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PAPER

First total synthesis of (+)-indicanone†

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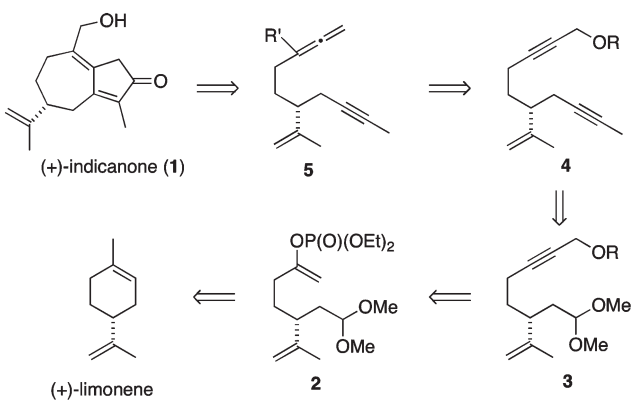
The first total synthesis of the guaiane-type sesquiterpene, (+)-indicanone (**1**), isolated from the root of *Wikstroemia indica*, was accomplished based on the rhodium(I)-catalyzed Pauson–Khand-type reaction of the allenyne derivative, which was derived from (+)-limonene. This total synthesis unambiguously confirmed the complete structure of (+)-indicanone involving its absolute stereochemistry.

Introduction

In 2005, Kitanaka[1] reported the isolation of a new guaiane-type sesquiterpene, (+)-indicanone (**1**), along with two known biflavonoids, sikokianin B and sikokianin C, from the root of *Wikstroemia indica* (Thymelaeceae), which is distributed in the southeast China. *Wikstroemia indica* has long been used as a traditional crude drug for the treatment of pneumonia, rheumatism, and bronchitis in China. (+)-Indicanone (**1**) was shown to inhibit not only nitric oxide production with a stronger IC_{50} at 9.3 μM than that of quercetine (IC_{50} at 24.8 μM),[2,3] but also the inducible nitric oxide synthase gene expression. The structure of this anti-inflammatory guaiane-type sesquiterpene **1**, except for its absolute configuration,[4] was elucidated by the spectral evidence, in particular, based on the careful examination of the ^{1}H NMR spectra. Recent efforts from our laboratory disclosed that the [RhCl(CO)dppp]$_2$-catalyzed Pauson–Khand-type reaction (PKTR) of the allenynes[5,6] consistently produced the corresponding bicyclo[5.3.0]decadienone skeletons in satisfactory yields. Described herein is the first total synthesis of (+)-**1** starting from (+)-limonene by taking advantage of the [RhCl(CO)dppp]$_2$-catalyzed PKTR of allenynes[5] for the construction of the core carbon framework of **1**.

The simple retrosynthesis of (+)-**1** afforded the reasonable tactics described in Scheme 1. The vinyl phosphate moiety of the known diene **2**,[7] derived from (+)-limonene, would be converted into the propargyl alcohol derivative **3**, which should be a precursor of the allenyl functional group in the latter stage. The acetal group of **3** would be transformed into the propyne derivative **4** by a conventional procedure. Finally, the rhodium(I)-catalyzed Pauson–Khand-type reaction of allenyne **5** would, after some chemical modification, lead to the formation of the target natural product (+)-**1** with the (*R*)-configuration.

Treatment of the vinyl phosphate derivative **2**[7] with LDA[8] unexpectedly produced an intractable mixture. After screening several bases, ^{n}BuLi and ^{s}BuLi were found to produce the alkyne derivative **6**, but the yields were rather low, presumably due to its volatility. Thus, compound **2** was exposed to ^{s}BuLi in THF at −78 °C to room temperature and the resulting acetylide was consecutively treated with paraformaldehyde providing the desired propargyl alcohol derivative **7** in 73% yield. Protection of the primary alcohol and deacetalization of **7** was achieved by *p*-methoxybenzylation and acid treatment under the standard conditions to afford the aldehyde **8** in 84% yield. The Ohira–Bestmann reagent[9] effected the transformation of the aldehyde moiety of **8** into a triple bond to furnish **9** in quantitative yield, which was subsequently treated with LHMDS and methyl iodide to give the internal alkyne derivative **10** in quantitative yield. Removal of *p*-methoxybenzyl group of **10** by DDQ easily proceeded to produce the propargyl alcohol derivative **11**, a precursor for the allene formation, in 92% yield. Compound **11** was then treated with choromethyl formate to furnish the carbonate **12** in quantitative yield. Upon exposure to Tsuji's conditions[10]



Scheme 1 Retrosynthetic analysis of (+)-indicanone from (+)-limonene.

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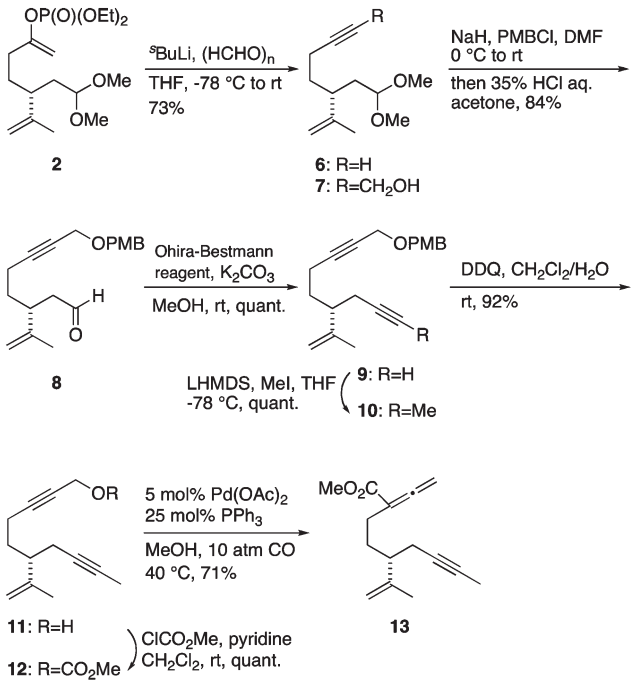
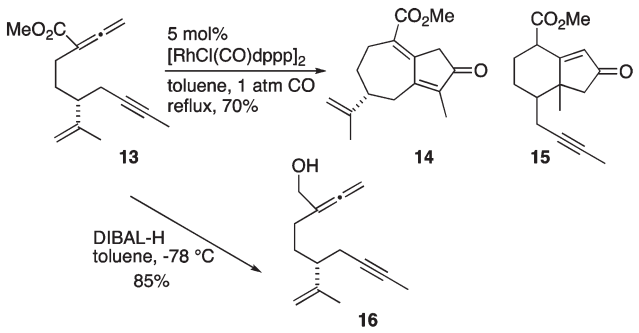


Scheme 2 Synthesis of allenyne derivative **13**.

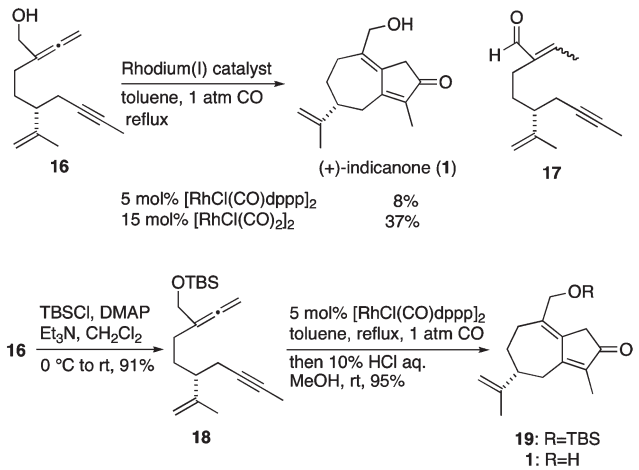
(5 mol% $Pd(OAc)_2$, 25 mol% PPh_3 in MeOH under 10 atm CO pressure), **12** underwent migration to provide the corresponding allenyl ester **13** with the required all carbon units of **1** in 71% yield (Scheme 2).

With the allene–alkyne detivative **13** in hand, we investigated its rhodium(I)-catalyzed PKTR.[5] There are two types of products would be possible from the PKTR of **13** judging from the previous results.[5,11] One is the desired bicyclo[5.3.0] product **14**[5] *via* the PKTR between the allene and alkyne moieties and the other is the bicyclo[4.3.0] compound **15**[11] *via* the reaction of the allene group with the alkene moiety. However, the fact that the PKTR of the allene with the 1,1-disubstituted alkene[11] tends to require a higher CO pressure (*e.g.* 5 atm) than the reaction with the alkyne (usually 1 atm) suggested the preferential formation of **14** over **15**. As a result, a solution of **13** in toluene was refluxed in the presence of 5 mol% $[RhCl(CO)dppp]_2$ for 1 h to provide the bicyclo[5.3.0]decadienone framework **14** in 70% yield as the main product along with a small amount of the bicyclo[4.3.0]nonenone skeleton **15** (obtained as a mixture of diastereoisomers),[12] which must have been formed *via* the [2 + 2 + 1]-type ring closure between the distal double bond of the allene functionality and isopropenyl group,[11] followed by migration of a double bond. The bicyclo[5.3.0]decadienone framework **14** was obtained in an acceptable yield, but we could not suppress the by-production of **15** despite several changes in the reaction conditions. In addition, the chemoselective reduction of the α,β-unsaturated ester group of bicyclo[5.3.0]decadienone derivative **14** in the presence of the α,β-unsaturated ketone moiety was not an easy task. Therefore, prior to the Pauson–Khand-type reaction, the methyl ester group of **13** was reduced with DIBAL-H to afford **16** in 85% yield (Scheme 3).

The PKTR of **16** was the next subject. The exposure of **16** to 5 mol% $[RhCl(CO)dppp]_2$ as described in Scheme 4 furnished



Scheme 3 Synthesis of bicyclo[5.3.0]decadienone **14**.



Scheme 4 Completion of total synthesis of (+)-indicanone.

(+)-indicanone (**1**) in a poor yield (8%) together with some amounts of the α,β-unsaturated aldehyde **17**.[13] Changing the rhodium(I) catalyst to $[RhCl(CO)_2]_2$ as well as increasing the loading amount of the catalyst (15 mol%) improved the yield of **1** (37%), but **17** was still consistently formed in some amounts. The production of **17** is obviously attributed to the unprotected allenyl alcohol of **16**. Therefore, the allenyl alcohol of **16** was protected by a silyl group to produce **18** in 91% yield, which was subsequently treated with 5 mol% $[RhCl(CO)dppp]_2$ in refluxing toluene under 1 atm CO atmosphere to give **19** in 37% yield. This ring-closing reaction was monitored by TLC indicating the efficient formation of **19** in the reaction vessel. We tentatively thought that the decomposition of **19** during workup and/or purification processes occurred which must be a major reason for its low isolation yield. Thus, after the PKTR of **18**, the resulting **19** without isolation was subsequently desilylated with aqueous HCl leading to the highly efficient production of (+)-indicanone (**1**)$\{[\alpha]_D^{21}$ +16.6° (lit. $[\alpha]_D^{23}$ +14.3°)$\}$[14,15] in 95% yield (Scheme 4).

In summary, we have efficiently completed the first total synthesis of (+)-indicanone (**1**) from the known phosphate (**2**) through 10 steps in a 29% overall yield. This total synthesis unambiguously established the absolute configuration of the natural (+)-indicanone to be (*R*) as indicated in Scheme 1.

Experimental

General

IR spectra were measured in $CHCl_3$. ^1H NMR spectra were taken in $CDCl_3$ unless otherwise stated. Tetramethylsilane (0.00 ppm) for compounds without a silyl group was used as internal standard unless otherwise stated. ^{13}C NMR spectra were recorded in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal standard unless otherwise stated. All reactions were carried out under a nitrogen atmosphere. Silica gel (silica gel 60, 230–400 mesh) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

(+)-(*R*)-8,8-Dimethoxy-6-isopropenyl-2-octyn-1-ol (7)

To a solution of (+)-**2**[7] (1.35 g, 3.86 mmol) in THF (38 mL) was added *s*-BuLi (1.0 M in hexane, 8.9 mL, 8.9 mmol) at −78 °C. The reaction mixture was stirred for 1 h at the same temperature. Then paraformaldehyde (365 mg) was added to the reaction mixture, which was stirred for an additional 1 h at room temperature. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the mixture was extracted with AcOEt. The extract was washed with water, brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (3 : 1) afforded (+)-**7** (635 mg, 73%) as a colorless oil; $[\alpha]_D^{28}$ +30.4 (*c* 1.0, $CHCl_3$); IR 3609, 3441 cm^{-1}; ^1H NMR δ 4.80 (brs, 1H), 4.76 (brs, 1H), 4.31 (dd, 1H, J = 7.1, 4.4 Hz), 4.27 (s, 2H), 3.30 (s, 3H), 3.28 (s, 3H), 2.34–2.27 (m, 1H) 2.19–2.01 (m, 3H), 1.60 (s, 3H), 1.68–1.51 (m, 4H); ^{13}C NMR δ 145.5, 113.0, 102.9, 86.0, 78.6, 53.1, 52.4, 51.2, 42.2, 35.9, 32.0, 17.8, 16.6; MS (DART) *m*/*z* 227 (M^+ + 1, 2.6); HRMS (DART) calcd for $C_{13}H_{23}O_3$ 227.1647, found 227.1655.

(+)-(*R*)-3-Isopropenyl-8-(4-methoxybenzyloxy)-6-octynal (8)

To a solution of (+)-**7** (53 mg, 0.23 mmol) in DMF (2.5 mL) was added 60% NaH in oil (28 mg, 0.70 mmol) at 0 °C. The reaction mixture was stirred for 1 h at the same temperature. Then PMBCl (0.060 mL, 0.47 mmol) was added to the reaction mixture, which was stirred for an additional 1 h at room temperature. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to give the crude acetal. To a solution of the crude acetal in acetone (3 mL) was added 35% aqueous HCl (0.2 mL) at 0 °C. The reaction mixture was stirred for 1 h at room temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (3 : 1) afforded (+)-**8** (59 mg, 84%) as a colorless oil; $[\alpha]_D^{28}$ +22.6 (*c* 0.56, $CHCl_3$); IR 1722 cm^{-1}; ^1H NMR δ 9.67 (t, 1H, J = 2.3 Hz), 7.29–7.26 (m, 2H), 6.89–6.86 (m, 2H), 4.88–4.84 (m, 1H), 4.84–4.82 (m, 1H), 4.51 (s, 2H), 4.11 (t, 2H, J = 1.8 Hz), 3.80 (s, 3H), 2.83 (quin, 1H, J = 7.3 Hz), 2.52–2.38 (m, 2H), 2.28–2.12 (m, 2H) 1.66 (s, 3H), 1.65–1.60 (m, 2H); ^{13}C NMR δ 201.8, 159.3, 144.6, 129.7, 129.6, 113.8, 113.3, 86.0, 76.5, 71.0, 57.3, 55.2, 47.1, 40.5, 31.8, 18.6, 16.5; MS (DART) *m*/*z* 301 (M^+ + 1, 30.3); HRMS (DART) calcd for $C_{19}H_{25}O_3$ 301.1804, found 301.1810.

(+)-(*R*)-4-Isopropenyl-8-(4-methoxybenzyloxy)-1,7-nonadiyne (9)

To a solution of (+)-**8** (894 mg, 2.97 mmol) in MeOH (30 mL) were added Ohira–Bestmann reagent (690 mg, 3.6 mmol) and K_2CO_3 (1.2 g, 8.9 mmol) at room temperature. The reaction mixture was stirred for 1 h at the same temperature. Then the reaction was quenched by addition of 10% aqueous HCl, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (12 : 1) afforded (+)-**9** (877 mg, quant.) as a colorless oil; $[\alpha]_D^{27}$ +24.4 (*c* 0.64, $CHCl_3$); IR 3307 cm^{-1}; ^1H NMR δ 7.30–7.26 (m, 2H), 6.91–6.86 (m, 2H), 4.88–4.86 (m, 1H), 4.84–4.80 (m, 1H), 4.52 (s, 2H), 4.12 (t, 2H, J = 2.1 Hz), 3.81 (s, 3H), 2.47–2.39 (m, 1H), 2.29–2.26 (m, 2H), 2.25–2.11 (m, 2H), 1.98 (t, 1H, J = 2.7 Hz), 1.84–1.76 (m, 1H), 1.67 (s, 3H), 1.65–1.57 (m, 1H); ^{13}C NMR δ 159.3, 145.1, 129.73, 129.66, 113.8, 112.8, 86.4, 82.6, 76.3, 71.0, 69.4, 57.3, 55.2, 45.0, 31.0, 23.2, 18.7, 16.7; MS (DART) *m*/*z* 297 (M^+ + 1, 5.4); HRMS (DART) calcd for $C_{20}H_{25}O_2$ 297.1855, found 297.1848.

(+)-(*R*)-6-Isopropenyl-1-(4-methoxybenzyloxy)-2,8-decadiyne (10)

To a solution of (+)-**9** (311 mg, 1.05 mmol) in THF (7.0 mL) was added LHMDS (0.5 M in THF, 2.4 mL, 1.2 mmol) at −78 °C. The reaction mixture was stirred for 1 h at the same temperature. Then MeI (0.40 mL, 5.3 mmol) was added to the reaction mixture, which was stirred for an additional 3 h at the same temperature. The reaction was quenched by addition of saturated aqueous NH_4Cl, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (20 : 1) afforded (+)-**10** (325 mg, quant.) as a colorless oil; $[\alpha]_D^{26}$ +20.7 (*c* 1.5, $CHCl_3$); ^1H NMR δ 7.30–7.28 (m, 2H), 6.90–6.86 (m, 2H), 4.85–4.83 (m, 1H), 4.79–4.76 (m, 1H), 4.52 (s, 2H), 4.12 (t, 2H, J = 2.1 Hz), 3.81 (s, 3H), 2.38–2.31 (m, 1H), 2.28–2.10 (m, 4H), 1.85–1.79 (m, 1H), 1.77 (t, 3H, J = 2.5 Hz), 1.66 (s, 3H), 1.63–1.54 (m, 1H); ^{13}C NMR δ 159.3, 145.8, 129.75, 129.68, 113.8, 112.3, 86.7, 77.2, 76.7, 76.1, 70.9, 57.3, 55.3, 45.5, 31.0, 23.6, 18.9, 16.7, 3.5; MS (DART) *m*/*z* 311 (M^+ + 1, 5.6); HRMS (DART) calcd for $C_{21}H_{27}O_2$ 311.2011, found 311.2001.

(+)-(*R*)-6-Isopropenyl-2,8-decadiyn-1-ol (11)

To a solution of (+)-**10** (757 mg, 2.44 mmol) in CH_2Cl_2 (12 mL) and H_2O (0.6 mL) was added DDQ (830 mg, 3.66 mmol) at room temperature. The reaction mixture was stirred for 1 h at the same temperature. Then the reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (8 : 1) afforded (+)-**11** (527 mg, 92%) as a colorless oil; $[\alpha]_D^{28}$ +34.85 (*c* 1.4, $CHCl_3$); IR 3609, 3447 cm^{-1}; ^1H NMR δ 4.85–4.82 (m, 1H), 4.78–4.76 (m, 1H),

4.25 (s, 2H), 2.35–2.20 (m, 1H), 2.26–2.07 (m, 4H), 1.83–1.74 (m, 1H), 1.78 (t, 3H, J = 2.5 Hz), 1.65 (s, 3H), 1.62–1.52 (m, 2H); ^{13}C NMR δ 145.7, 112.4, 86.2, 78.4, 77.3, 76.8, 51.4, 45.5, 30.9, 23.6, 18.9, 16.7, 3.5; MS (DART) m/z 191 (M^+ + 1, 79.9); HRMS (DART) calcd for $C_{13}H_{19}O$ 191.1436, found 191.1424.

(+)-(*R*)-6-Isopropenyl-1-methoxycarbonyloxy-2,8-decadiyne (12)

To a solution of (+)-**11** (411 mg, 2.16 mmol) in CH_2Cl_2 (10 mL) were added pyridine (1.0 mL, 13 mmol) and $ClCO_2Me$ (0.50 mL, 6.5 mmol) at 0 °C. The reaction mixture was stirred for 15 min at the same temperature. Then the reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (20 : 1) afforded (+)-**12** (536 mg, quant.) as a colorless oil; $[\alpha]_D^{27}$ +27.6 (c 0.10, $CHCl_3$); IR 1751 cm^{-1}; ^{1}H NMR δ 4.85–4.82 (m, 1H), 4.78–4.76 (m, 1H), 4.72 (t, 2H, J = 2.3 Hz), 3.80 (s, 3H), 2.33–2.22 (m, 1H), 2.21–2.06 (m, 4H), 1.77 (t, 3H, J = 2.5 Hz), 1.82–1.74 (m, 1H), 1.64 (s, 3H), 1.61–1.51 (m, 1H); ^{13}C NMR δ 155.3, 145.6, 112.4, 88.1, 77.2, 76.8, 73.5, 56.2, 55.0, 45.5, 30.7, 23.6, 18.9, 16.7, 3.5; MS (DART) m/z 249 (M^+ + 1, 10.2); HRMS (DART) calcd for $C_{15}H_{21}O_3$ 249.1491, found 249.1484.

(+)-(*R*)-6-Isopropenyl-3-methoxycarbonyl-1,2-decadien-8-yne (13)

To a solution of (+)-**12** (57.4 mg, 0.231 mmol) in MeOH (1.0 mL) were added $Pd(OAc)_2$ (2.6 mg, 0.012 mmol) and PPh_3 (12 mg, 0.046 mmol) at room temperature. The reaction mixture was warmed to 40 °C under CO (10 atm) and stirred for 24 h. Then MeOH was evaporated off, and the residue was chromatographed with hexane–AcOEt (80 : 1) to afford (+)-**13** (38 mg, 71%) as a colorless oil; $[\alpha]_D^{23}$ +7.0 (c 1.6, $CHCl_3$); IR 1965, 1936, 1713 cm^{-1}; ^{1}H NMR δ 5.14 (t, 2H, J = 3.2 Hz), 4.83–4.79 (m, 1H), 4.75 (brs, 1H), 3.74 (s, 3H), 2.27–2.16 (m, 4H), 2.15–2.07 (m, 1H), 1.76 (t, 3H, J = 2.3 Hz), 1.72–1.63 (m, 1H), 1.65 (s, 3H), 1.55–1.46 (m, 1H); ^{13}C NMR δ 213.8, 167.6, 146.2, 112.2, 100.0, 79.1, 77.6, 76.5, 52.2, 46.0, 30.3, 25.8, 23.8, 18.8, 3.5; MS (DART) m/z 233 (M^+ + 1, 100); HRMS (DART) calcd for $C_{15}H_{21}O_2$ 233.1542, found 233.1559.

(+)-(*R*)-6-Isopropenyl-3-hydroxymethyl-1,2-decadien-8-yne (16)

To a solution of (+)-**13** (116 mg, 0.500 mmol) in toluene (5.0 mL) was added DIBAL-H (1.0 M in toluene, 1.5 mL, 1.5 mmol) at −78 °C. The reaction mixture was stirred for 4 h at the same temperature. Then the reaction was quenched by addition of MeOH and saturated sodium potassium tartrate (Rochelle's salt), and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (10 : 1) afforded (+)-**16** (87 mg, 85%) as a colorless oil; $[\alpha]_D^{26}$ +7.9 (c 0.52, $CHCl_3$); IR 3605, 3450, 1958 cm^{-1}; ^{1}H NMR δ 4.90–4.87 (m, 2H), 4.80 (brs, 1H), 4.74 (brs, 1H), 4.04 (t, 2H, J = 3.0 Hz), 2.28–2.22 (m, 1H), 2.20–2.15 (m, 2H), 2.02–1.83 (m, 2H), 1.77 (t, 3H, J = 2.3 Hz), 1.75–1.66 (m, 1H), 1.64 (s, 3H), 1.55–1.45 (m, 2H); ^{13}C NMR δ 204.2, 146.4, 112.0, 104.5, 78.8, 77.6, 76.5, 62.9, 46.0, 29.7, 26.3, 23.8, 18.8, 3.5; MS (DART) m/z 205 (M^+ + 1, 8.3); HRMS (DART) calcd for $C_{14}H_{21}O$ 205.1592, found 205.1589.

(+)-(*R*)-3-(*tert*-Butyldimethylsilyloxy)-6-isopropenyl-1,2-decadien-8-yne (18)

To a solution of (+)-**16** (120 mg, 0.590 mmol) in CH_2Cl_2 (6 mL) were added TBSCl (134 mg, 0.886 mmol) and Et_3N (0.25 mL, 1.8 mmol) and DMAP (3.6 mg, 0.030 mmol) at 0 °C. The reaction mixture was stirred for 13 h at room temperature. Then the reaction was quenched by addition of water, and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane afforded (+)-**18** (170 mg, 91%) as a colorless oil; $[\alpha]_D^{22}$ +2.7 (c 1.0, $CHCl_3$); IR 1958 cm^{-1}; ^{1}H NMR δ 4.80–4.79 (m, 1H), 4.75–4.72 (m, 3H), 4.12 (t, 2H, J = 2.3 Hz), 2.28–2.22 (m, 1H), 2.20–2.17 (m, 2H), 2.02–1.92 (m, 1H), 1.91–1.83 (m, 1H), 1.77 (t, 3H, J = 2.5 Hz), 1.72–1.66 (m, 1H), 1.64 (s, 3H), 1.54–1.42 (m, 1H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR δ 205.7, 146.9, 112.2, 103.8, 78.1, 76.74, 76.70, 64.6, 46.5, 30.1, 26.4, 26.2, 24.1, 19.1, 18.7, 3.8, −5.0; MS (DART) m/z 319 (M^+ + 1, 10.5); HRMS (DART) calcd for $C_{20}H_{35}OSi$ 319.2457, found 319.2473.

(+)-Indicanone (1)

To a solution of (+)-**18** (14.7 mg, 0.0462 mmol) in toluene (1.0 mL) was added $[RhCl(CO)dppp]_2$ (3.0 mg, 2.6 × 10^{-3} mmol) at room temperature, and reaction mixture was warmed to refluxed under CO (1 atm) and stirred for 3 h. Then 10% aqueous HCl (0.5 mL) and MeOH (1 mL) was added to the reaction mixture, which was stirred for an additional 1 h at room temperature. The reaction was quenched by addition of saturated aqueous $NaHCO_3$, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–AcOEt (1 : 1) afforded (+)-indicanone (**1**) (10.2 mg, 95%) as a colorless oil; $[\alpha]_D^{23}$ +16.6 (c 0.73, MeOH); IR 3607, 3420, 1682 cm^{-1}; ^{1}H NMR δ 4.74 (s, 2H), 4.20 (s, 2H), 2.99 (s, 2H), 2.82 (dd, 1H, J = 15.5, 4.1 Hz), 2.73 (dd, 1H, J = 15.3, 8.9 Hz), 2.64 (ddd, 1H, J = 15.5, 8.4, 2.8 Hz), 2.55–2.44 (m, 2H), 2.05–1.97 (m, 2H), 1.80 (s, 3H), 1.84–1.77 (m, 1H), 1.77 (s, 3H); ^{1}H NMR (acetone-d_6) δ 4.74 (br s, 1H), 4.69 (quin, 1H, J = 1.3 Hz), 4.11, 4.08 (ABq, 2H, J_{AB} = 12.7 Hz), 2.95, 2.91 (ABq, 2H, J_{AB} = 20.6 Hz), 2.83 (dd, 1H, J = 15.4, 4.4 Hz), 2.77 (dd, 1H, J = 15.4, 8.5 Hz), 2.63 (ddd, 1H, J = 16.7, 8.5, 2.7 Hz), 2.54–2.45 (m, 2H), 1.99–1.94 (m, 1H), 1.78–1.71 (m, 4H), 1.70 (s, 3H); ^{13}C NMR δ 204.3, 167.1, 149.3, 140.2, 137.6, 133.9, 109.7, 65.7, 43.0, 39.0, 33.5, 32.4, 28.7, 20.5, 8.5; ^{13}C NMR (acetone-d_6) δ 203.5, 167.1, 150.6, 139.8, 139.5, 133.4, 109.7, 65.2, 43.9, 39.2, 33.9, 33.2, 28.9, 20.5, 8.3; MS (DART) m/z 233 (M^+ + 1, 100); HRMS (DART) calcd for $C_{15}H_{21}O_2$ 233.1542, found 233.1526.

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15 We are indebted to Professor S. Kitanaka, College of Pharmacy, Nihon University, for generously supplying the ^{1}H NMR spectrum of the natural (+)-indicanone in acetone-d_6.