Palladium-Catalyzed Enantioselective Carbonylative Cyclization of Aryl and Alkenyl Triflates with Carbon Monoxide

Tamio Hayashi,* Jun Tang, and Kazuhiko Kato

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

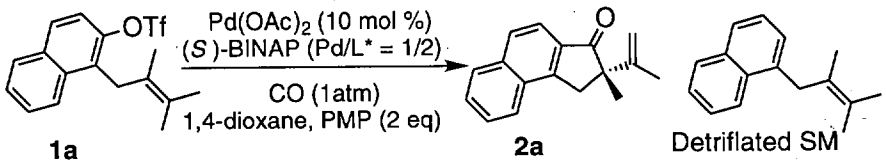
Supporting Data

General. All manipulations were carried out under a nitrogen atmosphere using conventional Schlenk techniques. ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra at 125 MHz in $CDCl_3$.

Materials. 1-(2,3-Dimethyl-2-butenyl)-2-naphthyl triflate (**1a**) was prepared by palladium-catalyzed addition of 2-naphthol to 2,3-dimethylbutadiene,[1] followed by treatment of the resulting 1-(2,3-dimethyl-2-butenyl)-2-naphthol with trifluoromethanesulfonic anhydride and pyridine in dichloromethane. A similar method was used for the preparation of **1b** and **1c**. Aryl triflates **1d~1j** were derived from the corresponding 2-(2,3-dimethyl-2-butenyl)phenol precursors. Alkenyl triflates **1k** and **1l** were prepared by the reported method.[2] Dioxane was distilled under nitrogen from sodium/benzophenone ketyl. Benzene was distilled from CaH_2. $Pd(OCOCF_3)_2$ was purchased from Fluka Chemical Co. Inc. PMP was purchased from Aldrich Chemical Co. Inc. Palladium diacetate was purified by recrystallization from hot benzene before use.

Catalytic Carbonylative Cyclization. Effects of solvents, chiral ligands, and palladium precursors on the reaction of **1a** are shown in text. We have also examined other factors including the temperature, amines, the ratio of palladium/ligands, CO pressure and the addition of MS 4A. Those effects are summarized in Tables 1~3.

Table 1. Effect of Temperature and the Addition of MS 4A on the Asymmetric Catalytic Carbonylative Cyclization of **1a**[a]

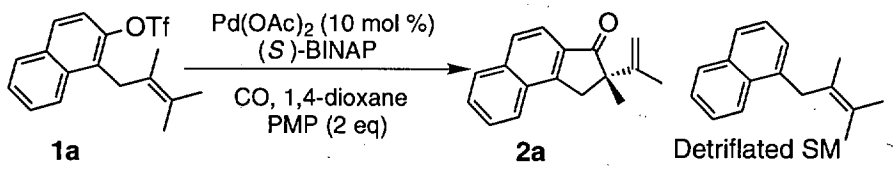


			(*S*)-**2a**		detriflated SM	SM recovery
entry	temp (°C)	time (h)	yield (%)[b]	%ee[c]	yield (%)[b]	yield (%)[b]
1	60	7	31	97	trace	60
2	70	7	54	95	trace	23
3	80	2.5	53	93	18	trace
4	80[d]	2.5	65	95	trace	20
5	100	2.5	13	92	50	trace

[a] The reaction was carried out with **1a** (0.2 mmol) in 1.8 mL of solvent under 1 atm of CO. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2). [d] In the presence of 50 mg of MS 4A.

Table 1 summarizes the effect of temperature and the addition of MS 4A, showing the general improving trend of % ee with the decreasing of temperature accompanied with the decreasing of the yield of **2a**. MS 4A plays an important role in preventing the generation of detriflated starting materials through the trapping of trace water presenting in the reaction system.

Table 2. Effect of CO Pressure and Palladium/Ligand Ratio on the Asymmetric Catalytic Carbonylative Cyclization of **1a**[a]

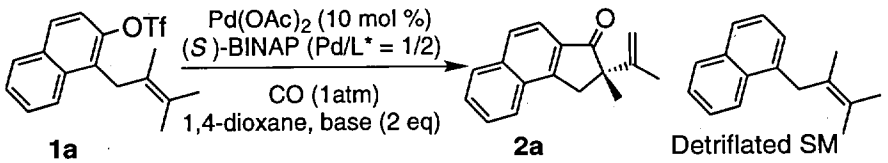


entry	Pd/ (S)-binap	CO pressure (atm)	(*S*)-**2a** yield (%)[b]	(*S*)-**2a** %ee[c]	detriflated SM yield (%)[b]	SM recovery yield (%)[b]
1	1	1	trace	ND	trace	87
2	0.5	0.3[d]	21	ND	14	41
3	0.5	1	53	93	18	trace
4	0.5	5	trace	ND	trace	85
5	0.3	1	57	93	14	trace

[a] The reaction was carried out with **1a** (0.2 mmol) in 1.8 mL of dioxane for 2.5 h. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2). [d] CO and N_2 mixture was used.

From the results shown in Table 2, 1 atm of CO pressure is mostly suitable to this asymmetric carbonylative cyclization. High CO pressure inhibits the reaction and low CO pressure results in sluggish reaction speed. When the ratio of Ligand/Pd is less than 2, Pd black precipitates to result in low conversion of triflate.

Table 3. Effect of Bases on the Asymmetric Catalytic Carbonylative Cyclization of **1a**[a]



		(*S*)-**2a**		detriflated SM	SM recovery
entry	base	yield (%)[b]	%ee[c]	yield (%)[b]	yield (%)[b]
1	proton sponge	60	95	trace	15
2	PMP	53	93	18	3
3	$^{i}Pr_2NEt$	40	93	24	trace
4	Cs_2CO_3	26	16.5	trace	trace
5	none	10	ND	trace	78

[a] The reaction was carried out with **1a** (0.2 mmol) in 1.8 mL of dioxane under 1 atm of CO for 2.5 h. Initial conditions: Pd precursor:Ligand:**1a**:base = 0.1:0.2:1:2. [b] Isolated yield by silica gel chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2).

Tertiary amines such as proton sponge, diisopropylethylamine, 1,2,2,6,6-pentametylpiperidine (PMP) are effective to this reaction. In contrast, inorganic bases such as Cs_2CO_3 resulted in obvious loss of enantioselectivity. In the absence of amine, the reaction proceeds slowly.

A Typical Procedure for Asymmetric Carbonylative Cyclization of 1a. A mixture of $Pd(OCOCF_3)_2$ (6.8 mg, 0.02 mmol), (*S*)-binap (25.6 mg, 0.04 mmol) and MS 4A (50 mg) was pumped up and changed to CO atmosphere. Dioxane (0.8 mL) was added to the above system and the mixture was stirred at room temperature for 10 min. Triflate **1a** (70.6 mg, 0.2 mmol) and PMP (62.1 mg, 0.4 mmol) in 1 mL dioxane were added to the resulting red suspention and the whole mixture was further stirred for another 10 min. The reaction mixture was heated at 80 °C under 1 atm of CO for 2.5 h and then eluted with a shot silica gel column (EtOAc) and evaporated under reduced pressure to give the crude residue. The residue was purified by preparative TLC (hexane/EtOAc=10/1) to give **(*S*)-2-isopropenyl-2-methyl-1-benzo[*e*]indanone (2a)** (42 mg, 89% yield). The enantiomeric excess was determined to be 95% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2): $[\alpha]_D^{20}$ +28.3 (c 0.78, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.47 (s, 3H), 1.67 (s, 3H), 3.25 (d, *J* = 17.7 Hz, 1H), 3.60 (d, *J* = 17.7 Hz, 1H), 4.99 (dq, *J* = 1.3, 1.3 Hz, 1H), 5.03 (br s, 1H), 7.62 (dd, *J* = 8.0, 8.2 Hz, 1H), 7.66 (dd, *J* = 8.0, 8.2 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 19.74, 22.67, 39.64, 54.38, 112.01, 119.98, 124.34, 126.99, 128.63, 128.85, 129.17, 130.20, 133.18, 136.69, 145.81, 153.78, 208.75. Anal. calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.54, H, 6.79.

(*S*)-2-Isopropenyl-2-methyl-1-benzo[*g*]indanone (2b). The enantiomeric excess was determined to be 93% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2, 82% yield): $[\alpha]_D^{20}$ –3.24 (c 0.65, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.44 (s, 3H), 1.66 (br s, 3H), 3.03 (d, *J* = 17.9 Hz, 1H), 3.40 (d, *J* = 17.9 Hz, 1H), 4.97 (dq, *J* = 1.4, 1.4 Hz, 1H), 5.01 (br s, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.54 (dd, *J* = 8.2, 8.3 Hz, 1H), 7.66 (dd, *J* = 8.3, 8.5 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 9.17 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR δ 19.80, 22.72, 41.53, 54.68, 111.98, 123.78, 124.02, 126.57, 128.09, 128.91, 129.67, 129.70, 132.79, 135.98, 146.09, 155.81, 209.47. Anal. calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.49, H, 6.80.

(*S*)-2-Isopropenyl-6-methoxy-2-methyl-1-benzo[*e*]indanone (2c). The enantiomeric excess was determined to be 96% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 94% yield): White solid (mp 92~93 °C); $[\alpha]_D^{20}$ +27.3 (c 1.38, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.47 (s, 3H), 1.68 (br s, 3H), 3.22 (d, *J* = 17.5 Hz, 1H), 3.57 (d, *J* = 17.5 Hz, 1H), 3.97 (s, 3H), 4.99 (dq, *J* = 1.2, 1.2 Hz, 1H), 5.03 (br s, 1H), 7.25 (d, *J* = 2.6 Hz, 1H), 7.33 (dd, *J* = 2.6, 9.1 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H) ; ^{13}C NMR δ 19.83, 22.78, 39.87, 54.51, 55.44, 102.86, 112.02, 117.82, 121.34, 128.35, 130.40, 131.52, 132.01, 133.67, 146.01, 152.32, 158.52, 209.08. Anal. calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.13, H, 6.78.

(*S*)-2-Isopropenyl-2,4,6-trimethyl-1-indanone (2d). The enantiomeric excess was determined to be 93% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 90% yield): $[\alpha]_D^{20}$ +6.88 (c 0.96, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.37 (s, 3H), 1.64 (br s, 3H), 2.31 (s, 3H), 2.37 (s, 3H), 2.79 (d, *J* = 17.4 Hz, 1H), 3.15 (d, *J* = 17.4 Hz, 1H), 4.94 (dq, *J* = 1.2, 1.2 Hz, 1H), 4.95 (br s, 1H), 7.26 (s, 1H), 7.42 (s, 1H); ^{13}C NMR δ 17.67, 19.83, 20.97, 22.72, 39.89, 54.74, 111.79, 121.83, 135.24, 135.85, 136.72, 137.65, 146.12, 148.96, 209.49. Anal. calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.90, H, 8.77.

(*S*)-2-Isopropenyl-5-methoxy-2-methyl-1-indanone (2e). A typical procedure using $Pd(OCOCF_3)_2$/(*S*)-tol-binap/benzene system is as follows: A mixture of $Pd(OCOCF_3)_2$ (6.8 mg, 0.02 mmol), (*S*)-tol-binap (27.2 mg, 0.04 mmol) and MS 4A (50 mg) was pumped up and changed to CO atmosphere. Benzene (0.8 mL) was added to the above system and the mixture was stirred at room temperature for 10 min. Triflate **2e** (67.7 mg, 0.2 mmol) and PMP (62.1 mg, 0.4 mmol) in 1 mL benzene were added to the resulting red suspension and it was further stirred for another 10 min. The reaction mixture was heated at 80 °C under 1 atm of CO for 8 h and then eluted with a shot silica gel column (EtOAc) and evaporated under reduced pressure to give the crude residue. The residue was purified by preparative TLC (hexane/EtOAc=10/1) to give (**2e**) (36.4 mg, 85% yield). The enantiomeric excess was

determined to be 91% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2): $[\alpha]_D^{20}$ +28.5 (c 0.79, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.37 (s, 3H), 1.64 (br s,3H), 2.90 (d, *J* = 17.5 Hz, 1H), 3.27 (d, *J* = 17.5 Hz, 1H), 3.89 (s, 3H), 4.94 (dq, *J* = 1.3, 1.3 Hz, 1H), 4.95 (br s, 1H), 6.88 (d, *J* = 2.1 Hz, 1H), 6.92 (dd, *J* = 2.1, 8.5 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR δ 19.80, 22.70, 41.30, 54.68, 55.62, 109.56, 111.86, 115.48, 126.22, 129.12, 146.13, 155.58, 165.54, 207.24. Anal. calcd for $C_{17}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.78, H, 7.51.

(*S*)-5-Chloro-2-isopropenyl-2-methyl-1-indanone (2f). The enantiomeric excess was determined to be 90% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 90% yield): $[\alpha]_D^{20}$ +24.0 (c 0.89, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.37 (s, 3H), 1.65 (br s, 3H), 2.93 (d, *J* = 17.7 Hz, 1H), 3.31 (d, *J* = 17.7 Hz, 1H), 4.94 (br s, 3H), 4.95 (dq, *J* = 1.2, 1.2 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.45 (s, 1H), 7.70 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR δ 19.80, 22.59, 40.93, 54.76, 112.32, 125.66, 126.64, 128.37, 134.29, 141.46, 145.38, 154.05, 207.48. Anal. calcd for $C_{13}H_{13}ClO$: C, 70.75; H, 5.94. Found: C, 71.05, H, 6.01.

(*S*)-2-Isopropenyl-2,5-dimethyl-1-indanone (2g). The enantiomeric excess was determined to be 87% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 86% yield): $[\alpha]_D^{20}$ +27.6 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.36 (s, 3H), 1.64 (br s, 3H), 2.44 (s, 3H), 2.90 (d, *J* = 17.5 Hz, 1H), 3.28 (d, *J* = 17.5 Hz, 1H), 4.94 (dq, *J* = 1.3, 1.3 Hz, 1H), 4.95 (br s, 1H), 6.88 (dd, *J* = 0.6, 7.9 Hz, 1H), 7.25 (d, *J* = 0.6 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR δ 19.80, 22.05, 22.65, 41.11, 54.62, 111.87, 124.36, 126.76, 128.78, 133.59, 146.02, 146.13, 153.53, 208.53. Anal. calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.69, H, 7.91.

(*S*)-2-Isopropenyl-2-methyl-4-(methoxycarbonyl)methyl-1-indanone (2h). The enantiomeric excess was determined to be 88% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 75% yield): White solid (mp 78~79 °C); $[\alpha]_D^{20}$ +31.7 (c 0.36, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.40 (s, 3H), 1.66 (br s, 3H), 3.00 (d, *J* = 17.5 Hz, 1H), 3.39 (d, *J* = 17.5 Hz, 1H), 3.96 (s, 3H),

4.95 (br s, 1H), 4.94 (dq, J = 1.2, 1.2 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 8.13 (s, 1H); ^{13}C NMR δ 19.83, 22.56, 24.24, 41.12, 52.53, 55.07, 112.37, 124.41, 127.80, 128.77, 135.76, 139.03, 145.31, 152.29, 166.36, 208.41. Anal. calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.72, H, 6.65.

(*S*)-5-Cyano-2-isopropenyl-2-methyl-1-indanone (2i). The enantiomeric excess was determined to be 88% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 82% yield): White solid (mp 75~76 °C); $[\alpha]_D^{20}$ +38.3 (c 0.41, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS) δ 1.39 (s, 3H), 1.67 (br s, 3H), 3.01 (d, J = 17.8 Hz, 1H), 3.40 (d, J = 17.8 Hz, 1H), 4.94 (s, 1H), 4.97 (s, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.78 (s, 1H), 7.86 (d, J = 7.9 Hz, 1H); ^{13}C NMR δ 19.80, 22.50, 40.90, 54.90, 112.76, 117.97, 118.03, 125.19, 130.57, 131.23, 138.82, 144.74, 152.36, 207.40. Anal. calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20. Found: C, 79.57, H, 6.13.

(*S*)-2-Isopropenyl-2-methyl-1-indanone (2j). The enantiomeric excess was determined to be 79% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak AS+AS, hexane/2-propanol = 98/2, 87% yield): $[\alpha]_D^{20}$ +23.9 (c 0.93, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS) δ 1.38 (s, 3H), 1.65 (br s, 3H), 2.96 (d, J = 17.4 Hz, 1H), 3.34 (d, J = 17.4 Hz, 1H), 4.95 (dq, J = 1.3, 1.3 Hz, 1H), 4.96 (br s, 1H), 7.39 (dd, J = 7.3, 7.7 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.60 (dd, J = 7.3, 7.7 Hz, 1H), 7.78 (d, J = 7.7 Hz); ^{13}C NMR δ 19.84, 22.61, 41.26, 54.51, 112.03, 124.53, 126.43, 127.50, 134.92, 135.85, 145,82, 152.62, 209.02. Anal. calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.95, H, 7.68.

(*S*)-2-Isopropenyl-2-methyl-4,5-dihydro-1-benzo[*g*]indanone (2k). The enantiomeric excess was determined to be 75% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OD-H, hexane/2-propanol = 98/2, 64% yield); : $[\alpha]_D^{20}$ +18.1 (c 0.56, $CHCl_3$); ^{1}H NMR ($CDCl_3$, TMS) δ 1.35 (s, 3H), 1.65 (dd, J = 1.1, 1.1 Hz, 3H), 2.51 (d, J = 19.4 Hz, 1H), 2.59~2.73 (m, 2H), 2.84 (d, J = 19.4 Hz, 1H), 2.98 (dd, J = 8.1, 8.1 Hz, 2H), 4.93~4.94 (m, 2H), 7.17~7.26 (m, 3H), 8.25 (d, J = 7.2 Hz, 1H); ^{13}C NMR δ 19.66, 22.62, 26.83, 27.53, 44.54, 53.53, 111.78, 124.04, 126.78, 127.55, 127.85,

129.11, 133.35, 134.47, 145.99, 172.29, 208.11. Anal. calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.69, H, 7.69.

(*S*)-2-Isopropenyl-2-methyl-8,9-dihydro-1-benzo[*e*]indanone (2l). The enantiomeric excess was determined to be 78% ee by HPLC analysis with a chiral stationary phase column (Daicel Chiralpak OJ, hexane/2-propanol = 98/2, 65% yield); : $[\alpha]_D^{20}$ –14.7 (c 1.94, $CHCl_3$); ^1H NMR ($CDCl_3$, TMS) δ 1.37 (s, 3H), 1.66 (br s, 3H), 2.50~2.56 (m, 2H),2.71 (dt, *J* = 2.5, 18.1 Hz, 1H), 2.95 (dd, *J* = 8.2, 8.2 Hz, 2H), 3.04 (dd, *J* = 2.5, 18.1 Hz, 1H), 4.95 (dq, *J* = 1.4, 1.4 Hz, 1H), 4.96 (br s, 1H), 7.26~7.31 (m, 2H), 7.34~7.38 (m, 2H); ^{13}C NMR δ 18.29, 19.66, 22.82, 27.91, 40.24 53.43, 111.72, 124.21, 126.83, 128.30, 130.89, 131.76, 136.03, 138.86, 146.15, 163.37, 209.82. Anal. calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.95, H, 7.71.

Preparation of MTPA Esters (3a) from (*S*)-2-isopropenyl-2-methyl-1-benzo[*e*]indanone (2a) and Assignment of the Absolute Configuration. Reduction of (*S*)-2-isopropenyl-2-methyl-1-benzo[*e*]indanone (**2a**) with LiBH(*sec*-Bu)$_3$ (1.0 M solution in THF) according the reported method[3] gave (1*R*,2*S*)-1-hydroxy-2-isopropenyl-2-methyl-2,3-dihydro-1*H*-benzo[*e*]indene (**4a**) (50% yield): ^1H NMR ($CDCl_3$, TMS) δ 1.23 (s, 3H), 1.97 (s, 3H), 3.04 (d, *J* = 15.8 Hz, 1H), 3.67 (d, *J* = 15.8 Hz, 1H), 4.89 (s, 1H), 5.05 (br s, 1H), 5.08 (dq, *J* = 1.4, 1.4 Hz, 1H), 7.47~7.54 (m, 2H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 20.69, 26.01, 39.45, 53.49, 82.69, 112.36, 123.32, 124.46, 125.81, 126.12, 127.61, 128.63, 130.66, 133.84, 139.45, 140.17, 149.02. MTPA Esters **3a** were obtained according to the reported method[3] in 60% yield. The absolute configuration of **3a** was assigned by ^1H NMR analysis of (*S*)-MTPA and (*R*)-MTPA esters according to Kakisawa's manner.[4] **(*S*)-MTPA Ester**: ^1H NMR δ 1.27 (s, 3H), 1.82 (br s, 3H), 3.09 (d, *J* = 15.5 Hz, 1H), 3.37 (s, 3H), 3.65 (d, *J* = 15.5 Hz, 1H), 4.95 (s, 1H), 5.02 (s, 1H), 6.29 (s, H), 7.18~7.89 (m, 9H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H). **(*R*)-MTPA Ester**: ^1H NMR δ 1.24 (s, 3H), 1.67 (s, 3H), 3.10 (d, *J* = 15.6 Hz, 1H), 3.32 (s, 3H), 3.69 (d, *J* = 15.6 Hz, 1H), 4.93 (br s, 1H), 6.25 (s, 1H), 7.12~7.91 (m, 9H), 7.64 (d, *J* = 8.5Hz, 1H), 7.74 (d, *J* = 8.5 Hz,

1H). The results are summarized in Figure S-1, revealing the absolute configuration of **3a** to be (1*R*,2*S*). It follows that the absolute configuration of **2a** is (+)-S.

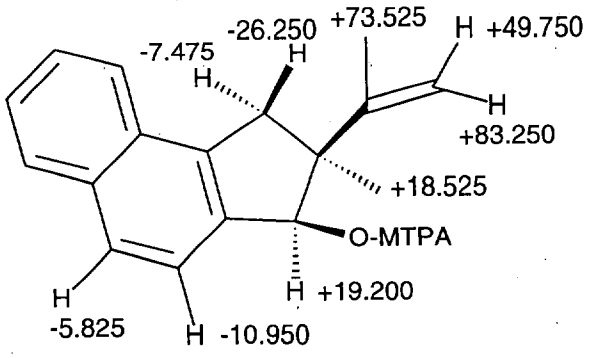


Figure S-1. Δδ values of MTPA esters of **3a.** $\Delta\delta = \delta_S - \delta_R$

References

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