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THE SYNTHETIC STUDIES OF CARBAZOLE ALKALOIDS

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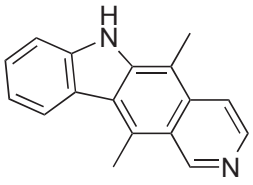
Abstract – The carbazole alkaloids have profound biological activities and material properties. We reported that 3, 4-substituted, 3-substituted and 4-substituted carbazoles were regioselectively synthesized from indoline derivatives by means of Diels-Alder reaction in the presence or absence of Pd catalyst and attained the synthesis of natural carbazole alkaloid from 3-substituted carbazole, too.

INTRODUCTION

Naturally occurring carbazoles[1,2] (Figure 1) have a broad range of biological activities, including psychotropic, anti-inflammatory, antihistaminic, antitumor, antibiotic, and anti-oxidative activities, as well as anti-aging activity.[1] Carbazoles have also been used in photorefractive materials, xerography, solar cells and organic light-emitting diodes.[3] Carbazole chemistry has been extensively reviewed, especially from the viewpoint of synthesis.[1,4,5] For example, Pindur's group first described the regioselective Diels-Alder reaction of 2-vinylindole and various dienophiles,[4c] and Ohno's group recently reported a palladium-catalyzed direct synthesis of carbazoles.[5b] We have developed a novel indole synthesis using Pd(II)-catalyzed cyclization,[6a] and in the present work, we described the synthetic studies for carbazole alkaloids from indole and indolines.



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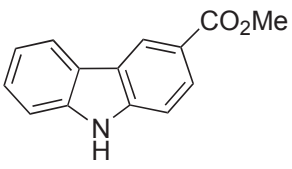
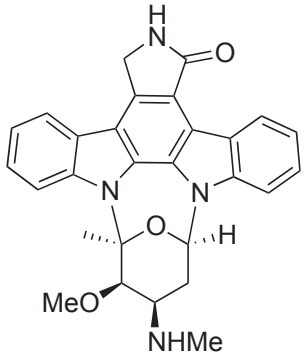


methyl carbazole-3-carboxylate



stauorsporine

Figure 1. Representative carbazole alkaloids

Carbazole alkaloids have some substituents on carbazole nucleus. The biological and material studies depend on the diversity of substituted groups on carbazole nucleus, so we aim regioselective synthesis of carbazole from common intermediates (Figure 2).

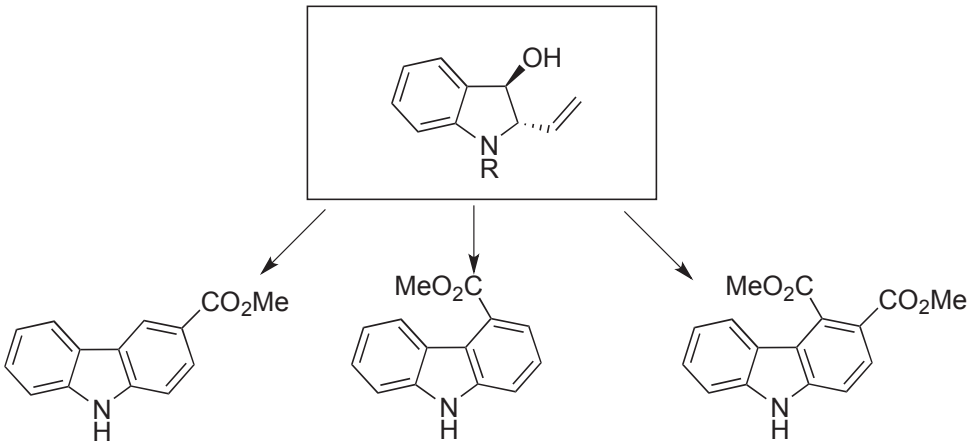
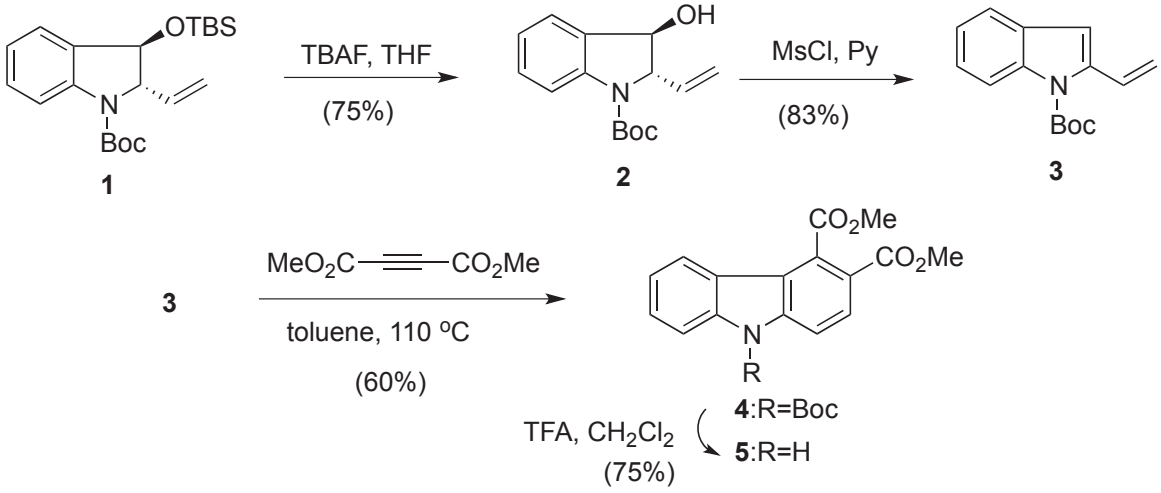


Figure 2

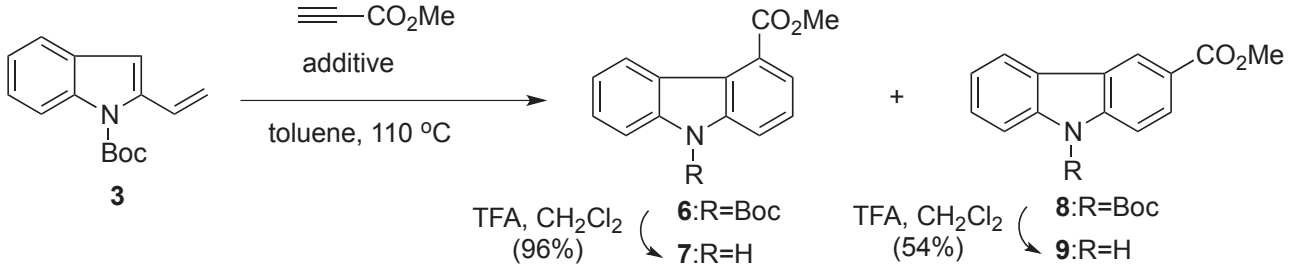
RESULTS AND DISCUSSION

The starting indoline (**1**) was prepared in 6 steps, as reported.[6a] Briefly, **1** was deprotected with TBAF in THF, followed by mesylation and elimination to give Boc-protected 2-vinylindole (**3**) (Scheme 1).[6a, 7] The 2-vinylindole derivative (**3**) and dimethyl 2-butynedioate were refluxed in toluene to afford the adduct (**4**), and deprotection with TFA in CH_2Cl_2 afforded dimethyl carbazole-3,4-dicarboxylate (**5**), as shown in Scheme 1.



Scheme 1

Next we examined Diels-Alder reaction of 2-vinylindole derivative (**3**) and methyl propiolate (Scheme 2). These compounds were refluxed in toluene to afford the *N*-Boc methyl carbazole-4-carboxylate (**6**)[8a] as the major product without formation of the *N*-Boc methyl carbazole-3-carboxylate (**8**). As shown in Table 1, the use of BHT or $AgNO_3$ improved the yield of the Diels-Alder reaction (Entries 2, 3). In the presence of palladium catalyst, *N*-Boc methyl carbazole-3-carboxylate (**8**)[8b] was isolated, instead of *N*-Boc methyl carbazole-4-carboxylate (**6**) (Entries 4, 5). Considering the yields, $PdCl_2(PhCN)_2$ catalyst is better than $PdCl_2(MeCN)_2$ catalyst. We examined several solvents and Lewis acids, but failed to improve the yields. And we see more reaction time lowered the yields of the reaction.



Scheme 2

Table 1. Selected data of Diels-Alder reaction

Entry	Conditions(Additive, Time)[a]	(**6**)Yield	(**8**)Yield
1	no, 19 h	10%	0%
2	BHT, 21 h	21%	0%
3	$AgNO_3$, 24 h	23% (+8%yield(**7**))	0%
4	$PdCl_2(MeCN)_2$, 10 h	0%	3%
5	$PdCl_2(PhCN)_2$, 9 h	0%	25%

[a] The reaction was carried out in toluene at reflux.

The mechanism involved was not established, but may involve steric effects[8,9] in the palladium-dienophile complex (Figure 3). In the presence of palladium catalyst, Pd was coordinated to the alkyne bond of methyl propiolate. The Diels-Alder reaction was carried on as like maximization of the interaction of diene and dienophile. There were four TS in this case. TS-a,b,c could have more steric repulsion between Pd complex and indole ring, than that of TS-d. TS-d would lead the 3-substituted carbazole (**8**).

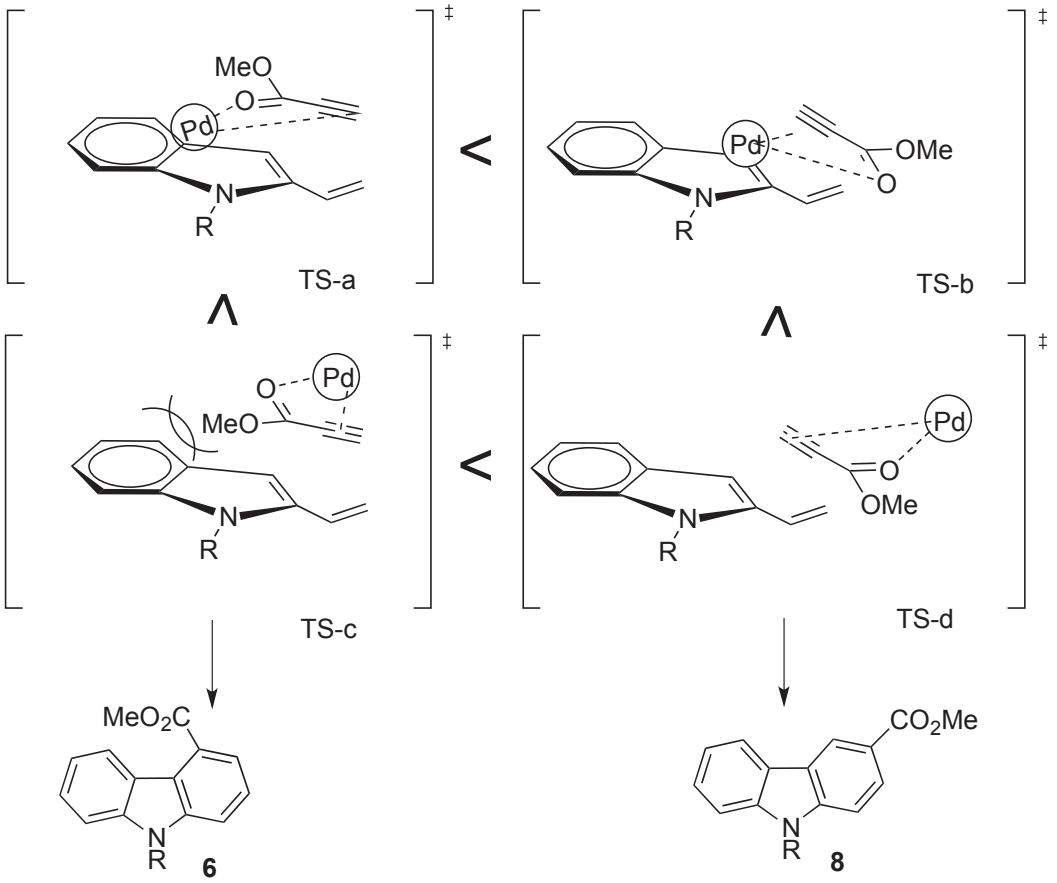
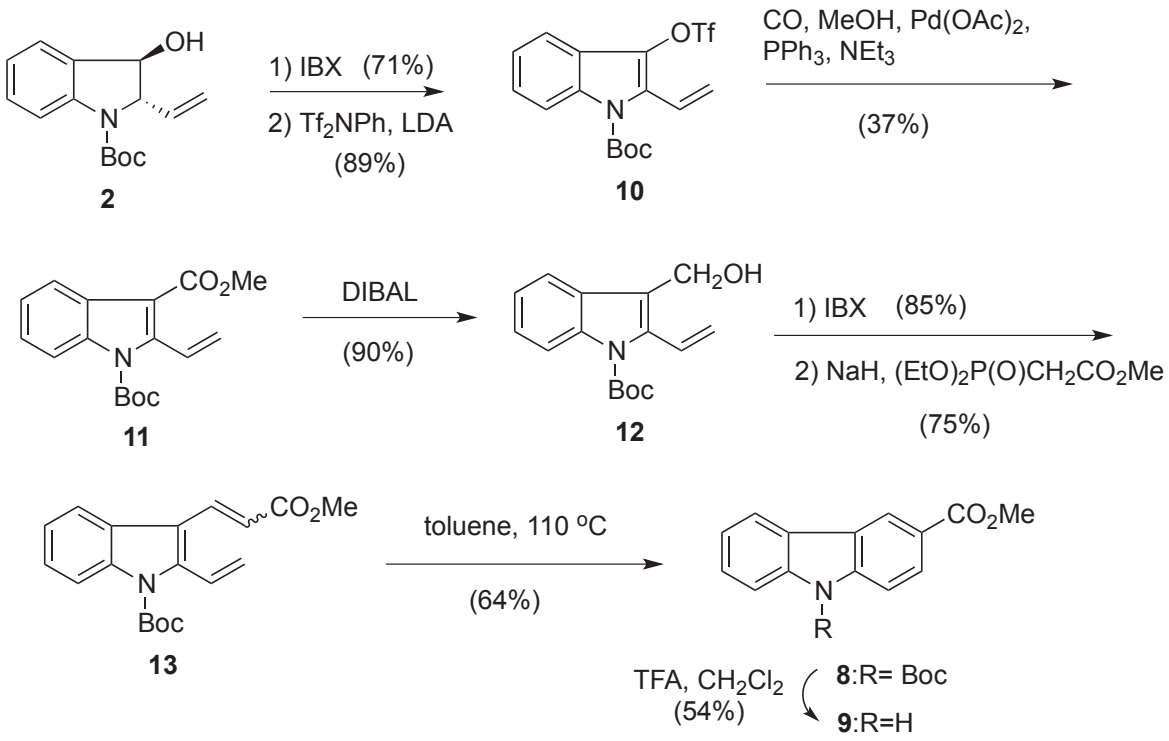


Figure 3

Next, to confirm the natural carbazole,[2c] we examined another synthesis of 3-substituted carbazole (Scheme 3). First, indoline (**2**) was oxidized with IBX to afford the ketone, which was transformed to enol triflate (**10**) by treatment with LDA and Tf_2NPh in THF at -78 °C. Carbonylation of **10** and reduction with DIBAL afforded the alcohol (**12**), which was oxidized and treated with Wittig reagent to afford triene (**13**), which was heated in toluene to afford *N*-Boc methyl carbazole-3-carboxylate (**8**) in 64% yield. At last, the acid treatment of 3-substituted carbazole (**8**) gave the natural methyl carbazole-3-carboxylate (**9**)[5c] in 54% yield. We investigated two different synthesis of the natural methyl carbazole-3-carboxylate (**9**). Former synthesis was short-step, regioselective and convenient method, but it was moderate yield. On the contrary, latter was accessible to many alkaloids, but it was long synthesis.



Scheme 3

In summary, we synthesized 3, 4-substituted, 3-substituted and 4-substituted carbazoles from indoline derivatives by means of Diels-Alder reaction in the presence or absence of Pd catalyst and attained the synthesis of natural methyl carbazole-3-carboxylate (**9**).

EXPERIMENTAL

^{1}H-NMR spectra and ^{13}C-NMR spectra were measured with JEOL JNM-ECX 300/TRH (300 MHz/75 MHz) and JEOL JNM-ECP 600 (600 MHz/150 MHz) spectrophotometers. Chemical shifts were relative to tetramethylsilane or chloroform (7.26 ppm) as an internal standard. Splitting patterns are designated as an s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broadened). Coupling constants were giving in Hz. Infrared spectra (IR) were recorded on JASCO Model FT/IR-7300 spectrophotometer. Data were given only the significant diagnostic bans. Mass spectra (MS) were obtained on JEOL JMS-700 spectrometer.

3-Hydroxy-2-vinyl-2,3-dihydroindole-1-carboxic acid *tert*-butyl ester (**2**)

To a solution of the TBS ether (**1**) (1.7 g, 4.49 mmol) in THF (18 mL) was added tetrabutylammonium fluoride solution (11.23 mL, 1.0 M in THF, 11.23 mmol) at 0 °C under an argon atmosphere, and the mixture was stirred at room temperature for 4 h. The mixture was quenched by an addition of saturated aqueous NH_4Cl. The mixture was extracted with Et_2O (7 mL x 3). The combined organic layers were

washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (3:7) as an eluent to afford the alcohol (**2**) (886 mg, 75%).

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.00-7.60 (brs, 1H), 7.38-7.35 (m, 1H), 7.34-7.31 (m, 1H), 7.04-7.01 (m, 1H), 5.72 (ddd, *J* = 6.60, 10.4, 17.1 Hz, 1H), 5.19 (dt, *J* = 1.20, 17.1 Hz, 1H), 5.12 (dt, *J* = 1.20, 10.4 Hz, 1H), 4.74 (d, *J* = 3.3 Hz, 1H), 4.68 (brs, 1H), 1.53 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 152.09, 134.60, 130.42, 125.73, 122.81, 115.84, 115.51, 75.46, 70.71, 60.39, 28.29, 20.99, 14.14.

IR(KBr) cm^{-1}; 3630-3100, 3100-2800.

EIMS *m/z* 261(M^+); HREIMS calcd. for $C_{15}H_{19}NO_3$ (M^+) 261.1365, found 261.1370.

***tert*-Butyl 2-vinylindole-1-carboxylate (3)**

To a solution of the alcohol (**2**) (151.4 mg, 0.58 mmol) and pyridine (0.14 mL, 1.74 mmol) in CH_2Cl_2 (5.8 mL) was added MsCl (0.07 mL, 0.87 mmol) at 0 ºC under an argon atmosphere, and the mixture was stirred at same temperature for 7 h. The reaction mixture was quenched with 1 N-HCl, saturated aqueous $NaHCO_3$ solution, and dry over $MgSO_4$. The filtrate was concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (1:9-1:1) as an eluent to afford the diene (**3**) (116.8 mg, 83%). The spectra of this diene (**3**) were in agreement with reported data.[6a,7]

***N-tert*-Butoxycarbonyldimethyl carbazole-3,4-dicarboxylate (4)**

To a solution of *N*-Boc-2-vinylindole (**3**) (10.0 mg, 0.041 mmol) in toluene (0.82 mL) was added dimethyl acetylenedicarboxylate (7.5 μL, 0.062 mmol) under argon atmosphere. The mixture was heated at reflux. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 1 / 6) to afford the *N*-Boc-carbazole (**4**) (9.5 mg, 60%).

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.48-8.45 (m, 1H), 8.34-8.30 (m, 1H), 8.18-8.14 (m, 1H), 7.85-7.82 (m, 1H), 7.55-7.50 (m, 1H), 7.39-7.34 (m, 1H), 4.14 (s, 3H), 3.96 (s, 3H), 1.77 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 169.45, 166.09, 150.52, 141.44, 139.15, 129.15, 128.64, 128.20., 123.71, 123.26, 122.31, 121.69, 121.08, 116.60, 116.29, 85.11, 53.04, 52.49, 28.31.

IR (KBr) cm^{-1}; 2946, 1721, 1584, 1437, 1365, 1278.

EIMS *m/z* 383(M^+); HREIMS calcd. for $C_{21}H_{21}NO_6$ (M^+) 383.1369, found 383.1367.

Dimethyl carbazole-3,4-dicarboxylate (5)

To a solution of the *N*-Boc-carbazole (**4**) (9.2 mg, 0.024 mmol) in CH_2Cl_2 (0.72 mL) was added TFA (0.11 mL) at 0 ºC under argon atmosphere. The mixture was stirred 15 min at same temperature, and allowed to warm to rt. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 1 /3) to afford the *N*-H-carbazole (**5**) (5.1 mg, 75%).

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.47-8.43 (brs, 1H), 8.10-8.07 (m, 1H), 7.93-7.89 (m, 1H), 7.49-7.44 (m, 3H), 7.28-7.25 (m, 1H), 4.16 (s, 3H), 3.94 (s, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 169.99, 166.62, 142.08, 140.06, 129.97, 127.60, 127.18, 121.56, 121.38, 120.80, 119.82, 118.32, 111.00, 110.91, 52.95, 52.30.
IR (KBr) cm^{-1} ; 3408, 3018, 2952, 1725, 1694, 1625, 1599, 1580, 1499, 1459.
EIMS *m/z* 283(M^+); HREIMS calcd. for $C_{16}H_{13}NO_4$ (M^+) 283.0845, found 283.0836.

***N-tert*-Butoxycarbonyl methyl carbazole-4-carboxylate (6)**

To a solution of *N*-Boc-2-vinylindole (**3**) (22.0 mg, 0.09 mmol) in toluene (1.8 mL) was added methyl propiolate (7.5 μL, 0.09 mmol) under argon atmosphere. The mixture was heated at reflux for 19 h. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 3 / 97) to afford the carbazole (**6**) (3.0 mg, 10%).
^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.70-8.60 (m, 2H), 8.37-8.33 (m, 1H), 7.88-7.84 (m, 1H), 7.53-7.48 (m, 2H), 7.38-7.33 (m, 1H), 4.06 (s, 3H), 1.77 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 168.34, 150.87, 139.51, 139.14, 127.89, 126.03, 125.48, 124.59, 124.45, 124.12, 123.03, 119.96, 115.76, 84.50, 52.37, 28.39.
IR (KBr) cm^{-1} ; 2979, 1727, 1591, 1477, 1451, 1242, 1394.
EIMS *m/z* 325(M^+); HREIMS calcd. for $C_{19}H_{19}NO_4$ (M^+) 325.1314, found 325.1300.

Methyl carbazole-4-carboxylate (7)

To a solution of the *N*-Boc-carbazole (**6**) (12.0 mg, 0.037 mmol) in CH_2Cl_2 (1.11 mL) was added TFA (0.11 mL) at 0 °C under argon atmosphere. The mixture was stirred 15 min at same temperature, and allowed to warm to rt. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 1 /6) to afford the *N*-H-carbazole (**7**) (8.0 mg, 96%). The spectra of this carbazole (**7**) were in agreement with reported data.[8a]
^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.87-8.83 (m, 1H), 8.28 (brs, 1H), 7.89-7.86 (m, 1H), 7.65-7.62 (m, 1H), 7.49-7.42 (m, 3H), 7.29-7.24 (m, 1H), 4.07 (s, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 168.38, 140.26, 140.22, 126.87, 125.66, 125.33, 124.79, 122.76, 121.94, 119.82, 114.88, 110.33, 52.14, 29.71.
IR (KBr) cm^{-1} ; 3407, 2950, 1703, 1620, 1604, 1573, 1504, 1457, 1437, 1324, 1308.
EIMS *m/z* 225(M^+).

***N-tert*-Butoxycarbonyl methyl carbazole-3-carboxylate (8)**

To a solution of the *N*-Boc-2-vinylindole (**3**) (97.6 mg, 0.40 mmol) in toluene (10 mL) was added methyl propiolate (49.7 mg, 0.59 mmol) and bis(benzonitrile)palladium(II) dichloride (17.5 mg, 4.6×10^{-2} mmol)

under argon atmosphere. The mixture was heated at reflux. The reaction mixture was filtered through a short pass silica gel and filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 3 / 97) to afford the carbazole (**8**) (33 mg, 25%).

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.70-8.69 (m, 1H), 8.38-8.35 (m, 1H), 8.31-8.29 (m, 1H), 8.18-8.15 (m, 1H), 8.06-8.04 (m, 1H), 7.52-7.49 (m, 1H), 7.42-7.38 (m, 1H), 3.99 (s, 3H), 1.78 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 167.26, 150.81, 141.45, 139.03, 128.48, 127.70, 125.76, 125.32, 124.88, 123.48, 121.58, 119.93, 116.39, 115.95, 84.64, 52.15, 28.37.

IR (neat) cm^{-1} ; 2934, 1725, 1604, 1452, 1432.

EIMS *m/z* 325(M^+) ; HREIMS calcd. for $C_{19}H_{19}NO_4$ (M^+) 325.1314, found 325.1331.

Methyl carbazole-3-carboxylate (**9**)

To a solution of the *N*-Boc-carbazole (**8**) (34.1 mg, 0.105 mmol) in CH_2Cl_2 (3.0 mL) was added TFA (4 drops) at 0 ºC under argon atmosphere. The mixture was stirred 15 min at same temperature, and allowed to warm to rt for 21 h. The reaction mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (AcOEt / *n*-hexane, 1 /6) to afford the *N*-H-carbazole (**9**) (12.7 mg, 54%). The spectra of this carbazole (**9**) were in agreement with reported data.[2c, 5c]

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.82 (d, *J* = 1.4 Hz, 1H), 8.14-8.12 (m, 2H), 7.48-7.43 (m, 3H), 7.31-7.28 (m, 1H), 3.98 (s, 3H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ ; 167.88, 142.25, 139.90, 127.45, 126.56, 123.31, 123.12, 122.89, 121.41, 120.62, 120.35, 110.88, 110.12, 51.95.

IR (KBr) cm^{-1} ; 3327, 2923, 2854, 1689, 1625, 1604, 1456, 1263.

EIMS *m/z* 225(M^+).

3-Methoxycarbonyl-2-vinyl- indole-1-carboxic acid *tert*-butyl ester (**11**)

To a solution of the alcohol (**2**) (445 mg, 1.7 mmol) in DMSO (8.5 mL) was added IBX (5.4 g, 19.2 mmol) under an argon atmosphere, and the mixture was stirred at rt. After the reaction was completed, the reaction mixture was quenched by an addition of saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$. The mixture was extracted with Et_2O (3 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (1:9) as an eluent to afford the ketone (315 mg, 71%).

A solution of potassium bis(trimethylsilyl)amide (1.2 mL, 0.5 M in toluene, 0.6 mmol) in THF (2 mL) was cooled to -78 ºC under a nitrogen atmosphere. The ketone (104 mg, 0.4 mmol) in THF (1 mL) was added to the solution at -78 ºC and the solution was stirred for 1 h. To a solution was added a solution of *N*-phenyl-bistrifluoromethanesulfonimide (257 mg, 0.72 mmol) in THF (1 mL) at -78 ºC. After 30 min,

the reaction mixture was quenched by an addition of saturated aqueous NH_4Cl. The mixture was extracted with AcOEt (1 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (3:97) as an eluent to afford the enol triflate (**10**) (140 mg, 89%).

To a solution of palladium diacetate (21 mg, 0.092 mmol) and triphenylphosphine (81 mg, 0.31 mmol) in MeOH (1.5 mL) was added triethylamine (0.28 mL, 1.86 mmol) and the enol triflate (**10**) (120 mg, 0.31 mmol) in MeOH (1.5 mL) under a carbon monoxide atmosphere, and the mixture was stirred at 60 ^oC. After the reaction was completed, the reaction mixture was cooled to rt, and quenched with saturated aqueous NH_4Cl solution. The mixture was extracted with CH_2Cl_2 (3 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (1:19) as an eluent to afford the ester (**11**) (34 mg, 37%).

^{1}H-NMR(600 MHz, $CDCl_3$) δ ; 8.08- 8.03 (m, 2H), 7.36-7.29 (m, 2H), 7.15 (dd, *J* = 11.6, 17.6 Hz, 1H), 5.65 (dd, *J* = 1.47, 11.6 Hz, 1H), 5.57 (dd, *J* = 1.47, 17.6 Hz, 1H), 3.92 (s, 3H), 1.66 (s, 9H).

^{13}C-NMR(150 MHz, $CDCl_3$) δ ; 165.28, 149.80, 143.16, 135.78, 127.75, 127.10, 125.00, 123.74, 121.76, 121.65, 114.59, 111.11, 85.30, 51.36, 29.68, 28.03.

IR (KBr) cm^{-1} ; 2980, 2950, 1740, 1706.

EIMS *m/z* 301(M^+); HREIMS calcd. for $C_{17}H_{19}NO_4$ (M^+) 301.1314, found 301.1308.

3-Hydroxymethyl-2-vinylindole-1-carboxic acid *tert*-butyl ester (12)

To a solution of the ester (**11**) (15.2 mg, 0.051 mmol) in THF (0.25 mL) was added DIBAL-H (0.5 mL, 1.0 M in *n*-hexane, 0.5 mmol) at -78 ^oC under an argon atmosphere, and the mixture was stirred at same temperature for 2.5 h. The reaction mixture was quenched with saturated aqueous Na_2SO_4 solution, and filtered through a celite. The filtrate was concentrated *in vacuo*. The residue was purified by column chromatography using AcOEt / *n*-hexane (1:9-1:1) as an eluent to afford the alcohol (**12**) (12.5 mg, 90%).

^{1}H-NMR (600 MHz, $CDCl_3$) δ ; 8.10 (d, *J* = 8.43 Hz, 1H), 7.71 (d, *J* = 8.43 Hz, 1H), 7.34-7.30 (m, 1H), 7.28-7.26 (m, 1H), 7.01 (dd, *J* = 11.4, 17.6 Hz, 1H), 5.55 (dd, *J* = 1.83, 17.6 Hz, 1H), 5.54 (dd, *J* = 1.83, 11.4 Hz, 1H), 4.84 (s, 2H), 1.68 (s, 9H).

^{13}C-NMR (150 MHz, $CDCl_3$) δ; 150.5, 137.5, 135.6, 129.2, 128.3, 124.8, 122.98, 119.0, 118.97, 115.6, 84.37, 55.9, 28.2.

IR(KBr) cm^{-1}; 3600-3100, 2976, 2930, 1717.

EIMS *m/z* 273(M^+); HREIMS calcd. for $C_{16}H_{19}NO_3$ (M^+) 273.1365, found 273.1363.

3-(2-Methoxycarbonyl-ethenyl)-2-vinylindole-1-carboxic acid *tert*-butyl ester (13)

To a solution of the alcohol (**12**) (5.5 mg, 0.020 mmol) in DMSO (0.1 mL) was added IBX (17 mg, 0.06 mmol) under an argon atmosphere, and the mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by addition of saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$. The mixture was extracted with Et_2O (1 mL × 3). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using AcOEt / *n*-hexane (3:17 – 1:2) mixture as eluent to afford the aldehyde (4.7mg, 85%).

To a suspension of NaH (2.9 mg, 55% in mineral oil, 0.066 mmol) in THF (0.2 mL) was added dropwise a solution of the phosphonate (15.6 mg, 0.074 mmol) in THF (0.1 mL) at 0 ℃ under an argon atmosphere and the mixture was stirred at room temperature for 30 min. The mixture was cooled to 0 ℃ and a solution of the aldehyde (11.1 mg, 0.041 mmol) in THF (0.1 mL) was added. The reaction mixture was stirred at rt for 2 h, and quenched with 10% HCl aqueous solution. The aqueous layer was extracted with Et_2O (1 mL × 3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using AcOEt / *n*-hexane (3:97) mixture as eluent to afford the ester (**13**) (16 mg, 75%).

^{1}H-NMR(600 MHz, $CDCl_3$) δ ; 8.19-8.16 (m, 0.5H), 8.12-8.07 (m, 0.5H), 7.92-7.87 (m, 1H), 7.38-7.20 (m, 2H), 7.17-7.02 (m, 1H), 6.95-6.905 (m, 0.5H), 6.63-6.58 (m, 0.5H), 6.15-6.11 (m, 0.5H), 5.75-5.72 (m, 0.5H), 5.62-5.58 (m, 0.5H), 5.45-5.41 (m, 1H), 3.82 (s, 1.5H), 3.57 (s, 1.5H), 1.697 (s, 9H).

***N-tert*-Butoxycarbonyl methyl carbazole-3-carboxylate (8)**

A solution of the triene (**13**) (3 mg, 9.61×10^{-3} mmol) in toluene (2 mL) was heated to 110 ºC under an argon atmosphere and the solution was stirred. After the reaction was completed, the reaction mixture was cooled to rt, and washed with water and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using AcOEt / *n*-hexane (3:97) mixture as eluent to afford the methyl *N*-Boccarbazole-3-carboxylate (**8**) (1.9 mg, 64%).

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9. See ref 8a that the steric effects were dominant in similar Diels-Alder reaction. And similar reversal of regioselectivity by Lewis acid(e.g. $AlCl_3$, Me_2AlCl) were reported in ref 8b.