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PAPER

Chiral phosphine-catalyzed asymmetric allylic alkylation of 3-substituted benzofuran-2(3*H*)-ones or oxindoles with Morita–Baylis–Hillman carbonates†

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An efficient chiral phosphine-catalyzed asymmetric substitution reaction of MBH carbonates with 3-substituted benzofuran-2(3*H*)-ones or 3-substituted oxindoles has been described in this context, giving the corresponding allylic alkylation products bearing adjacent quaternary and tertiary stereogenic centers in high yields, moderate diastereoselectivities and high enantioselectivities under mild conditions.

Introduction

Benzofuran-2(3*H*)-ones and oxindoles are important motifs which exist in a broad range of natural products[1,2] and pharmaceutically relevant compounds.[3] Many of them feature a chiral quaternary stereocenter at the C3 position of the corresponding heterocyclic rings (Fig. 1).[1d,e,2c] Therefore, a direct and valuable strategy for asymmetric synthesis of 3,3-disubstituted benzofuran-2(3*H*)-one or oxindole frameworks is highly desired.

Thus far, much effort has been devoted to asymmetric reactions using 3-substituted benzofuran-2(3*H*)-ones[4] or oxindoles[5] as pronucleophiles. Typically, the asymmetric allylic alkylation (AAA)[6] reaction of benzofuran-2(3*H*)-ones or oxindoles is fascinating not only because it can be used for the construction of quaternary stereocenters but also because a double bond can be induced at the same time, which allows for a number of useful organic transformations. Chen and his coworkers have presented the first organocatalytic AAA reaction of 3-substituted oxindoles[7] by means of a *Cinchona* alkaloid $(DHQD)_2AQN$ as the catalyst in 2009, giving the desired products in good yields with 86–97% ee values and 62 : 37–92 : 8 diastereoselectivities (dr). During the preparation of this manuscript, Cheng and Lin's group reported the AAA reaction of 3-substituted benzofuran-2(3*H*)-ones[8] using the same organocatalyst, furnishing the corresponding products in good yields with 67–95% ee values and 68 : 32–98 : 2 dr. Indeed, *Cinchona* alkaloids and their derivatives are powerful organocatalysts for AAA reactions, but there are still some limitations in their application. These alkaloids have no corresponding natural enantiomers, causing production of the enantiomers of the corresponding products in the same ee values to be more difficult because for example, $(DHQD)_2PHAL$ is a pseudo-enantiomer of $(DHQ)_2PHAL$. Furthermore, these organocatalysts cannot be easily modified which limits their wide application in organic synthesis.

Recently, we have been working on the development of chiral phosphine-catalyzed asymmetric substitution of Morita–Baylis–Hillman (MBH) adducts with various pronucleophiles and have established a chiral phosphine catalyzed asymmetric substitution reaction of MBH acetates with 2-trimethylsilyloxy furan, affording the corresponding products in good yields with high ee and dr values (Scheme 1).[9] During our ongoing investigations into the chiral phosphine catalyzed AAA reactions of MBH adducts using various nucleophiles,[10] we found that these chiral

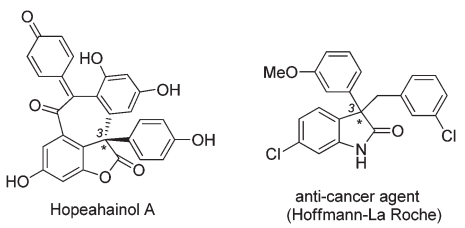
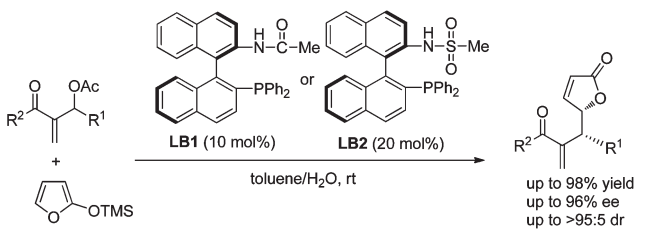


Fig. 1 Examples of biologically active chiral benzofuran-2(3*H*)-one and oxindole.



Scheme 1 Chiral phosphine catalyzed asymmetric substitution of MBH acetates with 2-trimethylsilyloxy furan.

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phosphines are also effective catalysts for the asymmetric substitution of MBH carbonates with 3-substituted benzofuran-2(3*H*)-ones or oxindoles, providing an efficient synthetic protocol for the preparation of these biologically interesting substances. In this context, we wish to report the details.

Results and discussion

We initially utilized 3-phenylbenzofuran-2(3*H*)-one **1a** (0.1 mmol, 1.0 equiv) and MBH carbonate **2a** (0.2 mmol, 2.0 equiv) as the substrates to investigate their reaction behavior in toluene at room temperature in the presence of 10 mol% chiral phosphines **LB1–LB11** (Fig. 2) as Lewis base catalysts for 24 h. It was found that using catalyst **LB1** afforded the desired product **3a** in 76% combined yield but with low diastereoselectivity (dr) as the ratio of two isomers was 55 : 45, with 94% ee value for the major product and 89% ee value for the minor product (Table 1, entry 1). Subsequently, we screened the other four chiral phosphine catalysts **LB2–LB5** for this reaction, and the results are summarized in Table 1 (entries 2–5). As can be seen from Table 1, catalyst **LB1** gave the best result and catalyst **LB3** afforded **3a** in the lowest yield, diastereo- and enantioselectivity as compared to the other catalysts. We also used **LB6** containing a sterically bulky group as the catalyst in this reaction and found that the diastereoselectivity increased to 63 : 37, while the yield and enantioselectivity declined significantly (Table 1, entry 6). We also examined the multifunctional chiral phosphine catalysts **LB7–LB10** shown in Fig. 2 in this reaction and the results are summarized in Table 1 (entries 7–10). Using **L8** and **L9** as catalysts, the desired products **3a** were obtained in 52% and 47% yields, 51 : 49 and 60 : 40 diastereoselectivities, and 92% (90%) and 92% (92%) enantioselectivities, respectively (Table 1, entries 8–9). While using **LB7** and **LB10** as catalysts afforded the products **3a** in 61 : 39 and 69 : 31 diastereoselectivities, slightly higher de values than that of **LB1**, but along with lower yields and enantioselectivities (Table 1, entries 7 and 10). We also examined chiral phosphine **LB11** derived from a natural amino acid in this reaction, but it only afforded a trace of product (Table 1, entry 11). With the identification of **LB1** as the best catalyst for this reaction, the examination of solvent effects revealed that in dichloromethane (DCM), the desired product **3a** could be obtained in 67% yield along with 57 : 43 dr and 92%

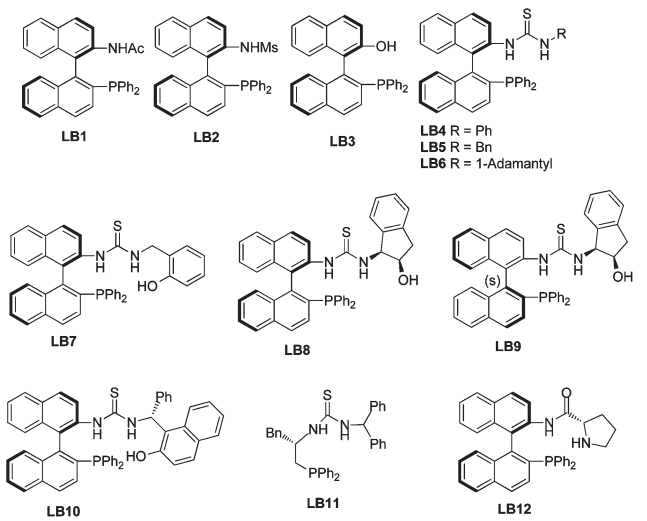
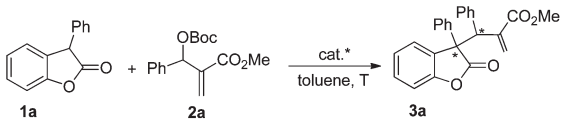


Fig. 2 Chiral phosphine catalysts **LB1–LB12**.

Table 1 Optimization of chiral phosphine catalyzed AAA reaction of 3-phenylbenzofuran-2(3*H*)-one **1a** and MBH carbonate **2a**



Entry[a]	Cat.*	Solvent	*T* (°C)	Yield[b] (%)	dr (*syn* : *anti*)[c]	ee % (*syn*/*anti*)[c]
1	**LB1**	Toluene	rt	76	55 : 45	94/89
2	**LB2**	Toluene	rt	33	60 : 40	83/79
3	**LB3**	Toluene	rt	27	51 : 49	67/65
4	**LB4**	Toluene	rt	53	59 : 41	92/86
5	**LB5**	Toluene	rt	50	59 : 41	92/89
6	**LB6**	Toluene	rt	28	63 : 37	86/85
7	**LB7**	Toluene	rt	60	61 : 39	91/89
8	**LB8**	Toluene	rt	52	51 : 49	92/90
9	**LB9**	Toluene	rt	47	60 : 40	−92/−92[d]
10	**LB10**	Toluene	rt	37	69 : 31	83/78
11	**LB11**	Toluene	rt	Trace	—	—
12	**LB1**	DCM	rt	67	57 : 43	92/91
13	**LB1**	THF	rt	40	55 : 45	91/88
14	**LB1**	CH_3CN	rt	NR	—	—
15[e]	**LB1**	Toluene	rt	96	55 : 45	94/89
16[e]	**LB1**	Toluene	0	95	67 : 33	94/91
17[e]	**LB1**	Toluene	−20	12	65 : 35	94/91

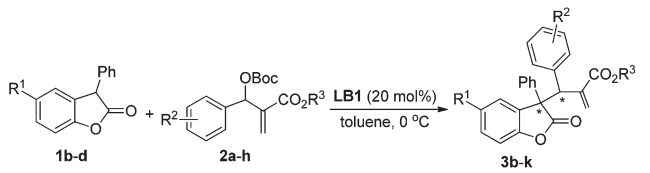
[a] The reactions were carried out with **1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (0.01 mmol) in solvent (1.0 mL) at room temperature for 24 h. [b] Isolated yield by column chromatography. [c] Determined by chiral HPLC analysis and *syn* and *anti* configurations were determined according to previous literature.[8,13] [d] The absolute configurations of each isomers are opposite to the others. [e] 0.02 mmol of catalyst was used and the reaction was carried out for 48 h.

(91%) ee (Table 1, entry 12). Using tetrahydrofuran (THF) as solvent gave **3a** in 40% yield with 55 : 45 dr and 91% (88%) ee under identical conditions (Table 1, entry 13). When the solvent was switched to acetonitrile (CH_3CN), no reaction occurred (Table 1, entry 14). Increasing the catalyst loading to 20 mol% and carrying out the reaction for 48 h could improve the yield of **3a** to 96% in toluene (Table 1, entry 15). Lowering the reaction temperature to 0 °C with 20 mol% catalyst loading could improve the yield of **3a** to 95% along with 67 : 33 dr and 94% (91%) ee value in toluene for 48 h (Table 1, entry 16). Further reducing the reaction temperature to −20 °C did not facilitate the reaction outcomes (Table 1, entry 17). Thus, we have established the optimal reaction conditions for this AAA reaction: using 20 mol% **LB1** as the catalyst and toluene as the solvent to perform the reaction at 0 °C for 48 h.

Under these optimized reaction conditions, the reaction generality was investigated by using various benzofuran-2(3*H*)-ones **1** in the reaction with several MBH carbonates **2**, and the results of these experiments are summarized in Table 2. All reactions proceeded smoothly to give the corresponding products **3** in good to excellent yields with moderate diastereoselectivities and excellent enantioselectivities under the optimal reaction conditions (Table 2). As can be seen from Table 2, three substituted benzofuran-2(3*H*)-ones **1b–1d** were used for the reactions with **2a**, affording the desired allylic-alkylation products **3b–3d** in excellent yields (91–93%), with moderate diastereoselectivities (56 : 44–71 : 29 dr), and high enantioselectivities (90–97% ee for *syn* products and 88–92% ee for *anti* products) (Table 2, entries 1–3). Then, seven different MBH carbonates **2b–2h** were tested in the reactions with **1a** (Table 2, entries 4–10). Introducing electron-withdrawing groups such as 3-Cl, 3-CN, 4-F, or 4-NO_2 on the aromatic ring of MBH carbonates, the corresponding products **3e–3h** were acquired in good yields (84–>99%) with moderate diastereoselectivities (56 : 44–64 : 36 dr), and excellent enantioselectivities (90–95% ee for *syn* products and 88–92% ee for *anti* products) (Table 2, entries 4–7). An MBH carbonate containing the electron-donating group 4-CH_3 also gave the desired product **3i** in high yield and ee values (for *anti*/*syn*-stereoisomers) (Table 2, entry 8). Changing the ester moiety of the MBH carbonate **2** (R^3) from Me to Et or the more sterically bulky *tert*-Bu provided similar reaction outcomes, affording the desired products **3j** and **3k** in 95% and 87% yields, and moderate diastereoselectivities of 55 : 45 and 54 : 46 along with 93% and 91% ee values for *syn* products and 88% and 85% ee values for *anti* products, respectively (Table 2, entries 9 and 10).

Encouraged by the results above, we attempted to use 3-substituted oxindoles instead of benzofuran-2(3*H*)-ones for this reaction. Thus, we used oxindole **4a** and MBH carbonate **2e** as substrates to investigate their AAA reaction behavior. We tested chiral phosphines **LB1**, **LB4**, **LB5**, and **LB12** in this reaction; the results are summarized in Table 3 (entries 1–4). Gratifyingly, the catalyst **LB1** was also suitable for this system. The results are indicated in Table 3. Using 20 mol% **LB1** as the catalyst gave **5a** in 67% combined yield with 55 : 45 dr and 84% (69%) ee values in THF for 48 h (Table 3, entry 1). An examination of solvent effects revealed that in dichloromethane (DCM), the desired product **5a** could be obtained in 80% combined yield along with 53 : 47 dr and 93% (84%) ee; using other solvents such as 1,2-dichloroethane (DCE) or toluene gave **5a** in 67% or 91% combined yield with 93% (83%) or 98% (89%) ee values and 45 : 55 or 67 : 33 dr under identical conditions (Table 3, entries 5, 6, and 8). Notably, no reaction occurred in CH_3CN (Table 3, entry 7). Toluene should be the solvent of choice for this reaction (Table 3, entry 8). Decreasing the catalyst loading

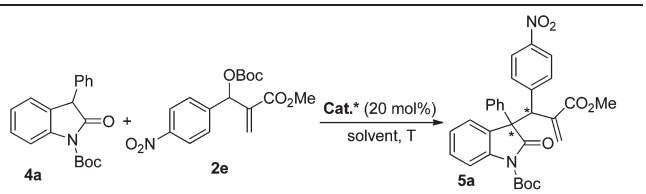
Table 2 Substrate scope of the reactions of benzofuran-2(3*H*)-ones **1** and MBH carbonates **2**



Entry[a]	**1** (R^1)	**2** (R^2/R^3)	Yield[b] (%)	dr (*syn* : *anti*)[c]	ee% (*syn*/*anti*)[c]
1	**1b** (Cl)	**2a** (H/Me)	**3b**: 93	56 : 44	92/91
2	**1c** (Br)	**2a** (H/Me)	**3c**: 90	71 : 29	97/92
3	**1d** (^{t}Bu)	**2a** (H/Me)	**3d**: 91	63 : 37	90/88
4	**1a** (H)	**2b** (3-Cl/Me)	**3e**: >99	56 : 44	94/90
5	**1a** (H)	**2c** (3-CN/Me)	**3f**: 84	56 : 44	90/88
6	**1a** (H)	**2d** (4-F/Me)	**3g**: 93	64 : 36	92/89
7[c]	**1a** (H)	**2e** (4-NO_2/Me)	**3h**: 98	58 : 42	95/92
8	**1a** (H)	**2f** (4-CH_3/Et)	**3i**: 85	56 : 44	95/92
9	**1a** (H)	**2g** (4-NO_2/Et)	**3j**: 95	55 : 45	93/88
10	**1a** (H)	**2h** (4-NO_2/^{t}Bu)	**3k**: 87	54 : 46	91/85 :

[a] The reactions were carried out with **1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (0.02 mmol) in toluene (1.0 mL) at 0 °C for 48 h. [b] Isolated yield by column chromatography and the isomers can not be easily separated by column chromatography. [c] Determined by chiral HPLC analysis and *syn* and *anti* configurations were determined according to previous literature.[8,13]

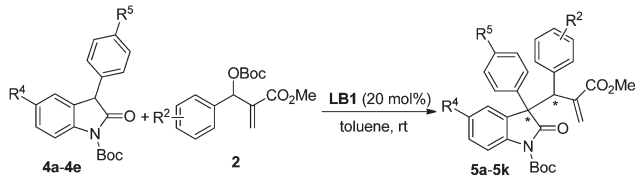
Table 3 Optimization of the reaction conditions of 3-phenyl oxindole **4a** and MBH carbonate **2e** in the presence of **LB1**



Entry[a]	Cat.*	Solvent	*T* (°C)	Yield[b] (%)	dr (*anti* : *syn*)[c]	ee% (*anti*/*syn*)[c]
1	**LB1**	THF	rt	67	55 : 45	84/69
2	**LB4**	THF	rt	62	54 : 46	60/52
3	**LB5**	THF	rt	57	55 : 45	73/67
4	**LB12**	THF	rt	53	57 : 43	82/60
5	**LB1**	DCM	rt	80	53 : 47	93/84
6	**LB1**	DCE	rt	67	45 : 55	93/83
7	**LB1**	CH_3CN	rt	—	—	—
8	**LB1**	Toluene	rt	91	67 : 33	98/89
9[d]	**LB1**	Toluene	rt	77	64 : 36	94/88
10	**LB1**	Toluene	0	68	66 : 34	96/85

[a] The reactions were carried out with **4a** (0.1 mmol), **2e** (0.2 mmol), catalyst (0.02 mmol) in solvent (1.0 mL) at room temperature for 24 h. [b] Total isolated yield by column chromatography and the isomers cannot be easily separated by column chromatography. [c] Determined by chiral HPLC analysis. [d] 0.01 mmol catalyst was used.

Table 4 Substrate scope of the reactions of oxindoles **4** and MBH carbonates **2**



Entry[a]	**4** (R^4/R^5)	**2** (R^2)	Yield[b] (%)	dr (*anti* : *syn*)[c]	ee% (*anti*/*syn*)[c]
1	**4a** (H/H)	**2e** (4-NO_2)	**5a**: 91	67 : 33	98/89
2	**4a** (H/H)	**2c** (3-CN)	**5b**: 86	62 : 38	94/80
3	**4a** (H/H)	**2b** (3-Cl)	**5c**: 93	51 : 49	92/87
4	**4a** (H/H)	**2i** (4-Cl)	**5d**: 92	59 : 41	93/88
5	**4a** (H/H)	**2d** (4-F)	**5e**: 86	58 : 42	93/85
6	**4a** (H/H)	**2j** (4-CH_3)	**5f**: 81	60 : 40	95/91
7[c]	**4a** (H/H)	**2a** (H)	**5g**: 89	57 : 43	93/89
8	**4b** (H/F)	**2a** (H)	**5h**: 82	60 : 40	92/89
9	**4c** (H/CH_3)	**2a** (H)	**5i**: 76	61 : 39	92/88
10	**4d** (F/H)	**2a** (H)	**5j**: 89	56 : 44	91/84
11	**4e** (CH_3/H)	**2a** (H)	**5k**: 78	64 : 36	96/94

[a] The reactions were carried out with **4** (0.1 mmol), **2** (0.2 mmol), catalyst (0.02 mmol) in toluene (1.0 mL) at room temperature for 48 h. [b] Total isolated yield by column chromatography and the isomers cannot be easily separated by column chromatography. [c] Determined by chiral HPLC analysis and *syn* and *anti* configurations were determined according to the previous literature.[7,13]

to 10 mol% afforded **5a** in 77% yield (Table 3, entry 9). Lowering the reaction temperature to 0 °C did not improve the result in toluene (Table 3, entry 10).

Having identified the optimal reaction conditions, we next set out to examine the scope and limitations of this AAA reaction catalyzed by **LB1** using various substituted oxindoles **4** with different MBH carbonates **2**, and the results are summarized in Table 4. As can be seen from Table 4, when R^2 on the aromatic group of the MBH carbonates was changed to 3-CN, 3-Cl, 4-Cl, 4-F or 4-CH_3 (Table 4, entries 2–6), the desired allylic alkylation products **5b–5f** were obtained in good to excellent yields (81–93%), with moderate diastereoselectivities (51 : 49–62 : 38 dr), and good enantioselectivities (92–95% ee for *anti* products and 80–91% ee for *syn* products). Subsequently, oxindoles having no substituent or bearing electron-donating or electron-withdrawing substituents (R^5) at the 3-aryl group were investigated in this reaction, affording the desired products **5g–5i** in 76–89% yields, 57 : 43–61 : 39 diastereoselectivities and good enantioselectivities (92–93% ee for *anti* products and 88–89% ee for *syn* products) (Table 4, entries 7–9). Introducing electron-donating or electron-withdrawing substituents (R^4) at the aryl ring of the oxindoles, the desire AAA products **5j** and **5k** were also formed in good yields, high ee values and moderate diastereoselectivities (Table 4, entries 10 and 11).

Conclusions

In conclusion, we have established an efficient chiral phosphine-catalyzed asymmetric allylic alkylation of MBH carbonates with 3-substituted benzofuran-2(3*H*)-ones or oxindoles to give the corresponding substitution products in high yields with moderate dr values and high ee values for major and minor diastereomeric products under mild conditions. For benzofuran-2(3*H*)-ones, the desired products could be obtained in high yields (84–>99%) with moderate diastereoselectivities (*syn* : *anti* = 54 : 46–71 : 29) and excellent ee values (90–97% for major products and 85–92% for minor products). While for oxindoles, the AAA reactions afforded the products in moderate to high yields (76–93%) with moderate diastereoselectivities (*anti* : *syn* = 51 : 49–67 : 33) and good ee values (91–98% for major products and 80–89% for minor products). These products bearing adjacent quaternary and tertiary stereogenic centers may have potential biological significance in medicinal chemistry. Our results suggested that compared to *Cinchona* alkaloid derived organocatalysts, the chiral phosphine catalyst can be also used for this type of reaction, giving the corresponding products in higher yields and good ee values. A plausible transition state for this asymmetric reaction is outlined in the ESI.† Further investigations on the reaction mechanism and improvement of the diastereoselectivity by new chiral phosphine catalyst are ongoing in our laboratory.

Experimental section

General remarks

^{1}H NMR spectra were recorded on a Bruker AM-300 or AM-400 spectrometer for solutions in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; *J*-values are in Hz. Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported in this paper gave satisfactory HRMS analytic data. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. THF and toluene were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN, 1,2-dichloroethane and dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF254 silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure.

Chiral phosphine catalysts **LB1–LB12** were synthesized according to our previous work.[9,10] All the 3-substituted benzofuran-2(3*H*)-ones[11] or oxindoles[5r] and MBH carbonates[12] were prepared according to the literature.

General procedure for the preparation of 3 from the reaction of 1 with 2 in the presence of LB1, using 3a as an example

To a mixture of **1a** (0.10 mmol, 21.0 mg), **2a** (0.20 mmol, 58.0 mg) and **LB1** (10.0 mg, 0.02 mmol) was added 1.0 mL of toluene at 0 °C. The reaction solution was monitored by TLC. After the reaction was complete, the solution was concentrated under reduced pressure and the residue was further purified by silica gel column chromatography (EtOAc–PE = 1 : 10) to give the target product **3a**.

Methyl 2-((2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)(phenyl)methyl)acrylate 3a. A white solid that is a known compound,[8] 95% yield, 36 mg (*syn* : *anti* = 67 : 33); $[\alpha]_D^{20} = -160.5$ (*c* 0.5, $CHCl_3$) for 94% ee (*syn*) and 91% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column, hexane–^{i}PrOH = 95 : 5, 0.5 mL min^{-1}, 230 nm, for *syn* product t_{major} = 27.323 min, t_{minor} = 35.282 min; for *anti* product t_{major} = 33.532 min, t_{minor} = 25.773 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.43 (s, 0.99H, CH_3), 3.65 (s, 2.01H, CH_3), 5.38 (s, 0.67H, =CH_2), 5.39 (s, 0.33H, =CH_2), 5.57 (d, J = 1.2 Hz, 0.33H, =CH_2), 5.63 (s, 0.67H, =CH_2), 6.27 (s, 0.33H, CH), 6.41 (s, 0.67H, CH), 6.79–6.82 (m, 1H, Ar), 6.90–7.03 (m, 2H, Ar), 7.07–7.19 (m, 4H, Ar), 7.26–7.39 (m, 5H, Ar), 7.47–7.65 (m, 2H, Ar); MS (ESI) *m*/*z* 407.4 (M + Na$^+$, 100). HRMS (MALDI) Calcd for $C_{25}H_{20}O_4Na$ requires (M + Na$^+$) 407.1270, Found: 407.1254.

Methyl 2-((5-chloro-2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)(phenyl)methyl)acrylate 3b. A white solid (41 mg, 93% yield, *syn* : *anti* = 56 : 44); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.46 (s, 1.32H, CH_3), 3.65 (s, 1.68H, CH_3), 5.35 (s, 0.56H, =CH_2), 5.39 (s, 0.44H, =CH_2), 5.55 (d, J = 1.2 Hz, 0.44H, =CH_2), 5.70 (s, 0.56H, =CH_2), 6.30 (s, 0.44H, CH), 6.43 (s, 0.56H), 6.81–6.89 (m, 2H, Ar), 6.92–6.98 (m, 2H, Ar), 7.10–7.21 (m, 3H, Ar), 7.25–7.37 (m, 4H, Ar), 7.43–7.61 (m, 2H, Ar) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 52.07, 52.31, 53.05, 53.58, 59.84, 60.15, 111.96, 112.16, 126.67, 127.22, 127.36, 127.53, 127.86, 127.87, 128.17, 128.20, 128.25, 128.28, 128.40, 128.69, 128.90, 129.15, 129.38, 129.55, 129.56, 129.63, 129.71, 130.70, 134.63, 135.85, 136.63, 137.19, 138.37, 139.23, 150.98, 151.51, 166.74, 167.49, 175.75, 176.04 ppm; IR (neat) ν 2949, 1805, 1718, 1466, 1262, 1132, 1065, 702 cm^{-1}; MS (ESI) *m*/*z* 441.4 (M + Na$^+$). HRMS (MALDI) Calcd for $C_{25}H_{19}O_4ClNa$ requires (M + Na$^+$): 441.0868, Found: 441.0864.

Methyl 2-((5-bromo-2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)(phenyl)methyl)acrylate 3c. A white solid, 90% yield, 41 mg, m.p. 94–95 °C, (*syn* : *anti* = 71 : 29); $[\alpha]_D^{20} = -172.7$ (*c* 0.6, $CHCl_3$) for 97% ee (*syn*) and 92% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column, hexane–^{i}PrOH = 98 : 2, 0.7 mL min^{-1}, 230 nm, for *syn* product t_{major} = 19.027 min, t_{minor} = 23.527 min; for *anti* product t_{major} = 21.727 min, t_{minor} = 16.977 min. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.47 (s, 0.87H, CH_3), 3.66 (s, 2.13H, CH_3), 5.35 (s, 0.71H, =CH_2), 5.38 (s, 0.29H, =CH_2), 5.55 (s, 0.29H, =CH_2), 5.70 (s, 0.71H, =CH_2), 6.30 (s, 0.29H, CH), 6.43 (s, 0.71H, CH), 6.81–7.01 (m, 4H, Ar), 7.13–7.22 (m, 3H, Ar), 7.31–7.36 (m, 3H, Ar), 7.42–7.74 (m, 3H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 52.10, 52.32, 53.11, 53.58, 59.81, 60.12, 112.44, 112.64, 116.43, 125.28, 127.24, 127.54, 127.88, 128.21, 128.22, 128.30, 128.72, 128.93, 129.01, 129.54, 129.59, 129.74, 130.10, 130.18, 132.29, 132.56, 134.65, 135.89, 137.22, 138.39, 139.29, 151.50, 152.02, 166.77, 167.50, 175.62, 175.92; IR (neat) ν 2916, 1806, 1719, 1466, 1234, 1135, 1065, 701 cm^{-1}; MS (ESI) *m*/*z* 485.3 (M + Na$^+$, 100). HRMS (ESI) Calcd for $C_{25}H_{19}BrO_4Na$ requires (M + Na$^+$) 485.0366, Found: 485.0359.

Methyl 2-((5-(*tert*-butyl)-2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)(phenyl)methyl)acrylate 3d. A colorless oil, 91% yield, 40 mg (*syn* : *anti* = 63 : 37); $[\alpha]_D^{20} = -134.6$ (*c* 2.0, $CHCl_3$) for 90% ee (*syn*) and 88% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column, hexane–^{i}PrOH = 93 : 7, 0.5 mL min^{-1}, 230 nm, for *syn* product t_{major} = 19.627 min, t_{minor} = 26.327 min; for *anti* product t_{major} = 18.077 min, t_{minor} = 15.177 min. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.25 (s, 5.67H, ^{t}Bu), 1.38 (s, 3.33H, ^{t}Bu), 3.44 (s, 1.11H, CH_3), 3.66 (s, 1.89H, CH_3), 5.38 (s, 0.37H, =CH_2), 5.40 (s, 0.63H, =CH_2), 5.41 (s, 0.67H, =CH_2), 5.58 (d, J = 1.2 Hz, 0.33H, =CH_2), 6.29 (s, 0.33H, CH), 6.39 (s, 0.67H, CH), 6.76–6.78 (m, 2H, Ar), 6.89–6.98 (m, 2H, Ar), 7.06–7.20 (m, 3H, Ar), 7.25–7.36 (m, 4H, Ar), 7.49–7.63 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 31.39, 31.52, 34.64, 34.71, 51.97, 52.26, 53.00, 53.39, 59.45, 59.67, 110.06, 110.09, 124.59, 125.98, 126.04, 127.29, 127.30, 127.58, 127.64, 127.66, 127.80, 127.90, 127.92, 128.01, 128.44, 128.60, 128.99, 129.61, 129.88, 135.12, 136.69, 137.77, 139.05, 139.78, 146.77, 146.84, 150.68, 150.86, 166.79, 167.71, 176.87, 177.17; IR (neat) ν 2957, 1801, 1720, 1488, 1264, 1145, 1065, 704, 702 cm^{-1}; MS (ESI) *m*/*z* 463.5 (M + Na$^+$, 100). HRMS (ESI) Calcd for $C_{29}H_{28}O_4Na$ requires (M + Na$^+$) 463.1889, Found: 463.1880.

Methyl 2-((3-chlorophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3e. White solid that is a known compound,[8] 99% yield, 41 mg (*syn* : *anti* = 56 : 44); $[\alpha]_D^{20} = -189.6$ (*c* 2.2, $CHCl_3$) for 94% ee (*syn*) and 90% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel REGIS column, hexane–^{i}PrOH = 100 : 0.5, 0.5 mL min^{-1}, 230 nm, for *syn* product t_{major} = 93.710 min, t_{minor} = 68.245 min; for *anti* product t_{major} = 71.377 min, t_{minor} = 86.127 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.46 (s, 1.32H, CH_3), 3.67 (s, 1.68H, CH_3), 5.33 (s, 0.56H, =CH_2), 5.37 (s, 0.44H, =CH_2), 5.58 (s, 0.44H, =CH_2), 5.60 (s, 0.56H, =CH_2), 6.31 (s, 0.44H, CH), 6.44 (s, 0.56H, CH), 6.67–6.74 (m, 1H, Ar), 6.90 (d, J = 6.8 Hz, 1H, Ar), 7.01–7.18 (m, 4H, Ar), 7.27–7.39 (m, 5H, Ar), 7.47–7.51 (m, 2H, Ar).

Methyl 2-((3-cyanophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3f. A white solid, 84% yield, 34 mg, m.p. 124–126 °C, (*syn* : *anti* = 56 : 44); $[\alpha]_D^{20} = -254.8$ (*c* 1.8, $CHCl_3$) for 90% ee (*syn*) and 88% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column, hexane–^{i}PrOH = 93 : 7, 0.5 mL min^{-1}, 230 nm, for *syn* product t_{major} = 55.027 min, t_{minor} = 61.327 min; for *anti* product t_{major} = 45.677 min, t_{minor} = 50.477 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.49 (s, 1.32H, CH_3), 3.67 (s, 1.68H, CH_3), 5.37 (s, 0.56H, =CH_2), 5.41 (s, 0.44H, =CH_2), 5.63 (d, J = 1.2 Hz, 0.44H, =CH_2), 5.71 (s, 0.56H, =CH_2), 6.35 (s, 0.44H, CH), 6.48 (s, 0.56H, CH), 6.88–7.08 (m, 2H, Ar), 7.13–7.38 (m, 8H, Ar), 7.40–7.63 (m, 3H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 52.20, 52.41, 52.62, 53.05, 59.24, 59.30, 111.22, 111.85, 111.96, 118.36, 124.17, 124.24, 126.11, 126.79, 127.22, 127.39, 128.06, 128.16, 128.29, 128.33, 128.58, 128.74, 128.77, 128.80, 128.96, 129.37, 129.82, 129.93, 131.00, 131.33, 133.20, 133.23, 134.13, 134.38, 136.03, 137.05, 137.13, 137.59, 138.32, 138.61, 152.52, 152.77, 166.43, 166.95, 176.06, 176.13; IR (neat) ν 2952, 2230, 1800, 1719, 1462, 1271, 1066, 753, 699 cm^{-1}; MS (ESI) *m*/*z* 432.3 (M + Na$^+$, 100). HRMS (ESI) Calcd for $C_{26}H_{19}NO_4Na$ requires (M + Na$^+$) 432.1216, Found: 432.1206.

Methyl 2-((4-fluorophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3g. A white solid that is a known compound,[8] 93% yield, 37 mg (*syn* : *anti* = 64 : 36); $[\alpha]_D^{20}$ = −228.7 (*c* 1.85, $CHCl_3$) for 92% ee (*syn*) and 89% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 97 : 3, 0.5 mL min^{-1}, 210 nm, for *syn* product t_{major} = 17.460 min, t_{minor} = 31.167 min; for *anti* product t_{major} = 26.322 min, t_{minor} = 43.432 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.46 (s, 1.08H, CH_3), 3.66 (s, 1.92H, CH_3), 5.34 (s, 0.64H, =CH_2), 5.38 (s, 0.36H, =CH_2), 5.57 (d, *J* = 1.2 Hz, 0.36H, =CH_2), 5.65 (s, 0.64H, =CH_2), 6.27 (s, 0.36H, CH), 6.40 (s, 0.64H, CH), 6.76–6.80 (m, 3H, Ar), 6.92–6.96 (m, 1H, Ar), 6.99–7.16 (m, 2H, Ar), 7.23–7.35 (m, 5H, Ar), 7.46–7.51 (m, 2H, Ar); ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ −114.83, −114.69.

Methyl 2-((4-nitrophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3h. A white solid that is a known compound,[8] 98% yield, 42 mg (*syn* : = 58 : 42); $[\alpha]_D^{20}$ = −171.4 (*c* 2.8, $CHCl_3$) for 95% ee (*syn*) and 92% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 90 : 10, 1.0 mL min^{-1}, 210 nm, for *syn* product t_{major} = 22.917 min, t_{minor} = 28.935 min; for *anti* product t_{major} = 51.235 min, t_{minor} = 44.657 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.49 (s, 1.26H, CH_3), 3.66 (s, 1.74H, CH_3), 5.45 (s, 0.58H,=CH_2), 5.52 (s, 0.42H,=CH_2), 5.65 (d, *J* = 1.2 Hz, 0.42H,=CH_2), 5.75 (s, 0.58H,=CH_2), 6.37 (s, 0.42H, CH), 6.49 (s, 0.58H, CH), 6.95–7.05 (m, 3H, Ar), 7.15–7.19 (m, 1H, Ar), 7.22–7.25 (m, 1H, Ar), 7.29–7.38 (m, 4H, Ar), 7.44–7.49 (m, 2H, Ar), 7.95–7.97 (m, 2H, Ar).

Ethyl 2-((2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)(*p*-tolyl)methyl)acrylate 3i. A colorless oil, 85% yield, 35 mg (*syn* : *anti* = 56 : 44); $[\alpha]_D^{20}$ = −187.7 (*c* 1.2, $CHCl_3$) for 95% ee (*syn*) and 92% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, hexane–^{i}PrOH = 98 : 2, 1.0 mL min^{-1}, 210 nm, for *syn* product t_{major} = 14.540 min, t_{minor} = 29.405 min; for *anti* product t_{major} = 33.103 min, t_{minor} = 42.455 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.07 (t, *J* = 9.6 Hz, 1.32H, CH_3), 1.18 (t, *J* = 9.6 Hz, 1.68H, CH_3), 2.20 (s, 1.32H, CH_3), 2.24 (s, 1.68H, CH_3), 3.75–3.96 (m, 0.88H, CH_2), 4.00–4.17 (m, 1.12H, CH_2), 5.35 (s, 0.56H, =CH_2), 5.37 (s, 0.44H, =CH_2), 5.55 (s, 0.44H, =CH_2), 5.56 (s, 0.56H, =CH_2), 6.25 (s, 0.44H, CH), 6.38 (s, 0.56H, CH), 6.67–6.84 (m, 2H, Ar), 6.88–7.04 (m, 3H, Ar), 7.23–7.37 (m, 5H, Ar), 7.48–7.66 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.86, 13.95, 20.99, 21.43, 52.65, 53.21, 59.51, 59.59, 60.95, 61.09, 110.84, 111.00, 123.67, 123.72, 125.26, 126.85, 127.41, 127.47, 127.54, 127.71, 127.83, 127.96, 128.19, 128.36, 128.48, 128.61, 128.73, 128.99, 129.23, 129.45, 129.50, 129.71, 132.06, 133.99, 136.64, 136.90, 137.15, 137.91, 139.13, 139.92, 152.69, 153.17, 166.39, 167.35, 176.50, 176.79; IR (neat) ν 2980, 1796, 1712, 1460, 1232, 1127, 1061, 734, 696 cm^{-1}; MS (ESI) *m*/*z* 413.1 (M + H$^+$, 100). HRMS (ESI) Calcd for $C_{27}H_{25}O_4$ requires (M + H$^+$) 413.1675, Found: 413.1738.

Ethyl 2-((4-nitrophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3j. A yellowish solid, 95% yield, 42 mg, m.p. 65–67 °C, (*syn* : *anti* = 55 : 45); $[\alpha]_D^{20}$ = −229.1 (*c* 2.0, $CHCl_3$) for 93% (*syn*) and 88% (*anti*) ee; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 95 : 5, 0.8 mL min^{-1}, 230 nm, for *syn* product t_{major} = 15.727 min, t_{minor} = 19.227 min; for *anti* product t_{major} = 34.527 min, t_{minor} = 31.077 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.08 (t, *J* = 6.8 Hz, 1.35H, CH_3), 1.18 (t, *J* = 6.8 Hz, 1.65H, CH_3), 3.86–4.00 (m, 0.90H, CH_2), 4.03–4.17 (m, 1.10H, CH_2), 5.45 (s, 0.55H, =CH_2), 5.53 (s, 0.45H, =CH_2), 5.65 (d, *J* = 1.2 Hz, 0.45H, =CH_2), 5.72 (s, 0.55H, =CH_2), 6.37 (s, 0.45H, CH), 6.49 (s, 0.55H, CH), 6.95–7.06 (m, 3H, Ar), 7.15–7.37 (m, 6H, Ar), 7.43–7.49 (m, 2H, Ar), 7.61–7.97 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.88, 13.93, 52.87, 52.91, 59.25, 59.45, 61.34, 61.43, 111.26, 111.28, 122.78, 123.01, 124.15, 124.27, 126.19, 126.79, 127.23, 127.30, 128.10, 128.31, 128.33, 128.88, 129.00, 129.12, 129.83, 129.93, 130.71, 130.75, 136.29, 137.06, 137.93, 138.54, 143.34, 144.99, 146.90, 147.27, 152.53, 152.75, 165.95, 176.13; IR (neat) ν 2981, 1800, 1716, 1597, 1521, 1347, 1065, 757, 699 cm^{-1}; MS (ESI) *m*/*z* 466.4 (M + Na$^+$, 100). HRMS (ESI) Calcd for $C_{26}H_{21}NO_6Na$ requires (M + Na$^+$) 466.1268, Found: 466.1261.

***tert*-Butyl 2-((4-nitrophenyl)(2-oxo-3-phenyl-2,3-dihydrobenzofuran-3-yl)methyl)acrylate 3k.** A white solid, 87% yield, 41 mg, m.p. 147–149 °C, (*syn* : *anti* = 54 : 46); $[\alpha]_D^{20}$ = −119.7 (*c* 1.8, $CHCl_3$) for 91% ee (*syn*) and 85% ee (*anti*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 93 : 7, 0.5 mL min^{-1}, 230 nm, for *syn* product t_{major} = 17.477 min, t_{minor} = 14.977 min; for *anti* product t_{major} = 19.777 min, t_{minor} = 16.177 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.22 (s, 4.14H, ^{t}Bu), 1.34 (s, 4.86H, ^{t}Bu), 5.41 (s, 0.54H, =CH_2), 5.52 (s, 0.46H, =CH_2), 5.55 (s, 0.54H, =CH_2), 5.61 (s, 0.46H, =CH_2), 6.33 (s, 0.46H, CH), 6.40 (s, 0.54H, CH), 6.90–7.07 (m, 3H, Ar), 7.15–7.49 (m, 8H, Ar), 7.96 (d, *J* = 7.2 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.64, 27.78, 52.41, 52.79, 59.00, 59.71, 81.69, 81.77, 111.18, 111.27, 122.68, 122.90, 124.04, 124.29, 126.33, 126.83, 127.16, 127.31, 127.85, 128.13, 128.25, 128.32, 128.45, 128.93, 129.77, 129.87, 130.66, 130.73, 136.58, 137.04, 139.21, 139.50, 143.72, 145.52, 146.72, 147.14, 152.58, 152.69, 165.00, 165.51, 176.10, 176.29; IR (neat) ν 2978, 1801, 1709, 1604, 1524, 1347, 1146, 1065, 757 cm^{-1}; MS (ESI) *m*/*z* 494.5 (M + Na$^+$, 100). HRMS (MALDI) Calcd for $C_{28}H_{25}NO_6Na$ requires (M + Na$^+$) 494.1579, Found: 494.1574.

General procedure for the preparation of 5 from the reaction of 4a with 2e in the presence of LB1, using 5a as an example

To a mixture of **1a** (0.10 mmol, 31.0 mg), **2a** (0.20 mmol, 67.0 mg) and **LB1** (10.0 mg, 0.02 mmol) was added 1.0 mL of toluene at room temperature. The reaction solution was monitored by TLC. After the reaction was complete, the solution was concentrated under reduced pressure and the residue was further purified by silica gel column chromatography (EtOAc–PE = 1 : 10) to give the target product **5a**.

***tert*-Butyl 3-(2-(methoxycarbonyl)-1-(4-nitrophenyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5a.** A white solid, 91% yield, 48 mg, m.p. 90–92 °C, (*anti* : *syn* = 67 : 33); $[\alpha]_D^{20}$ = −200.0 (*c* 0.1, $CHCl_3$) for 98% ee (*anti*) and 89% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel

AD-H column, hexane–^{i}PrOH = 80 : 20, 0.7 mL min^{-1}, 230 nm, for *anti* product t_{major} = 7.057 min, t_{minor} = 8.517 min; for *syn* product t_{major} = 9.900 min, t_{minor} = 17.785 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.56 (s, 9.00H, for *syn* and *anti*, Boc), 3.48 (s, 0.99H, CH_3), 3.64 (s, 2.01H, CH_3), 5.40 (s, 0.67H, =CH_2), 5.53 (s, 0.33H, =CH_2), 5.59 (s, 0.33H, =CH_2), 5.97 (s, 0.67H, =CH_2), 6.32 (s, 0.33H, CH), 6.49 (s, 0.67H, CH), 6.99 (d, J = 8.8 Hz, 2H, Ar), 7.13–7.21 (m, 1H, Ar), 7.25–7.35 (m, 5H, Ar), 7.39–7.44 (m, 2H, Ar), 7.60–7.66 (m, 1H, Ar), 7.91 (d, J = 8.8 Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.88, 28.03, 52.15, 52.31, 53.17, 53.26, 60.15, 60.28, 84.76, 115.05, 115.19, 122.54, 122.72, 124.17, 124.27, 125.53, 126.60, 127.57, 127.80, 127.86, 127.96, 128.60, 128.80, 128.95, 129.03, 129.20, 130.70, 130.82, 136.95, 137.36, 137.99, 138.74, 138.94, 139.60, 143.88, 145.37, 146.75, 147.09, 148.40, 166.75, 167.25, 175.19, 175.43; IR (neat) ν 2982, 1793, 1762, 1719, 1604, 1522, 1251, 1147, 738 cm^{-1}; MS (ESI) m/z 551.4 (M + Na^{+}, 100). HRMS (ESI) Calcd for $C_{30}H_{28}N_2O_7Na$ requires (M + Na^{+}) 551.1797, Found: 551.1789.

***tert*-Butyl 3-(1-(3-cyanophenyl)-2-(methoxycarbonyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5b.** A white solid that is a known compound.[7] 86% yield, 43 mg (*anti* : *syn* = 62 : 38); $[\alpha]_D^{20}$ = −98.0 (*c* 0.15, $CHCl_3$) for 94% ee (*anti*) and 80% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 90 : 10, 1.0 mL min^{-1}, 254 nm, for *anti* product t_{major} = 5.607 min, t_{minor} = 6.290 min; for *syn* product t_{major} = 7.147 min, t_{minor} = 8.542 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.57 (s, 3.42H, Boc), 1.59 (s, 5.58H, Boc), 3.49 (s, 1.14H, CH_3), 3.65 (s, 1.86H, CH_3), 5.32 (s, 0.62H, =CH_2), 5.43 (s, 0.38H, =CH_2), 5.59 (d, J = 1.6 Hz, 0.38H, =CH_2), 5.98 (s, 0.62H, =CH_2), 6.32 (s, 0.38H, CH), 6.48 (s, 0.62H, CH), 6.95–7.03 (m, 1H, Ar), 7.10–7.17 (m, 2H, Ar), 7.22–7.45 (m, 9H, Ar), 7.59–7.71 (m, 1H, Ar).

***tert*-Butyl 3-(1-(3-chlorophenyl)-2-(methoxycarbonyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5c.** A white solid that is a known compound.[7] 93% yield, 48 mg (*anti* : *syn* = 51 : 49); $[\alpha]_D^{20}$ = −254.6 (*c* 1.85, $CHCl_3$) for 92% ee (*anti*) and 87% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, hexane–^{i}PrOH = 95 : 5, 0.9 mL min^{-1}, 254 nm, for *anti* product t_{major} = 4.915 min, t_{minor} = 14.830 min; for *syn* product t_{major} = 5.487 min, t_{minor} = 16.798 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.55 (s, 4.41H, Boc), 1.58 (s, 4.59H, Boc), 3.46 (s, 1.47H, CH_3), 3.65 (s, 1.53H, CH_3), 5.29 (s, 0.51H, =CH_2), 5.39 (s, 0.49H, =CH_2), 5.54 (d, J = 1.2 Hz, 0.49H, =CH_2), 5.88 (s, 0.51H, =CH_2), 6.26 (s, 0.49H, CH), 6.43 (s, 0.51H, CH), 6.64–6.82 (m, 1H, Ar), 6.94–7.15 (m, 4H, Ar), 7.23–7.36 (m, 5H, Ar), 7.42–7.46 (m, 2H, Ar), 7.59–7.74 (m, 1H, Ar).

***tert*-Butyl 3-(1-(4-chlorophenyl)-2-(methoxycarbonyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5d.** A white solid that is a known compound.[7] 92% yield, 47 mg, m.p. 134–136 °C, (*anti* : *syn* = 59 : 41); $[\alpha]_D^{20}$ = −203.0 (*c* 0.1, $CHCl_3$) for 93% ee (*anti*) and 88% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 90 : 10, 0.7 mL min^{-1}, 230 nm, for *anti* product t_{major} = 6.652 min, t_{minor} = 7.385 min; for *syn* product t_{major} = 7.985 min, t_{minor} = 13.052 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.54 (s, 3.69H, Boc), 1.57 (s, 5.31H, Boc), 3.44 (s, 1.23H, CH_3), 3.64 (s, 1.77H, CH_3), 5.28 (s, 0.59H, =CH_2), 5.39 (s, 0.41H, =CH_2), 5.51 (d, J = 1.2 Hz, 0.41H, =CH_2), 5.88 (s, 0.59H, =CH_2), 6.22 (s, 0.41H, CH), 6.41 (s, 0.59H, CH), 6.72–6.89 (m, 2H, Ar), 6.98–7.14 (m, 3H, Ar), 7.22–7.37 (m, 5H, Ar), 7.42–7.46 (m, 2H, Ar), 7.59–7.73 (m, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.94, 27.98, 51.96, 52.19, 52.88, 53.09, 60.25, 60.48, 84.37, 84.45, 114.93, 115.14, 123.85, 124.06, 125.74, 126.99, 127.65, 127.70, 127.77, 127.83, 127.91, 128.07, 128.37, 128.61, 128.69, 128.96, 131.12, 131.20, 132.94, 133.28, 134.34, 135.87, 137.10, 138.08, 138.51, 139.07, 139.66, 140.00, 148.55, 148.61, 167.03, 167.82, 175.32, 175.83; IR (neat) ν 2927, 1793, 1762, 1735, 1491, 1368, 1287, 1148, 738 cm^{-1}; MS (ESI) m/z 494.5 (M + Na^{+}, 100). HRMS (ESI) Calcd for $C_{30}H_{28}ClNO_5Na$ requires (M + Na^{+}) 540.1563, Found: 540.1548.

***tert*-Butyl 3-(1-(4-fluorophenyl)-2-(methoxycarbonyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5e.** A white solid that is a known compound.[7] 86% yield, 43 mg (*anti* : *syn* = 58 : 42); $[\alpha]_D^{20}$ = −236.0 (*c* 1.9, $CHCl_3$) for 93% ee (*anti*) and 85% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, hexane–^{i}PrOH = 99 : 1, 1.0 mL min^{-1}, 254 nm, for *anti* product t_{major} = 6.793 min, t_{minor} = 35.273 min; for *syn* product t_{major} = 8.958 min, t_{minor} = 52.310 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.54 (s, 3.78H, Boc), 1.57 (s, 5.22H, Boc), 3.44 (s, 1.26H, CH_3), 3.64 (s, 1.74H, CH_3), 5.30 (s, 0.58H, =CH_2), 5.40 (s, 0.42H, =CH_2), 5.52 (d, J = 1.2 Hz, 0.42H, =CH_2), 5.90 (s, 0.58H, =CH_2), 6.21 (s, 0.42H, CH), 6.40 (s, 0.58H, CH), 6.71–6.79 (m, 3H, Ar), 6.88–7.14 (m, 2H, Ar), 7.22–7.36 (m, 5H, Ar), 7.42–7.47 (m, 2H, Ar), 7.61–7.72 (m, 1H, Ar).

***tert*-Butyl 3-(2-(methoxycarbonyl)-1-(*p*-tolyl)allyl)-2-oxo-3-phenylindoline-1-carboxylate 5f.** A white solid, 81% yield, 39 mg, m.p. 82–84 °C, (*anti* : *syn* = 60 : 40); $[\alpha]_D^{20}$ = −89.5 (*c* 1.2, $CHCl_3$) for 95% ee (*anti*) and 91% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column, hexane–^{i}PrOH = 90 : 10, 0.7 mL min^{-1}, 214 nm, for *anti* product t_{major} = 11.627 min, t_{minor} = 25.043 min; for *syn* product t_{major} = 15.877 min, t_{minor} = 22.543 min; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 1.52 (s, 3.60H, Boc), 1.57 (s, 5.40H, Boc), 2.19 (s, 1.20H, CH_3), 2.22 (s, 1.80H, CH_3), 3.42 (s, 1.20H, CH_3), 3.64 (s, 1.80H, CH_3), 5.31 (s, 0.60H, =CH_2), 5.38 (s, 0.40H, =CH_2), 5.51 (s, 0.40H, =CH_2), 5.79 (s, 0.60H, =CH_2), 6.18 (s, 0.40H, CH), 6.38 (s, 0.60H, CH), 6.66–6.79 (m, 2H, Ar), 6.84–7.14 (m, 3H, Ar), 7.25–7.34 (m, 5H, Ar), 7.35–7.51 (m, 2H, Ar), 7.62–7.74 (m, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.97, 27.93, 27.99, 51.89, 52.15, 53.02, 53.51, 60.33, 60.57, 84.03, 84.17, 114.82, 115.06, 123.65, 123.84, 126.13, 127.24, 127.42, 127.55, 127.63, 127.86, 128.22, 128.46, 128.72, 129.60, 129.69, 132.44, 134.05, 136.54, 136.79, 137.27, 138.67, 138.84, 139.18, 140.18, 140.26, 148.74, 167.21, 168.24, 175.43, 176.05; IR (neat) ν 2981, 1759, 1724, 1463, 1345, 1287, 1146, 1098, 734, 697 cm^{-1}; MS (ESI) m/z 520.2 (M + Na^{+}, 100). HRMS (ESI) Calcd for $C_{31}H_{31}O_5Na$ requires (M + Na^{+}) 520.2202, Found: 520.2086.

***tert*-Butyl 3-(2-(methoxycarbonyl)-1-phenylallyl)-2-oxo-3-phenylindoline-1-carboxylate 5g.** A white solid that is a known

compound.[7] 89% yield, 42 mg (*anti* : *syn* = 57 : 43); $[\alpha]_D^{20}$ = −196.0 (*c* 0.1, $CHCl_3$) for 93% ee (*anti*) and 89% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, hexane–^{i}PrOH = 95 : 5, 0.9 mL min^{-1}, 254 nm, for *anti* product t_{major} = 6.295 min, t_{minor} = 12.578 min; for *syn* product t_{major} = 8.940 min, t_{minor} = 18.340 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.52 (s, 3.87H, Boc), 1.57 (s, 5.13H, Boc), 3.43 (s, 1.29H, CH_3), 3.63 (s, 1.71H, CH_3), 5.34 (s, 0.57H, =CH_2), 5.42 (s, 0.43H, =CH_2), 5.53 (d, *J* = 0.8 Hz, 0.43H, =CH_2), 5.85 (s, 0.57H, =CH_2), 6.22 (s, 0.43H, CH), 6.40 (s, 0.57H, CH), 6.79–6.92 (m, 2H, Ar), 6.95–7.12 (m, 4H, Ar), 7.24–7.33 (m, 5H, Ar), 7.44–7.50 (m, 2H, Ar), 7.61–7.72 (m, 1H, Ar).

***tert*-Butyl 3-(4-fluorophenyl)-3-(2-(methoxycarbonyl)-1-phenylallyl)-2-oxoindoline-1-carboxylate 5h.** A white solid that is a known compound.[7] 82% yield, 41 mg (*anti* : *syn* = 60 : 40); $[\alpha]_D^{20}$ = −147.7 (*c* 1.1, $CHCl_3$) for 92% ee (*anti*) and 89% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 95 : 5, 1.0 mL min^{-1}, 254 nm, for *anti* product t_{major} = 5.468 min, t_{minor} = 7.813 min; for *syn* product t_{major} = 5.998 min, t_{minor} = 8.328 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.52 (s, 3.60H, Boc), 1.57 (s, 5.40H, Boc), 3.46 (s, 1.20H, CH_3), 3.64 (s, 1.80H, CH_3), 5.30 (s, 0.60H, =CH_2), 5.35 (s, 0.40H, =CH_2), 5.52 (s, 0.40H, =CH_2), 5.72 (s, 0.60H, =CH_2), 6.22 (s, 0.40H, CH), 6.39 (s, 0.60H, CH), 6.78–6.89 (m, 3H, Ar), 6.94–7.14 (m, 5H, Ar), 7.25–7.37 (m, 2H, Ar), 7.41–7.49 (m, 2H, Ar), 7.59–7.73 (m, 1H, Ar).

***tert*-Butyl 3-(2-(methoxycarbonyl)-1-phenylallyl)-2-oxo-3-(*p*-tolyl)indoline-1-carboxylate 5i.** A white solid that is a known compound.[7] 76% yield, 38 mg (*anti* : *syn* = 61 : 39); $[\alpha]_D^{20}$ = −177.8 (*c* 1.85, $CHCl_3$) for 92% ee (*anti*) and 88% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 95 : 5, 0.8 mL min^{-1}, 254 nm, for *anti* product t_{major} = 6.902 min, t_{minor} = 8.437 min; for *syn* product t_{major} = 7.322 min, t_{minor} = 18.025 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.51 (s, 3.51H, Boc), 1.56 (s, 5.49H, Boc), 2.29 (s, 1.17H, CH_3), 2.31 (s, 1.83H, CH_3), 3.43 (s, 1.13H, CH_3), 3.63 (s, 1.87H, CH_3), 5.31 (s, 0.61H, =CH_2), 5.39 (s, 0.39H, =CH_2), 5.54 (d, *J* = 1.2 Hz, 0.39H, =CH_2), 5.86 (s, 0.61H, =CH_2), 6.22 (s, 0.39H, CH), 6.40 (s, 0.61H, CH), 6.81 (d, *J* = 7.2 Hz, 1H, Ar), 6.92 (t, *J* = 8.4 Hz, 1H, Ar), 7.01–7.14 (m, 6H, Ar), 7.22–7.36 (m, 4H, Ar), 7.60–7.71 (m, 1H, Ar).

***tert*-Butyl 5-fluoro-3-(2-(methoxycarbonyl)-1-phenylallyl)-2-oxo-3-phenylindoline-1-carboxylate 5j.** A white soli that is a known compound.[7] 82% yield, 41 mg (*anti* : *syn* = 56 : 44); $[\alpha]_D^{20}$ = −155.0 (*c* 0.25, $CHCl_3$) for 97% ee (*anti*) and 84% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column, hexane–^{i}PrOH = 95 : 5, 0.9 mL min^{-1}, 254 nm, for *anti* product t_{major} = 5.585 min, t_{minor} = 12.665 min; for *syn* product t_{major} = 6.605 min, t_{minor} = 9.740 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.52 (s, 3.96H, Boc), 1.56 (s, 5.04H, Boc), 3.44 (s, 1.32H, CH_3), 3.64 (s, 1.68H, CH_3), 5.31 (s, 0.56H, =CH_2), 5.41 (s, 0.44H, =CH_2), 5.49 (d, *J* = 1.6 Hz, 0.44H, =CH_2), 5.87 (s, 0.56H, =CH_2), 6.23 (s, 0.44H, CH), 6.41 (s, 0.56H, CH), 6.67–6.83 (m, 2H, Ar), 6.91–6.96 (m, 1H, Ar), 7.04–7.12 (m, 3H, Ar), 7.28–7.38 (m, 4H, Ar), 7.41–7.47 (m, 2H, Ar), 7.62–7.72 (m, 1H, Ar).

***tert*-Butyl 3-(2-(methoxycarbonyl)-1-phenylallyl)-5-methyl-2-oxo-3-phenylindoline-1-carboxylate 5k.** A colorless oil that is a known compound.[7] 78% yield, 38 mg (*anti* : *syn* = 64 : 36); $[\alpha]_D^{20}$ = −32.7 (*c* 0.25, $CHCl_3$) for 96% ee (*anti*) and 94% ee (*syn*); Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column, hexane–^{i}PrOH = 95 : 5, 1.0 mL min^{-1}, 254 nm, for *anti* product t_{major} = 7.887 min, t_{minor} = 11.732 min; for *syn* product t_{major} = 9.095 min, t_{minor} = 13.745 min; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 1.51 (s, 3.24H, Boc), 1.55 (s, 5.78H, Boc), 2.29 (s, 1.92H, CH_3), 2.42 (s, 1.08H, CH_3), 3.44 (s, 1.08H, CH_3), 3.64 (s, 1.92H, CH_3), 5.31 (s, 0.64H, =CH_2), 5.40 (s, 0.36H, =CH_2), 5.53 (d, *J* = 1.2 Hz, 0.36H, =CH_2), 5.90 (s, 0.64H, =CH_2), 6.22 (s, 0.36H, CH), 6.40 (s, 0.64H, CH), 6.73–6.93 (m, 2H, Ar), 7.03–7.14 (m, 4H, Ar), 7.24–7.33 (m, 4H, Ar), 7.40–7.59 (m, 3H, Ar).

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References

1 For selected examples for benzofuran-2(3*H*)-ones see: (*a*) N. Lindquist, W. Fenical, G. D. Van Duyne and J. Clardy, *J. Am. Chem. Soc.*, 1991, **113**, 2303; (*b*) C. M. Passreiter, H. Weber, D. Blaser and R. Boese, *Tetrahedron*, 2002, **58**, 279; (*c*) B. Sontag, M. Ruth, P. Spiteller, N. Arnold, W. Steglich, M. Reichert and G. Bringmann, *Eur. J. Org. Chem.*, 2006, 1023; (*d*) Y.-J. Kwon, M.-J. Sohn, C.-J. Zheng and W.-G. Kim, *Org. Lett.*, 2007, **9**, 2449; (*e*) H. M. Ge, C. H. Zhu, D. H. Shi, L. D. Zhang, D. Q. Xie, J. Yang, S. W. Ng and R. X. Tan, *Chem.–Eur. J.*, 2008, **14**, 376.

2 For selected examples for oxindoles see: (*a*) A. B. Dounay and L. E. Overman, *Chem. Rev.*, 2003, **103**, 2945; (*b*) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748; (*c*) F. Zhou, Y.-L. Liu and J. Zhou, *Adv. Synth. Catal.*, 2010, **352**, 1381.

3 (*a*) S. A. Adediran, D. Vabaret, B. Drouillat, R. F. Pratt and M. Wakselman, *Bioorg. Med. Chem.*, 2001, **9**, 1175; (*b*) E. K. Panisheva, L. M. Alekseeva, M. I. Evstratova, S. S. Kiselev and V. G. Granik, *Pharm. Chem. J.*, 2007, **41**, 549.

4 (*a*) X. Li, Z. G. Xi, S. Z. Luo and J.-P. Cheng, *Adv. Synth. Catal.*, 2010, **352**, 1097; (*b*) X. Li, S. S. Hu, Z. G. Xi, L. Zhang, S. Z. Luo and J.-P. Cheng, *J. Org. Chem.*, 2010, **75**, 8697; (*c*) C.-L. Zhu, F.-G. Zhang, W. Meng, J. Nie, D. Cahard and J.-A. Ma, *Angew. Chem., Int. Ed.*, 2011, **50**, 5869; (*d*) C. Cassani, X. Tian, E. C. Escudero-Adan and P. Melchiorre, *Chem. Commun.*, 2011, **47**, 233; (*e*) X. Li, Y.-Y. Zhang, X.-S. Xue, J.-L. Jin, B.-X. Tan, C. Liu, N. Dong and J.-P. Cheng, *Eur. J. Org. Chem.*, 2012, 1774.

5 For selected examples of catalytic asymmetric syntheses of 3,3-disubstituted oxindoles see: (*a*) T. Bui, N. R. Candeias and C. F. Barbas, III, *J. Am. Chem. Soc.*, 2010, **132**, 5574; (*b*) S. Mouri, Z. Chen, H. Mitsunuma, M. Furutachi, S. Matsunaga and M. Shibasaki, *J. Am. Chem. Soc.*, 2010, **132**, 1255; (*c*) A. M. Taylor, R. A. Altman and S. L. Buchwald, *J. Am. Chem. Soc.*, 2009, **131**, 9900; (*d*) R. He, S. Shirakawa and K. Maruoka, *J. Am. Chem. Soc.*, 2009, **131**, 16620; (*e*) R. He, C. Ding and K. Maruoka, *Angew. Chem., Int. Ed.*, 2009, **48**, 4559; (*f*) Y. Kato, M. Furutachi, Z. Chen, H. Mitsunuma, S. Matsunaga and M. Shibasaki, *J. Am. Chem. Soc.*, 2009, **131**, 9168; (*g*) T. A. Duffey, S. A. Shaw and E. Vedejs, *J. Am. Chem. Soc.*, 2009, **131**, 14; (*h*) E. C. Linton and M. C. Kozlowski, *J. Am. Chem. Soc.*, 2008, **130**,

16162; (*i*) B. M. Trost, N. Cramer and S. M. Silverman, *J. Am. Chem. Soc.*, 2007, **129**, 12396; (*j*) B. K. Corkey and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 2764; (*k*) T. B. Poulsen, L. Bernardi, J. Alemán, J. Overgaard and K. A. Jørgensen, *J. Am. Chem. Soc.*, 2007, **129**, 441; (*l*) E. P. Kündig, T. M. Seidel, Y.-X. Jia and G. Bernardineli, *Angew. Chem., Int. Ed.*, 2007, **46**, 8484; (*m*) I. D. Hills and G. C. Fu, *Angew. Chem., Int. Ed.*, 2003, **42**, 3291; (*n*) Y.-L. Liu, B.-L. Wang, J.-J. Cao, L. Chen, C. Zhang, Y.-X. Wang and J. Zhou, *J. Am. Chem. Soc.*, 2010, **132**, 15176; (*o*) T. Itoh, H. Ishikawa and Y. Hayashi, *Org. Lett.*, 2009, **11**, 3854; (*p*) J. Itoh, S. B. Han and M. J. Krische, *Angew. Chem., Int. Ed.*, 2009, **48**, 6313; (*q*) R. Shintani, M. Inoue and T. Hayashi, *Angew. Chem., Int. Ed.*, 2006, **45**, 3353; (*r*) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru and S. Kanemasa, *J. Am. Chem. Soc.*, 2006, **128**, 16488; (*s*) L. Cheng, L. Liu, D. Wang and Y.-C. Chen, *Org. Lett.*, 2009, **11**, 3874; (*t*) H.-L. Cui, J.-R. Huang, J. Lei, Z.-F. Wang, S. Chen, L. Wu and Y.-C. Chen, *Org. Lett.*, 2010, **12**, 720–723; (*u*) H.-L. Cui, X. Feng, J. Peng, J. Lei, K. Jiang and Y.-C. Chen, *Angew. Chem., Int. Ed.*, 2009, **48**, 5737; (*v*) X. Feng, Y.-Q. Yuan, H.-L. Cui, K. Jiang and Y.-C. Chen, *Org. Biomol. Chem.*, 2009, **7**, 3660; (*w*) D. Wang, J.-J. Jiang, R. Zhang and M. Shi, *Tetrahedron: Asymmetry*, 2011, **22**, 1133.

6 For reviews on AAA reactions, see: (*a*) O. Belda and C. Moberg, *Acc. Chem. Res.*, 2004, **37**, 159; (*b*) B. M. Trost, M. R. Machacek and A. Aponick, *Acc. Chem. Res.*, 2006, **39**, 747.

7 K. Jiang, J. Peng, H.-L. Cui and Y.-C. Chen, *Chem. Commun.*, 2009, 3955.

8 C. Liu, B.-X. Tan, J.-L. Jin, Y.-Y. Zhang, N. Dong, X. Lin and J.-P. Cheng, *J. Org. Chem.*, 2011, **76**, 5838.

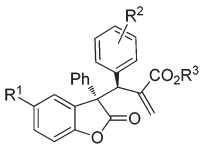
9 Y.-Q. Jiang, Y.-L. Shi and M. Shi, *J. Am. Chem. Soc.*, 2008, **130**, 7202.

10 (*a*) Y.-L. Yang, C.-K. Pei and M. Shi, *Org. Biomol. Chem.*, 2011, **9**, 3349; (*b*) H.-P. Deng and M. Shi, *Eur. J. Org. Chem.*, 2012, 183; (*c*) H.-P. Deng, Y. Wei and M. Shi, *Eur. J. Org. Chem.*, 2012, 1956; (*d*) H.-P. Deng, Y. Wei and M. Shi, *Adv. Synth. Catal.*, 2012, **354**, 783; (*e*) G.-N. Ma, S.-H. Cao and M. Shi, *Tetrahedron: Asymmetry*, 2009, **20**, 1086.

11 A. Padwa, D. Dehm, T. Oine and G. A. Lee, *J. Am. Chem. Soc.*, 1975, **97**, 1837.

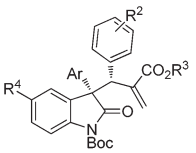
12 J. Feng, X. Lu, A. Kong and X. Han, *Tetrahedron*, 2007, **63**, 6035.

13 Determination of absolute configuration: for AAA reaction of 3-substituted benzofuran-2(3*H*)-ones, *anti* products can be determined as below on the basis of chiral HPLC according to ref. 8.



(*anti* product)

For AAA reaction of 3-substituted oxindoles, *syn* products can be determined as below on the basis of chiral HPLC according to ref. 7.



(*syn* product)