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Trisoxazoline/Cu(II)-catalyzed asymmetric intramolecular Friedel–Crafts alkylation reaction of indoles

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ABSTRACT

Intramolecular Friedel–Crafts alkylation reaction of indoles catalyzed by trisoxazoline/copper(II) is described. This annulation provides an easy access to polycyclic indole derivatives with up to 90% ee in up to 99% yield.

1. Introduction

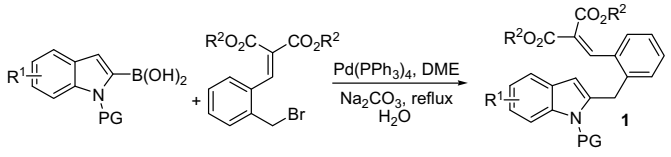
Polycyclic indoles, such as carbolines, pyranoindole, carbozoles, possess a wide diversity of biologically activities.[1] The development of practical and effective protocol for the preparation of polycyclic indoles has always been an attractive and challenging area to chemical community.[1,2] Of the methods developed, intramolecular indole annulation provides an easy access to such compounds.[2–6] Compared with the asymmetric intermolecular alkylation of indoles, however, the enantioselective intramolecular alkylation remains undeveloped except a few examples of those related to asymmetric Pictet–Spengler reaction (PS reaction)[5] and asymmetric Friedel–Crafts alkylation reaction (FC alkylation reaction)[6] of unsaturated indolyl aldehydes and ketones. Very recently, we[7] developed highly efficient asymmetric intermolecular Friedel–Crafts reaction[8,9] of indole with alkylidene malonates. Herein, we wish to report the enantioselective intramolecular alkylation reaction of indolyl alkylidene malonates **1**.

2. Results and discussion

Indolyl alkylidene malonate derivatives **1a**–**1j** are readily available from the corresponding indole boric acids[10] by the coupling reactions[11] with benzyl bromides[12] in the presence of catalytic $Pd(PPh_3)_4$ in good to excellent yields (Table 1).

Using compound **1a** as a model substrate and $Cu(OTf)_2$ (10 mol %)/^{i}Pr-TOX **L1** (12 mol %) as catalyst, solvent effects were examined first. As shown in Table 2, indolyl alkylidene malonates **1a** could be converted smoothly into tetracyclic indole **2a** in CH_2Cl_2 (DCM) with 36% ee in almost quantitative yield (entry 1, Table 2). Compared with DCM, other solvents screened gave lower yields but with higher enantioselectivities (entries 2–6, Table 2). The highest ee was achieved in ^{t}BuOH (62% ee, entry 6, Table 2). Further studies showed that the ratio of the mixed solvent of ^{t}BuOH with toluene, as well as the concentration of both the substrate and the catalyst, influenced the yields as well as the enantioselectivities (entries 7–15, Table 2). For example, increasing the content of ^{t}BuOH resulted in a diminished enantioselectivity (entries 7–10, Table 1). Lowering the concentration of the substrate or the catalyst improved the ee (entry 9 vs entries 12–15). Under the optimal conditions, using the mixed solvent of ^{t}BuOH and toluene (1:3, v/v) at 15 °C, 71% ee was obtained (entry 13, Table 1).

Table 1
Preparation of substrates[a]



Entry	Substrates	R^1	R^2	PG	Yield[b] [%]
1	**1a**	H	Me	Boc	87
2	**1b**	H	Et	Boc	80
3	**1c**	4-Br	Me	Boc	52
4	**1d**	4-OMe	Me	Boc	79
5	**1e**	5-Br	Me	Boc	52
6	**1f**	5-OMe	Me	Boc	83
7	**1g**	6-OMe	Me	Boc	92
8	**1h**	H	Me	CO_2Me	73
9	**1i**	5-OMe	Me	CO_2Me	76
10	**1j**	Pyrrole	Me	Boc	38

[a] Reaction conditions: indole boric acids (4.68 mmol), benzyl bromides (3.35 mmol), $Pd(PPh_3)_4$ (197 mg, 0.17 mmol), Na_2CO_3 (1.49 g, 14.1 mmol), DME (30 mL), H_2O (3 mL).
[b] Isolated yield.

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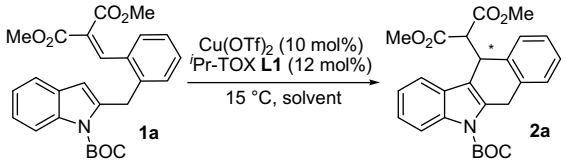
Table 2
Effects of solvent on asymmetric intramolecular alkylation of indoles[a]



Ent.	Solvent	Volume [mL]	Time [h]	Yield[b] [%]	ee[c] [%]
1	DCM	1	5 (min)	99	36
2	DME	1	3	64	56
3[d]	EtOAc	1	2	94	45
4	PhMe	1	24	88	51
5	^{i}PrOH	1	0.5	73	54
6	^{t}BuOH	1	0.5	65	62
7[e]	^{t}BuOH/PhMe(3:1)	1	2	86	55
8[e]	^{t}BuOH/PhMe(1:1)	1	2	89	54
9[e]	^{t}BuOH/PhMe(1:3)	1	2	89	62
10[e]	^{t}BuOH/PhMe(1:6)	1	6	95	67
11[e]	^{t}BuOH/PhMe(1:9)	1	8	90	64
12[e]	^{t}BuOH/PhMe(1:3)	2	4	90	68
13[e,f]	^{t}BuOH/PhMe(1:3)	4	6	99	71
14[e,f]	^{t}BuOH/PhMe(1:3)	6	6	99	69
15[e,f]	^{t}BuOH/PhMe(1:3)	10	8	96	67

[a] Reaction conditions: **1a** (45 mg, 0.1 mmol), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol), ^{i}Pr-TOX (4.5 mg, 0.012 mmol), 15 °C.
[b] Isolated yield.
[c] Determined by chiral HPLC (OD-H).
[d] At 20 °C.
[e] ^{t}BuOH/PhMe: v/v.
[f] Improved work-up procedure, see Supplementary data.

To further improve the enantioselection, different oxazoline ligands **L1**–**L9** in Figure 1 were evaluated and the structure of ligand proves to influence the ee strongly. As shown in Table 3, trisoxazolines **L1**–**L4**, varying the substituents on the pendant oxazoline moiety from ^{i}Pr, ^{t}Bu, Ph to Bn, afforded very similar ee values in excellent yields (entries 1–4, Table 3). Ligand **L5**, with indene-derived oxazoline, proved to be the optimal one and up to 77% ee was achieved (entry 5, Table 3). Chiral 2-amino-2-phenylethanol-derived ligand **L6** gave poor enantioselection (entry 6, Table 3). Bisoxazoline **L7** with an ester group catalyzed this reaction in almost quantitative yields with 64% ee (entry 7, Table 3). Compared with trisoxazoline **L1**–**L5**, the parental bisoxazoline **L8**–**L9** gave much lower enantioselectivities (entries 8–9, Table 3).

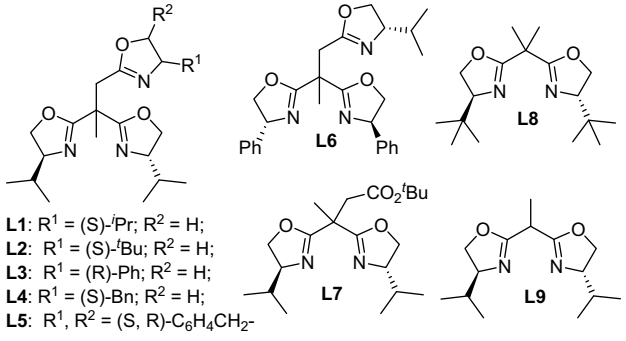
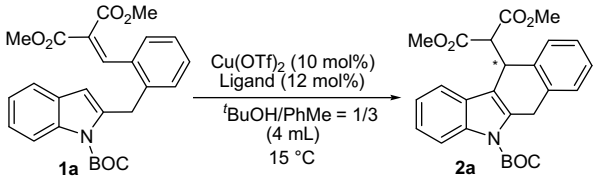


Figure 1. Ligands screened.

Under the optimized reaction conditions, a variety of indolyl alkylidene malonates have been examined to investigate the generality of the current reaction. As summarized in Table 4, methyl ester gave better ee than ethyl ester (entry 1 vs entry 2).

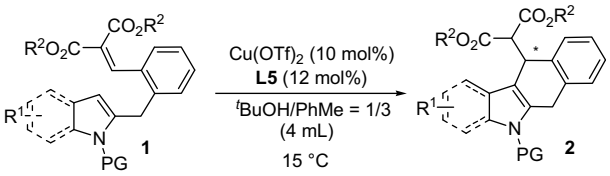
Table 3
Screening of ligands in asymmetric intramolecular alkylation reaction of indoles[a]



Entry	Ligand	Time [h]	Yield[b] [%]	ee[c] [%]
1	**L1**	4	99	71
2	**L2**	4	99	71
3	**L3**	4	99	70
4	**L4**	4	99	69
5	**L5**	4	99	77
6	**L6**	4	99	−21
7	**L7**	4	99	64
8	**L8**	10	99	50
9	**L9**	10	99	41

[a] Reaction conditions: **1a** (45 mg, 0.1 mmol), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol), ligand (0.012 mmol), 15 °C.
[b] Isolated yield.
[c] Determined by chiral HPLC (OD-H).

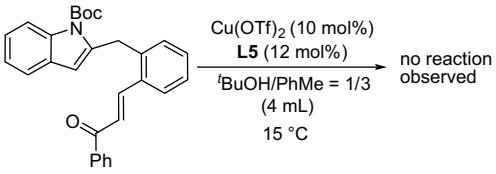
Table 4
Asymmetric intramolecular FC alkylation reaction of indolesa[a]



Ent.	R^1	R^2	PG	Product	Yield[b] (%)	ee[c] (%)
1	**1a**, H	Me	Boc	**2a**	99	78
2	**1b**, H	Et	Boc	**2b**	80	60
3[d]	**1c**, 4-Br	Me	Boc	**2c**	94	82
4	**1d**, 4-OMe	Me	Boc	**2d**	98	62
5	**1e**, 5-Br	Me	Boc	**2e**	97	90
6	**1f**, 5-OMe	Me	Boc	**2f**	99	86
7[e]	**1g**, 6-OMe	Me	Boc	**2g**	94	74
8	**1h**, H	Me	CO_2Me	**2h**	90	86
9	**1i**, 5-OMe	Me	CO_2Me	**2i**	99	90
10	**1j**, pyrrole	Me	Boc	**2j**	99	26

[a] Reaction conditions: **1** (0.1 mmol), $Cu(OTf)_2$ (3.6 mg, 0.01 mmol), **L5** (5.1 mg, 0.012 mmol), 15 °C.
[b] Isolated yield.
[c] Determined by chiral HPLC.
[d] 15 mmol% of catalyst.
[e] At 5 °C.

Substituents on indole ring were well tolerant to give the desired products in very high yields but affected the enantioselectivities (entries 3–7, Table 4). 5-Bromolindole **1e** afforded the highest level of enantioselectivity (90% ee, entry 5, Table 4) and 4-methoxylindole **1d** gave 62% ee (entry 4, Table 4). 6-Methoxylindole **1g** is more reactive than both 4-methoxylindole **1d** and 5-methoxylindole **1f**. Good ee was also achieved for **1g** at 5 °C (74% ee, entry 7, Table 4). Using methoxylcarbonyl group instead of Boc group in substrates **1a** and **1f** increased the enantioselectivities obviously (entry 1 vs 8 and entry 6 vs 9, Table 4). Interestingly, under the same reaction conditions, the substrate **1j** derived from pyrrole underwent this annulation reaction very smoothly to deliver the corresponding product in an almost quantitative yield with 26% ee (entry 10, Table 4). The use of α,β-unsaturated ketone instead of the alkylidene malonate resulted in no reaction (Eq. 1).



(1)

3. Conclusions

In summary, we have developed an intramolecular Friedel–Crafts alkylation reaction of indolyl alkylidene malonates catalyzed by $Cu(OTf)_2$-trisoxazoline. This reaction provides an easy access to polycyclic indole derivatives, in particular for the 4-substituted polycyclic indoles, with modest to high enantioselectivities in high to excellent yields.

4. Experimental

4.1. General

All reactions were carried out under dry nitrogen atmosphere. Dichloromethane (DCM) and 1,2-dichloro ethane were distilled over calcium hydride prior to use. Toluene, dimethoxyethane (DME), isopropanol, isobutanol, and ethyl acetate (EtOAc) were purified with standard methods.[13] *N*-Boc indole boronic acid[10] and substrate was synthesized according to the literature.[11,12]

^1H NMR was recorded on a Varian Mercury-300 (300 MHz). Chemical shifts are reported in ppm, using residual $CDCl_3$ (7.26 ppm) as an internal standard.

4.2. Typical procedures for asymmetric intramolecular Friedel–Crafts reaction of indole derivatives by TOX/Cu(II)

A mixture of $Cu(OTf)_2$ (0.01 mmol) and oxazoline ligand (0.012 mmol) in toluene/^{t}BuOH=3 mL/1 mL was stirred at 40 °C for 2 h under nitrogen atmosphere. After the mixture was cooled to 15 °C, substrate **1a** (0.1 mmol, 45 mg) was added and the resulting mixture was stirred at 15 °C until the reaction is complete (determined by ^1H NMR). The mixture was filtered through a thin layer (40 mm) of silicon gel (300–400 mesh), and eluted with ethyl acetate (50 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography.

*4.2.1. Dimethyl 2-(5-(tert-butoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2a**)*

At 15 °C, 4 h, colourless oil, 99% yield, 78% ee determined on HPLC with Chiral OD-H column: hexane/isopropanol=100:1, flow rate=0.7 mL/min, 230 nm. $[\alpha]_D^{20}$ +64.2 (*c* 1.08, $CHCl_3$, 76% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 8.14–8.11 (m, 1H), 7.59–7.56 (m, 1H), 7.44 (dd, *J*=1.5, 6.9 Hz, 1H), 7.33 (dd, *J*=1.8, 8.7 Hz, 1H), 7.28–7.20 (m, 4H), 5.14 (d, *J*=6.6 Hz, 1H), 4.55 (ABd, *J*=21.9 Hz, 1H), 4.33 (ABd, *J*=21.9 Hz, 1H), 3.51 (s, 3H), 3.47 (s, 3H), 1.74 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.5, 168.0, 150.5, 136.1, 136.0, 135.6, 135.0, 129.1, 128.6, 127.5, 126.9, 126.2, 123.7, 122.6, 118.1, 115.9, 115.5, 84.0, 58.4, 52.5, 52.2, 38.3, 31.2, 28.3; IR (neat) 2978, 2941, 1730, 1453, 1363, 1253, 1157, 1141, 748 cm^{-1}; LRMS–ESI (*m*/*z*): 450.0 $(M+H)^+$, 472.0 $(M+Na)^+$. Anal. Calcd for $C_{26}H_{27}NO_6$: C, 69.47; H, 6.05; N, 3.12. Found: C, 69.16; H, 5.98; N, 2.79.

*4.2.2. Diethyl 2-(5-(tert-butoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2b**)*

At 15 °C, 5 h, colourless oil, 80% yield, 60% ee determined on HPLC with Chiral OD-H column: hexane/isopropanol=95:5, flow rate=0.5 mL/min, 230 nm. $[\alpha]_D^{20}$ +50.1 (*c* 0.925, $CHCl_3$, 60% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 8.15–8.12 (m, 1H), 7.61–7.59 (m, 1H), 7.50–7.47 (m, 1H), 7.34–7.18 (m, 5H), 5.16 (d, *J*=6.6 Hz, 1H), 4.54 (ABd, *J*=21.6 Hz, 1H), 4.34 (ABd, *J*=21.6 Hz, 1H), 4.01–3.89 (m, 4H), 3.72 (d, *J*=6.6 Hz, 1H), 1.74 (s, 9H), 1.05 (t, *J*=6.9 Hz, 3H), 1.00 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.3, 167.7, 150.5, 136.1, 136.0, 135.6, 135.2, 129.0, 128.8, 127.7, 126.8, 126.2, 123.7, 122.6, 118.3, 116.3, 115.5, 84.0, 61.5, 61.2, 58.7, 38.0, 31.3, 28.3, 13.7 (1), 13.6 (8); IR (neat) 2979, 1730, 1453, 1366, 1253, 1141, 1119, 1037, 748 cm^{-1}; LRMS–ESI (*m*/*z*): 478.9 $(M+H)^+$, 499.6 $(M+Na)^+$. Anal. Calcd for $C_{28}H_{31}NO_6$: C, 70.42; H, 6.54; N, 2.93. Found: C, 70.34; H, 6.55; N, 2.68.

*4.2.3. Dimethyl 2-(1-bromo-5-(tert-butoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2c**)*

At 15 °C, 14 h, colourless oil, 94% yield, 82% ee determined on HPLC with Daicel Chiralcel OD-H column: hexane/isopropanol=100:5, flow rate=0.7 mL/min, 254 nm. $[\alpha]_D^{20}$ +66.6 (*c* 1.0, $CHCl_3$, 83% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 8.19 (d, *J*=8.4 Hz, 1H), 7.72 (dd, *J*=4.8, 8.4 Hz, 1H), 7.39 (d, *J*=8.4 Hz, 1H), 7.28–7.08 (m, 3H), 7.11 (t, *J*=8.4 Hz, 1H), 5.86 (s, 1H), 4.43 (ABd, *J*=21.6 Hz, 1H), 4.27 (ABd, *J*=21.3 Hz, 1H), 4.13 (d, *J*=2.7 Hz, 1H), 3.76 (s, 3H), 3.30 (s, 3H), 1.73 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.33, 168.11, 149.95, 137.66, 137.58, 134.97, 133.70, 129.48, 128.56, 127.37, 126.97, 126.28, 125.94, 124.53, 115.81, 114.84, 112.48, 84.75, 58.55, 52.49, 52.01, 37.19, 31.27, 28.25; IR (neat) 2976, 2951, 2852, 1736, 1629, 1557, 1474, 1455, 1425, 1371, 1328, 1309, 1263, 1215, 1142, 1089, 1069, 771 cm^{-1}; LRMS–ESI (*m*/*z*): 550.3 $(M+Na)^+$; HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{26}H_{26}BrNO_6$: 550.0841, found: 550.0836.

*4.2.4. Dimethyl 2-(5-(tert-butoxycarbonyl)-1-methoxy-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2d**)*

At 15 °C, 15 h, colourless oil, 98% yield, 62% ee determined on HPLC with Chiral OD-H column: hexane/isopropanol=90:10, flow rate=0.7 mL/min, 254 nm. $[\alpha]_D^{20}$ +85.1 (*c* 0.5, $CHCl_3$, 63% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (d, *J*=8.4 Hz, 1H), 7.62 (t, *J*=5.1 Hz, 1H), 7.29–7.17 (m, 4H), 6.68 (d, *J*=8.4 Hz, 1H), 5.49 (d, *J*=3 Hz, 1H), 4.47 (dd, *J*=21.3, 2.4 Hz, 1H), 4.29 (ABd, *J*=21.6, 3.6 Hz, 1H), 4.16 (d, *J*=2.1 Hz, 1H), 3.89 (s, 3H), 3.83 (s, 3H), 3.24 (s, 3H), 1.73 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.20, 168.51, 152.75, 150.55, 137.60, 135.25, 133.88, 133.45, 129.20, 128.67, 126.67, 126.02, 124.50, 117.28, 116.13, 108.95, 103.37, 83.97, 58.61, 54.99, 52.32, 51.76, 38.03, 30.95, 28.27; IR (neat) 2980, 2950, 2938, 1731, 1584, 1576, 1496, 1457, 1442, 1404, 1395, 1367, 1356, 1330, 1316, 1283, 1264, 1142, 1107, 1044, 1026, 958, 741 cm^{-1}; LRMS–ESI (*m*/*z*): 502.3 $(M+Na)^+$. Anal. Calcd for $C_{27}H_{29}NO_7$: C, 67.63; H, 6.10; N, 2.92. Found: C, 67.60; H, 6.29; N, 2.69.

*4.2.5. Dimethyl 2-(2-bromo-5-(tert-butoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2e**)*

At 15 °C, 15 h, colourless oil, 97% yield, 90% ee determined on HPLC with Chiral AD-H column: hexane/isopropanol=100:2, flow rate=0.7 mL/min, 238 nm. $[\alpha]_D^{20}$ +47.7 (*c* 1.0, $CHCl_3$, 89% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J*=9.3 Hz, 1H), 7.67 (d, *J*=1.5 Hz, 1H), 7.44–7.41 (m, 1H), 7.35–7.32 (m, 2H), 7.25–7.22 (m, 2H), 5.04 (d, *J*=6.6 Hz, 1H), 4.50 (ABd, *J*=21.6 Hz, 1H), 4.30 (ABd, *J*=21.6 Hz, 1H), 3.67 (d, *J*=7.2 Hz, 1H), 3.56 (s, 3H), 3.51 (s, 3H), 1.73 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.09, 167.94, 150.04, 137.64, 135.18, 134.83, 134.77, 129.22, 129.15, 128.53, 127.04, 126.43, 126.40, 120.87, 117.00, 115.98, 115.06, 84.58, 58.52, 52.54, 52.37, 38.20, 31.24, 28.24; IR (neat) 2979, 2951, 2846, 1733, 1597, 1577, 1492, 1476, 1451, 1396, 1357, 1325, 1307, 1279, 1252, 1218, 1143, 1111, 1062, 1040, 1022, 957, 842, 807, 739 cm^{-1}; LRMS–ESI (*m*/*z*): 550.3 $(M+Na)^+$; HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{26}H_{26}BrNO_6$: 550.0841, found: 550.0836.

4.2.6. Dimethyl 2-(5-(tert-butoxycarbonyl)-2-methoxy-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2f**)

At 15 °C, 15 h, colourless oil, 99% yield, 86% ee determined on HPLC with Daicel Chiralcel OD-H column: hexane/isopropanol=100:5, flow rate=0.7 mL/min, 254 nm. $[\alpha]_D^{20}$ +66.0 (*c* 0.955, $CHCl_3$, 85% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, *J*=9.0 Hz), 7.36–7.33 (m, 1H), 7.26–7.24 (m, 1H), 7.17–7.13 (m, 2H), 6.99 (d, *J*=2.1 Hz, 1H), 6.79 (dd, *J*=9.0, 2.7 Hz, 1H), 5.02 (d, *J*=7.2 Hz, 1H), 4.47 (ABd, *J*=21.3 Hz, 1H), 4.22 (ABd, *J*=21.3 Hz, 1H), 3.81 (s, 3H), 3.62 (d, *J*=7.2 Hz, 1H), 3.43 (s, 3H), 3.41 (s, 3H), 1.65 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.55, 168.06, 155.74, 150.41, 136.79, 135.57, 135.06, 130.60, 129.12, 128.55, 128.32, 126.93, 126.24, 116.25, 115.87, 112.05, 101.13, 83.90, 58.43, 55.67, 52.49, 52.27, 38.50, 31.24, 28.28; IR (neat) 2977, 2952, 2834, 1728, 1613, 1478, 1453, 1435, 1403, 1370, 1312, 1258, 1220, 1192, 1164, 1135, 1108, 1040, 957, 847, 754 cm^{-1}; LRMS–ESI (*m*/*z*): 502.3 $(M+Na)^+$. Anal. Calcd for $C_{27}H_{29}NO_7$: C, 67.63; H, 6.10; N, 2.92. Found: C, 67.51; H, 6.24; N, 2.72.

4.2.7. Dimethyl 2-(5-(tert-butoxycarbonyl)-3-methoxy-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2g**)

At 5–8 °C, 9 h, colourless oil, 94% yield, 74% ee determined on HPLC with Chiral AD-H column: hexane/isopropanol=100:2, flow rate=0.7 mL/min, 238 nm. $[\alpha]_D^{20}$ +60.9 (*c* 0.85, $CHCl_3$, 73% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J*=2.4 Hz, 1H), 7.47–7.40 (m, 2H), 7.34–7.31 (m, 1H), 7.25–7.20 (m, 2H), 6.89 (dd, *J*=2.4, 8.7 Hz, 1H), 5.09 (d, *J*=6.9 Hz, 1H), 4.51 (ABd, *J*=21.3 Hz, 1H), 4.29 (ABd, *J*=21.9 Hz, 1H), 3.87 (s, 3H), 3.70 (d, *J*=7.2 Hz, 1H), 3.52 (s, 3H), 3.48 (s, 3H), 1.74 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.49, 168.04, 157.24, 150.52, 137.05, 135.65, 135.10, 134.53, 129.09, 128.54, 126.84, 126.19, 121.42, 118.64, 115.81, 111.30, 100.39, 83.89, 58.59, 55.53, 52.46, 52.21, 38.43, 31.27, 28.28; IR (neat) 2926, 2853, 1731, 1686, 1616, 1579, 1492, 1442, 1367, 1310, 1285, 1141, 1034, 848, 805, 764, 737 cm^{-1}; LRMS–ESI (*m*/*z*): 502.3 $(M+Na)^+$; HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{27}H_{29}NO_7$: 502.1842, found: 502.1836.

4.2.8. Dimethyl 2-(5-(methoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2h**)

At 15 °C, 7 h, colourless oil, 90% yield, 86% ee determined on HPLC with Chiral OD-H column: hexane/isopropanol=95:5, flow rate=0.7 mL/min, 230 nm. $[\alpha]_D^{20}$ +80.5 (*c* 0.95, $CHCl_3$, 83% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 8.15–8.12 (m, 1H), 7.58–7.55 (m, 1H), 7.45–7.42 (m, 1H), 7.34–7.22 (m, 5H), 5.11 (d, *J*=6.3 Hz, 1H), 4.48 (ABd, *J*=21.6 Hz, 1H), 4.32 (ABd, *J*=21.6 Hz, 1H), 4.09 (s, 3H), 3.73 (d, *J*=6.9 Hz, 1H), 3.50 (s, 3H), 3.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.46, 167.25, 152.38, 135.96, 135.92, 135.35, 134.87, 129.06, 128.60, 127.62, 126.96, 126.29, 123.97, 122.96, 118.25, 116.52, 115.52, 58.26, 53.57, 52.44, 52.23, 38.20, 30.86; IR (neat) 3022, 2956, 1737, 1454, 1440, 1365, 1251, 1146, 1043, 759 cm^{-1}; LRMS–ESI (*m*/*z*): 407.7 $(M+H)^+$, 430.1 $(M+Na)^+$. Anal. Calcd for $C_{23}H_{21}NO_6$: C, 67.80; H, 5.20; N, 3.44. Found: C, 67.81; H, 5.12; N, 3.28.

4.2.9. Dimethyl 2-(2-methoxy-5-(methoxycarbonyl)-6,11-dihydro-5H-benzo[b]carbazol-11-yl)malonate (**2i**)

At 15 °C, 15 h, colourless oil, 99% yield, 90% ee determined on HPLC with Chiralcel OD-H column: hexane/isopropanol=90:10, flow rate=0.9 mL/min, 280 nm. $[\alpha]_D^{20}$ +69.6 (*c* 1.7500, $CHCl_3$, 90% ee); ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J*=9.2 Hz, 1H), 7.42 (dd, *J*=1.6, 7.2 Hz, 1H), 7.33 (d, *J*=6.8 Hz, 1H), 7.26–7.19 (m, 2H), 7.06 (d, *J*=2.8 Hz, 1H), 6.87 (dd, *J*=2.8, 9.2 Hz, 1H), 5.07 (d, *J*=6.8 Hz, 1H), 4.39 (ABd, *J*=55.6, 20.4 Hz, 2H), 4.07 (s, 3H), 3.89 (s, 3H), 3.69 (d, *J*=6.8 Hz, 1H), 3.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.49, 168.00, 156.02, 152.29, 136.63, 135.35, 134.96, 130.47, 129.09, 128.59, 128.50, 126.98, 126.30, 116.50, 116.26, 112.25, 101.32, 58.29, 55.68, 53.50, 52.46, 52.26, 38.41, 30.90; IR (neat) 2954, 1736, 1477, 1440, 1403, 1369, 1313, 1261, 1219, 1139, 1108, 1027, 755, 665 cm^{-1}; LRMS–ESI (*m*/*z*): 460.2 $(M+Na)^+$; HRMS–ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{24}H_{24}NO_7^+$: 438.1553, found: 438.1563.

4.2.10. Dimethyl 2-(1-(tert-butoxycarbonyl)-4,9-dihydro-1H-benzo[f]indol-4-yl)malonate (**2j**)

At 15 °C, 15 h, colourless oil, 99% yield, 26% ee determined on HPLC with Daicel Chiralcel AD-H column: hexane/isopropanol=100:2, flow rate=0.7 mL/min, 238 nm. $[\alpha]_D^{20}$ +4.3 (*c* 0.935, $CHCl_3$, 83% ee); ^1H NMR (300 MHz, $CDCl_3$): δ 7.30–7.15 (m, 5H), 6.12 (d, *J*=3.0 Hz, 1H), 4.77 (d, *J*=7.5 Hz, 1H), 4.39 (ABd, *J*=21.3 Hz, 1H), 4.11 (ABd, *J*=19.5 Hz, 1H), 3.62 (s, 3H), 3.61 (d, *J*=7.5 Hz, 1H), 3.59 (s, 3H), 1.62 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.47, 168.05, 149.30, 135.37, 135.15, 129.33, 129.28, 128.35, 126.73, 126.12, 120.59, 120.06, 110.04, 83.56, 59.95, 52.33, 52.29, 39.90, 29.74, 28.01; IR (neat) 2979, 2952, 2852, 1743, 1495, 1478, 1458, 1434, 1394, 1371, 1345, 1321, 1286, 1261, 1164, 1134, 1104, 1021, 961, 940, 855, 752, 732 cm^{-1}; LRMS–ESI (*m*/*z*): 422.2 $(M+Na)^+$; HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{25}NO_6$: 422.1580, found: 422.1574.

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Supplementary data

^1H NMR, ^{13}C NMR for new compounds, and HPLC spectra for **2a**–**2j**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.071.

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