

Asymmetric Friedel–Crafts alkylation of indoles with 3-nitro-2*H*-chromenes catalyzed by diphenylamine-linked bis(oxazoline) and bis(thiazoline) Zn(II) complexes†

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An efficient diastereo- and enantioselective Friedel–Crafts alkylation of indoles with 3-nitro-2*H*-chromenes catalyzed by diphenylamine-linked bis(oxazoline) and bis(thiazoline) Zn(II) complexes has been developed. This asymmetric Friedel–Crafts alkylation led to medicinally privileged indolyl(nitro)chromans in good yields with high enantioselectivities (up to 95% ee) and diastereoselectivities under mild reaction conditions.

## Introduction

As an important class of compounds, chroman derivatives are widely found in naturally occurring compounds,<sup>1</sup> many of which exhibit useful biological activity.<sup>2</sup> For example, they have been identified as apoptosis-inducing agents,<sup>3</sup> anti-HIV agents,<sup>4,5</sup> modulators of the estrogen receptors,<sup>6</sup> antibacterials,<sup>7</sup> antioxidants<sup>8</sup> and anticonvulsants.<sup>9</sup> Likewise, indole and many of its derivatives are important units because of their pharmacological and biological properties.<sup>10</sup> So the synthesis of chiral fused heterocyclic systems containing both chroman and indole moieties should be significant work. There has been some evidence demonstrating the biological activity of this kind of fused heterocyclic system.<sup>11</sup> 3-Nitro-2*H*-chromenes, which can be easily prepared from salicylaldehyde and nitroethylene,<sup>12</sup> are valuable intermediates for the synthesis of chroman derivatives. For example, they present high reactivity for conjugate addition with nucleophiles<sup>13</sup> and 1,3-dipolar cycloaddition with azomethine, azide, and diazo compounds.<sup>14</sup> Yao's group studied the Friedel–Crafts alkylation of indole with 3-nitro-2*H*-chromene to achieve fused heterocyclic systems,<sup>15</sup> but no asymmetric reaction was tried.

Our group has developed various diphenylamine-linked bis(oxazoline) ligands and bis(thiazoline) ligands in recent years,<sup>16</sup> which have been successfully applied in the asymmetric Henry reaction of  $\alpha$ -ketoesters,<sup>16a,b</sup> asymmetric Michael addition of nitroethanes to nitroalkenes,<sup>16c</sup> and asymmetric Friedel–Crafts

alkylation of different electron-rich heteroaromatics with nitroalkenes<sup>16d-f</sup> in the subsequent research. Inspired by the mechanism, we attempted to apply this kind of ligand to the asymmetric Friedel–Crafts alkylation<sup>17,18</sup> of 3-nitro-2*H*-chromenes and indoles. To our delight, good yields, enantioselectivities and diastereoselectivities were obtained as expected. In this paper, we wish to report an efficient method to afford indolyl(nitro)chromans in high yields with good enantioselectivities and diastereoselectivities.

## Results and discussion

We initially performed the Friedel–Crafts alkylation of indole **1a** with 3-nitro-2*H*-chromene **2a** in toluene at room temperature using **L1**–Zn(OTf)<sub>2</sub> as the catalyst. The desired product **3a** was obtained in 73% yield with 65% ee and 98 : 2 dr. To identify a more efficient ligand, we screened a series of diphenylamine-linked bis(oxazoline) ligands **L2**–**L6** and bis(thiazoline) ligands **L7** and **L8** (Fig. 1). The results are summarized in Table 1. When ligand **L2** was used, excellent yield and an obvious increase in the enantioselectivity (93% ee) were observed though the diastereoselectivity slightly decreased. So we studied ligands

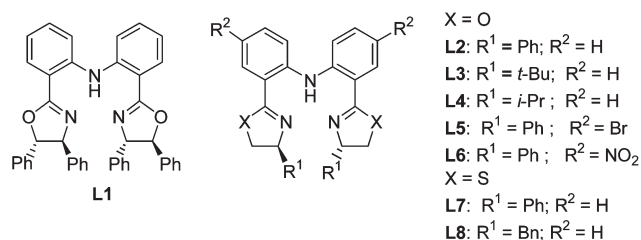


Fig. 1 Diphenylamine-linked bis(oxazoline) and bis(thiazoline) ligands.

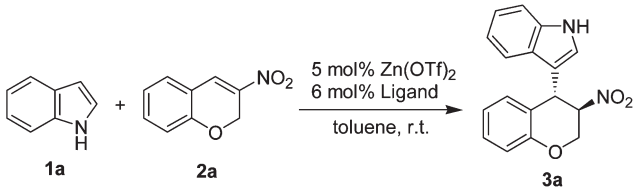
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† Electronic supplementary information (ESI) available: <sup>1</sup>H NMR spectra, <sup>13</sup>C NMR spectra and HPLC diagrams. CCDC reference numbers 868579. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob25360g

with only one substitution group on the heterocycles (Table 1, entries 3–4 and 7–8). Interestingly, the catalyst **L2**–Zn(OTf)<sub>2</sub> furnished overwhelmingly better results than the other bis(oxazoline) or bis(thiazoline)–Zn(OTf)<sub>2</sub> catalysts in enantioselectivity. We wondered whether the electronic effect of the substitution group on the diphenylamine skeleton would promote the result, so ligand **L5** and **L6** were tested. However, no surpassing results were achieved (Table 1, entries 5–6). Therefore, **L2**–Zn(OTf)<sub>2</sub> was selected as the best catalyst for further optimization.

To get the optimal reaction conditions, we further evaluated different solvents, temperatures, and zinc salts. As presented in Table 2, the Friedel–Crafts alkylation could be efficiently

**Table 1** Screening of ligands for the asymmetric Friedel–Crafts alkylation of indole with 3-nitro-2*H*-chromene<sup>a</sup>



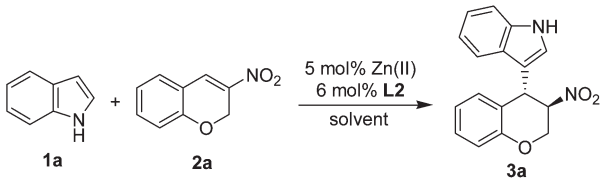
Entry	Ligand	Yield <sup>b</sup> (%)	Anti/syn <sup>c</sup>	ee <sup>c,d</sup> (%)
1	<b>L1</b>	73	98 : 2	65
2	<b>L2</b>	96	84 : 16	93
3	<b>L3</b>	81	88 : 12	81
4	<b>L4</b>	71	77 : 23	83
5	<b>L5</b>	91	77 : 23	81
6	<b>L6</b>	60	86 : 14	71
7	<b>L7</b>	96	83 : 17	86
8	<b>L8</b>	90	86 : 14	73

<sup>a</sup> All the reactions were conducted in a 0.3 mmol scale in 3 mL of toluene at room temperature for 48 h. <sup>b</sup> Isolated yields after column chromatography purification. <sup>c</sup> Determined by chiral HPLC analysis. <sup>d</sup> Enantiomeric excess of the *anti*-product.

performed in all solvents tested, but variation of the solvents had a pronounced effect on the selectivity. Our catalyst exhibited high catalytic activity in toluene with 93% ee and 84 : 16 dr. Xylene led to an obvious decrease in the enantioselectivity, in spite of a slight improvement in the diastereoselectivity (Table 2, entry 2). The use of chlorobenzene produced **3a** in excellent yield, but with moderate enantioselectivity and diastereoselectivity (Table 2, entry 3). Other solvents tested led to moderate to low enantioselectivities (Table 2, entries 4–6). Then we conducted a temperature effect study using toluene as the solvent. A decrease in the yield was observed when the reaction temperature dropped. But taking the enantioselectivities and diastereoselectivities into account comprehensively, we chose 0 °C as the final reaction temperature. As for zinc salts, the role of Zn(OTf)<sub>2</sub> could not be carried out by ZnCl<sub>2</sub>, ZnBr<sub>2</sub> or Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (Table 2, entries 9–11).

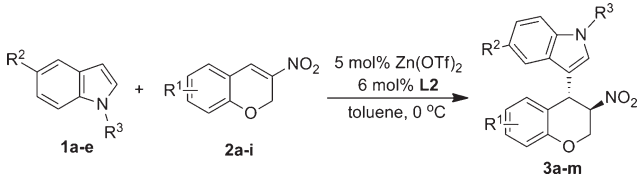
With the optimal reaction conditions established, we explored the substrate scope of this asymmetric Friedel–Crafts alkylation. The results are summarized in Table 3. We first surveyed a variety of 3-nitro-2*H*-chromenes **2a–i** bearing different substituents (Table 3, entries 1–9). They could react with indole in moderate to good yields that varied from 61% to 94%, with good diastereoselectivities. As for enantioselectivities, the substitution on the phenyl of 3-nitro-2*H*-chromene, with either electron-donating or electron-withdrawing groups, led to good enantioselectivities (83–89% ee, Table 3, entries 2–3 and 5–9), except for the substrate **2d** (Table 3, entry 4), with which the product was obtained in moderate enantioselectivity (54% ee). The generality of the reaction was further demonstrated by variation of indoles. When electron-rich 5-methylindole **1b** and 5-methoxyindole **1c** were used, the reaction proceeded very smoothly with good yields, enantioselectivities and diastereoselectivities (Table 3, entries 10–11). However, an electron-withdrawing substituent chlorine in the 5-position of the indole ring caused a moderate decrease in both yield and selectivity, providing **3l** in 68% yield, 62% ee and 82 : 18 dr (Table 3, entry 12). When we

**Table 2** Optimization of reaction conditions for the asymmetric Friedel–Crafts alkylation of indole with 3-nitro-2*H*-chromene<sup>a</sup>



Entry	Solvent	T (°C)	Zn(II) Salt	Yield <sup>b</sup> (%)	Anti/syn <sup>c</sup>	ee <sup>c,d</sup> (%)
1	Toluene	rt	Zn(OTf) <sub>2</sub>	96	84 : 16	93
2	Xylene	rt	Zn(OTf) <sub>2</sub>	92	90 : 10	86
3	Chlorobenzene	rt	Zn(OTf) <sub>2</sub>	97	72 : 28	77
4	Chloroform	rt	Zn(OTf) <sub>2</sub>	74	76 : 24	78
5	THF	rt	Zn(OTf) <sub>2</sub>	73	89 : 11	48
6	Ethanol	rt	Zn(OTf) <sub>2</sub>	62	81 : 19	23
7	Toluene	0	Zn(OTf) <sub>2</sub>	80	89 : 11	94
8	Toluene	–20	Zn(OTf) <sub>2</sub>	78	91 : 9	91
9	Toluene	0	ZnCl <sub>2</sub>	82	79 : 21	0
10	Toluene	0	ZnBr <sub>2</sub>	80	72 : 28	3
11	Toluene	0	Zn(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O	80	75 : 25	20

<sup>a</sup> All the reactions were conducted in a 0.3 mmol scale in 3 mL of solvent for 48 h. <sup>b</sup> Isolated yields after column chromatography purification. <sup>c</sup> Determined by chiral HPLC analysis. <sup>d</sup> Enantiomeric excess of the *anti*-product.

**Table 3** Asymmetric Friedel–Crafts alkylation of indoles **1** with 3-nitro-2*H*-chromenes **2** catalyzed by **L2**–Zn(OTf)<sub>2</sub><sup>a,b</sup>


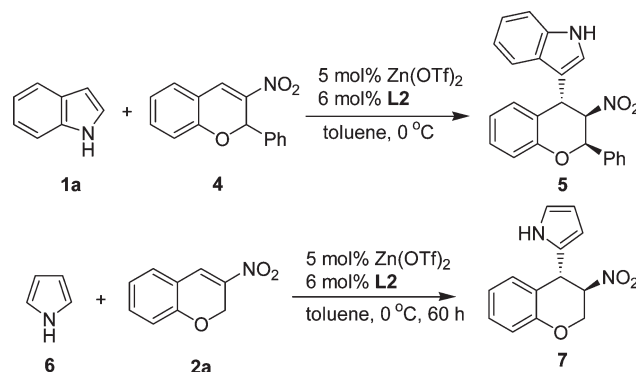
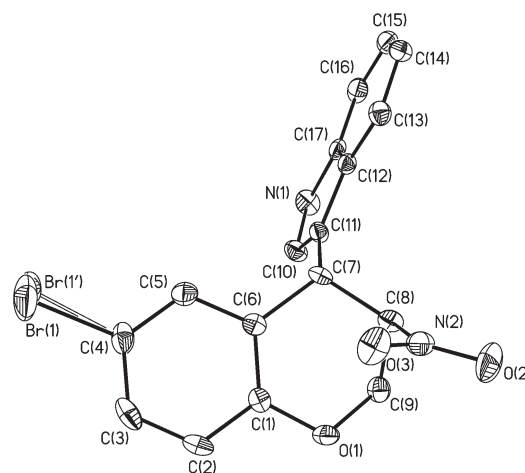
Entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Product	Time (h)	Yield <sup>c</sup> (%)	<i>Anti/syn</i> <sup>d</sup>	ee <sup>d,e</sup> (%)
1	H	H	H	<b>3a</b>	46	80	89 : 11	94
2	6-Cl	H	H	<b>3b</b>	48	80	88 : 12	83
3	6-Br	H	H	<b>3c</b>	48	94	84 : 16	86
4	6-NO <sub>2</sub>	H	H	<b>3d</b>	60	80	90 : 10	54
5	8-MeO	H	H	<b>3e</b>	60	84	89 : 11	89
6	8-EtO	H	H	<b>3f</b>	60	92	92 : 8	88
7	5,6-benzo	H	H	<b>3g</b>	60	61	95 : 5	88
8	6,8-Cl <sub>2</sub>	H	H	<b>3h</b>	60	90	90 : 10	83
9	6,8-Br <sub>2</sub>	H	H	<b>3i</b>	60	90	92 : 8	87
10	H	Me	H	<b>3j</b>	60	88	94 : 6	92
11	H	MeO	H	<b>3k</b>	60	92	91 : 9	93
12	H	Cl	H	<b>3l</b>	60	68	82 : 18	62
13	H	H	Me	<b>3m</b>	60	94	92 : 8	95

<sup>a</sup> All the reactions were conducted in a 0.3 mmol scale in 3 mL of toluene. <sup>b</sup> The absolute configuration of adduct **3c** was assigned by single X-ray crystallography, configurations of other adducts were assigned by analogy. <sup>c</sup> Isolated yields after column chromatography purification. <sup>d</sup> Determined by chiral HPLC analysis. <sup>e</sup> Enantiomeric excess of the *anti*-product.

introduced a methyl substituent to the indolic nitrogen atom, to our delight, the reaction proceeded very well, giving the corresponding product **3m** in high yield with good enantioselectivity and diastereoselectivity (Table 3, entry 13).

To further extend the scope of this methodology, we also examined other substituted chromenes, such as 3-nitro-2-phenyl-2*H*-chromene **4**, and other heterocycle pyrroles (Scheme 1). Under the optimal reaction conditions we established, 3-nitro-2-phenyl-2*H*-chromene **4** reacted with indole **1a** giving the desired alkylation product in 45% yield after 3 days. The major diastereomer **5** was obtained with 58% ee and 86 : 14 dr. To the best of our knowledge, the asymmetric Friedel–Crafts alkylation of pyrrole with chromenes has not been developed though the racemic form has been attempted.<sup>13d</sup> To our delight, the asymmetric Friedel–Crafts alkylation of pyrrole **6** with 3-nitro-2*H*-chromene **2a** proceeded smoothly and the product **7** was obtained with 88% yield, 77% ee and 65 : 35 dr.

To determine the absolute configuration of the major isomer of products **3a–m**, a single crystal suitable for X-ray crystallographic analysis was fortunately obtained from recrystallization of *anti*-**3c** bearing a bromine atom. As shown in Fig. 2, the absolute configuration of the major enantiomer of *anti*-**3c** is (3*R*,4*S*).<sup>19</sup> On the basis of the configuration of the product and the XRD structure of the ligand we have published before,<sup>16a,20</sup> we postulate the proposed transition state of the reaction as illustrated in Fig. 3. Our catalyst works in a bifunctional form, the NH– $\pi$  interaction directs the indole attack from the back side,<sup>16e,20</sup> and the Lewis acid activates the chromene molecule through coordination of the zinc cation with the two oxygen atoms in the nitro group. The hydrogen atom is directed to the back side to eliminate the steric repulsion between the phenyl group and incoming indole.

**Scheme 1** Further investigation of substrate scope.**Fig. 2** X-ray crystal structure of enantiopure *anti*-**3c**.

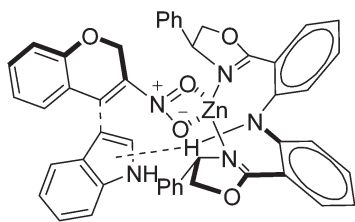


Fig. 3 Proposed transition state of the asymmetric Friedel-Crafts alkylation catalyzed by **L2**-Zn(OTf)<sub>2</sub> complex.

## Conclusions

In conclusion, the diphenylamine-linked bis(oxazoline) **L2**-Zn(OTf)<sub>2</sub> complex showed excellent performance in asymmetric Friedel-Crafts alkylation of indoles with 3-nitro-2*H*-chromenes. Moderate to high levels of reactivity, enantioselectivity, and diastereoselectivity are achieved with a wide variety of indolyl (nitro)chromans, which have a wide range of potential applications in pharmaceutical chemistry. The transition state was proposed on the basis of the absolute configuration of *anti*-**3c**. This methodology was also effective in the reaction of pyrrole with 3-nitro-2*H*-chromene. Further studies on asymmetric Friedel-Crafts alkylation of other functional nitroalkenes are underway in our laboratory, and will be reported in due course.

## Experimental

### General methods

Commercially available compounds were used without further purification. Toluene was purified according to standard procedures. Column chromatography was performed using silica gel (200–300 mesh). Melting points were determined on a XT-4 melting point apparatus without correction. The <sup>1</sup>H NMR spectra were measured on a Varian Mercury-plus 400 MHz spectrometer. Chemical shifts were recorded in ppm ( $\delta$ ) relative to tetramethylsilane (TMS) as the internal standard. <sup>13</sup>C NMR spectra were measured at 100 MHz. Chemical shifts were reported in ppm with the solvent resonance as internal standard (DMSO-d<sub>6</sub>,  $\delta$  = 39.43; CDCl<sub>3</sub>,  $\delta$  = 77.0; CD<sub>3</sub>COCD<sub>3</sub>,  $\delta$  = 30.83). Infrared spectra were obtained with a Perkin Elmer Spectrum One spectrometer. ESI-HRMS spectra were measured with a Bruker APEX IV Fourier-Transform mass spectrometer. Optical rotations were measured with a WZZ-3 polarimeter after the products were recrystallized. Enantiomeric excesses and diastereomeric ratios were determined by chiral HPLC using an Agilent 1200 LC instrument with a Daicel Chiralpak IB, IA or AS-H column. The absolute configuration of compound *anti*-**3c** was determined by single crystal X-ray analysis and others were tentatively assigned by analogy.

### Preparation of 3-nitro-2*H*-chromenes **2a–i** and **4**

The 3-nitro-2*H*-chromenes were prepared following the reported procedures.<sup>12,21</sup>

### General procedure for asymmetric Friedel-Crafts alkylation of indoles with 3-nitro-2*H*-chromenes

To a flame-dried Schlenk tube Zn(OTf)<sub>2</sub> (5.5 mg, 0.015 mmol) and ligand **L2** (8.3 mg, 0.018 mmol) were added under argon, followed by addition of toluene (3 mL). After the mixture was stirred at room temperature for 1.5 h, 3-nitro-2*H*-chromene **2** or **4** (0.3 mmol) was added and the mixture was cooled to 0 °C. After 10 min, indole **1** (0.3 mmol) was added and the mixture was stirred at 0 °C for the corresponding time. Then the mixture was separated directly by silica gel column chromatography with petroleum ether–ethyl acetate (10:1) as eluent to afford the desired products **3a–m** or **5**.

**3-(3-Nitrochroman-4-yl)-1*H*-indole (3a)**. The title compound **3a** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a white solid (70.4 mg, 80% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (89 : 11 dr, 94% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol = 95 : 5 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer: *t*<sub>R</sub> (major) = 52.6 min, *t*<sub>R</sub> (minor) = 33.1 min; *syn* diastereomer: *t*<sub>R</sub> = 42.8 min, 56.6 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. [ $\alpha$ ]<sub>D</sub><sup>20</sup> +138.2 (*c* 0.50, CH<sub>2</sub>Cl<sub>2</sub>); m. p. 190–193 °C; IR (KBr, cm<sup>-1</sup>):  $\nu$  3406, 3116, 3055, 2925, 2889, 1585, 1547, 1488, 1462, 1426, 1385, 1357, 1222, 1209, 1093, 747, 618, 588; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.11 (s, 1H, NH), 7.45–7.40 (m, 2H, ArH), 7.26–7.10 (m, 4H, ArH), 6.97–6.89 (m, 2H, ArH), 6.80 (s, 1H, ArH), 5.22 (d, *J* = 2.8 Hz, 1H, CH), 5.08 (s, 1H, CH), 4.67 (dd, *J* = 11.4 Hz, 4.2 Hz, 1H, CH), 4.42 (d, *J* = 11.6 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>):  $\delta$  (ppm) 152.8, 136.4, 130.2, 128.0, 125.3, 121.6, 121.4, 121.3, 118.9, 118.1, 116.2, 114.6, 111.8, 82.5, 63.3, 35.7; HRMS (ESI): *m/z* calcd for C<sub>17</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 295.10772, found: 295.10829.

**3-(6-Chloro-3-nitrochroman-4-yl)-1*H*-indole (3b)**. The title compound **3b** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a pale yellow solid (78.9 mg, 80% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (88 : 12 dr, 83% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 95 : 5 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer: *t*<sub>R</sub> (major) = 26.9 min, *t*<sub>R</sub> (minor) = 31.3 min; *syn* diastereomer: *t*<sub>R</sub> = 36.2 min, 48.3 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 199–203 °C; [ $\alpha$ ]<sub>D</sub><sup>20</sup> +106.3 (*c* 0.54, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3404, 3111, 3063, 2925, 1582, 1549, 1480, 1458, 1358, 1264, 1224, 1178, 1091, 825, 747, 614; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.16 (s, 1H, NH), 7.47 (d, *J* = 8.0 Hz, 1H, ArH) 7.42 (d, *J* = 8.0 Hz, 1H, ArH), 7.29–7.26 (m, 2H, ArH), 7.17 (d, *J* = 7.6 Hz, 1H, ArH), 7.12 (s, 1H, ArH), 6.90 (d, *J* = 8.8 Hz, 1H, ArH), 6.80 (s, 1H), 5.19 (s, 1H, CH), 5.04 (s, 1H, CH), 4.69 (d, *J* = 11.6 Hz, 1H, CH), 4.39 (d, *J* = 11.6 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>COCD<sub>3</sub>):  $\delta$  (ppm) 154.2, 138.9, 131.7, 130.0, 127.5, 127.3, 125.5, 123.9, 121.3, 120.1, 120.0, 116.9, 113.8, 84.2, 65.6, 37.8; HRMS (ESI): *m/z* calcd for C<sub>17</sub>H<sub>14</sub>ClN<sub>2</sub>O<sub>3</sub>



$[M + H]^+$ : 329.06785, found: 329.06910; calcd for  $C_{17}H_{13}ClN_2NaO_3$   $[M + Na]^+$ : 351.05069, found: 351.05094.

**3-(6-Bromo-3-nitrochroman-4-yl)-1H-indole (3c).** The title compound **3c** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a white solid (105.2 mg, 94% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (84 : 16 dr, 86% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 95 : 5 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 27.7 min,  $t_R$  (minor) = 33.0 min; *syn* diastereomer:  $t_R$  = 38.5 min, 49.9 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 212–214 °C;  $[\alpha]_D^{20} +80.0$  (*c* 0.27, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3404, 3109, 3062, 2922, 1729, 1578, 1547, 1478, 1458, 1357, 1265, 1224, 1177, 1094, 822, 747, 607; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.16 (s, 1H, NH), 7.48 (d, *J* = 7.6 Hz, 1H, ArH), 7.42 (d, *J* = 8.4 Hz, 1H, ArH), 7.32–7.26 (m, 3H, ArH), 7.18–7.15 (m, 1H, ArH), 6.85 (d, *J* = 8.8 Hz, 1H, ArH), 6.79 (s, 1H, ArH), 5.19 (s, 1H, CH), 5.04 (s, 1H, CH), 4.68 (dd, *J* = 12.0 Hz, 3.2 Hz, 1H, CH), 4.38 (d, *J* = 12.0 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 152.5, 136.6, 132.9, 131.5, 124.7, 123.1, 122.7, 120.5, 118.8, 118.1, 115.9, 114.0, 111.8, 82.2, 63.5, 35.9; HRMS (ESI): *m/z* calcd for  $C_{17}H_{14}BrN_2O_3$   $[M + H]^+$ : 373.01823, found: 373.01856; calcd for  $C_{17}H_{13}BrN_2NaO_3$   $[M + Na]^+$ : 395.00018, found: 395.00058.

**3-(6-Nitro-3-nitrochroman-4-yl)-1H-indole (3d).** The title compound **3d** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a white solid (81.9 mg, 80% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (90 : 10 dr, 54% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 21.6 min,  $t_R$  (minor) = 24.8 min; *syn* diastereomer:  $t_R$  = 33.6 min, 40.7 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 98–100 °C;  $[\alpha]_D^{20} +60.0$  (*c* 0.35, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3412, 3061, 2923, 1620, 1589, 1551, 1517, 1487, 1458, 1343, 1259, 1236, 1093, 908, 747, 606; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.30 (s, 1H, NH), 8.11–8.08 (m, 2H, ArH) 7.48 (d, *J* = 8.0 Hz, 1H, ArH), 7.42 (d, *J* = 8.4 Hz, 1H, ArH), 7.29–7.24 (m, 1H, ArH), 7.19–7.15 (m, 1H, ArH), 7.06–7.04 (m, 1H, ArH), 6.70 (d, *J* = 2.4 Hz, 1H, ArH), 5.25 (s, 1H, CH), 5.10–5.08 (m, 1H, CH), 4.82–4.78 (m, 1H, CH), 4.43 (dd, *J* = 12.2 Hz, 2.0 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 158.3, 142.2, 136.6, 126.8, 124.8, 124.6, 124.3, 123.3, 121.3, 120.6, 117.8, 115.2, 112.0, 81.4, 63.6, 35.9; HRMS (ESI): *m/z* calcd for  $C_{17}H_{14}N_3O_5$   $[M + H]^+$ : 340.09280, found: 340.09301; calcd for  $C_{17}H_{13}N_3NaO_5$   $[M + Na]^+$ : 362.07474, found: 362.07499.

**3-(8-Methoxy-3-nitrochroman-4-yl)-1H-indole (3e).** The title compound **3e** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a white solid (82.1 mg, 84% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (89 : 11 dr, 89% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak AS-H column, *n*-hexane–2-propanol 85 : 15 v/v, flow rate

1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 41.1 min,  $t_R$  (minor) = 30.8 min; *syn* diastereomer:  $t_R$  = 27.5 min, 33.9 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 72–75 °C;  $[\alpha]_D^{20} +85.4$  (*c* 0.52, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3368, 2935, 2838, 1589, 1549, 1484, 1457, 1358, 1337, 1266, 1120, 1035, 1011, 910, 767, 744, 730; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.17 (s, 1H, NH), 7.44 (d, *J* = 7.6 Hz, 1H, ArH), 7.37 (d, *J* = 8.0 Hz, 1H, ArH), 7.24–7.21 (m, 1H, ArH), 7.14–7.10 (m, 1H, ArH), 6.86–6.81 (m, 2H, ArH), 6.75 (d, *J* = 2.4 Hz, 1H, ArH), 6.72–6.70 (m, 1H, ArH), 5.20 (d, *J* = 4.0 Hz, 1H, CH), 5.06–5.03 (m, 1H, CH), 4.76–4.72 (m, 1H, CH), 4.44 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H, CH), 3.90 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 148.0, 142.8, 136.5, 125.0, 124.8, 122.7, 122.0, 121.3, 120.1, 118.2, 115.9, 111.7, 110.0, 82.5, 63.8, 55.9, 36.1; HRMS (ESI): *m/z* calcd for  $C_{18}H_{17}N_2O_4$   $[M + H]^+$ : 325.11828, found: 325.11882; calcd for  $C_{18}H_{16}N_2NaO_4$   $[M + Na]^+$ : 347.10023, found: 347.10068.

**3-(8-Ethoxy-3-nitrochroman-4-yl)-1H-indole (3f).** The title compound **3f** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a pale yellow solid (94.1 mg, 92% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (92 : 8 dr, 88% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 18.4 min,  $t_R$  (minor) = 27.5 min; *syn* diastereomer:  $t_R$  = 21.4 min, 25.1 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 215–218 °C;  $[\alpha]_D^{20} +137.6$  (*c* 1.00, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3436, 3133, 3091, 2980, 2924, 2896, 1584, 1551, 1486, 1458, 1397, 1360, 1208, 1075, 875, 824, 806, 765, 725, 748, 726; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.17 (s, 1H, NH), 7.43 (d, *J* = 7.6 Hz, 1H, ArH), 7.38 (d, *J* = 8.0 Hz, 1H, ArH), 7.23 (t, *J* = 7.8 Hz, 1H, ArH), 7.12 (t, *J* = 7.4 Hz, 1H, ArH), 6.85–6.77 (m, 3H, ArH), 6.70 (dd, *J* = 7.2 Hz, 1.6 Hz, 1H, ArH), 5.18 (d, *J* = 4.0 Hz, 1H, CH), 5.08–5.05 (m, 1H, CH), 4.73 (dd, *J* = 11.8 Hz, 5.0 Hz, 1H, CH), 4.46 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H, CH), 4.12 (q, *J* = 6.8 Hz, 2H, OCH<sub>2</sub>), 1.49 (t, *J* = 6.8 Hz, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO):  $\delta$  (ppm) 149.6, 145.4, 138.9, 127.2, 123.8, 123.7, 122.7, 121.2, 120.1, 117.5, 113.7, 113.3, 84.7, 65.8, 65.4, 38.0, 16.2; HRMS (ESI): *m/z* calcd for  $C_{19}H_{19}N_2O_4$   $[M + H]^+$ : 339.13393, found: 339.13459; calcd for  $C_{19}H_{18}N_2NaO_4$   $[M + Na]^+$ : 361.11588, found: 361.11660.

**3-[2,3-Dihydro-2-nitro-1H-naphtho[2,1-b]pyran-1-yl]-1H-indole (3g).** The title compound **3g** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a pale yellow solid (62.8 mg, 61% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (95 : 5 dr, 88% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 15.5 min,  $t_R$  (minor) = 21.2 min; *syn* diastereomer:  $t_R$  = 19.4 min, 23.1 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 228–232 °C;  $[\alpha]_D^{20} +295.2$  (*c* 0.36, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3413, 3112, 3058, 2923, 1625, 1600, 1546,

1515, 1470, 1458, 1353, 1241, 1222, 1098, 961, 906, 814, 747;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.00 (s, 1H, NH), 7.85 (d,  $J = 7.2$  Hz, 1H, ArH), 7.77–7.71 (m, 2H, ArH), 7.59 (d,  $J = 7.6$  Hz, 1H, ArH), 7.42–7.40 (m, 1H, ArH), 7.33–7.25 (m, 4H, ArH), 7.13 (d,  $J = 8.8$  Hz, 1H, ArH) 6.52 (d,  $J = 2.4$  Hz, 1H, ArH), 5.74 (s, 1H, CH), 5.08 (d,  $J = 1.6$  Hz, 1H, CH), 4.90–4.85 (m, 1H, CH), 4.42 (dd,  $J = 12.6$  Hz, 1.8 Hz, 1H, CH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 151.0, 136.5, 132.3, 129.8, 129.4, 128.5, 126.7, 125.2, 124.9, 123.8, 123.04, 122.96, 120.5, 118.4, 117.9, 116.8, 111.8, 111.3, 81.2, 61.8, 32.2; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_3$   $[\text{M} + \text{H}]^+$ : 345.12337, found: 345.12381; calcd for  $\text{C}_{21}\text{H}_{16}\text{N}_2\text{NaO}_3$   $[\text{M} + \text{Na}]^+$ : 367.10531, found: 367.10554.

**3-(6,8-Dichloro-3-nitrochroman-4-yl)-1H-indole (3h).** The title compound **3h** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a yellow oil (98.3 mg, 90% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (90 : 10 dr, 83% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak AS-H column, *n*-hexane–2-propanol 95 : 5 v/v, flow rate 1.3 mL  $\text{min}^{-1}$ , detection at 254 nm): *anti* diastereomer:  $t_{\text{R}}$  (major) = 32.6 min,  $t_{\text{R}}$  (minor) = 42.5 min; *syn* diastereomer:  $t_{\text{R}}$  = 45.9 min, 49.1 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 75–78 °C;  $[\alpha]_{\text{D}}^{20} +79.5$  ( $c$  0.42,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  3419, 3060, 2923, 1619, 1551, 1468, 1420, 1356, 1243, 1180, 1101, 1038, 1012, 936, 909, 865, 852, 745. 706;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.18 (s, 1H, NH), 7.46 (d,  $J = 8.0$  Hz, 1H, ArH), 7.40 (d,  $J = 8.0$  Hz, 1H, ArH), 7.31 (d,  $J = 2.8$  Hz, 1H, ArH), 7.26–7.24 (m, 1H, ArH), 7.18–7.14 (m, 1H, ArH), 7.04–7.03 (m, 1H, ArH), 6.74 (d,  $J = 2.4$  Hz, 1H, ArH), 5.18 (d,  $J = 3.2$  Hz, 1H, CH), 5.05–5.02 (m, 1H, CH), 4.79 (dd,  $J = 12.2$  Hz, 4.2 Hz, 1H, CH), 4.42 (dd,  $J = 12.0$  Hz, 1.6 Hz, 1H, CH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 147.9, 136.5, 128.9, 128.5, 126.3, 124.75, 124.71, 123.5, 123.2, 122.6, 120.5, 117.9, 115.2, 111.9, 81.7, 63.9, 36.0; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{17}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_3$   $[\text{M} + \text{H}]^+$ : 363.02977, found: 363.02995; calcd for  $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{N}_2\text{NaO}_3$   $[\text{M} + \text{Na}]^+$ : 385.01172, found: 385.01152.

**3-(6,8-Dibromo-3-nitrochroman-4-yl)-1H-indole (3i).** The title compound **3i** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a yellow oil (122.8 mg, 90% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (92 : 8 dr, 87% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 80 : 20 v/v, flow rate 1.0 mL  $\text{min}^{-1}$ , detection at 254 nm): *anti* diastereomer:  $t_{\text{R}}$  (major) = 14.5 min,  $t_{\text{R}}$  (minor) = 9.8 min; *syn* diastereomer:  $t_{\text{R}}$  = 12.8 min, 17.3 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 95–98 °C;  $[\alpha]_{\text{D}}^{20} +68.1$  ( $c$  0.41,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  3426, 3061, 2919, 1550, 1462, 1443, 1357, 1243, 1169, 1101, 911, 836, 746, 679;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.18 (s, 1H, NH), 7.60 (d,  $J = 2.0$  Hz, 1H, ArH), 7.47 (d,  $J = 8.0$  Hz, 1H, ArH), 7.40 (d,  $J = 8.0$  Hz, 1H, ArH), 7.29–7.15 (m, 3H, ArH), 6.72 (d,  $J = 2.4$  Hz, 1H, ArH), 5.18 (d,  $J = 2.8$  Hz, 1H, CH), 5.03–5.01 (m, 1H, CH), 4.79 (dd,  $J = 12.0$  Hz, 4.0 Hz, 1H,

CH), 4.41 (dd,  $J = 12.0$  Hz, 1.6 Hz, 1H, CH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 149.2, 136.4, 134.4, 132.1, 124.8, 124.7, 123.9, 123.1, 120.5, 117.8, 115.3, 113.7, 111.9, 111.7, 81.7, 64.0, 35.9; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{17}\text{H}_{13}\text{Br}_2\text{N}_2\text{O}_3$   $[\text{M} + \text{H}]^+$ : 450.92874, found: 450.92904.

**5-Methyl-3-(3-nitrochroman-4-yl)-1H-indole (3j).** The title compound **3j** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a bright yellow solid (81.4 mg, 88% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (94 : 6 dr, 92% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL  $\text{min}^{-1}$ , detection at 254 nm): *anti* diastereomer:  $t_{\text{R}}$  (major) = 11.3 min,  $t_{\text{R}}$  (minor) = 15.4 min; *syn* diastereomer:  $t_{\text{R}}$  = 14.6 min, 19.6 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 169–173 °C;  $[\alpha]_{\text{D}}^{20} +107.7$  ( $c$  0.54,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  3412, 3117, 3032, 2927, 2882, 1586, 1547, 1487, 1462, 1450, 1383, 1357, 1216, 1178, 1119, 1094, 1040, 859, 805, 758, 616, 602;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.01 (s, 1H, NH), 7.30–7.25 (m, 2H, ArH), 7.22–7.18 (m, 1H, ArH), 7.12–7.06 (m, 2H, ArH), 6.96–6.89 (m, 2H, ArH), 6.70 (d,  $J = 2.4$  Hz, 1H, ArH), 5.18 (d,  $J = 4.0$  Hz, 1H, CH), 5.07–5.04 (m, 1H, CH), 4.70–4.65 (m, 1H, CH), 4.39 (dd,  $J = 12.0$  Hz, 2.4 Hz, 1H, CH), 2.44 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 153.2, 134.8, 130.5, 129.6, 128.4, 125.3, 124.9, 124.4, 121.8, 120.5, 117.7, 116.8, 115.8, 111.4, 82.6, 63.3, 36.0, 21.5; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_3$   $[\text{M} + \text{H}]^+$ : 309.12337, found: 309.12335; calcd for  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{NaO}_3$   $[\text{M} + \text{Na}]^+$ : 331.10531, found: 331.10536.

**5-Methoxy-3-(3-nitrochroman-4-yl)-1H-indole (3k).** The title compound **3k** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a pale yellow solid (89.2 mg, 92% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (91 : 9 dr, 93% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL  $\text{min}^{-1}$ , detection at 254 nm): *anti* diastereomer:  $t_{\text{R}}$  (major) = 19.7 min,  $t_{\text{R}}$  (minor) = 21.8 min; *syn* diastereomer:  $t_{\text{R}}$  = 30.2 min, 34.7 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 146–150 °C;  $[\alpha]_{\text{D}}^{20} +102.6$  ( $c$  0.57,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr,  $\text{cm}^{-1}$ ):  $\nu$  3416, 2997, 2936, 2832, 1586, 1548, 1488, 1458, 1358, 1295, 1219, 1173, 1048, 1026, 909, 802, 757, 734;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.06 (s, 1H, NH), 7.25–7.16 (m, 2H, ArH), 7.10 (d,  $J = 7.6$  Hz, 1H, ArH), 6.95–6.86 (m, 3H, ArH), 6.82 (s, 1H, ArH), 6.71 (d,  $J = 2.0$ , 1H, ArH), 5.14 (d,  $J = 4.4$  Hz, 1H, CH), 5.02–4.99 (m, 1H, CH), 4.64 (dd,  $J = 11.8$  Hz, 5.0 Hz, 1H, CH), 4.38 (dd,  $J = 11.8$  Hz, 2.2 Hz, 1H, CH), 3.77 (s, 3H,  $\text{OCH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 154.2, 153.2, 131.5, 130.4, 128.4, 125.5, 125.4, 121.8, 120.5, 116.7, 115.6, 112.7, 112.5, 100.1, 82.7, 63.4, 55.8, 36.2; HRMS (ESI):  $m/z$  calcd for  $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_4$   $[\text{M} + \text{H}]^+$ : 325.11828, found: 325.11834; calcd for  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{NaO}_4$   $[\text{M} + \text{Na}]^+$ : 347.10023, found: 347.10017.

**5-Chloro-3-(3-nitrochroman-4-yl)-1H-indole (3l).** The title compound **3l** (the mixture of the *syn* and *anti* diastereomer) was

obtained according to the general procedure as a pale yellow solid (66.9 mg, 68% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (82 : 18 dr, 62% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 12.1 min,  $t_R$  (minor) = 14.3 min; *syn* diastereomer:  $t_R$  = 17.0 min, 20.7 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 120–122 °C;  $[\alpha]_D^{20}$  +49.5 (*c* 0.63, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3426, 3397, 3123 3032, 2922, 1586, 1547, 1489, 1460, 1357, 1281, 1222, 1099, 895, 805, 759; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.19 (s, 1H, NH), 7.35 (d, *J* = 2.0 Hz, 1H, ArH), 7.31–7.29 (m, 1H, ArH), 7.21–7.17 (m, 2H, ArH), 7.06 (d, *J* = 6.8 Hz, 1H, ArH), 6.98–6.90 (m, 2H, ArH), 6.84 (d, *J* = 2.4 Hz, 1H, ArH), 5.14 (d, *J* = 5.2 Hz, 1H, CH), 5.04–5.00 (m, 1H, CH), 4.67–4.62 (m, 1H, CH), 4.42 (dd, *J* = 11.8 Hz, 2.6 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 153.1, 134.9, 130.2, 128.6, 126.2, 126.1, 125.8, 123.1, 121.9, 120.2, 117.7, 116.9, 115.5, 112.8, 82.7, 63.6, 36.3; HRMS (ESI): *m/z* calcd for C<sub>17</sub>H<sub>14</sub>ClN<sub>2</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 329.06875, found: 329.06861; calcd for C<sub>17</sub>H<sub>13</sub>ClN<sub>2</sub>NaO<sub>3</sub> [M + Na]<sup>+</sup>: 351.05069, found: 351.05063.

**1-Methyl-3-(3-nitrochroman-4-yl)-1H-indole (3m).** The title compound **3m** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure as a light pink solid (86.8 mg, 94% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (92 : 8 dr, 95% ee for the major *anti* diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): *anti* diastereomer:  $t_R$  (major) = 11.4 min,  $t_R$  (minor) = 15.8 min; *syn* diastereomer:  $t_R$  = 17.5 min, 24.2 min. The *anti* diastereomer was obtained by recrystallization from petroleum ether–ethyl acetate. m.p. 111–115 °C;  $[\alpha]_D^{20}$  +126.2 (*c* 0.23, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3045, 3025, 2934, 2891, 1583, 1547, 1487, 1452, 1359, 1231, 1059, 760, 752; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.42 (d, *J* = 8.0 Hz, 1H, ArH), 7.31 (d, *J* = 8.0 Hz, 1H, ArH), 7.27–7.15 (m, 2H, ArH), 7.10 (t, *J* = 6.8 Hz, 1H, ArH), 6.94–6.87 (m, 2H, ArH), 6.59 (s, 1H, ArH), 5.17 (d, *J* = 3.6 Hz, 1H, CH), 5.03–5.00 (m, 1H, CH), 4.61 (dd, *J* = 11.8 Hz, 4.6 Hz, 1H, CH), 4.36 (dd, *J* = 12.0 Hz, 2.4 Hz, 1H, CH), 3.66 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 153.2, 137.3, 130.4, 129.2, 128.3, 125.4, 122.3, 121.7, 120.7, 119.6, 118.3, 116.7, 114.5, 109.8, 82.8, 63.4, 36.1, 32.7; HRMS (ESI): *m/z* calcd for C<sub>18</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 309.12337, found: 309.12350; calcd for C<sub>18</sub>H<sub>16</sub>N<sub>2</sub>NaO<sub>3</sub> [M + Na]<sup>+</sup>: 331.10531, found: 331.10548.

**3-(3-Nitro-2-phenylchroman-4-yl)-1H-indole (5).**<sup>15b</sup> The title compound **5** (the mixture of diastereomers) was obtained according to the general procedure as a colorless solid (50.3 mg, 45% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 58% ee for the major diastereomer) by HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 90 : 10 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): major diastereomer:  $t_R$  (major) = 14.1 min,  $t_R$  (minor) = 13.0 min; minor diastereomer:  $t_R$  = 19.4 min, 22.8 min. The major diastereomer was obtained by

recrystallization from hexane–ethyl acetate. m.p. 245–248 °C;  $[\alpha]_D^{20}$  –5.7 (*c* 0.88, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3414, 3055, 2918, 1583, 1550, 1488, 1457, 1379, 1232, 1101, 745, 710; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 8.14 (s, 1H, NH), 7.65 (d, *J* = 8.0 Hz, 1H, ArH), 7.46 (d, *J* = 8.4 Hz, 1H, ArH), 7.33–7.28 (m, 7H, ArH), 7.21 (d, *J* = 7.2 Hz, 2H, ArH), 7.13 (d, *J* = 8.4 Hz, 1H, ArH), 7.01 (t, *J* = 7.2 Hz, 1H, ArH), 6.73 (d, *J* = 2.8 Hz, 1H, ArH), 5.37 (d, *J* = 2.4 Hz, 1H, CH), 5.34 (t, *J* = 2.4 Hz, 1H, CH), 5.02 (s, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 154.0, 136.6, 135.7, 130.5, 128.7, 128.6, 128.5, 125.7, 125.2, 123.1, 121.8, 120.5, 120.0, 118.1, 117.7, 117.0, 111.8, 87.4, 72.6, 37.1.

**2-(3-Nitrochroman-4-yl)-1H-pyrrole (7).** The title compound **7** (the mixture of the *syn* and *anti* diastereomers) was obtained according to the general procedure using 3-nitro-2H-chromene **2a** (0.5 mmol) and pyrrole **6** (0.5 mmol) as a brown oil (100 mg, 88% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (65 : 35 dr, 77% ee for the major diastereomer) by HPLC (Daicel Chiralpak IA column, *n*-hexane–2-propanol 80 : 20 v/v, flow rate 1.0 mL min<sup>-1</sup>, detection at 254 nm): major diastereomer:  $t_R$  (major) = 6.0 min,  $t_R$  (minor) = 5.2 min; minor diastereomer:  $t_R$  = 8.2 min, 8.4 min. The major diastereomer was obtained by silica gel column chromatography (petroleum ether–ethyl acetate 10 : 1).  $[\alpha]_D^{20}$  +171.3 (*c* 0.48, CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr, cm<sup>-1</sup>):  $\nu$  3426, 3099, 2923, 1586, 1550, 1489, 1461, 1384, 1359, 1225, 1099, 1029, 857, 806, 756, 728; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.97 (s, 1H, NH), 7.07 (t, *J* = 7.2 Hz, 1H, ArH), 6.96 (d, *J* = 7.6 Hz, 1H, ArH), 6.82 (d, *J* = 7.2 Hz, 1H, ArH), 6.79 (d, *J* = 7.6 Hz, 1H, ArH), 6.52 (s, 1H, ArH), 6.01 (d, *J* = 2.8 Hz, 1H, ArH), 5.81 (s, 1H, ArH), 4.82 (d, *J* = 3.2 Hz, 1H, CH), 4.75–4.72 (m, 1H, CH), 4.50 (dd, *J* = 12.0 Hz, 4.4 Hz, 1H, CH), 4.17 (dd, *J* = 12.0 Hz, 2.4 Hz, 1H, CH); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 153.2, 130.3, 129.9, 128.8, 121.9, 119.1, 118.2, 117.0, 109.0, 108.1, 83.4, 63.6, 37.3; HRMS (ESI): *m/z* calcd for C<sub>13</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub> [M + H]<sup>+</sup>: 245.09207, found: 245.09222.

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