, 130.2, 128.5, 126.8, 126.6, 121.9, 118.0, 117.5, 115.8, 77.5, 57.5, 33.7, 28.5, 21.8, 21.7, 17.9; IR (KBr) ν_{max}: 3110.0, 2959.4, 2876.8, 2736.8, 1716.0, 1553.7, 1443.4, 1373.4, 1169.5, 804.1, 665.7, 581.3, 539.9 cm^{-1}; MS (ESI) calcd for $C_{22}H_{23}BrN_2NaO_5S$ $[M+Na]^+$ 529.0, Found: 529.0; HRMS (ESI) calcd for $C_{22}H_{27}BrN_3O_5S$ $[M+NH_4]^+$ 524.0849, Found: 524.0830.

(*S*)-2-((*R*)-1-(5-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)heptanal (4m): Reaction at −15 °C, pale yellow oil, 95% yield (101.7 mg), >99% ee, dr = 97/3. HPLC: Chiralcel AD-H, hexane/i-PrOH = 95:5, flow rate: 0.8 mL·min^{-1}, λ = 254 nm, t_{major} = 26.867 min, t_{minor} = 23.952 min; $[\alpha]_D^{25}$ = +15.91 (c 3.37, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.71 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 1.2 Hz, 1H), 7.50 (s, 1H), 7.43 (dd, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.79–4.67 (m, 2H), 4.05–3.96 (m, 1H), 2.93–2.86 (m, 1H), 2.34 (s, 3H), 1.57–1.42 (m, 2H), 1.32–1.12 (m, 6H), 0.81 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 145.7, 134.4, 134.0, 131.2, 130.2, 128.5, 126.8, 126.4, 122.0, 117.9, 117.5, 115.7, 77.2, 52.6, 34.5, 31.7, 27.6, 26.3, 22.4, 21.7, 14.0; IR (KBr) ν_{max}: 3105.5, 2931.3, 2862.1, 2726.9, 1719.5, 1555.1, 1444.8, 1373.7, 1169.0, 1118.4, 805.5, 666.7, 581.1, 542.9 cm^{-1}; MS (ESI) calcd for $C_{24}H_{27}BrN_2NaO_5S$ $[M+Na]^+$ 557.1, Found: 557.0; HRMS (ESI) calcd for $C_{24}H_{31}BrN_3O_5S$ $[M+NH_4]^+$ 552.1162,

Found: 552.1145.

(*S*)-2-((*R*)-1-(5-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)octanal (4n): Reaction at −15 °C, pale yellow oil, 92% yield (101.1 mg), >99% ee, dr = 97/3. HPLC: Chiralcel AD-H, hexane/i-PrOH = 95:5, flow rate: 0.8 mL·min^{-1}, λ = 254 nm, t_{major} = 30.827 min, t_{minor} = 28.821 min; $[\alpha]_D^{25}$ = +15.01 (c 4.11, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, *J* = 1.6 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.59 (s, 1H), 7.50 (s, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.79–4.67 (m, 2H), 4.03–3.96 (m, 1H), 2.93–2.85 (m, 1H), 2.34 (s, 3H), 1.59–1.41 (m, 2H), 1.31–1.12 (m, 8H), 0.82 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 145.7, 134.4, 134.0, 131.2, 130.2, 128.5, 126.8, 126.4, 122.0, 117.9, 117.5, 115.7, 77.2, 52.6, 34.6, 31.5, 29.2, 27.7, 26.5, 22.6, 21.7, 14.1; IR (KBr) ν_{max}: 3115.0, 2930.0, 2860.6, 2726.2, 1720.9, 1556.0, 1447.3, 1372.2, 1168.7, 1118.1, 804.0, 667.0, 581.1, 542.6 cm^{-1}; MS (ESI) calcd for $C_{25}H_{29}BrN_2NaO_5S$ $[M+Na]^+$ 571.1, Found: 571.1; HRMS (ESI) calcd for $C_{25}H_{33}BrN_3O_5S$ $[M+NH_4]^+$ 566.1319, Found: 566.1302.

(*S*)-2-((*R*)-1-(5-Methoxy-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)pentanal (4o): Reaction at −30 °C, white oil, 98% yield (89.9 mg), >99% ee, dr > 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH = 80:20, flow rate: 0.8 mL·min^{-1}, λ = 254 nm, t_{major} = 44.523 min, t_{minor} = 33.691 min; $[\alpha]_D^{25}$ = +15.02 (c 4.36, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.47 (s, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.88 (s, 1H), 4.80–4.68 (m, 2H), 4.06–3.99 (m, 1H), 3.80 (s, 3H), 2.93–2.85 (m, 1H), 2.30 (s, 3H), 1.57–1.22 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 156.8, 145.3, 134.6, 130.5, 130.0, 126.7, 125.8, 118.6, 115.2, 114.2, 102.0, 77.2, 55.8, 52.5, 34.7, 29.6, 21.7, 20.0, 14.1; IR (KBr) ν_{max}: 3112.3, 2947.8, 2873.3, 2727.6, 1721.4, 1600.9, 1557.5, 1460.5, 1369.8, 1217.3, 1166.5, 1133.0, 844.2, 815.4, 671.5, 586.1, 545.0 cm^{-1}; MS (ESI) calcd for $C_{23}H_{26}N_2NaO_6S$ $[M+Na]^+$ 481.1, Found: 481.1; HRMS (ESI) calcd for $C_{23}H_{30}N_3O_6S$ $[M+NH_4]^+$ 476.1850, Found: 476.1844.

(*S*)-2-((*R*)-1-(5-Methoxy-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)heptanal (4p): Reaction at −15 °C, white oil, 98% yield (95.4 mg), >99% ee, dr = 98/2. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} =

19.750 min, t_{minor} = 20.991 min; $[\alpha]_D^{25}$ = +20.16 (c 2.46, CH_3COCH_3); ^1H NMR (300 MHz, $CDCl_3$): δ 9.70 (s, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.44 (s, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 1H), 6.86 (d, *J* = 1.2 Hz, 1H), 4.79–4.65 (m, 2H), 4.06–3.96 (m, 1H), 3.82 (s, 3H), 2.93–2.83 (m, 1H), 2.32 (s, 3H), 1.59–1.41 (m, 2H), 1.31–1.08 (m, 6H), 0.80 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 156.8, 145.3, 134.6, 130.5, 130.0, 126.8, 125.8, 118.6, 115.2, 114.2, 102.0, 77.3, 55.8, 52.7, 34.7, 31.7, 27.5, 26.4, 22.4, 21.7, 14.0; IR (KBr) ν_{max}: 3114.3, 2936.0, 2861.7, 2724.2, 1722.1, 1603.7, 1554.9, 1461.9, 1372.0, 1219.2, 1170.3, 1133.0, 812.1, 672.8, 587.6, 544.1 cm^{-1}; MS (ESI) calcd for $C_{25}H_{30}N_2NaO_6S$ $[M+Na]^+$ 509.2, Found: 509.1; HRMS (ESI) calcd for $C_{25}H_{34}N_3O_6S$ $[M+NH_4]^+$ 504.2163, Found: 504.2160.

(*S*)-2-((*R*)-1-(5-Methoxy-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)octanal (4q): Reaction at −15 °C, white oil, 97% yield (97.1 mg), >99% ee, dr = 98/2. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 18.403 min, t_{minor} = 19.530 min; $[\alpha]_D^{25}$ = +18.37 (c 4.10, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.48 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.94 (dd, *J* = 9.0 Hz, 1H), 6.88 (d, *J* = 2.4 Hz, 1H), 4.80–4.68 (m, 2H), 4.07–4.00 (m, 1H), 3.80 (s, 3H), 2.93–2.86 (m, 1H), 2.30 (s, 3H), 1.58–1.40 (m, 2H), 1.31–1.10 (m, 8H), 0.80 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 156.8, 145.2, 134.6, 130.5, 130.0, 126.7, 125.8, 118.6, 115.1, 114.2, 102.0, 77.3, 55.8, 52.7, 34.6, 31.5, 29.2, 27.5, 26.6, 22.5, 21.6, 14.1; IR (KBr) ν_{max}: 3120.0, 2932.1, 2859.5, 2728.1, 1721.8, 1600.9, 1555.1, 1461.8, 1371.3, 1218.8, 1169.9, 848.0, 809.7, 673.9, 587.9, 543.8 cm^{-1}; MS (ESI) calcd for $C_{26}H_{32}N_2NaO_6S$ $[M+Na]^+$ 523.2, Found: 523.2; HRMS (ESI) calcd for $C_{26}H_{36}N_3O_6S$ $[M+NH_4]^+$ 518.2319, Found: 518.2318.

(*S*)-2-((*R*)-1-(6-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)pentanal (4r): Reaction at −30 °C, pale yellow solid (m.p. 94.0–95.0 °C), 96% yield (97.4 mg), >99% ee, dr = 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH = 85:15, flow rate: 0.8 mL·min^{-1}, λ = 210 nm, t_{major} = 33.930 min, t_{minor} = 31.559 min; $[\alpha]_D^{25}$ = +9.94 (c 1.47, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 8.15 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H),

7.49 (s, 1H), 7.39–7.33 (m, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.79–4.68 (m, 2H), 4.08–4.01 (m, 1H), 2.92–2.84 (m, 1H), 2.33 (s, 3H), 1.55–1.19 (m, 4H), 0.77 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 145.8, 135.9, 134.4, 130.3, 128.3, 127.3, 126.8, 125.5, 120.4, 119.3, 118.4, 117.3, 77.3, 52.6, 34.5, 29.7, 21.7, 20.0, 14.1; IR (KBr) ν_{max}: 3106.8, 2949.8, 2866.8, 2719.0, 1721.6, 1550.6, 1420.2, 1372.0, 1173.1, 1119.8, 809.3, 667.6, 582.7 cm^{-1}; MS (ESI): calcd for $C_{22}H_{23}BrN_2NaO_5S$ $[M+Na]^+$ 529.0, Found: 529.0; HRMS (ESI): calcd for $C_{22}H_{27}BrN_3O_5S$ $[M+NH_4]^+$ 524.0849, Found: 524.0845.

(2*S*,3*R*)-3-(6-Bromo-1-tosyl-1*H*-indol-3-yl)-2-isopropyl-4-nitrobutanal (4s): Reaction at 0 °C, white solid (m.p. 118.0 °C), 98% yield (99.5 mg), >99% ee, dr > 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH = 85:15, flow rate: 0.8 mL·min^{-1}, λ = 210 nm, t_{major} = 29.995 min, t_{minor} = 31.167 min; $[\alpha]_D^{25}$ = +7.97 (c 0.59, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (d, J = 1.2 Hz, 1H), 8.14 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.49 (s, 1H), 7.39–7.33 (m, 2H), 7.25 (d, J = 8.0 Hz, 2H), 4.69 (d, J = 6.8 Hz, 2H), 4.17–4.10 (m, 1H), 2.99–2.93 (m, 1H), 2.33 (s, 3H), 1.82–1.73 (m, 1H), 1.13 (d, J = 7.2 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 145.8, 136.0, 134.4, 130.3, 128.2, 127.3, 126.8, 125.7, 120.3, 119.2, 118.5, 117.4, 77.7, 57.7, 33.7, 28.5, 21.8, 21.76, 17.8; IR (KBr) ν_{max}: 3116.4, 2959.2, 2727.6, 1720.2, 1551.0, 1427.9, 1370.7, 1168.0, 1148.6, 810.2, 666.1, 585.0 cm^{-1}; MS (ESI): calcd for $C_{22}H_{23}BrN_2NaO_5S$ $[M+Na]^+$ 529.0, Found: 529.0; HRMS (ESI): calcd for $C_{22}H_{27}BrN_3O_5S$ $[M+NH_4]^+$ 524.0849, Found: 524.0831.

(*S*)-2-((*R*)-1-(6-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)heptanal (4t): Reaction at −15 °C, pale yellow solid (m.p. 139.0–140.0 °C), 93% yield (99.6 mg), >99% ee, dr = 98/2. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major}= 13.970 min, t_{minor} = 15.796 min; $[\alpha]_D^{25}$ = +19.34 (c 2.05, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, J = 1.2 Hz, 1H), 8.15 (s, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.49 (s, 1H), 7.39–7.33 (m, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.78–4.68 (m, 2H), 4.08–4.01 (m, 1H), 2.91–2.83 (m, 1H), 2.34 (s, 3H), 1.56–1.39 (m, 2H), 1.31–1.05 (m, 6H), 0.79 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 145.8, 135.9, 134.4, 130.3, 128.3, 127.2, 126.8, 125.5, 120.4, 119.3, 118.4,

117.3, 77.3, 52.8, 34.5, 31.7, 27.6, 26.3, 22.4, 21.7, 14.0; IR (KBr) ν_{max}: 3106.4, 2932.8, 2859.4, 2728.4, 1721.2, 1550.0, 1423.9, 1372.0, 1172.0, 1132.1, 808.2, 667.9, 584.1 cm^{-1}; MS (ESI): calcd for $C_{24}H_{27}BrN_2NaO_5S$ $[M+Na]^+$ 557.1; Found: 557.1; HRMS (ESI): calcd for $C_{24}H_{31}BrN_3O_5S$ $[M+NH_4]^+$ 552.1162, Found: 552.1161.

(*S*)-2-((*R*)-1-(6-Bromo-1-tosyl-1*H*-indol-3-yl)-2-nitroethyl)octanal (4u): Reaction at −15 °C, pale yellow solid (m.p. 118.0–119.0 °C), 92% yield (101.1 mg), >99% ee, dr > 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH = 85:15, flow rate: 0.8 mL·min^{-1}, λ = 210 nm, t_{major} = 24.128 min, t_{minor} = 27.467 min; $[\alpha]_D^{25}$ = +19.35 (c 1.24, CH_3COCH_3); ^1H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 8.14 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.50 (s, 1H), 7.39–7.33 (m, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 4.78–4.68 (m, 2H), 4.08–4.01 (m, 1H), 2.91–2.84 (m, 1H), 2.33 (s, 3H), 1.66–1.40 (m, 2H), 1.31–1.11 (m, 8H), 0.81 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 145.7, 135.9, 134.4, 130.3, 128.3, 127.2, 126.8, 125.5, 120.4, 119.3, 118.4, 117.3, 76.9, 52.8, 34.5, 31.5, 29.2, 27.6, 26.6, 22.5, 21.7, 14.1; IR (KBr) ν_{max}: 3104.4, 2928.6, 2857.9, 2729.4, 1717.6, 1551.8, 1425.9, 1371.6, 1171.4, 1133.0, 806.7, 668.3, 582.5 cm^{-1}; MS (ESI): calcd for $C_{25}H_{29}BrN_2NaO_5S$ $[M+Na]^+$ 571.1, Found: 571.1; HRMS (ESI): calcd for $C_{25}H_{33}BrN_3O_5S$ $[M+NH_4]^+$ 566.1319, Found: 566.1315.

(*S*)-2-((*R*)-1-(2-Methyl-1-tosyl-1H-indol-3-yl)-2-nitroethyl)pentanal (4v): Reaction at –30 °C, pale yellow oil, 98% yield (86.7 mg), >99% ee, dr = 97/3. HPLC: Chiralcel AS-H, hexane/i-PrOH = 85:15, flow rate: 0.8 mL·min^{-1}, λ = 254 nm, t_{major} = 36.956 min, t_{minor} = 28.893 min; $[\alpha]_D^{25}$ = –17.19 (c 4.05, CH_3COCH_3); ^1H NMR (300 MHz, $CDCl_3$): δ 9.65 (d, *J* = 1.8 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.25–7.13 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 4.66–4.59 (m, 2H), 4.05–3.93 (m, 1H), 3.02–2.90 (m, 1H), 2.50 (s, 3H), 2.23 (s, 3H), 1.28–1.18 (m, 4H), 0.53 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 145.1, 137.0, 136.5, 135.8, 130.1, 130.0, 126.1, 124.6, 124.0, 118.3, 115.6, 115.1, 76.6, 51.5, 34.5, 29.8, 22.7, 21.7, 19.4, 13.0; IR (KBr) ν_{max}: 2959.6, 2934.3, 2872.4, 2734.0, 1721.6, 1554.5, 1378.0, 1177.0, 749.4, 661.0, 576.6 cm^{-1}; MS (ESI): calcd for $C_{23}H_{26}N_2NaO_5S$ $[M+Na]^+$ 465.1, Found: 465.1; HRMS (ESI): calcd for $C_{23}H_{26}N_2NaO_5S$ $[M+Na]^+$ 465.1455, Found: 465.1446.

(*S*)-2-((*R*)-1-(4-Methyl-1-tosyl-1H-indol-3-yl)-2-nitroethyl)pentanal (4w): Reaction at –30 °C, yellow oil, 90% yield (79.7 mg), >99% ee, dr = 99/1. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 18.439 min, t_{minor} = 19.581 min; $[\alpha]_D^{25}$ = +43.97 (c 2.90, CH_3COCH_3); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.64 (d, *J* = 2.1 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.45 (s, 1H), 7.18–7.06 (m, 3H), 6.89 (d, *J* = 7.5 Hz, 1H), 4.80–4.71 (m, 1H), 4.64–4.57 (m, 1H), 4.41–4.32 (m, 1H), 2.86–2.77 (m, 1H), 2.56 (s, 3H), 2.22 (s, 3H), 1.31–1.13 (m, 4H), 0.74 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.3, 145.4, 135.4, 134.6, 130.9, 130.06, 128.4, 126.9, 126.3, 125.2, 124.3, 120.2, 111.9, 78.1, 54.6, 35.1, 30.2, 21.7, 20.9, 20.5, 14.2; IR (KBr) ν_{max}: 3137.1, 2962.2, 2870.3, 2736.1, 1722.1, 1553.0, 1401.3, 1384.2, 1098.6, 812.3, 666.2, 576.0 cm^{-1}; MS (ESI): calcd for $C_{23}H_{26}N_2NaO_5S$ $[M+Na]^+$ 465.1, Found: 465.1; HRMS (ESI): calcd for $C_{23}H_{26}N_2NaO_5S$ $[M+Na]^+$ 465.1455, Found: 465.1444.

(*S*)-2-((*R*)-1-(6-Chloro-1-tosyl-1H-indol-3-yl)-2-nitroethyl)pentanal (4x): Reaction at –30 °C, yellow oil, 98% yield (90.7 mg), >99% ee, dr = 99/1. HPLC: Chiralcel AS-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 21.870 min, t_{minor} = 20.519 min; $[\alpha]_D^{25}$ = +10.48 (c 4.20, CH_3COCH_3); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.60 (d, *J* = 1.8 Hz, 1H), 7.90 (d, *J* = 1.5 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.43 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.18–7.10 (m, 3H), 4.73–4.60 (m, 2H), 4.01–3.92 (m, 1H), 2.85–2.75 (m, 1H), 2.24 (s, 3H), 1.31–1.11 (m, 4H), 0.68 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 145.7, 135.6, 134.4, 131.5, 130.2, 127.9, 126.8, 125.6, 124.5, 120.1, 118.4, 114.3, 77.3, 52.6, 34.5, 29.6, 21.7, 20.0, 14.1. IR (KBr) ν_{max}: 2960.2, 2932.7, 2872.5, 2733.1, 1722.1, 1554.2, 1426.5, 1376.9, 1174.2, 1142.3, 811.8, 671.1, 579.9 cm^{-1}; MS (ESI): calcd for $C_{22}H_{23}ClN_2NaO_5S$ $[M+Na]^+$ 485.1, Found: 485.1; HRMS (ESI): calcd for $C_{22}H_{23}ClN_2NaO_5S$ $[M+Na]^+$ 485.0908, Found: 485.0891.

(*S*)-2-((*R*)-2-Nitro-1-(7-nitro-1-tosyl-1H-indol-3-yl)ethyl)pentanal (4y): Reaction at –30 °C, pale yellow oil, 91% yield (86.2 mg), >99% ee, dr = 98/2. HPLC: Chiralcel AS-H, hexane/i-PrOH = 70:30, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 49.337 min, t_{minor} = 40.093 min; $[\alpha]_D^{25}$ = +44.20 (c 4.05, CH_3COCH_3); ^{1}H NMR (300 MHz,

$CDCl_3$): δ 9.60 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.66–7.49 (m, 4H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 4.78–4.62 (m, 2H), 4.10–3.99 (m, 1H), 2.88–2.77 (m, 1H), 2.31 (s, 3H), 1.50–1.14 (m, 4H), 0.73 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 145.8, 139.7, 134.8, 133.4, 130.0, 129.5, 127.0, 125.7, 124.1, 123.7, 121.3, 119.7, 77.0, 52.7, 33.9, 29.5, 21.8, 20.0, 14.0. IR (KBr) ν_{max}: 3111.9, 2962.1, 2932.2, 2873.6, 2734.9, 1721.6, 1553.9, 1425.2, 1377.6, 1176.6, 1089.3, 809.6, 731.0, 668.8, 579.5 cm^{-1}; MS (ESI): calcd for $C_{22}H_{23}N_3NaO_7S$ $[M+Na]^+$ 496.1, Found: 496.0; HRMS (ESI): calcd for $C_{22}H_{23}N_3NaO_7S$ $[M+Na]^+$ 496.1149, Found: 496.1133.

(*S*)-2,2-Dimethyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butanal (4z): Reaction at −15 °C, pale yellow solid (m.p. 56.0–57.0 °C), 26% yield (21.6 mg), 87% ee. The enantiomeric excess was determined by HPLC [Daicel Chiralcel OD-H, hexane/i-PrOH (80:20) , flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 28.579 min, t (minor) = 25.367 min]; $[\alpha]_D^{25}$ = –3.85 (c 0.26, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.55 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.28-7.23 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.84–4.72 (m, 2H), 4.17–4.09 (m, 1H), 2.96–2.87 (m, 1H), 2.32 (s, 3H), 1.18 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 145.4, 134.8, 134.6, 130.1, 127.3, 126.9, 125.5, 124.9, 123.9, 119.6, 118.0, 113.9, 76.9, 48.8, 39.1, 21.9, 21.8, 19.1; IR (KBr) ν_{max}: 3125.9, 2963.6, 2929.8, 2871.2, 2714.8, 1723.0, 1554.4, 1448.0, 1371.1, 1171.4, 1129.1, 754.4, 670.9, 576.7 cm^{-1}; MS (ESI): calcd for $C_{21}H_{22}N_2NaO_5S$ $[M+Na]^+$ 437.1, Found: 437.1; HRMS (ESI): calcd for $C_{21}H_{26}N_3O_5S$ $[M+NH_4]^+$ 432.1588, Found: 432.1574.

General Procedure for Synthesis of *γ*-Formyl Nitro Compound 5. (*S*)-diphenylprolinol trimethylsilyl ether **1j** (6.51 mg, 0.02 mmol) and *trans*-3-(2-nitroethenyl)-*N*-tosylindole (0.20 mmol) were dissolved in DCM (1 mL) at room temperature. The solution was stirred for 10 min, and then citronellal (1.00 mmol) was added. The reaction mixture was then stirred until the nitroalkene no longer reduced (monitored by TLC). After 48 hours, the solvent was evaporated and the residue was purified by flash column silica-gel chromatography (PE/EA = 8/1) to provide the corresponding Michael adduct.

(*S*)-3,7-Dimethyl-2-((*R*)-2-nitro-1-(1-tosyl-1*H*-indol-3-yl)ethyl)oct-6-enal (5a and 5b). Reaction at room temperature. **5a**: White oil, 52% yield (51.6 mg), >99% ee. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 17.444 min, t_{minor} = 15.292 min; $[\alpha]_D^{25}$ = +57.23 (c 1.73, CH_3COCH_3); **5b**: White solid (m.p. 89.0–90.0 °C), 31% yield (30.8 mg), >99% ee. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 21.117 min, t_{minor} = 15.855 min; $[\alpha]_D^{25}$ = –16.91 (c 0.48, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (d, *J* = 1.6 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.50–7.44 (m, 2H), 7.36–7.29 (m, 1H), 7.28–7.22 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 4.73–4.66 (m, 3H), 4.24–4.13 (m, 1H), 3.03–2.97 (m, 1H), 2.31 (s, 3H), 1.91–1.82 (m, 1H), 1.69–1.61 (m, 1H), 1.49 (s, 3H), 1.41 (s, 3H), 1.29–1.23 (m, 1H), 1.13 (t, *J* = 6.8 Hz, 3H), 1.08–0.97 (m, 1H), 0.90–0.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 145.3, 135.5, 134.7, 132.6, 130.1, 129.4, 126.9, 125.5, 125.3, 123.9, 123.1, 119.2, 118.7, 114.4, 77.9, 58.0, 33.5, 32.6, 32.2, 25.7, 25.65, 21.7, 18.8, 17.7; IR (KBr) ν_{max}: 3109.4, 3054.3, 2918.7, 2862.1, 2745.0, 1719.4, 1550.8, 1447.2, 1368.3, 1171.4, 1121.1, 814.9, 749.9, 668.2, 575.8 cm^{-1}; MS (ESI) calcd for $C_{27}H_{32}N_2NaO_5S$ $[M+Na]^+$ 519.2, Found: 519.2; HRMS (ESI) calcd for $C_{27}H_{36}N_3O_5S$ $[M+NH_4]^+$ 514.2370, Found: 514.2363.

General Procedure for Synthesis of 1,4-Nitro Alcohols 6a and 6b. The catalyst **1j** (6.51 mg, 0.02 mmol) and **3h** or **3a** (0.20 mmol) were dissolved in DCM (1 mL) respectively at –15 °C or –30 °C. The solution was stirred for 10 min, and then aldehyde **2a** or **2i** (1.00 mmol) was added. The reaction mixture was then stirred at respective temperature until the complete consumption of nitroalkene (monitored by TLC). After the solvent was evaporated, the residue was dissolved in methanol (1 mL), then $NaBH_4$ (3.0 equiv.) was added portionwise at room temperature. The reaction finished in 6 hours. Subsequently, methanol was evaporated and the residue was purified by flash column silica-gel chromatography (PE/EA = 4/1) to provide the corresponding reductive product **6a** or **6b**.

(2*S*,3*R*)-3-(6-Bromo-1-tosyl-1*H*-indol-3-yl)-2-ethyl-4-nitrobutan-1-ol (6a): Reaction at –15 °C then rt, pale yellow solid (m.p. 119.0–120.0 °C), 94% yield (93.1

mg), >99% ee, dr = 99/1. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 0.8 mL·min^{-1}, λ = 210 nm, t_{major} = 29.137 min, t_{minor} = 30.419 min; $[\alpha]_D^{25}$ = –30.09 (c 1.17, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 1.2 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.48 (s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.34 (dd, *J* = 8.4 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.87 (d, *J* = 8.0 Hz, 2H), 3.99 (q, J_1= 14.6 Hz, J_2= 7.4 Hz, 1H), 3.69 (dd, *J* = 11.2 Hz, 1H), 3.51–3.45 (m, 1H), 2.33 (s, 3H), 1.91 (s, 1H), 1.84–1.79 (m, 1H), 1.32–1.23 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 135.9, 134.4, 130.2, 129.3, 127.0, 126.8, 124.7, 120.8, 120.3, 119.0, 117.0, 77.8, 61.8, 44.5, 37.1, 21.8, 21.7, 12.1; IR (KBr) ν_{max}: 3434.4, 3098.9, 2956.2, 2929.2, 2348.1, 1600.8, 1548.4, 1418.5, 1370.9, 1168.7, 1133.7, 1097.5, 1022.7, 804.0, 665.8, 582.7 cm^{-1}; MS (ESI) calcd for $C_{21}H_{23}BrN_2NaO_5S$ $[M+Na]^+$ 517.0, Found: 517.1; HRMS (ESI) calcd for $C_{21}H_{27}BrN_3O_5S$ $[M+NH_4]^+$ 512.0849, Found: 512.0852.

(2*S*,3*R*)-2-Methyl-4-nitro-3-(1-tosyl-1*H*-indol-3-yl)butan-1-ol (6b): Reaction at –30 °C then rt, pale yellow oil, 95% yield (76.5 mg), >99% ee, dr = 96/4. HPLC: Chiralcel OD-H, hexane/i-PrOH = 85:15, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 24.494 min, t_{minor} = 17.941 min; $[\alpha]_D^{25}$ = –13.69 (c 0.94, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.47 (s, 1H), 7.33–7.27 (m, 1H), 7.27–7.22 (m, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 4.91–4.75 (m, 2H), 4.05–3.98 (m, 1H), 3.55 (dd, *J* = 10.8 Hz, 1H), 3.40–3.35 (m, 1H), 2.30 (s, 3H), 2.15–2.09 (m, 1H), 1.96 (s, 1H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 135.2, 134.7, 130.6, 130.1, 126.8, 125.3, 124.4, 123.7, 119.8, 119.5, 113.9, 78.2, 65.4, 37.7, 37.5, 21.7, 14.2; IR (KBr) ν_{max}: 3438.0, 3114.8, 2956.7, 2922.0, 1601.3, 1552.4, 1446.7, 1370.9, 1170.5, 1121.5, 1029.7, 806.9, 669.8, 576.1 cm^{-1}; MS (ESI) calcd for $C_{20}H_{22}N_2NaO_5S$ $[M+Na]^+$ 425.1, Found: 425.1; HRMS (ESI) calcd for $C_{20}H_{26}N_3O_5S$ $[M+NH_4]^+$ 420.1588, Found: 420.1589.

General Procedure for Synthesis of Cyclic Tryptamine Derivative 7. A mixture of the γ-formyl nitro compound **4g** (62.5 mg, 0.146 mmol) and Pd/C (10 mol%) in 1.5 mL of anhydrous methanol was hydrogenated at 10 bar for 24 hours by using an

autoclave. The reaction mixture was filtered through a small plug of celite and concentrated in vacuo. The crude product was dissolved in dichloromethane (1.0 mL), cooled to 0 °C and treated with triethylamine (65 μL, 3 eq) followed by *p*-toluenesulfonyl chloride (30.6 mg, 1.1 eq) for 12 hours. After aqueous workup, the organic concentrate was purified by silica gel column chromatography (PE/EA = 5/1) to afford 45.8 mg (58 % overall yield from **4g**) of the chiral pyrrolidine compound **7**.

3-((3*R*,4*S*)-4-Isopropyl-1-tosylpyrrolidin-3-yl)-1-tosyl-1*H*-indole (7): White solid (m.p. 45.0–46.0 °C), 58% yield (45.8 mg), >99% ee, dr = 94/6. HPLC: Chiralcel OD-H, hexane/i-PrOH = 80:20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 16.050 min, t_{minor} = 20.290 min; $[\alpha]_D^{25}$ = –2.31 (c 2.25, CH_3COCH_3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.39–7.27 (m, 4H), 7.24 (s, 1H), 7.19 (d, *J* = 8.0 Hz, 3H), 3.70–3.61 (m, 1H), 3.55 (t, *J* = 9.0 Hz, 1H), 3.24–3.14 (m, 2H), 3.11 (t, *J* = 9.4 Hz, 1H), 2.48 (s, 3H), 2.33 (s, 3H), 2.24–2.14 (m, 1H), 1.61–1.51 (m, 1H), 0.79 (d, *J* = 6.4 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 144.0, 135.6, 135.2, 133.4, 130.02, 129.97, 129.8, 127.8, 126.9, 125.1, 123.4, 123.0, 122.8, 119.7, 114.1, 54.2, 50.7, 50.2, 39.2, 30.0, 21.8, 21.7, 21.5, 19.3; IR (KBr) ν_{max}: 3233.7, 2959.3, 2879.6, 1618.0, 1448.4, 1369.8, 1175.0, 1121.5, 813.4, 748.2, 664.7, 575.8 cm^{-1}; MS (ESI) calcd for $C_{29}H_{32}N_2NaO_4S_2$ $[M+Na]^+$ 559.2, Found: 559.2; HRMS (ESI) calcd for $C_{29}H_{32}N_2NaO_4S_2$ $[M+Na]^+$ 559.1696, Found: 559.1714.

General Procedure for Synthesis of Tryptamine Derivative 8. $NaBH_4$ (45 mg, 1.2 mmol) was added portionwise during 10 min to a solution of the Michael adduct **4a** (165 mg, 0.4 mmol) in 4 mL methanol at 0 °C. Then the reaction mixture was stirred for 6 hours at room temperature. After aqueous workup, a mixture of the organic concentrate and Pd/C (10 mol%, 38 mg) in 4 mL of anhydrous methanol was hydrogenated at 1 bar for 36 hours by using an autoclave. Subsequently the reaction mixture was filtered through a small plug of celite. To the filtrate were added Mg (144 mg, 6.0 mmol) and NH_4Cl (91 mg, 1.7 mmol). The reaction was stirred and monitored

by TLC for completion. Upon consumption of the starting material the solution was evaporated and the residue was poured into a separatory funnel containing a saturated solution of NH_4Cl and extracted with EtOAc (3x15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. MeOH (3 mL) and $(Boc)_2O$ (100 mg, 0.46 mmol) was added subsequently. The reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (PE/EA = 3:1). The chiral tryptamine derivative **8** was obtained as a white oil (98.5 mg) in 74% yield for four steps.

tert-Butyl (2*R*,3*S*)-3-(hydroxymethyl)-2-(1*H*-indol-3-yl)pentylcarbamate (**8**): white oil, 74% yield (98.5 mg), 99% ee, dr = 98/2. HPLC: Chiralcel AD-H, hexane/i-PrOH = 90:10, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t_{major} = 9.748 min, t_{minor} = 11.806 min; $[\alpha]_D^{25}$ = –12.11 (c 2.63, CH_3COCH_3); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.91 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 4.78–4.70 (m, 1H), 3.82–3.69 (m, 2H), 3.66–3.55 (m, 1H), 3.46–3.22 (m, 2H), 2.97 (s, 1H), 1.82 (s, 1H), 1.39 (s, 9H), 1.29–1.21 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 136.6, 127.5, 122.6, 121.9, 119.3, 115.4, 111.5, 79.4, 62.2, 44.9, 43.1, 38.3, 28.5, 21.6, 12.1; IR (KBr) ν_{max}: 3419.9, 3058.0, 2968.6, 2932.7, 2874.4, 1690.5, 1508.9, 1457.6, 1366.6, 1249.9, 1169.2, 1012.8, 863.6, 741.5, 582.4 cm^{-1}; MS (ESI): calcd for $C_{19}H_{28}N_2NaO_3$ $[M+Na]^+$ 355.2, Found: 355.2; HRMS (ESI): calcd for $C_{19}H_{28}N_2NaO_3$ $[M+Na]^+$ 355.1992, Found: 355.1993.

General Procedure for the Synthesis of Cyclic Tryptamine Derivative 9. To a solution of the Michael adduct **4a** (160 mg, 0.39 mmol) in 6 mL methanol were added Mg (144 mg, 6.0 mmol) and NH_4Cl (91 mg, 1.7 mmol). The reaction was stirred and monitored by TLC for completion. Upon consumption of the starting material the solution was evaporated and the residue was poured into a separatory funnel containing a saturated solution of NH_4Cl and extracted with EtOAc (3x15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. $NaBH_4$ (19 mg, 0.5 mmol) was added in portionwise during 10 min to a

solution of the residue in methanol 4 mL at 0 °C. After the reaction mixture was stirred for 6 hours at room temperature, $(Boc)_2O$ (100 mg, 0.46 mmol) was added subsequently. The reaction mixture was stirred at room temperature for another 6 hours. Finally the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleumether /ethyl acetate = 6:1). The cyclic tryptamine derivative **9** was obtained as a white oil (16.2 mg) in 13% yield for three steps.

(3*S*,4*R*)-tert-Butyl 3-ethyl-4-(1*H*-indol-3-yl)pyrrolidine-1-carboxylate (9): white oil, 13% yield (16.2 mg), 82% ee, dr = 94/6. HPLC: Chiralcel AD-H, hexane/i-PrOH = 95:5, flow rate: 1.0 mL·min^{-1}, λ = 210 nm, t_{major} = 18.606 min, t_{minor} = 19.845 min; $[\alpha]_D^{25}$ = +16.00 (c 0.75, CH_3COCH_3); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.21–7.14 (m, 1H), 7.13–7.05 (m, 1H), 7.01 (s, 1H), 3.94–3.63 (m, 2H), 3.55–3.40 (m, 1H), 3.29–3.14 (m, 1H), 3.12–2.98 (m, 1H), 2.35–2.25 (m, 1H), 1.52–1.43 (m, 9H), 1.29–1.20 (m, 2H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.9, 136.7, 130.0, 122.3, 121.2, 119.5, 119.3, 115.5, 111.6, 79.3, 52.9, 51.5, 46.0, 42.2, 28.80, 28.75, 25.4, 12.6. IR (KBr) ν_{max}: 3419.9, 2966.4, 2928.2, 2854.1, 2360.2, 1670.5, 1558.4, 1249.6, 1174.8, 1140.5, 879.8, 740.1, 669.2, 580.5 cm^{-1}; MS (ESI): calcd for $C_{19}H_{26}N_2NaO_2$ $[M+Na]^+$ 337.2, Found: 337.1; HRMS (ESI): calcd for $C_{19}H_{26}N_2NaO_2$ $[M+Na]^+$ 337.1886, Found: 337.1895.

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ASSOCIATED CONTENT

Supporting Information

The effect of additive on the Michael reaction, X-ray crystallographic data of **4u**, the copies of ^{1}H and ^{13}C NMR spectra of the products, and HPLC chromatograms. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCE

(1) (a) Faulkner, D. J. *Nat.Prod. Rep.* **2002**, *19*, 1. (b) O'Connor, S. E.; Maresh, J. J. *Nat.Prod. Rep.* **2006**, *23*, 532.

(2) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489.

(3) Kinsman, A. C.; Kerr, M. A. *Org. Lett.* **2001**, *3*, 3189.

(4) Hanessian, S.; Stoffman, E.; Mi, X.; Renton, P. *Org. Lett.* **2011**, *13*, 840.

(5) Zhang, X.; Mu, T.; Zhan, F.; Ma, L.; Liang, G. *Angew. Chem., Int. Ed.* **2011**, *50*, 6164.

(6) Sperry, J. *Tetrahedron Lett*. **2011**, *52*, 4537.

(7) King, D.; Meng, Z.; Denhart, D.; Mattson, R.; Kimura, R.; Wu, D.; Gao, Q.; Macor, J. E. *Org. Lett.* **2005**, *7*, 3437.

(8) Chen, T.; Xu, X.-P.; Ji, S.-J. *J. Comb. Chem.* **2010**, *12*, 659.

(9) For selected examples of the Michael addition of carbonyl compounds to nitroalkenes, see: (a) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877. (b) Ishii, T.; Fujioka, S.; Sekiguchi, Y.; Kotsuki, H. *J. Am. Chem. Soc.* **2004**, *126*, 9558. (c) Li, H.; Wang, Y.; Tang, L.; Deng, L. *J. Am. Chem. Soc.* **2004**, *126*, 9906. (d) Ye, J.; Dixon, D. J.; Hynes, P. S. *Chem. Commun.* **2005**, 4481. (e) Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X.; Takemoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 119. (f) Wang, J.; Li, H.; Duan, W.; Zu, L.; Wang, W. *Org. Lett.* **2005**, *7*, 4713. (g) Xu, Y.; Córdova, A. *Chem.*

Commun. **2006**, 460. (h) Huang, H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2006**, *128*, 7170. (i) Bui, T.; Syed, S.; Barbas III, C. F. *J. Am. Chem. Soc.* **2009**, *131*, 8758. (j) Kato, Y.; Furutachi, M.; Chen, Z.; Mitsunuma, H.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 9168. (k) Choudhury, A. R.; Mukherjee, S. *Org. Biomol. Chem.* **2012**, *10*, 7313. (l) Chen, X.; Zhu, W.; Qian, W.; Feng, E.; Zhou, Y.; Wang, J.; Jiang, H.; Yao, Z.-J.; Liu, H. *Adv. Synth. Catal.* **2012**, *354*, 2151.

(10) For selected examples of the Michael addition of nitroalkanes to α,β-unsaturated carbonyl compounds, see: (a) Hanessian, S.; Pham, V. *Org. Lett.* **2000**, *2*, 2975. (b) Halland, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2002**, *67*, 8331. (c) Ooi, T.; Takada, S.; Fujioka, S.; Maruoka, K. *Org. Lett.* **2005**, *7*, 5143. (d) Ooi, T.; Takada, S.; Doda, K.; Maruoka, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 7606. (e) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701. (f) Malmgren, M.; Granander, J.; Amedjkouh, M. *Tetrahedron: Asymmetry* **2008**, *19*, 1934. (g) Wu, B.; Liu, G.-G.; Li, M.-Q.; Zhang, Y.; Zhang, S.-Y.; Qiu, J.-R.; Xu, X.-P.; Ji, S.-J.; Wang, X.-W. *Chem. Commun.* **2011**, *47*, 3 992.

(11) (a) Johnston, G. A. R. *Pharmacol. Ther.* **1996**, *69*, 173. (b) Chi, Y.; Guo, L.; Gellman, S. H. *J. Am. Chem. Soc.* **2008**, *130*, 5608.

(12) List, B.; Pojarliev, P.; Martin, H. J. *Org. Lett.* **2001**, *3*, 2423.

(13) Betancort, J. M.; Barbas III, C. F. *Org. Lett.* **2001**, *3*, 3737.

(14) For asymmetric organocatalysis, see: (a) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520. (b) Erkkilä, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416. (c) Mukherjee, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471. (d) Dondoni, A.; Massi, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 4638. (e) MacMillan, D. W. C. *Nature* **2008**, *455*, 304. (f) Bertelsen, S.; Jørgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178.

(15) For selected examples, see: (a) Alexakis, A.; Andrey, O. *Org. Lett.* **2002**, *4*, 3611. (b) Mase, N.;

Barbas III, C. F. *Org. Lett.* **2004**, *6*, 2527. (c) Wang, W.; Wang, J.; Li, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 1369. (d) Zu, L.; Li, H.; Wang, J.; Yu, X.; Wang, W. *Tetrahedron Lett.* **2006**, *47*, 5131. (e) Li, Y.; Liu, X.; Zhao, G. *Tetrahedron: Asymmetry* **2006**, *17*, 2034. (f) Barros, M. T.; Phillips, A. M. F. *Eur. J. Org. Chem.* **2007**, 178. (g) Wiesner, M.; Revell, J. D.; Tonazzi, S.; Wennemers, H. *J. Am. Chem. Soc.* **2008**, *130*, 5610. (h) García-García, P.; Ladépêche, A.; Halder, R.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 4719. (i) Hayashi, Y.; Itoh, T.; Ohkubo, M.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4722. (j) Quintard, A.; Bournaud, C.; Alexakis, A. *Chem. Eur. J.* **2008**, *14*, 7504. (k) Zhang, X.; Liu, S.; Li, X.; Yan, M.; Chan, A. S. C. *Chem. Commun.* **2009**, 833. (l) Chang, C.; Li, S.-H.; Reddy, R. J.; Chen, K. *Adv. Synth. Catal.* **2009**, *351*, 1273. (m) Lu, D.; Gong, Y.; Wang, W. *Adv. Synth. Catal.* **2010**, *352*, 644. (n) Husmann, R.; Jörres, M.; Raabe, G.; Bolm, C. *Chem. Eur. J.* **2010**, *16*, 12549. (o) Jentzsch, K. I.; Min, T.; Etcheson, J. I.; Fettinger, J. C.; Franz, A. K. *J. Org. Chem.* **2011**, *76*, 7065. (p) Arakawa, Y.; Wiesner, M.; Wennemersa, H. *Adv. Synth. Catal.* **2011**, *353*, 1201. (q) Cao, X.; Wang, G.; Zhang, R.; Wei, Y.; Wang, W.; Sun, H.; Chen, L. *Org. Biomol. Chem.* **2011**, *9*, 6487. (r) Watts, J.; Luu, L.; McKee, V.; Carey, E.; Kelleher, F. *Adv. Synth. Catal.* **2012**, *354*, 1035. (s) Zhao, L.; Shen, J.; Liu, D.; Liub, Y.; Zhang, W. *Org. Biomol. Chem.* **2012**, *10*, 2840.

(16) For recent examples, see: (a) Lalonde, M. P.; Chen, Y.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 6366. (b) Reyes, E.; Vicario, J. L.; Badía, D.; Carrillo, L. *Org. Lett.* **2006**, *8*, 6135. (c) Ruiz, N.; Reyes, E.; Vicario, J. L.; Badía, D.; Carrillo, L.; Uria, U. *Chem. Eur. J.* **2008**, *14*, 9357. (d) Belot, S.; Massaro, A.; Tenti, A.; Mordini, A.; Alexakis, A. *Org. Lett.* **2008**, *10*, 4557. (e) Zhu, S.; Yu, S.; Ma, D. *Angew. Chem., Int. Ed.* **2008**, *47*, 545. (f) He, T.; Qian, J.-Y.; Song, H.-L.; Wu, X.-Y. *Synlett.* **2009**, *19*, 3195. (g) Belot, S.; Quintard, A.; Krause, N.; Alexakis, A. *Adv. Synth. Catal.* **2010**, *352*, 667. (h) Enders, D.; Wang, C.; Greb, A. *Adv. Synth. Catal.* **2010**, *352*, 987. (i) Cao, X.-Y.; Zheng, J.-C.; Li,

Y.-X.; Shu, Z.-C.; Sun, X.-L.; Wang, B.-Q.; Tang, Y. *Tetrahedron* **2010**, *66*, 9703.

(17) reactions of indolylnitroalkene: (a) Xing, J.; Chen, G.; Cao, P.; Liao, J. *Eur. J. Org. Chem.* **2012**, 1230. (b) Baron, M.; Métay, E.; Lemaire, M.; Popowycz, F. *J. Org. Chem.* **2012**, *77*, 3598.

(18) (a) Austin, J. F.; Kim, S.-G.; Sinz, C. J.; Xiao, W.-J.; MacMillan, D. W. C. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5482. (b) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576. (c) Bonini, B. F.; Capitò, E.; Comes-Franchini, M.; Fochi, M.; Ricci, A.; Zwanenburg, B. *Tetrahedron: Asymmetry* **2006**, *17*, 3135. (d) Fleming, E. M.; McCabe, T.; Connon, S. J. *Tetrahedron Lett.* **2006**, *47*, 7037. (e) Li, C.-F.; Liu, H.; Liao, J.; Cao, Y.-J.; Liu, X.-P.; Xiao, W.-J. *Org. Lett.* **2007**, *9*, 1847. (f) Chen, J.-R.; Li, C.-F.; An, X.-L.; Zhang, J.-J.; Zhu, X.-Y.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 2489. (g) Itoh, J.; Fuchibe, K.; Akiyama, T.; *Angew. Chem. Int. Ed.* **2008**, *47*, 4016. (h) Liu, H.; Lu, S.-F.; Xu, J.; Du, D.-M. *Chem. Asian J.* **2008**, *3*, 1111. (i) Arai, T.; Yokoyama, N.; Yanagisawa, A. *Chem. Eur. J.* **2008**, *14*, 2052. (j) Ganesh, M.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 16464. (k) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608.

(19) For selected examples, see: (a) Huang, Y.; Walji, A. M.; Larsen, C. H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 15051. (b) Dalton King, H.; Meng, Z.; Denhart, D.; Mattson, R.; Kimura, R.; Wu, D.; Gao, Q.; Macor, J. E. *Org. Lett.* **2005**, *7*, 3437. (c) Ye, M.-C.; Yang, Y.-Y.; Tang, Y.; Sun, X.-L.; Ma, Z.; Qin, W.-M. *Synlett* **2006**, 1240. (d) Chi, Y.; Scroggins, S. T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6322. (e) Raimondi, W.; Baslé, O.; Constantieux, T.; Bonne, D.; Rodriguez J. *Adv. Synth. Catal.* **2012**, *354*, 563.

(20) (a) Dobish, M. C.; Johnston, J. N. *Org. Lett.* **2010**, *12*, 5744. (b) Fochi, M.; Gramigna, L.; Mazzanti, A.; Duce, S.; Fantini, S.; Palmieri, A.; Petrini, M.; Bernardi, L. *Adv. Synth. Catal.* **2012**, *354*, 1373.

(21) (a) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 794. (b) Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4212. (c) Palomo, C.; Mielgo A. *Angew. Chem., Int. Ed.* **2006**, *45*, 7876. (d) Xu, L.-W.; Li, L.; Shi, Z.-H. *Adv. Synth. Catal.* **2010**, *352*, 243. (e) Jensen, K. M.; Dickmeiss, G.; Jiang, H.; Albrecht, Ł.; Jørgensen, K. A. *Acc. Chem. Res.* **2012**, *45*, 248.

(22) CCDC-880614 (for **4u**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See the Supporting Information for details.

(23) For the preparation of indolylnitroalkenes **3a–3l**: (a) Canoira, L.; Rodriguez, J. G.; Subirats, J. B.; Escario, J.-A.; Jimenez, I.; Martinez-Fernandez, A. R. *Eur. J. Med. Chem.* **1989**, *24*, 39. (b) Kinsman, A. C.; Kerr, M. A. *Org. Lett.* **2001**, *3*, 3189. (c) Muratore, M. E.; Holloway, C. A.; Pilling, A. W.; Storer, R. I.; Trevitt, G.; Dixon, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 10796. (d) Lee, S.; Park, S. B. *Org. Lett.* **2009**, *11*, 5214.