Supporting Information

AN EFFICIENT SYNTHESIS OF (±)-CYCLOILLICINONE

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General

All chemicals were obtained from commercial suppliers and used without further purification. Anhydrous THF was distilled from sodium/benzophenone before use. Anhydrous dichloromethane was distilled from calcium hydride (10 % w/v) under positive pressure of nitrogen. The other anhydrous solvents and reagents were purchased from Aldrich or Fisher. All reactions were carried out under nitrogen atmosphere unless specified. NMR spectra were obtained using a Jeol ECA 400 (400 MHz) and EX 270 (270 MHz) NMR spectrometers with TMS as the internal standard. All chemical shifts are reported in ppm. Mass spectra were recorded on a Agilent G6530A Accurate-Mass Q-TOF LC/MS spectrometer. HPLC was carried out on a Waters HPLC system equipped with a Daicel Chiralpak IC chiral column (150mm x 4.6mm x 5μm). Analytical thin layer chromatography (TLC) was carried out on Merck precoated aluminum silica gel sheets (Kieselgel 60 F-254). Column chromatography was done with silica gel 60 (230-400 mesh) from Merck. All target compounds were characterized by ¹H, ¹³C, 2D NMR and MS analyses.

Synthesis of (±)-cycloillicinone (1)

To a solution of (*S*)-(-)-*o*-tolyl-CBS-oxazaborolidine (0.5 M solution in toluene, 400 μL, 0.2 mmol) at -25 °C was added trifluoromethanesulfonimide (0.5 M solution in CH₂Cl₂, freshly prepared, 400 μL, 0.2 mmol) dropwise. After 10 min at -25 °C, a colorless homogeneous catalyst solution was formed. A solution of illicinone A (**7**) (246 mg, 1 mmol) in CH₂Cl₂ (1.0 mL) and β-*trans*-ocimene (666 μL, 544 mg, 4 mmol) were added successively at -78 °C. The reaction mixture was stirred for 2 h at -40 °C and then another 8 h at room temperature before quenched by addition of 20 μL of Et₃N. The solvent was removed by rotary evaporation and the residue was purified by silica gel chromatography (gradient elution with 10-20% EtOAc-hexanes) to afford adduct (**1**) (210 mg, 55%).

Table S1. Diels-Alder reaction of illicinone A **7** and β -*trans*-ocimene

Entry	Conditions ^a	mol %	Solvent	Temp (°C)	Time (h)	Isolated yield (%) ^b			
						($\pm$)- 1	5	6	8
1	Thermal condition in pressure tube	-	toluene	130	24	47	35	10	2
2	-	-	toluene	rt	2	-	-	-	-
3	CF ₃ SO ₃ H	20	CH ₂ Cl ₂	-20°C	2	16	55	10	8
4	CF ₃ SO ₃ H	20	toluene	-20°C	2	15	50	10	5
5	ZnCl ₂	20	CH ₂ Cl ₂	-20°C	36	25	-	-	-
6	ZnCl ₂	20	toluene	-20°C	36	20	-	-	-
7	AlCl ₃	20	CH ₂ Cl ₂	-20°C	2	29	45	5	2
8	AlCl ₃	20	toluene	-20°C	2	29	45	5	3
9	BF ₃ ·Et ₂ O	20	CH ₂ Cl ₂	-20°C	2	30	35	10	15
10	BF ₃ ·Et ₂ O	20	toluene	-20°C	2	30	35	10	15
11	(<i>S</i>)-(-)- <i>o</i> -tolyl-CBS-oxazaborolidine, Tf ₂ NH activated	20	CH ₂ Cl ₂	-40°C to rt	8	55	-	-	-
12	(<i>S</i>)-(-)- <i>o</i> -tolyl-CBS-oxazaborolidine, Tf ₂ NH activated	20	toluene	-40°C to rt	8	50	-	-	-
13	(<i>S</i>)-(-)- <i>o</i> -tolyl-CBS-oxazaborolidine, Tf ₂ NH activated	20	THF	-40°C to rt	8	15	-	-	-
14	TiCl ₄	20	CH ₂ Cl ₂	-20°C	2	-	-	-	-
15	AlBr ₃	20	CH ₂ Cl ₂	-20°C	2	-	-	-	-
16	Et ₂ AlCl	20	CH ₂ Cl ₂	-20°C	2	-	-	-	-

^a Reaction conditions: dienophile **7** (1.0 equiv), diene β -*trans*-ocimene (4 equiv), catalyst 20 mol%, solvent 4ml/mmol.

^b Isolated yield after chromatography.

Table S2 ^1H NMR for synthetic ($\pm$)-cycloillicinone **1** compared with literature data.

Position	^1H NMR data δ ($J_{\text{H-H}}$ in Hz) ^a		
	Synthetic (400 MHz, CDCl_3)	Literature ^{S1} (600 MHz, CDCl_3) ^b	Literature ^{S2} (400 MHz, CDCl_3) ^c
H-3	2.51 (m)	2.51 (dd, $J = 11.5, 6.0$)	2.50 (m)
H-6	5.55 (s)	5.55 (s)	5.54 (s)
H ₂ -7	2.36 (dd, $J = 13.9, 6.8$) 2.52 (dd, $J = 14.0, 8.0$)	2.36 (dd, $J = 14.0, 6.9$) 2.56 (dd, $J = 14.0, 8.0$)	2.36 (dd, $J = 13.8, 6.7$) 2.55 (dd, $J = 13.8, 8.1$)
H-8	5.85 (m)	5.75 (dddd, $J = 17.0, 8.0, 7.9, 6.9$)	5.85 (m)
H ₂ -9	5.00 (d, $J = 9.5$) 5.04 (d, $J = 17.1$)	5.00 (d, $J = 7.9$) 5.04 (d, $J = 17.0$)	5.00 (d, $J = 9.5$) 5.13 (d, $J = 17.3$)
H ₂ -10	2.17 (dd, $J = 15.6, 7.6$) 2.49 (dd, $J = 15.4, 5.8$)	2.17 (dd, $J = 15.4, 7.8$) 2.49 (dd, $J = 15.4, 5.8$)	2.17 (dd, $J = 15.6, 7.3$) 2.45 (m)
H-11	5.16 (br, s)	5.16 (dd, $J = 7.8, 5.8$)	5.16 (br s)
Me-13	1.72 (s)	1.72 (s)	1.72 (s)
Me-14	1.57 (s)	1.56 (s)	1.57 (s)
H ₂ -15	5.41 (s) 5.55 (s)	5.41 (s) 5.55 (s)	5.41 (s) 5.44 (s)
H ₂ -16	1.95 (m) 2.23 (m)	1.97 (ddd, $J = 15.1, 11.5, 5.5$) 2.23 (ddd, $J = 15.1, 7.4, 6.0$)	1.95 (m) 2.23 (m)
H-17	5.59 (d, $J = 5.0$)	5.59 (ddq, $J = 7.4, 5.5, 1.6$)	5.59 (d, $J = 4.9$)
Me-19	1.68 (s)	1.68 (d, $J = 1.6$)	1.68 (s)
H-20	2.12 (dd, $J = 10.2, 4.6$)	2.12 (dd, $J = 10.4, 4.7$)	2.12 (dd, $J = 10.2, 4.6$)
H ₂ -21	1.95 (m)	1.93 (m)	1.95 (m)
H-22	5.00 (m)	4.99 (m)	5.00 (m)
Me-24	1.50 (s)	1.50 (s)	1.50 (s)
Me-25	1.63 (s)	1.63 (s)	1.63 (s)

^a Chemical shifts (δ) measured in ppm. ^b Natural product cycloillicinone. ^c Natural product illicarbonene A. ^{S1} Kubo, M.; Shima, N.; Harada, K.; Fukuyama, Y. *Chem. Pharm. Bull.* **2011**, 59, 898-901. ^{S2} Liaw, C. C.; Chen, Y. C.; Fazary, A. E.; Hsieh, J. L.; Chen, S. Y.; Chien, C. T.; Sheu, S. Y.; Kuo, Y. H.; Chiang, B. L.; Shen, Y. C. *Phytochemistry Lett.* **2013**, 6, 397-402.

Table S3 ^{13}C NMR data for synthetic ($\pm$)-cycloillicinone **1** compared with literature data.

Position	^{13}C NMR data ^a		
	Synthetic (100 MHz, CDCl_3)	Literature ^{S1} (150 MHz, CDCl_3) ^b	Literature ^{S2} (100 MHz, CDCl_3) ^c
C-1	201.5	201.5	201.5
C-2	53.9	53.9	53.9
C-3	40.8	40.7	40.8
C-4	83.9	83.9	83.9
C-5	172.6	172.6	172.6
C-6	99.4	99.4	99.3
C-7	45.2	45.2	45.2
C-8	134.9	134.9	134.9
C-9	118.0	118.0	118.0
C-10	37.2	37.1	37.2
C-11	116.6	116.5	116.5
C-12	136.4	136.4	136.3
C-13	18.3	18.4	18.3
C-14	25.9	25.9	25.9
C-15	97.9	97.9	97.9
C-16	24.0	24.0	24.0
C-17	121.6	121.6	121.6
C-18	142.1	142.1	142.1
C-19	24.3	24.4	24.3
C-20	51.3	51.3	51.3
C-21	29.7	29.7	29.7
C-22	123.4	123.4	123.4

C-23	132.1	132.2	132.1
C-24	17.8	17.8	17.8
C-25	25.6	25.6	25.6

^a Chemical shifts (δ) measured in ppm. ^b Natural product cycloillicinone. ^c Natural product illicarbonene A. ^{S1} Kubo, M.; Shima, N.; Harada, K.; Fukuyama, Y. *Chem. Pharm. Bull.* **2011**, 59, 898-901. ^{S2} Liaw, C. C.; Chen, Y. C.; Fazary, A. E.; Hsieh, J. L.; Chen, S. Y.; Chien, C. T.; Sheu, S. Y.; Kuo, Y. H.; Chiang, B. L.; Shen, Y. C. *Phytochemistry Lett.* **2013**, 6, 397-402.

Figure S1 HPLC chromatogram of separation of ($\pm$)-cycloillicinone by Daisel Chiralpak IC chiral column (150mm x 4.6mm x 5 μ m). Experimental conditions: flow rate: 1.0 ml/min; solvent system: *n*-hexane: isopropanol (100:0; 92:8; 80:20, v/v)

Figure S2 ESI-MS of (±)-cycloillicinone (**1**)

Figure S3 ^1H NMR of ($\pm$)-cycloillicinone

Figure S4 ^{13}C NMR of ($\pm$)-cycloillicinone

Figure S5 NOESY spectrum of ($\pm$)-cycloillicinone