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Squaramide-catalyzed diastereo- and enantioselective Michael addition of 3-substituted oxindoles to nitroalkenes

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ABSTRACT

An efficient diastereo- and enantioselective Michael addition of 3-substituted oxindoles onto nitroalkenes catalyzed by a bifunctional chiral squaramide catalyst has been developed. This organocatalytic reaction with 2 mol % of catalyst proceeded smoothly to afford 3,3-disubstituted oxindoles in high yields with good diastereoselectivities and enantioselectivities (up to 98:2 dr, 88% ee).

1. Introduction

Hydrogen bonding as an activating force is widespread in organocatalysis.[1] As a novel type of hydrogen-bonding donor organocatalyst, chiral squaramide is being increasingly utilized.[2] After the pioneering work reported by Rawal, many chiral squaramide catalysts have been developed and successfully applied in various asymmetric reactions.[3] In recent years, our group has also conducted research in this area.[4] Oxindoles, especially those with a quaternary stereocenter at the 3-position, are important structural motifs in numerous biologically and pharmaceutically active natural alkaloids.[5] In this context, various catalytic enantioselective approaches to oxindoles have been developed.[6] As a continuation of research on asymmetric catalysis using squaramide catalysts, we attempted to develop a squaramide-catalyzed asymmetric Michael addition of 3-substituted oxindoles to nitroalkenes, which would provide straightforward access to synthetically useful β-aminooxindoles bearing adjacent quaternary–tertiary stereocenters. To date, several efficient catalytic enantioselective methods to perform this reaction have been reported.[7] Barbas III et al. first reported the highly asymmetric Michael addition of *N*-Boc protected 3-alkyloxindoles to nitroalkenes catalyzed by chiral thioureas,[7a] while Shibasaki et al. independently developed efficient homodinuclear $Mn(III)_2$–Schiff base complexes to promote this reaction.[7b] In the same year, Maruoka described chiral quaternary ammonium salts for the Michael addition of *N*-Boc protected 3-aryloxindoles to nitroalkenes in a water-rich solvent.[7c] Subsequently, Cheng et al. reported the addition of 3-methyl-*N*-phenyloxindole to nitroalkenes catalyzed by a simple alkyl-substituted bifunctional thiourea,[7d] and Yuan developed a chiral $Ni(OAc)_2$–diamine complex catalyst for 3-alkyloxindoles bearing an *N*-carbonyl group.[7e] Impressively, Zhou and co-workers reported a cinchonidine-derived phosphoramide-catalyzed highly enantioselective Michael addition of unprotected 3-substituted oxindoles to nitroalkenes with a wide scope toward substrates.[7f] During the preparation of this manuscript, Enders et al. reported the asymmetric Michael addition of *N*-Boc protected oxindoles to nitroalkenes catalyzed by a chiral secondary amine.[7g] Despite these achievements, the development of other new, efficient catalytic systems with low catalyst loading is still needed. Herein we report the asymmetric Michael addition of 3-substituted oxindoles to nitroalkenes catalyzed by chiral squaramide catalysts.

2. Results and discussion

Initially, 5 mol % squaramide catalyst **I** was employed to promote the Michael addition of oxindole **1a** with β-nitrostyrene **2a** in CH_2Cl_2 at −20 °C. The reaction proceeded well for 12 h to furnish the corresponding adduct **3aa** in 90% yield with 80% ee. Encouraged by the promising result, we prepared a small library of squaramide catalysts **I**–**IX** (Fig. 1) and evaluated their catalytic performance in this Michael addition. As shown in Table 1, all of squaramide catalysts screened could promote the reaction efficiently. Squaramide **II** with 4-CF_3 substitution on the aromatic ring gave comparable diastereoselectivity but lower enantioselectivity (Table 1, entry 2). When squaramides **III** and **IV** bearing a piperidinyl group were examined, better enantioselectivities (84% ee and 85% ee, respectively) were obtained (Table 1, entries 3 and 4). Both squaramides **V** and **VI** derived from cinchona alkaloid only gave moderate enantioselectivities (Table 1, entries 5 and 6). Subsequently, three C_2-symmetric squaramides **VII**–**IX** were tested, but no obviously superior result was obtained (Table 1, entries 7–9). It should be noted that quinine/hydroquinine-derived squaramides **VIII** and **IX** slightly improved enantioselectivity but decreased diastereoselectivity. Based on a comprehensive consideration of yield, enantioselectivity, and diastereoselectivity, squaramide **III** was selected as the best catalyst for the optimization of reaction conditions.

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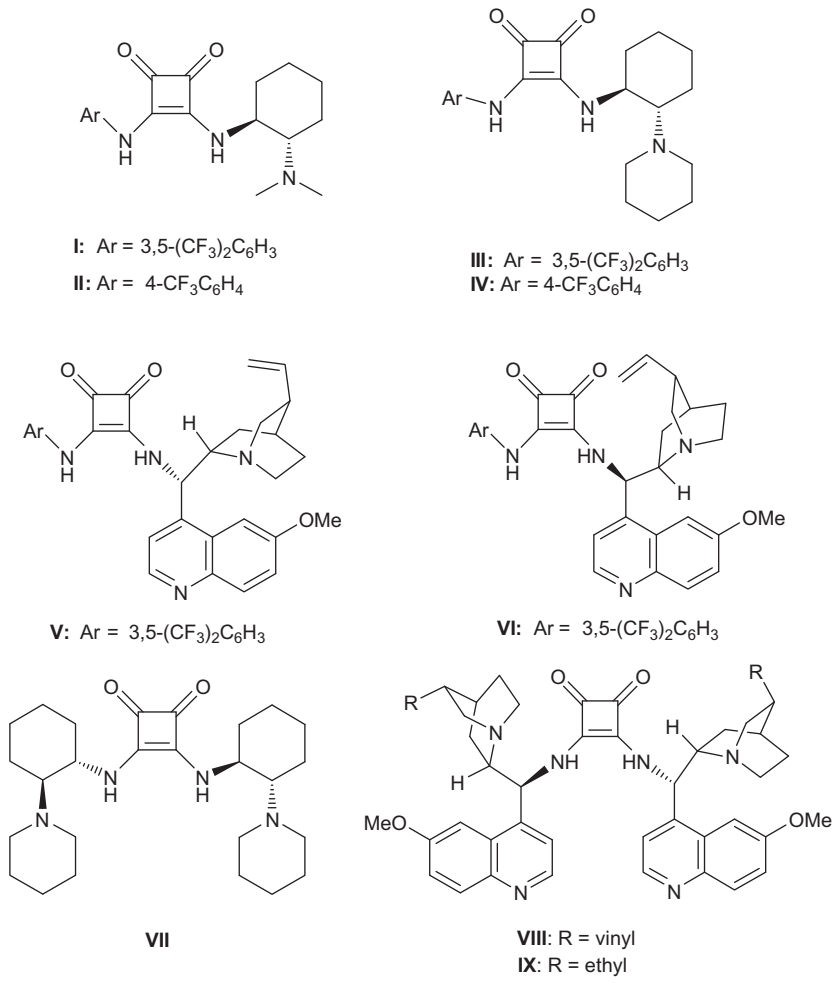
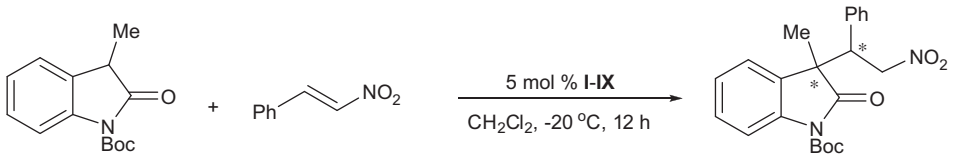


Figure 1. Squaramide catalysts **I**–**IX**.

Table 1
Screening of squaramide catalysts[a]



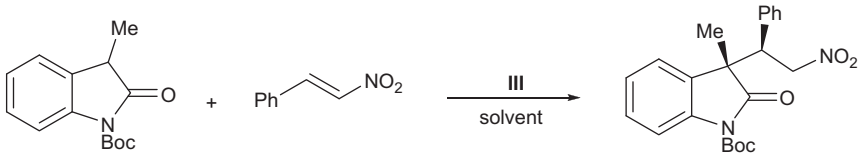
1a **2a** **3aa**

Entry	Catalyst	Yield[b] (%)	dr[c]	ee[d] (%)
1	**I**	90	98:2	80
2	**II**	95	96:4	68
3	**III**	98	97:3	84
4	**IV**	93	95:5	85
5	**V**	94	95:5	66
6	**VI**	88	96:4	−58
7	**VII**	90	92:8	80
8	**VIII**	95	86:14	86
9	**IX**	94	83:17	89

[a] Reactions were carried out with oxindole **1a** (0.2 mmol) and β-nitrostyrene **2a** (0.2 mmol) in CH_2Cl_2 (0.5 mL).
[b] Isolated yield after column chromatography purification.
[c] Determined by chiral HPLC analysis.
[d] Enantiomeric excess for the major diastereomer was determined by chiral HPLC analysis.

With the optimal catalyst in hand, we investigated several reaction parameters involving solvent, catalyst loading, and temperature for the optimal conditions. The results are summarized in Table 2. The solvent screening identified chloroform as the best reaction medium. Variation of the solvent had a limited effect on the process. The common solvents all gave the desired adduct

Table 2
Optimization of the reaction conditions[a]

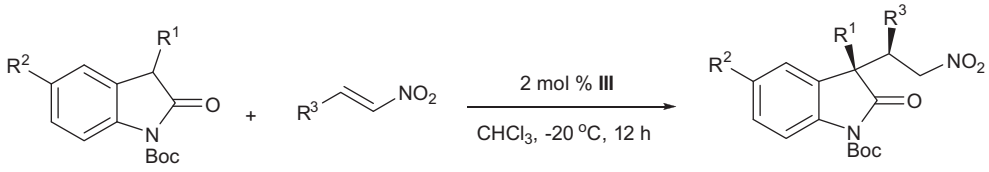


1a **2a** **3aa**

Entry	Solvent	Loading	Temp (°C)	Time (h)	Yield[b] (%)	dr[c]	ee[d,e] (%)
1	CH_2Cl_2	5	−20	12	98	97:3	84
2	THF	5	−20	12	98	98:2	78
3	PhMe	5	−20	12	96	96:4	77
4	MeOH	5	−20	12	92	94:6	84
5	$CHCl_3$	5	−20	12	99	97:3	85
6	$ClCH_2CH_2Cl$	5	−20	12	94	97:3	83
7	$CHCl_3$	10	−20	12	98	98:2	85
8	$CHCl_3$	2	−20	12	97	98:2	86
9	$CHCl_3$	1	−20	12	78	94:6	83
10	$CHCl_3$	2	−40	36	81	92:8	80
11	$CHCl_3$	2	rt	4	93	58:42	22
12	$CHCl_3$	2	0	8	91	93:7	80

[a] Unless noted otherwise, reactions were carried out with oxindole **1a** (0.2 mmol) and β-nitrostyrene **2a** (0.2 mmol) in solvent (0.5 mL).
[b] Isolated yield after column chromatography purification.
[c] Determined by chiral HPLC analysis.
[d] Enantiomeric excess for the major diastereomer was determined by chiral HPLC analysis.
[e] The configuration was determined by comparison of the specific rotation with literature data.[7a]

Table 3
Substrate scope of the catalytic asymmetric Michael addition of oxindoles to nitroalkenes[a]



1a-f **2a-l** **3aa-fa**

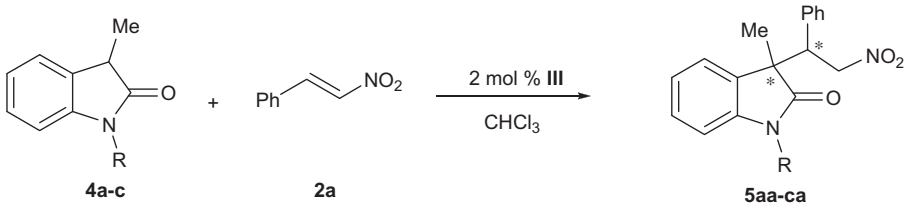
1a: R^1 = Me, R^2 = H; **1b**: R^1 = Et, R^2 = H;
1c: R^1 = Bn, R^2 = H; **1d**: R^1 = Ph, R^2 = H;
1e: R^1 = Me, R^2 = F; **1f**: R^1 = Me, R^2 = OMe

Entry	R^1	R^2	R^3	Product	Yield[b] (%)	dr[c]	ee[d,e] (%)
1	Me	H	Ph **2a**	**3aa**	97	98:2	86
2	Me	H	4-$MeOC_6H_4$ **2b**	**3ab**	95	97:3	87
3	Me	H	3,4-$(MeO)_2$ C_6H_3 **2c**	**3ac**	84	97:3	79
4	Me	H	4-MeC_6H_4 **2d**	**3ad**	95	98:2	88
5	Me	H	4-FC_6H_4 **2e**	**3ae**	94	79:21	64
6	Me	H	4-ClC_6H_4 **2f**	**3af**	94	87:13	80
7	Me	H	2-ClC_6H_4 **2g**	**3ag**	90	74:26	85
8	Me	H	4-BrC_6H_4 **2h**	**3ah**	92	88:12	81
9	Me	H	2-Furanyl **2i**	**3ai**	83	90:10	76
10	Me	H	2-Thienyl **2j**	**3aj**	86	84:16	70
11	Me	H	2-Phenylethyl **2k**	**3ak**	79	94:6	76
12[f]	Me	H	Et **2l**	**3al**	33	97:3	88
13	Et	H	Ph **2a**	**3ba**	97	79:21	87
14	Bn	H	Ph **2a**	**3ca**	95	90:10	86
15	Ph	H	Ph **2a**	**3da**	96	87:13	44
16	Me	OMe	Ph **2a**	**3ea**	96	88:12	84
17	Me	F	Ph **2a**	**3fa**	96	90:10	79

[a] Unless noted otherwise, reactions were carried out with oxindole **1** (0.2 mmol) and nitroalkene **2** (0.2 mmol) in $CHCl_3$ (0.5 mL).
[b] Isolated yield after column chromatography purification.
[c] Determined by chiral HPLC analysis.
[d] Enantiomeric excess for the major diastereomer was determined by chiral HPLC analysis.
[e] The configuration was determined by comparison of the specific rotation with literature data[7a–c]
[f] Reaction was performed at 0 °C for 3 d.

3aa in excellent yields, with high diastereoselectivities and good enantioselectivities ranging from 77 to 85% (Table 2, entries 1–6). Subsequently, the effect of catalyst loading was investigated. When the model reaction was performed with 10 or 2 mol %

Table 4
Further investigation of substrate scope



4a-c **2a** **5aa-ca**

4a: R = H; **4b**: R = Ph; **4c**: R = CO_2Et

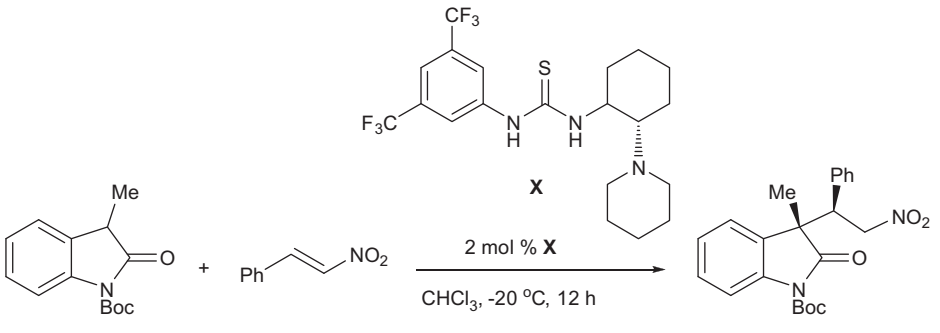
Entry	4	T (°C)	Time	Product	Yield[a] (%)	dr[b]	ee[b] (%)
1	**4a**	−20	3 d	**5aa**	Trace	—	—
2	**4a**	0	5 d	**5aa**	45	60:40	89/85
3	**4a**	rt	36 h	**5aa**	73	61:39	85/79
4	**4b**	0	3 d	**5ba**	Trace	—	—
5	**4b**	rt	24 h	**5ba**	91	73:27	54/76
6	**4c**	−20	12 h	**5ca**	90	96:4	91

[a] Isolated yield after column chromatography purification.
[b] Determined by chiral HPLC analysis.

squaramide **III**, the excellent yield and good stereoselectivity were maintained (Table 2, entries 7 and 8). Reducing the catalyst loading further to 1 mol % led to a decrease in both the yield and stereoselectivity (Table 2, entry 9). However, neither cooling nor heating the reaction gave a better result (Table 2, entries 10–12). It is noteworthy that the reaction proceeded at room temperature with very low diastereoselectivity and enantioselectivity (58:42 dr, 22% ee).

With the optimal reaction conditions established, the scope of the asymmetric Michael addition of 3-substituted oxindoles to nitroalkenes was explored. The results are shown in Table 3. Generally, a variety of aromatic nitroalkenes **2b**–**h** with different substituents on the phenyl ring reacted smoothly with oxindole **1a** to afford the corresponding adducts in high yields with good to high diastereoselectivities and enantioselectivities (Table 3, entries 2–8). The electronic properties of the substituent have an effect on the diastereoselectivity. The electron-rich substrates gave much better diastereoselectivities than those bearing electron-withdrawing groups. When heteroaromatic nitroalkenes **2i** and **2j** were used as acceptors, the desired products were obtained with good yields and diastereoselectivities but lower enantioselectivities (Table 3, entries 9 and 10). Aliphatic nitroalkenes **2k** and **2l** gave good diastereoselectivities and enantioselectivities, but **2l** showed **a** much lower reactivity (Table 3, entries 11 and 12). When other branched aliphatic nitroalkenes (R^3 = *i*-Pr, cyclohexyl) were examined, no reactions occurred. Oxindoles **1b**–**f** with different groups were also evaluated. Oxindoles **1b** and **1c** with an ethyl or benzyl group at the 3-position worked well to give the corresponding adducts in high yields and with good diastereoselectivities and enantioselectivities (Table 3, entries 13 and 14). When oxindole **1d** with a phenyl group was used, a high yield and good diastereoselectivity but low enantioselectivity were observed (Table 3, entry 15). The result indicated that this catalytic system is not suitable for an oxindole with an aryl group at the 3-position to achieve good enantioselectivity. Oxindoles **1e** and **1f** with variations on the aromatic ring gave high yields and good diastereoselectivities and enantioselectivities (Table 3, entries 16 and 17).

Further substrate scope with varitions on the 1-position of oxindole was investigated, and the results are shown in Table 4. Unprotected oxindole **4a** showed much lower reactivity than Boc-protected oxindole **1a**. The reaction hardly occurred at −20 °C but gave a moderate yield at 0 °C for 5 d (Table 4, entries 1 and 2). When the reaction was performed at room temperature, the desired adduct **5aa** was obtained in good yield with good enantioselectivities for both diastereomers (85% ee and 79% ee, respectively), albeit with low diastereoselectivity (Table 4, entry 3). The *N*-phenyl protected oxindole **4b** reacted with β-nitrostyrene **2a** at room temperature to give **5ba** in high yield but only moderate diastereoselectivity and enantioselectivity (Table 4, entry 5). The results indicated that a Boc protecting group facilitates the enolization of oxindole to enhance its reactivity. The reaction of oxindole **4c**



1a **2** **3aa**

70% yield, 84:16 dr, 87% ee

Scheme 1. Thiourea-catalyzed Michael addition of oxindole **1a** to β-nitrostyrene **2a**.

and β-nitrostyrene **2a** proceeded well to afford adduct **5ca** in high yield with high diastereoselectivity and enantioselectivity (Table 4, entry 6). In addition, a control experiment with the corresponding thiourea-based catalyst **X** was performed in order to compare the differences in the catalytic activity. Under otherwise identical conditions, thiourea **X** gave the corresponding adduct **3aa** in 70% yield with 84:16 dr and 87% ee. This result demonstrates that the squaramide gives higher reactivity and diastereoselectivity than the corresponding thiourea catalyst (see Scheme 1).

Based on the absolute configuration of adduct **3aa**, a possible transition state model is hypothesized and shown in Figure 2. The squaramide **III** may act as a bifunctional chiral catalyst. The squaramide moiety activates nitroalkene **2a** through double hydrogen bonding. Meanwhile, the tertiary amino moiety serves as a base for the deprotonation of the acidic proton of the oxindole. In the transition state, the phenyl ring faces away from the cyclohexane ring of the squaramide catalyst, and the bulky Boc protecting group is far from the piperidinyl group. Therefore, the proposed transition state is favored.[7a] The oxindole attacks the activated nitroalkene from the *Si*-face to afford the (3*S*,1'*R*)-configured adduct, which is consistent with the observed result.

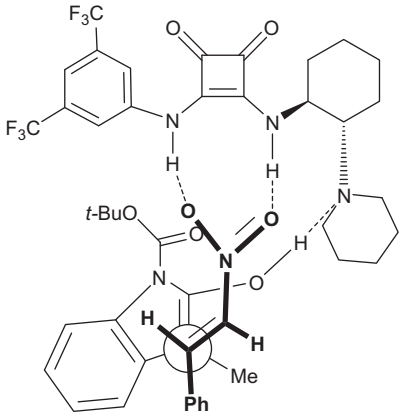


Figure 2. Proposed transition state model.

3. Conclusion

In conclusion, we have developed an efficient squaramide-catalyzed diastereo- and enantioselective Michael addition of 3-substituted oxindoles to nitroalkenes. This organocatalytic reaction with a low catalyst loading (2 mol %) afforded the corresponding adducts in high yields with good diastereoselectivities and enantioselectivities. This process provides an easy route to chiral multifunctional oxindole derivatives bearing adjacent quaternary-tertiary stereocenters. Further studies on asymmetric reactions catalyzed by squaramides are currently underway in our laboratory.

4. Experimental

4.1. General methods

Commercially available compounds were used without further purification, unless otherwise stated. Column chromatography was carried out with silica gel (200–300 mesh). Melting points were measured with an XT-4 melting point apparatus without correction. ^{1}H NMR spectra were recorded with a Varian Mercury-plus or a Bruker AVIII 400 M spectrometer. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br s = broad singlet), coupling constant(s) in Hz, integration assignment. ^{13}C NMR spectra were recorded at 100 MHz spectrometer. Infrared spectra were obtained with a Perkin–Elmer Spectrum One spectrometer. The ESI-MS spectra were obtained with a Bruker APEX IV mass spectrometer. Optical rotations were measured with a Krüss P8000 polarimeter at the indicated concentration with units of g/100 mL. The enantiomeric excesses of the products were determined by chiral HPLC using an Agilent 1200 LC instrument with Daicel Chiralpak columns (IB, IA or AS-H). The absolute configurations of the known adducts were assigned by HPLC and specific rotation comparisons with the reported data;[7a–c] those of unknown adducts were assigned by analogy.

4.2. Materials

3-Substituted oxindoles **1a**–**f** were prepared according to the literature procedures.[8] Racemic samples of **3aa**–**fa** and **5aa-ca** were prepared with 10 mol % DBU as the catalyst. The squaramide catalysts **I**–**X** were prepared by following the reported procedures.[4a,4b,4f,9,10]

4.3. General procedure for the Michael addition of 3-substituted oxindoles to nitroalkenes

A mixture of 3-substituted oxindole **1** (0.2 mmol, 1.0 equiv) and catalyst **III** (2 mol %) in chloroform (0.5 mL) was stirred at −20 °C for 30 min, after which nitroalkene **2** (0.2 mmol, 1.0 equiv) was added. After stirring at −20 °C for 12 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford a mixture of both diastereomers **3**. The mixture was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction by chiral HPLC. The major diastereomer was then obtained by another column chromatography separation on silica gel, and used for characterization.

4.3.1. (3*S*)-*tert*-Butyl 3-methyl-3-[(1*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3aa[7e]

The title compound **3aa** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (76.9 mg, 97% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (98:2 dr, 86% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA and AS-H column in series, *n*-hexane/2-propanol = 95:5, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{minor} = 33.6 min, t_{major} = 36.4 min; minor diastereomer: t_R = 28.0, 30.7 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 100–102 °C, $[\alpha]_D^{28} = +27.6$ (*c* 1.63, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.0 Hz, 1H, ArH), 7.31 (t, J = 7.2 Hz, 1H, ArH), 7.18–7.10 (m, 4H, ArH), 7.03 (d, J = 7.6 Hz, 1H, ArH), 6.82 (d, J = 7.2 Hz, 1H, ArH), 5.04 (dd, J_1 = 12.6 Hz, J_2 = 3.8 Hz, 1H, CH_2), 4.90 (t, J = 12.0 Hz, 1H, CH), 3.95 (dd, J_1 = 10.8 Hz, J_2 = 3.6 Hz, 1H, CH_2), 1.52 (s, 12 H, CH_3) ppm.

4.3.2. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(4-methoxyphenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ab[7b]

The title compound **3ab** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (81.0 mg, 95% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (97:3 dr, 87% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 11.7 min, t_{minor} = 16.4 min;

minor diastereomer: t_R = 9.6 min. The major diastereomer was purified by flash chromatography and obtained as a colorless oil. $[\alpha]_D^{20} = +6.3$ (*c* 1.08, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.33 (t, *J* = 7.6 Hz, 1H, ArH), 7.18 (t, *J* = 7.2 Hz, 1H, ArH), 7.02 (d, *J* = 7.2 Hz, 1H, ArH), 6.75 (d, *J* = 8.0 Hz, 2H, ArH), 6.66 (d, *J* = 8.0 Hz, 2H, ArH), 5.00 (dd, J_1 = 12.6 Hz, J_2 = 3.8 Hz, 1H), 4.85 (t, *J* = 12.0 Hz, 1H), 3.90 (dd, J_1 = 11.2 Hz, J_2 = 3.6 Hz, 1H), 3.71 (s, 3H, OCH_3), 1.53 (s, 9H, CH_3), 1.51 (s, 3H, CH_3) ppm.

4.3.3. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(3,4-dimethoxyphenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ac

The title compound **3ac** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (76.7 mg, 84% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (97:3 dr, 79% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 19.5 min, t_{minor} = 25.9 min; minor diastereomer: t_R = 15.4 min. The major diastereomer was purified by flash chromatography and obtained as a yellow foam, mp 53–55 °C. $[\alpha]_D^{22} = +1.7$ (*c* 2.46, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.4 Hz, 1H, ArH), 7.34 (dt, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H, ArH), 7.20 (t, *J* = 7.2 Hz, 1H, ArH), 7.10 (d, *J* = 7.6 Hz, 1H, ArH), 6.63 (d, *J* = 8.0 Hz, 1H, ArH), 6.44 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H, ArH), 6.18 (d, *J* = 1.6 Hz, 1H, ArH), 5.03 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2), 4.85 (t, *J* = 12.0 Hz, 1H, CH), 3.92 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.78 (s, 3H, OCH_3), 3.58 (s, 3H, OCH_3), 1.54 (s, 3H, CH_3), 1.52 (s, 9H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.8, 148.8, 148.3, 148.2, 139.7, 129.3, 129.0, 126.1, 124.2, 123.3, 121.2, 115.3, 111.2, 110.5, 84.2, 75.7, 55.6, 55.4, 51.2, 50.6, 27.8, 20.7 ppm. IR (KBr): ν 2979, 2936, 2838, 1790, 1765, 1732, 1607, 1593, 1556, 1520, 1481, 1467, 1371, 1350, 1301, 1264, 1151, 1104, 1073, 1027, 1010, 960, 844, 815, 767, 640 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_2NaO_7$ $[M+Na]^+$ 479.17887, found 479.17867.

4.3.4. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(4-methylphenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ad

The title compound **3ad** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (80.1 mg, 95% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (98:2 dr, 88% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 16.6 min, t_{minor} = 24.6 min; minor diastereomer: t_R = 14.5 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 86–87 °C. $[\alpha]_D^{22} = +13.0$ (*c* 0.97, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 7.33 (t, *J* = 7.0 Hz, 1H, ArH), 7.18 (t, *J* = 6.8 Hz, 1H, ArH), 7.01 (d, *J* = 6.4 Hz, 1H, ArH), 6.94 (d, *J* = 6.8 Hz, 2H, ArH), 6.71 (d, *J* = 7.2 Hz, 2H, ArH), 5.00 (dd, J_1 = 12.6 Hz, J_2 = 4.0 Hz, 1H, CH_2), 4.86 (t, *J* = 12.0 Hz, 1H, CH), 3.90 (dd, J_1 = 10.8 Hz, J_2 = 4.0 Hz, 1H, CH_2), 2.23 (s, 3H, CH_3), 1.53 (s, 9H, CH_3), 1.51 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.8, 148.5, 139.5, 138.0, 130.8, 129.3, 129.0, 128.8, 128.6, 124.3, 123.4, 115.2, 84.2, 75.7, 50.9, 50.6, 27.9, 21.0, 20.7 ppm. IR (KBr): ν 2980, 2932, 1790, 1766, 1732, 1608, 1557, 1515, 1481, 1467, 1371, 1349, 1300, 1289, 1253, 1153, 1104, 1072, 1108, 961, 844, 825, 766, 680 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{23}H_{26}N_2NaO_5$ $[M+Na]^+$ 433.17339, found 433.17403.

4.3.5. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(4-fluorophenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ae

The title compound **3ae** (the mixture of the major and minor diastereomer) was obtained as a white solid (mp 112–114 °C) according to the general procedure (78.4 mg, 94% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (79:21 dr, 64% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 9.2 min, t_{minor} = 14.0 min; minor diastereomer: t_R = 8.2 min. $[\alpha]_D^{22} = +11.8$ (*c* 0.97, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.4 Hz, 1H), 7.35 (dt, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.21 (dt, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.08 (d, *J* = 7.2 Hz, 1H, ArH), 6.86–6.77 (m, 4H, ArH), 5.99 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2), 4.85 (t, *J* = 12.0 Hz, 1H, CH), 3.96 (dd, J_1 = 11.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 1.54 (s, 9H, CH_3), 1.52 (s, 3H, CH_3) ppm. ^{13s}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 162.5 (d, $^1J_{C-F}$ = 246.3 Hz), 148.3, 139.4, 130.4 (d, $^3J_{C-F}$ = 8.1 Hz), 129.3, 128.8, 124.5, 123.3, 115.3, 115.1(d, $^2J_{C-F}$ = 21.3 Hz), 84.5, 75.6, 50.9, 50.2, 27.9, 20.8 ppm. IR (KBr): ν 2981, 2933, 1789, 1763, 1734, 1607, 1559, 1511, 1481, 1467, 1372, 1349, 1290, 1252, 1152, 1108, 1008, 961, 840, 757 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{23}FN_2NaO_5$ $[M+Na]^+$ 437.14832, found 437.14906.

4.3.6. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(4-chlorophenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3af[7b]

The title compound **3af** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (81.1 mg, 94% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (87:13 dr, 80% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 10.7 min, t_{minor} = 17.7 min; minor diastereomer: t_R = 9.4 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 72–74 °C. $[\alpha]_D^{20} = +7.5$ (*c* 1.31, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.35 (t, *J* = 8.0 Hz, 1H, ArH), 7.21 (t, *J* = 7.2 Hz, 1H, ArH), 7.13–7.08 (m, 2H, ArH), 6.77 (d, *J* = 8.4 Hz, 2H, ArH), 4.99 (dd, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1H, CH_2), 4.84 (t, *J* = 12.0 Hz, 1H, CH), 3.95 (dd, J_1 = 11.2 Hz, J_2 = 3.6 Hz, 1H, CH_2), 1.54 (s, 9H, CH_3), 1.52 (s, 3 H, CH_3) ppm.

4.3.7. (3*S*)-*tert*-Butyl 3-[(1*S*)-1-(2-chlorophenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ag

The title compound **3ag** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (77.3 mg, 90% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (74:26 dr, 85% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA and IB column in series, *n*-hexane/2-propanol = 97:3, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 30.8 min, t_{minor} = 38.8 min; minor diastereomer: t_R = 32.2, 34.2 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 116–118 °C. $[\alpha]_D^{20} = +40.8$ (*c* 0.74, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.4 Hz, 1H, ArH), 7.42–7.33 (m, 3H, ArH), 7.28–7.22 (m, 2H, ArH), 7.15 (t, *J* = 7.6 Hz, 1H, ArH), 6.94 (d, *J* = 7.6 Hz, 1H, ArH), 4.87 (t, *J* = 12.8 Hz, 1H, CH), 4.78–4.72 (m, 2H, CH_2), 1.64 (s, 9H, CH_3), 1.39 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 148.8, 138.9, 136.5, 132.6, 130.4, 130.0, 129.4, 129.1, 128.7, 126.9, 124.9, 123.1, 115.0, 84.9, 75.2, 49.6, 44.5, 28.0, 20.9 ppm. IR (KBr): *ν* 2981, 2934, 1790, 1760, 1733, 1607, 1558, 1480, 1468, 1372, 1348, 1289, 1252, 1151, 1105, 1056, 1037, 1007, 962, 843, 775, 754, 688 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{23}ClN_2NaO_5$ $[M+Na]^+$ 453.11877, found 453.11889.

4.3.8. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(4-bromophenyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ah[7b]

The title compound **3ah** (the mixture of the major and minor diastereomer) was obtained according to the general procedure

(87.8 mg, 92% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (88:12 dr, 81% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 23.2 min, t_{minor} = 38.3 min; minor diastereomer: t_r = 20.5 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 109–111 °C. $[\alpha]_D^{20} = +4.2$ (*c* 1.57, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.6 Hz, 1H, ArH), 7.35 (t, *J* = 7.2 Hz, 1H, ArH), 7.28–7.26 (m, 2H, ArH), 7.21 (t, *J* = 7.2 Hz, 1H, ArH), 7.09 (d, *J* = 7.2 Hz, 1H, ArH), 6.71 (d, *J* = 8.0 Hz, 2H, ArH), 4.98 (dd, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1H, CH_2), 4.84 (t, *J* = 12.0 Hz, 1H, CH), 3.93 (dd, J_1 = 11.2 Hz, J_2 = 4.0 Hz, 1H, CH_2), 1.54 (s, 9H, CH_3), 1.52 (s, 3 H, CH_3) ppm.

4.3.9. (3*S*)-*tert*-Butyl 3-[(1*R*)-1-(2-furanyl)-2-nitroethyl]-3-methyl-2-oxoindoline-1-carboxylate 3ai[7b]

The title compound **3ai** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (64.2 mg, 83% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (90:10 dr, 76% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA and IB column in series, *n*-hexane/2-propanol = 95:5, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 29.0 min, t_{minor} = 33.6 min; minor diastereomer: t_R = 25.8, 28.1 min. The major diastereomer was purified by flash chromatography and obtained as colorless oil. $[\alpha]_D^{20} = +48.3$ (*c* 1.27, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.4 Hz, 1H, ArH), 7.32–7.27 (m, 2H, ArH), 7.09 (t, *J* = 7.4 Hz, 1H, ArH), 6.66 (d, *J* = 7.6 Hz, 1H, ArH), 6.28 (s, 1H, ArH), 6.09 (s, 1H, ArH), 5.10 (dd, J_1 = 13.2 Hz, J_2 = 3.6 Hz, 1H, CH_2), 4.91 (t, *J* = 12.2 Hz, 1H, CH), 3.98 (dd, J_1 = 11.2 Hz, J_2 = 3.6 Hz, 1H, CH_2), 1.64 (s, 9H, CH_3), 1.52 (s, 3H, CH_3) ppm.

4.3.10. (3*S*)-*tert*-Butyl 3-methyl-3-[(1*R*)-2-nitro-1-(2-thienyl)-ethyl]-2-oxoindoline-1-carboxylate 3aj[7b]

The title compound **3aj** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (69.2 mg, 86% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (84:16 dr, 70% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane/2-propanol = 97:3, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{minor} = 21.1 min, t_{major} = 22.8 min; minor diastereomer: t_R = 16.5, 17.1 min. The major diastereomer was purified by flash chromatography and obtained as a colorless oil. $[\alpha]_D^{20} = +18.0$ (*c* 1.28, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 1H, ArH), 7.35 (t, *J* = 7.2 Hz, 1H, ArH), 7.20–7.12 (m, 2H, ArH), 7.00 (d, *J* = 7.2 Hz, 1H, ArH), 6.83 (d, *J* = 3.2 Hz, 1H, ArH), 6.70 (s, 1H, ArH), 5.05 (dd, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1H, CH_2), 4.80 (t, *J* = 12.0 Hz, 1H, CH), 4.29 (dd, J_1 = 10.8 Hz, J_2 = 3.2 Hz, 1H, CH_2), 1.57 (s, 9H, CH_3), 1.55 (s, 3H, CH_3) ppm.

4.3.11. (3*S*)-*tert*-Butyl 3-methyl-3-[(1*R*)-1-nitromethyl-3-phenylpropyl]-2-oxoindoline-1-carboxylate 3ak

The title compound **3ak** (the mixture of the major and minor diastereomer) was obtained as a colorless oil according to the general procedure (67.2 mg, 79% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (94:6 dr, 76% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 95:5, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 15.0 min, t_{minor} = 16.6 min; minor diastereomer: t_R = 12.4, 13.4 min. $[\alpha]_D^{20} = +27.2$ (*c* 1.30, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.0 Hz, 1H, ArH), 7.35–7.31 (m, 1H, ArH), 7.25 (t, *J* = 7.2 Hz, 2H, ArH), 7.20–7.14 (m, 3H, ArH), 7.10–7.08 (m, 2H, ArH), 4.45 (dd, J_1 = 13.2 Hz, J_2 = 4.8 Hz, 1H, CH_2), 4.43 (dd, J_1 = 13.2 Hz, J_2 = 7.2 Hz, 1H, CH_2), 2.93–2.87 (m, 1H, CH), 2.66–2.50 (m, 2H, CH_2), 1.98–1.89 (m, 1H, CH_2), 1.64 (s, 9H, CH_3), 1.62–1.59 (m, 1H, CH_2), 1.45 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1, 148.9, 140.7, 139.0, 130.4, 128.9, 128.4, 128.3, 126.2, 124.8, 122.8, 115.3, 84.8, 76.4, 50.1, 44.3, 34.0, 30.8, 28.0, 22.7 ppm. IR (KBr): ν 3027, 2980, 2932, 2872, 1790, 1764, 1733, 1607, 1555, 1481, 1465, 1371, 1348, 1291, 1252, 1152, 1105, 1006, 963, 843, 753, 701, 679 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}NaN_2O_5$ $[M+Na]^+$ 447.18904, found 447.18928.

4.3.12. (3*S*)-*tert*-Butyl 3-methyl-3-[(1*R*)-1-nitromethylpropyl]-2-oxoindoline-1-carboxylate 3al

The title compound **3al** (the mixture of the major and minor diastereomer) was obtained as a colorless oil according to the general procedure (22.7 mg, 33% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (97:3 dr, 88% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 90:10, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 10.1 min, t_{minor} = 11.3 min; minor diastereomer: t_R = 9.3 min. $[\alpha]_D^{28} = +43.5$ (*c* 1.13, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.0 Hz, 1H, ArH), 7.36–7.32 (m, 1H, ArH), 7.19 (d, *J* = 8.4 Hz, 2H, ArH), 4.44 (dd, J_1 = 13.2 Hz, J_2 = 4.8 Hz, 1H, CH_2NO_2), 4.32 (dd, J_1 = 13.2 Hz, J_2 = 7.2 Hz, 1H, CH_2NO_2), 2.84–2.77 (m, 1H, CH), 1.65 (s, 9H, CH_3), 1.48 (s, 3H, CH_3), 1.34–1.26 (m, 2H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 149.0, 139.1, 130.6, 128.8, 124.8, 122.8, 115.3, 84.7, 76.0, 50.3, 46.2, 28.0, 22.7, 21.9, 12.0 ppm. IR (KBr): ν 2977, 2937, 2879, 1790, 1762, 1733, 1607, 1556, 1481, 1464, 1371, 1346, 1290, 1251, 1151, 1007, 842, 775, 756 cm^{-1}. HRMS (ESI): *m*/*z* calcd for $C_{18}H_{24}NaN_2O_5$ $[M+Na]^+$ 371.15774, found 371.15769.

4.3.13. (3*S*)-*tert*-Butyl 3-ethyl-3-[(1*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3ba[7a]

The title compound **3ba** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (79.7 mg, 97% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (79:21 dr, 87% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 97:3, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 18.5 min, t_{minor} = 23.9 min; minor diastereomer: t_R = 15.3, 16.3 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 92–94 °C. $[\alpha]_D^{20} = +15.5$ (*c* 1.92, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.4 Hz, 1H, ArH), 7.38–7.27 (m, 2H, ArH), 7.23–7.16 (m, 2H, ArH), 7.13–7.05 (m, 2H, ArH), 6.81 (d, *J* = 7.2 Hz, 2H, ArH), 4.99 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2), 4.88 (t, *J* = 12.0 Hz, 1H, CH), 3.97 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.16–2.07 (m, 1H, CH_2), 2.02–1.93 (m, 1H, CH_2), 1.51 (s, 9H, CH_3), 0.6 (t, *J* = 7.2 Hz, 3H, CH_3) ppm.

4.3.14. (3*S*)-*tert*-Butyl 3-benzyl-3-[(1*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3ca[7b]

The title compound **3ca** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (89.6 mg, 95% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (90:10 dr, 86% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 97:3, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 41.1 min, t_{minor} = 42.6 min; minor diastereomer: t_R = 24.0, 25.6 min. The major diastereomer was purified by flash chromatography and obtained as a colorless oil. $[\alpha]_D^{20} = +3.0$ (*c* 1.22, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.42 (m, 1H, ArH), 7.30–7.28 (m, 1H, ArH), 7.25–7.16 (m, 5H, ArH), 7.05–6.95 (m, 5H, ArH), 6.75 (d, *J* = 7.6 Hz, 2H, ArH), 5.02–4.95 (m, 2H, CH_2), 4.16 (dd, J_1 = 9.0 Hz, J_2 = 6.6 Hz, 1H

CH), 3.28 (d, J = 12.8 Hz, 1H, CH_2), 3.14 (d, J = 12.8 Hz, 1H, CH_2), 1.45 (s, 9H, CH_3) ppm.

4.3.15. (3*R*)-*tert*-Butyl 3-phenyl-3-[(1*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3da[7c]

The title compound **3da** (the mixture of the major and minor diastereomer) was obtained as a white foam according to the general procedure (88.3 mg, 96% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (87:13 dr, 44% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane/2-propanol = 98:2, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 21.7 min, t_{minor} = 19.9 min; minor diastereomer: t_R = 17.3, 30.9 min. $[\alpha]_D^{20} = +64.3$ (*c* 2.11, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, J = 8.0 Hz, 1H, ArH), 7.61 (d, J = 8.4 Hz, 2H, ArH), 7.42–7.38 (m, 3H, ArH), 7.36–7.30 (m, 3H, ArH), 7.09–7.03 (m, 3H, ArH), 6.78 (d, J = 8.0 Hz, 2H, ArH), 4.98–4.87 (m, 2H, CH_2), 4.74 (dd, J_1 = 11.6 Hz, J_2 = 1.6 Hz, 1H, CH), 1.44 (s, 9H, CH_3) ppm.

4.3.16. (3*S*)-*tert*-Butyl 5-methoxy-3-methyl-3-[(*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3ea[7b]

The title compound **3ea** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (81.9 mg, 96% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (88:12 dr, 84% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 85:15, flow rate 0.5 mL/min, detection at 254 nm), major diastereomer: t_{major} = 13.4 min, t_{minor} = 27.6 min; minor diastereomer: t_R = 11.9 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 139–140 °C. $[\alpha]_D^{28} = -5.1$ (*c* 1.50, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, J = 8.8 Hz, 1H, ArH), 7.23–7.14 (m, 3H, ArH), 6.89 (d, J = 7.2 Hz, 2H, ArH), 6.83 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H, ArH), 6.48 (d, J = 2.4 Hz, 1H, ArH), 5.05 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2), 4.91 (dd, J_1 = 12.8 Hz, J_2 = 11.2 Hz, 1H, CH_2), 3.91 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H, CH), 3.76 (s, 3H, OCH_3), 1.53 (s, 9H, CH_3), 1.50 (s, 3H, CH_3) ppm.

4.3.17. (3*S*)-*tert*-Butyl 5-fluoro-3-methyl-3-[(*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 3fa[7b]

The title compound **3fa** (the mixture of the major and minor diastereomer) was obtained according to the general procedure (79.6 mg, 95% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (90:10 dr, 79% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane/2-propanol = 90:10, flow rate 0.8 mL/min, detection at 254 nm), major diastereomer: t_{major} = 9.0 min, t_{minor} = 14.1 min; minor diastereomer: t_R = 7.5, 8.1 min. The major diastereomer was purified by flash chromatography and obtained as a white solid, mp 105–107 °C. $[\alpha]_D^{28} = +28.6$ (*c* 1.52, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.67 (m, 1H, ArH), 7.24–7.14 (m, 3H, ArH), 7.02 (dt, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H, Ar), 6.87 (d, J = 7.6 Hz, 2H, Ar), 6.67 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 1H, Ar), 5.06 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2), 4.91 (dd, J_1 = 12.8 Hz, J_2 = 11.2 Hz, 1H, CH_2), 3.93 (dd, J_1 = 10.8 Hz, J_2 = 4.0 Hz, 1H, CH), 1.53 (s, 9H, CH_3), 1.51 (s, 3H, CH_3) ppm.

4.4. Further investigation of substrate scope

4.4.1. 3-Methyl-3-(2-nitro-1-phenylethyl)indolin-2-one 5aa[7f]

According to the general procedure, the reaction was performed with 3-methyl oxindole **4a** (58.9 mg, 0.4 mmol) and β-nitrostyrene **2a** (59.6 mg, 0.4 mmol) at room temperature for 36 h. The mixture was concentrated and directly purified by silica gel column chromatography to afford a mixture of the major and minor diastereomer **5aa** (86.6 mg, 73% yield). White foam, mp 62–64 °C. $[\alpha]_D^{25} = -27.8$ (*c* 0.80, CH_2Cl_2). The mixture was analyzed to determine the diastereoselectivity and enantioselectivity (61:39 dr, 85% ee for the major diastereomer and 79% ee for the minor diastereomer) of the reaction by chiral HPLC (Daicel Chiralpak IA column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 22.6 min, t_{minor} = 25.7 min; minor diastereomer: t_{major} = 18.1 min, t_{minor} = 20.4 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (s, 1H, NH), 7.27–7.23 (m, 1H, ArH), 7.20–7.13 (m, 3H), 7.07–7.03 (m, 1H, ArH), 6.97–6.94 (m, 3H, ArH), 6.83 (d, J = 7.6 Hz, 1H, ArH), 5.06 (dd, J_1 = 12.6 Hz, J_2 = 4.4 Hz, 1H), 4.93 (t, J = 12.0 Hz, 1H, CH), 3.93 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H, CH_2), 1.47 (s, 3H, CH_3) ppm.

4.4.2. 3-Methyl-3-(2-nitro-1-phenylethyl)-1-phenyl-indolin-2-one 5ba[7d]

According to the general procedure, the reaction was performed with 3-methyl-1-phenyloxindole **4b** (44.7 mg, 0.2 mmol) and β-nitrostyrene **2a** (35.8 mg, 0.24 mmol) at room temperature for 24 h. The mixture was concentrated and directly purified by silica gel column chromatography to afford a mixture of the major and minor diastereomer **5ba** (68.0 mg, 91% yield). White solid, mp 112–114 °C. $[\alpha]_D^{28} = +5.8$ (*c* 2.11, CH_2Cl_2). The mixture was analyzed to determine the diastereoselectivity and enantioselectivity (73:27 dr, 54% ee for the major diastereomer and 76% ee for the minor diastereomer) of the reaction by chiral HPLC (Daicel Chiralpak IA column, *n*-hexane/2-propanol = 85:15, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 21.5 min, t_{minor} = 8.4 min; minor diastereomer: t_{major} = 7.0 min, t_{minor} = 11.6 - min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.31 (m, 3H, ArH), 7.24–7.19 (m, 3H, ArH), 7.16–7.10 (m, 3H, ArH), 6.83 (d, J = 7.6 Hz, 2H, ArH), 6.75 (d, J = 7.2 Hz, 2H, ArH), 6.55 (d, J = 7.2 Hz, 1H, ArH), 5.16 (dd, J_1 = 12.4 Hz, J_2 = 4.8 Hz, 1H, CH_2), 4.98 (dd, J_1 = 12.4 Hz, J_2 = 11.2 Hz, 1H, CH_2), 4.09 (dd, J_1 = 11.2 Hz, J_2 = 4.8 Hz, 1H, CH), 1.64 (s, 3H) ppm.

4.4.3. (3*S*)-Ethyl 3-methyl-3-[(1*R*)-2-nitro-1-phenylethyl]-2-oxoindoline-1-carboxylate 5ca[7e]

According to the general procedure, the reaction was performed with ethyl 3-methyl-2-oxoindoline-1-carboxylate **4c** (43.8 mg, 0.2 mmol) and β-nitrostyrene **2a** (29.8 mg, 0.2 mmol) at −20 °C for 12 h. The mixture was concentrated and directly purified by silica gel column chromatography to afford a mixture of the major and minor diastereomer **5ca** (66.3 mg, 90% yield). White solid, mp 102–104 °C. $[\alpha]_D^{28} = +18.4$ (*c* 3.06, CH_2Cl_2). The mixture was analyzed to determine the diastereoselectivity and enantioselectivity (96:4 dr, 91% ee for the major diastereomer) of the reaction by chiral HPLC (Daicel Chiralpak IA column, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm), major diastereomer: t_{major} = 15.2 min, t_{minor} = 12.9 min; minor diastereomer: t_R = 9.6 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.4 Hz, 1H, ArH), 7.34–7.28 (m, 1H, ArH), 7.20 (t, J = 7.2 Hz, 2H, ArH), 7.13 (t, J = 7.2 Hz, 2H, ArH), 7.03 (d, J = 7.2 Hz, 1H, ArH), 6.85 (d, J = 7.2 Hz, 2H, ArH), 5.02 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H, CH_2NO_2), 4.91 (dd, J_1 = 12.8 Hz, J_2 = 11.2 Hz, 1H, CH_2NO_2), 4.34 (q, J = 7.2 Hz, 2H, CH_2), 3.96 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H, CH), 1.53 (s, 3H, CH_3), 1.35 (t, J = 7.2 Hz, 3H, CH_3) ppm.

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