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Synthetic Studies on Ciguatoxin—Synthesis of H–I–J Ring System

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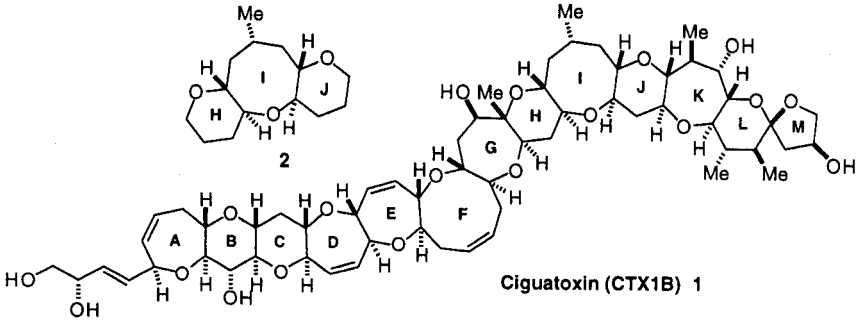
Abstract—Synthesis of a tricyclic ring system corresponding to H–I–J rings of ciguatoxin was stereoselectively achieved in 13 steps from a sugar derivative as a model study directed toward the total synthesis of ciguatoxin.

Ciguatoxin is a marine *trans*-fused polycyclic compound causing ciguatera poisoning.[1] Our approach required a new cyclization to prepare ring systems with stereochemical control. We have been addressing this goal by applying the Nicholas reaction[2] to acetylene biscobalthexacarbonyl complexes[3] for the formation of medium-sized ether rings.[4] These cyclization products, *endo* cobalt complexes of acetylenes, are convertible into olefins through reductive decomplexation methods: for example, hydrogenation with rhodium catalyst, hydrosilylation or tin hydride reduction.[3,4] The complex was designed to assist the cyclization of 7-, 8-, 9- and 10-membered ether rings by affecting the entropy effect which otherwise leads to poor cyclization without the biscobalt.[5] These methodologies have been reviewed in a feature article describing the complexation to biscobalthexacarbonyl, cyclization to cyclic ethers and decomplexation.[5] This paper describes the synthesis of the H–I–J ring system (**2**) using this methodology.

The retrosynthetic analysis for tricyclic compound (**2**) is illustrated in Scheme 1. Ring-H in the target molecule **A** was planned to be derived from a D-sugar, a hexopyranoside precursor in optically active form. Opening the ring-J generates a precursor **B**, where the olefin is derived from acetylene biscobalthexacarbonyl precursor of **C** according to our methodology.[5] The stereochemistry of its methyl group has to be introduced. Ring-I could be prepared from a cation intermediate **D** stabilized by the acetylene biscobalt complex. The requisite acetylene compound is accessible from a palladium-mediated coupling between a vinyl halide **E** (X=Br, I) and an acetylene **F**, prepared from known tosylate **G**.

The starting material tosylate **4** was synthesized according to the route reported by Martin et al.[6] Addition of a THF solution of **4** to vinylmagnesium bromide[7] at 0°C in the presence of catalytic amount of copper(I) iodide[8] and stirring at room temperature for two days gave vinylsilane **5**. A high concentration (6.2 M in THF) was required in this step. Exposure of the corresponding acetate **5** to iodine solution in anhydrous and degassed dichloromethane at 0°C afforded the vinyl iodide **6**.[9] It was noted that acetyl group was stable under this condition, while the *tert*-butyldimethylsilyl group was unstable to iodine. Sonogashira coupling[10] of the vinyl iodide **6** with a protected propargyl alcohol in the presence of catalytic amount of palladium(0) provided



Keywords: ciguatoxin; acetylene biscobalthexacarbonyl complex; cyclization.

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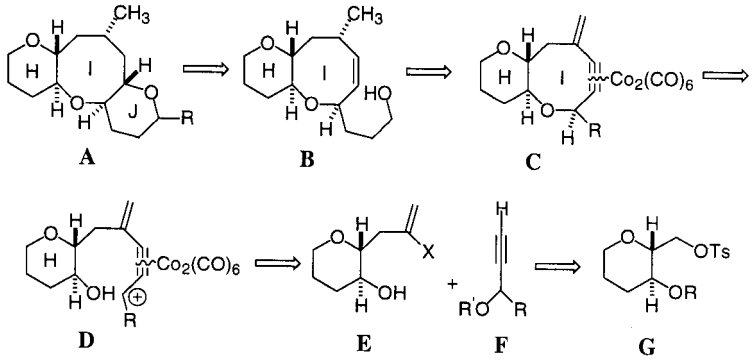
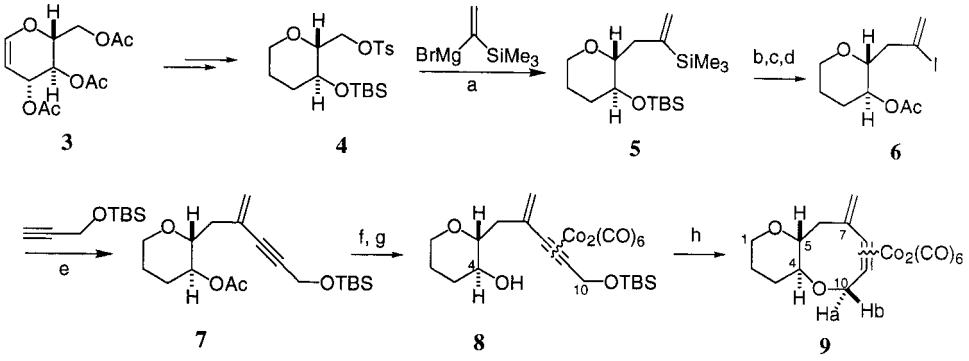


Scheme 1. Retrosynthetic analysis.



Scheme 2. *Reagents, conditions and yields*: (a) CuI (cat), THF, 0°C to rt, 82%. (b) TsOH, MeOH, 93%. (c) Ac_2O, Py, 100%. (d) I_2, CH_2Cl_2, 0°C to rt, 71%. (e) CuI, *n*-$BuNH_2$, Pd(0), benzene, rt, 69%. (f) K_2CO_3, MeOH, rt. (g) $Co_2(CO)_8$, CH_2Cl_2, 0°C to rt, 100% (2 steps). (h) $BF_3{\cdot}OEt_2$, 0°C, CH_2Cl_2, 87%.

compound **7**. Deacetylation of **7** with potassium carbonate in methanol followed by complexation of the acetylene with biscobaltoctacarbonyl provided the key intermediate **8** in good yield.

The stage is now set for the annulation of the oxocane ring. Upon treatment of **8** with boron trifluoride etherate (degassed CH_2Cl_2, 0°C), the desired ring closure took place to afford the bicyclic compound **9** in 87% yield. NOE experiments indicated that one of the C-10 protons, C-10 Ha (δ 5.11, doublet, $J_{H10a,\ H10b}$=16 Hz), is spatially proximate to the C-4 proton (Scheme 2).

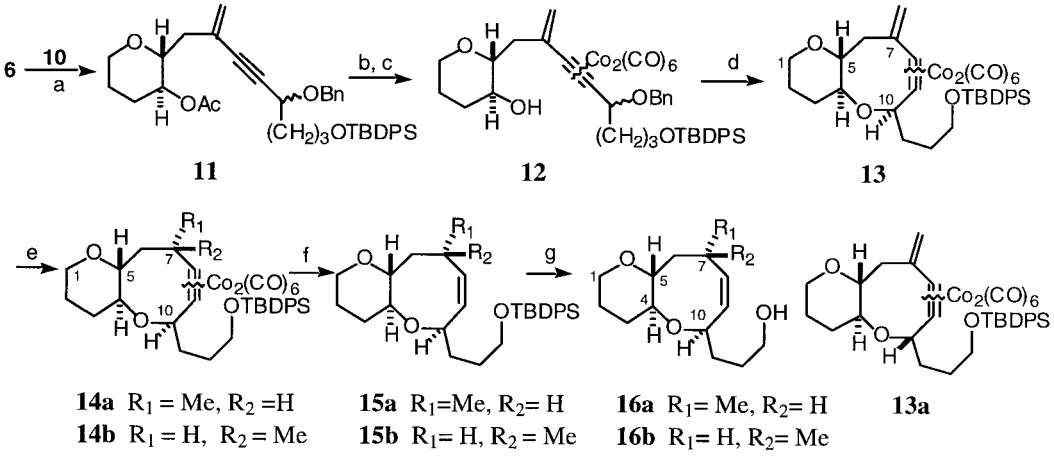
These results encouraged us to use a longer acetylene in the Sonogashira coupling step, so that we could have a side chain precursor to ring-J. Hex-5-yn-1,4-diol,[11] was prepared as its protected form **10**, and was coupled with **6**, to provide compound **11**. Cobalt complexation and cyclization were achieved under similar conditions to afford bicyclic compound **13** as a single stereoisomer in 94% yield.

At this stage, the crucial stereoselectivity of the oxocane ring formation (**12→13**) was investigated. Interestingly, if this oxocane ring forming reaction was quenched shortly after the addition of boron trifluoride etherate, then a mixture of stereoisomeric cyclization products, epimeric at C-10 (**13a**) was produced. On prolonged reaction time, however, the *anti* isomer **13a** (H-10, δ 5.00, dd, J=11, 2 Hz) equilibrated in situ and ultimately underwent conversion to the desired stereoisomer **13** (H-10, δ 4.61, dd, J=10, 3 Hz), presumably through a process involving the cation intermediate **D** (Scheme 1), and the results are summarized in Table 1. In addition, lower temperature also disfavored the formation of **13** presumably due to slower equilibration (entry 4). Compound **13** thus emerged as the product of a thermodynamically controlled ring closure.[4] The stereochemistry of **13** was demonstrated by two-dimensional ^{1}H NOESY experiments. The observation of an noe between H-4 (δ 3.14) and H-10 was indicative of a *syn* relationship between these protons (Scheme 3).

Reduction of the terminal olefin in compound **13** with diimide[12] in methanol in the presence of triethylamine as an acid scavenger resulted in a mixture of two diastereoisomers, which was separated by chromatography to provide the desired isomer **14a** in 63% and the undesired isomer **14b** in 24% yield, respectively. The configuration of the newly formed methyl-bearing stereocenter at position C-7 was assigned in a later stage. It was noted that other conditions for the reduction of the conjugated terminal olefin **13**, such as normal-pressure catalytic hydrogenation

Table 1. Cobalt complex assisted thermodynamically-controlled cyclization of **12→13** (The reaction **12→13** was carried out in CH_2Cl_2 solvent and 4 mM $BF_3{\cdot}OEt_2$. The ratios of *syn*/*anti* were determined from the H-10 signal intensity in ^{1}H NMR spectra)

Entry	Conditions	*syn*/*anti* **13**/**13a**	Yield (%)
1	0°C, 1 min	3:1	60
2	0°C, 15 min	20:1	88
3	0°C, 40 min	>100:1	94
4	−20°C, 50 min	9:1	76



Scheme 3. *Reagents, conditions and yields*: (a) *n*-$BuNH_2$, CuI, Pd(0), benzene, rt, 89%. (b) MeOH, K_2CO_3, rt, 96%. (c) $Co_2(CO)_8$, CH_2Cl_2, 0°C to rt, 87%. (d) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0°C, 94%. (e) [HN=NH], rt, [**14a**, 63%; **14b**, 24%]. (f) *n*-Bu_3SnH, benzene, [**15a**, 96%; **15b**, 86%]. (g) TBAF, THF, rt, [**16a**, 85%; **16b**, 85%].

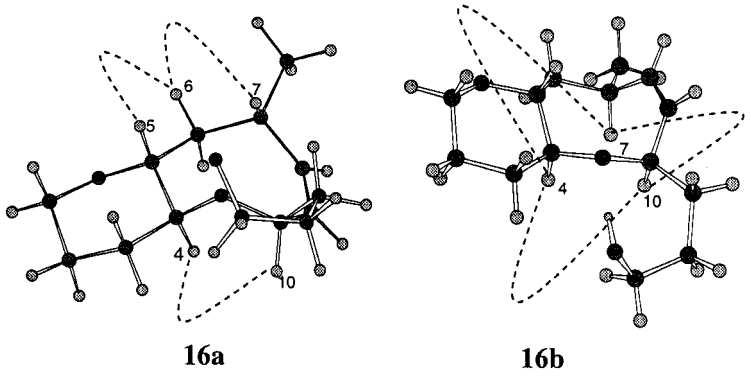


Figure 1. Conformation of **16a** and **16b** (calculated by MacroModel. Dashed lines indicate NOE to explain the validity of these conformations).

(Rh, Pd/C, PtO_2, Raney Ni),[2] or high-pressure hydrogenation[4af] (>110 atm) with Wilkinson catalyst, simply gave no reactions in this particular case, presumably due to the low reactivity of the double bond in this complex system. Reductive decomplexation of the acetylene–biscobalthexacarbonyl complex **14a**,**b** with tri-*n*-butyltin hydride[4e] (benzene, 50°C) afforded the corresponding *cis*-olefins **15a**,**b** in 96% and 86% yields, respectively. These olefins were allowed to assist the cyclization for ring-J. Thus, removal of the *tert*-butyldiphenylsilyl group in compounds **15a**,**b** with tetrabutylammonium fluoride in THF provided alcohols **16a**,**b** (85, 85%, respectively) as potential precursors for ring-J cyclization. At this stage, the configuration of the methyl group at C-7 in compounds **16a**,**b** was determined by analysis of their NOESY data. Particularly revealing was the observation of noe between H-7 and H-4; H-7 and H-10 in the NOESY spectrum for **16b**, which strongly suggests that the methyl group in **16b** is concluded as β-orientation. This result was supported by the data from conformational analysis studies on **16b** (MM2* force field in MacroModel version 4.5), which revealed that the H-7 in **16b** resides in spatial proximity to H-4 (2.45 Å) and H-10 (2.18 Å). Similarly, the calculated conformational data for **16a** are also consistent with the result from NOESY experiments (Fig. 1).

With the compound **16a** in hands, our attention was then turned to the elaboration of J-ring, where the *trans* juncture at C9-C10 has to be established. Our first attempt for the construction of this six-membered ether ring was an oxymercuration reaction.[13,14] After an analysis of steric and stereo-electronic effects,[15] it was found that mercury could engage the $\Delta^{8,9}$ double bond in **16a** from its less hindered face, namely, from the bottom direction of the double bond (Fig. 2), then the nucleophilic hydroxyl group would attack C-9 from the back side of the mercuric ion. Thus, the *cis* product would be favored. Indeed, treatment of **16a** with mercury(II) acetate in CH_2Cl_2, followed by washing with brine, led to the isolation of chloromercury compound **17**, albeit in modest yield. As expected, *cis* stereochemistry for the juncture C9-C10 was deduced from its ^1H NMR spectra ($J_{9H,10H}$=2 Hz). Reductive demercuration of **17** with tri-*n*-butyltin hydride and catalytic amount of AIBN (toluene, 55°C)[16] afforded *cis* tricyclic compound **18** ($J_{H9,H10}$=2.0 Hz) in 86% yield (Scheme 4).

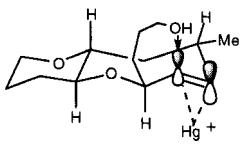
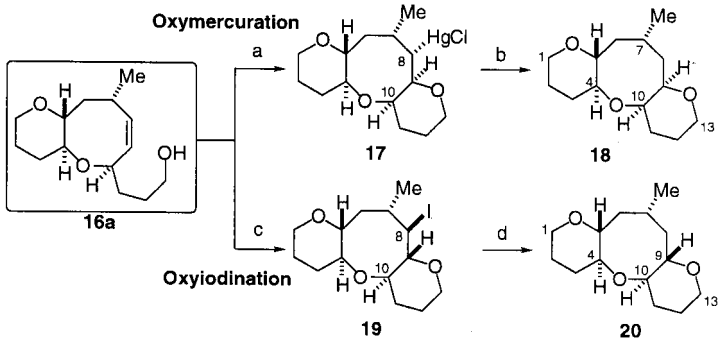


Figure 2.



Scheme 4. *Reagents, conditions and yields*: (a) $Hg(OAc)_2$, CH_2Cl_2, then brine, 50%. (b) *n*-Bu_3SnH, AIBN(cat), toluene, 86%. (c) I_2, CH_3CN, 0°C to rt, 56%. (d) *n*-Bu_3SnH, AIBN (cat), toluene, 72%.

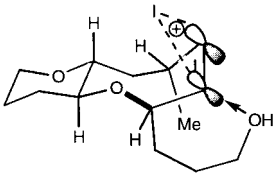
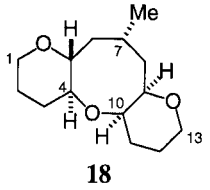


Figure 3.

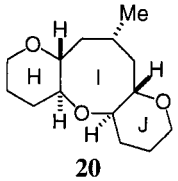
We selected to test the feasibility of oxyiodination reaction.[17] Treatment of **16a** with iodine in acetonitrile[18b] at 0°C provided **19** as a major product (56%). Surprisingly, it was demonstrated to be a *trans* isomer ($J_{H9,H10}$=9 Hz). To account for this result, it was presumed that the conformational transition state such as the one in Fig. 3 predominated in this reaction, in which case iodine might engage the $\Delta^{8,9}$ double bond in **16a** from either top or bottom direction, however, the attack of the hydroxyl group to the C-9 from bottom direction would favor the new bond forming, for the adjacent electron-withdrawing C–O bond (the bold one) antiparallel to the orbital of the double bond as well as the attack direction of the nucleophile (Fig. 3) in this case. Thus, *trans* product would be favored. Reductive removal of the iodine in **19** with *n*-Bu_3SnH and AIBN in toluene at 55°C[18] afforded the *trans* tricyclic product **20** ($J_{9,10}$=9.5 Hz) in 72% yield (Scheme 4). The NMR data of **18** and **20** are very similar to each other as listed in Table 2.

The tricyclic compound **20** (*trans–syn–trans*) has a symmetry plane in the center of its planar structure, so that one expected to have 8 lines in its ^{13}C NMR spectrum (^1H decoupled at room temperatures). It, however, afforded 14 lines rather than 8 lines. This fact suggested non-symmetric conformers around the lowest energy. ^1H NMR spectra of

Table 2. The comparison of the chemical shifts for compound **18** and **20**



18



20

Position	Chemical shifts of **18**		Chemical shifts of **20**	
	^1H	^{13}C	^1H	^{13}C
1	Ha: 3.28, ddd, *J*=11, 9, 5 Hz Hb: 3.84, ddd, *J*=11, 5, 2.0 Hz	66.7	Ha: 3.40, ddd, *J*=12, 10, 5 Hz Hb: 3.86–3.93, m	67.5
2	1.61–1.71, m	21.2	1.66–1.73, m, total 2H	25.6
3	Ha: 1.35–1.44, m Hb: 2.00–2.09, m	26.3	Ha: 1.36, dd, *J*=13, 6 Hz Hb: 2.02, ddd, *J*=13, 9, 2 Hz	29.4
4	3.07, td, *J*=10, 5 Hz	75.5	3.02, td, *J*=9, 6 Hz	75.8
5	3.16, td, *J*=10, 2 Hz	81.0	2.98, td, *J*=9, 4 Hz	78.4
6	Ha: 1.52, ddd, *J*=12, 10, 4 Hz Hb:1.82–1.88, m	29.6	Ha: 1.20, ddd, *J*=12, 9, 4 Hz Hb: 1.96, dt, *J*=12, 5 Hz	36.0
7	2.11–2.22, m	43.0	1.46–1.52, m	39.1
8	Ha: 1.53–1.60, m Hb: 1.82, ddd, *J*=11, 5, 2 Hz	32.1	Ha: 1.26, ddd, *J*=12, 6, 2 Hz Hb: 1.40–1.49, m	38.6
9	3.59, dd, *J*=5, 2 Hz	82.1	3.19, td, *J*=9.5, 2 Hz	80.6
10	3.62, dd, *J*=4, 2 Hz	75.9	4.08, td, *J*=9.5, 7 Hz	77.8
11	Ha: 1.58–1.64, m Hb: 2.00–2.06, m	26.2	Ha: 1.42–1.48, m Hb: 1.80, ddd, *J*=12, 7, 2 Hz	31.9
12	1.84–1.92, m, 2H	23.7	1.86–1.92, m, 2H	25.7
13	Ha: 3.45, td, *J*=11, 3 Hz Hb: 3.92, ddd, *J*=11, 5, 2 Hz	67.8	Ha: 3.74, dd, *J*=13, 7 Hz Hb: 3.84, dd *J*=13, 6 Hz	67.8
14	1.01, d, *J*=7 Hz, 3H	18.1	0.89, d, *J*=7 Hz, 3H	17.7

the C7-Me appeared around 0.9 ppm in different intensities at different temperatures (25, 35, 45, 55°C in $CDCl_3$) as shown in Fig. 6, in which three sets of doublet (J=7 Hz) exist at 25°C. One of the minor ones increased at higher temperatures. Signals became broad at temperatures higher than 45°C. On the other hand, ^{13}C NMR spectra did not change so clearly to show different chemical shifts, indicating that no symmetric conformer appeared in these temperatures. Signal difference according to these temperatures might correspond to some other conformers which could not be specified from these experiments. As a consequence it is likely that **20** exists as a mixture of various conformers at ordinary temperatures. To account for this result, it is presumed that the symmetric crown-conformer (Fig. 4) is not the most stable one, but the non-crown unsymmetric conformers such as the one in Fig. 5 turned out to be more stable. This presumption was supported by computer calculated conformational studies on **20**. The results of Molecular Mechanics Calculations for **20** from MacroModel are consistent with that from BioGraf package, which revealed that the minimum energy of one of the most stable unsymmetric conformers is 0.4~0.5 kcal (Table 3) lower than the symmetric one.

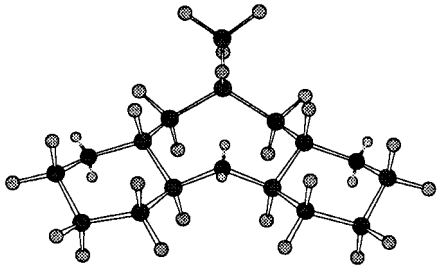


Figure 4. View of the symmetric conformation of **20** (not global minimum).

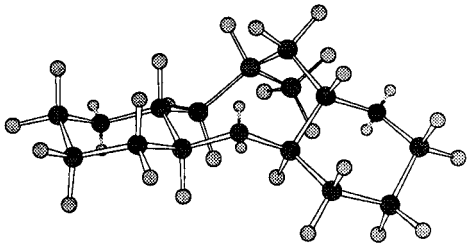


Figure 5. View of one of the stable conformers of **20**.

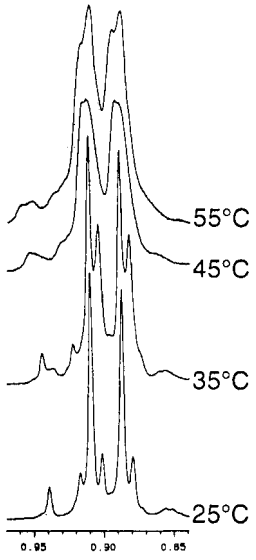


Figure 6. Change of Me signal in ^1H NMR spectra of **20** at different temperatures.

Table 3. Calculated energy of **20** for its two conformers (Figs. 4 and 5).

20 (symmetric crown conformer)		**20** (unsymmetric non-crown conformer)	
BioGraf		**BioGraf**	
Total energy	52.916	Total energy	52.368
Bonds	5.102	Bonds	4.963
Angles	15.636	Angles	12.123
Torsion	4.715	Torsion	7.451
van der Waals	27.463	van der Waals	27.831
MacroModel		**MacroModel**	
Total energy (kcal/mol)	21.74	Total energy (kcal/mol)	21.52
Stretch:	7.61	Stretch:	8.05
Bend:	39.61	Bend:	30.01
Prop Torsion:	52.60	Prop Torsion:	60.25
Electrostatic:	−79.51	Electrostatic:	−80.42
van der Waals:	67.14	van der Waals:	69.14

We have demonstrated a study toward the synthesis of the H–I–J ring system of ciguatoxin. Further extension of above methodology is now in progress and will be reported elsewhere.

Experimental

General

All melting points were recorded on a Yanaco MP-S3 hot stage melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm^{-1}). Proton NMR spectra (^1H NMR) were recorded on a Varian Gemini 2000 (300 MHz) or a Bruker ARX-400 (400 MHz). All samples were dissolved in $CDCl_3$, and chemical shift values are reported in parts per million (ppm) with tetramethylsilane (TMS, δ 0.00) as an internal standard. Data are reported as follows: chemical shift (integrated intensity, multiplicity, coupling constants in Hertz, assignment). NOE experiments were performed with a Bruker ARX-400 (400 MHz). Carbon NMR spectra (^{13}C NMR) were recorded on a Varian Gemini 2000 (75.4 MHz) or a BRUKER ARX-400 (100 MHz) with proton decoupling. Chemical shift values are reported as δ in parts per million (ppm) with $CDCl_3$ (δ 77.0) as an internal standard.

Low-resolution mass spectra (EI) were obtained on a JEOL DX-300 spectrometer. High-resolution mass spectra (HRMS) and elemental analyses were performed by the Analytical Laboratory, School of Bioagricultural Sciences, Nagoya University. Optical rotations were measured on a JASCO DIP-370 automatic digital polarimeter with a sodium lamp in 100 mm cell of 2 or 10 mL capacity and reported as follows: $[\alpha]_D^t$ (°C) λ, [c (g/100 mL), solvent].

Analytical thin-layer chromatography (TLC) was conducted on 0.25 mm E. Merk silica gel 60F-254 plates. Column chromatography was performed on Merk Silica gel 60 (70–230 mesh). Flash chromatography was performed using the forced flow of indicated solvent system on Merck Silica Gel 60 (230–400 mesh).

Unless otherwise noted, all non-aqueous reactions were carried out under an atmosphere of nitrogen or argon in glassware which had been either flame-dried or oven-dried (120°C). Operations of degassed solvent were performed on dualbank vacuum manifold through a three-way stopcock and repeated twice before used. THF was distilled from potassium metal/benzophenone ketyl. CH_2Cl_2 and DMF were dried over activated molecular sieves 4 Å (250°C, several hours). Pyridine was dried over KOH. All other commercially available reagents were used as received.

Trimethylsilylethenylmagnesium bromide

To a dry three-necked flask equipped with a mechanical stirrer, a water condenser, and a constant-pressure dropping funnel were placed THF (30 mL) and magnesium turnings (1.56 g, 64.91 mmol). To this mixture was added 0.10 mL of 1,2-dibromoethane to initiate the reaction (heat the solution if necessary), followed by dropwise addition of (1-bromovinyl)trimethylsilane (9.68 mL, 63.64 mmol) under nitrogen atmosphere. After addition, the mixture was heated at 70°C for 1 h. The resulting mixture was cooled to room temperature and used directly in the next step.

Protected vinylsilane (5). To the above Grignard reagent were added CuI (592 mg, 3.11 mmol) and a solution of the tosylate **4** (12.46 g, 31.15 mmol) in THF (5 mL) at 0°C under nitrogen atmosphere. After stirring at 0°C for 3 h and then at room temperature for 2 days, the reaction was quenched with saturated aqueous NH_4Cl solution (250 mL), the mixture was extracted with CH_2Cl_2 (×3), the organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was purified by chromatography on silica gel (2.5→40% diethyl ether in hexane) to afford the vinylsilane **5** (7.61 g, 82%,) as a colorless oil. Small amount (9%) of SM was recovered. $[\alpha]_D^{25}=+33.7$ (c 0.70, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (6H, s, Me_2Si), 0.10 (9H, s, Me_3Si), 0.88 (9H, s, ^{t}BuSi), 1.36–1.50 (1H, m, H-3), 1.58–1.71 (2H, m, H-2×2), 1.99–2.07 (2H, m, H-6, H-3), 2.83 (1H, dd, J=15.0, 1.5 Hz, H-6), 3.15 (1H, td J=10.0, 2.0 Hz, H-5), 3.2-3.31 (2H, m, H-1, H-4), 3.86 (1H, dt, J=11.0, 2.0 Hz, H-1), 5.39 (1H, dd, J=3.0, 1.5 Hz, C=CH_2), 5.65 (1H, dd,2.0, 1.0 Hz, C=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, −4.1, −1.4, 17.8, 25.6, 25.7, 33.6, 39.6, 67.6, 71.5, 81.7 125.9, 149.6. IR (KBr): 2956, 2939, 2859, 1249, 1128, 1099, 837 cm^{-1}. Anal. Calcd for $C_{17}H_{36}O_2Si$: C, 62.13; H, 11.04. Found: C, 62.26; H, 11.21.

Hydroxyvinylsilane (5a). A solution of **5** (7.27 g, 23.15 mmol) in methanol (200 mL) was treated with *p*-toluenesulfonic acid monohydrate (421 mg, 2.2 mmol) at room temperature for 10 h. The reaction was quenched with trimethylamine (0.6 mL, 4.5 mmol). The solvent was evaporated and the residue was purified by chromatography on silica gel (33% diethyl ether in hexane) to afford the alcohol intermediate (**5a**) (4.51 g, 93%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (9H, s, ^{t}BuSi), 1.33–1.47 (1H, m, H-3a), 1.58–1.73 (2H, m, H-2×2), 2.06–2.14 (1H, m, H-3b), 2.29 (1H, ddt, J=15.0, 9.0, 1.0 Hz, H-6a), 2.72 (1H, ddt, J=15.0, 4.5, 1.0 Hz, H-6b), 3.18 (1H, td J=9.0, 4.0 Hz, H-5), 3.24–3.40 (2H, m, H-1a, H-4), 3.87 (1H, br d J=11.0 Hz, H-1b), 5.43 (1H, dt J=3.0, 1.0 Hz, C=CH_2), 5.71 (1H, dt, J=3.0, 1.5 Hz, C=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.3, 25.4, 32.7, 40.0, 67.4, 70.9, 81.2, 126.6, 149.9. IR (KBr): 3412, 2954, 2855, 1248, 1096, 1034, 838 cm^{-1}.

Acetoxyvinylsilane (5b). A mixture of **5a** (4.43 g, 20.21 mmol), acetic anhydride (5.97 mL, 63.30 mmol), pyridine (33.78 mL, 422 mmol) and 4-dimethylaminopyridine (710 mg, 6.3 mmol) in dichloromethane (100 mL) was stirred at room temperature for 1 h. The resulting solution was diluted with CH_2Cl_2 (300 mL), washed sequentially with cold 1N aqueous HCl solution, saturated aqueous $NaHCO_3$ solution (×2), brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (20% diethyl ether in hexane) to afford the vinylsilane **5b** (5.32 g, 100%) as a colorless oil. $[\alpha]_D^{25}=+34.5$ (c 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (9H, s, ^{t}BuSi), 1.37–1.41 (1H, m, H-3a), 1.62–1.83 (2H, m, H-2×2), 2.04 (3H, s, CH_3CO), 2.15–2.24 (2H, m, H-3b, H-6a), 2.47 (1H, dd, J=15.0 Hz, 1.0 Hz, H-6b), 3.39 (1H, td, J=12.0, 3.0 Hz, H-1a), 3.34 (1H, td, J=10.0, 3.0 Hz, H-5), 3.89 (1H, ddd, J=12.0, 4.0, 2.0 Hz, H-1b), 4.50 (1H, td J=10.0, 4.5 Hz, H-4), 5.39 (1H, dd, J=3.0, 1.0 Hz, C=CH_2), 5.62 (1H, dd, J=2.0, 1.0 Hz, C=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.4, 21.1, 25.0, 29.3, 39.3, 67.4, 72.1, 78.7, 126.6, 148.7, 170.3. IR (KBr): 2954, 2853, 1745, 1375, 1240, 1099, 1037, 839 cm^{-1}. Anal. Calcd for $C_{13}H_{24}O_3Si$: C, 60.89; H, 9.43. Found: C, 60.89; H, 9.63.

Vinyliodide (6). To a solution of iodine (12.50 g, 49.2 mmol) in degassed CH_2Cl_2 (130 mL) was added dropwise a solution of the silane **5b** (4.13 g, 16.40 mmol) in CH_2Cl_2 (40 mL). After stirring at room temperature for 30 min, the reaction was quenched with cold saturated aqueous Na_2SO_3 solution. The mixture was stirred until the yellow color of the solution disappeared, and extracted with CH_2Cl_2 (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel (14→20% diethyl ether in hexane) to afford **6** (3.61 g, 71%) as a pale yellow oil. R_f=0.33 (silica gel, 1:3, ether–hexane). $[\alpha]_D^{24}=+11.4$ (c 1.03, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43–1.57 (1H, m, H-3a), 1.65–1.84 (2H, m, H-2×2), 2.06 (3H, s, CH_3CO), 2.14–2.24 (1H, m, H-3b), 2.43 (1H, ddd, J=15.0, 9.0, 1.0 Hz, H-6a), 2.63 (1H, ddt, J=15.0, 3.0, 1.5 Hz, H-6b), 3.39 (1H, td, J=11.0, 3.0 Hz, H-1a), 3.53 (1H, td, J=9.0, 3.0 Hz, H-5), 3.94 (1H, ddt, J=11.0, 4.0, 2.0 Hz, H-1b), 4.59 (1H, ddd, J=10.5, 9.0, 5.0 Hz, H-4), 5.80 (1H, dd, J=2.0, 1.0 Hz, C=CH_2), 6.12 (1H, dd J=2.5, 1.0 Hz, C=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 24.9, 29.3, 47.6, 67.8, 71.2, 77.9, 106.9, 128.0, 170.3. IR (KBr): 2946, 2855, 1741, 1619, 1434, 1375, 1239, 1102, 893 cm^{-1}. Anal. Calcd for $C_{10}H_{15}O_3Si$: C, 38.73; H, 4.88. Found: C, 38.73; H, 5.03.

En-yne compound (7). A slurry of palladium(II) acetate

(22 mg, 0.1 mmol) and copper(I) iodide (15 mg, 0.08 mmol) in benzene (5 mL) was treated with triphenylphosphine (51 mg, 0.2 mmol) at 25°C for 15 min. A solution of **6** (300 mg, 0.97 mmol) and protected propargyl alcohol (330 mg, 0.2 mmol) in benzene (5 mL) was added to above solution, the resulting mixture was degassed twice with an argon line, and then treated with *n*-butylamine (0.14 mL, 0.15 mmol). After stirring at room temperature over night under argon atmosphere, the color of the solution changed from brown to orange. The reaction mixture was poured into saturated NH_4Cl solution (15 mL), and extracted with diethyl ether (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by chromatography on silica gel (20% diethyl ether in hexane) to afford compound **7** (234 mg, 69%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.15 (6H, s, Me_2Si), 0.94 (9H, s, ^{t}BuSi), 1.40–1.54 (1H, m, H-3a), 1.65–1.83 (2H, m, H-2×2), 2.04 (3H, s, CH_3CO), 2.13–2.22 (1H, m, H-3b), 2.24 (1H, dd, J=14.0, 9.0 Hz, H-6a), 2.44 (1H, dt, J=14.0, 2.0 Hz, H-6b), 3.31 (1H, td, J=11.0, 3.5 Hz, H-1a), 3.58 (1H, td, J=9.0, 3.0 Hz, H-5), 3.93 (1H, ddd, J=11.0, 3.5, 2.0 Hz, H-1b), 4.46 (2H, s, H-10×2), 4.54 (1H, ddd, J=10.0, 9.0, 4.5 Hz, H-4), 5.30 (1H, s, C=CH_2) 5.40 (1H, s, C=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.2, 18.2, 21.1, 25.0, 25.8, 29.4, 40.0, 52.1, 67.8, 71.9, 77.2, 84.5, 88.0, 123.5, 127.6, 170.3. MS-EI (*m*/*z*): 337 (M^+−Me), 295 (M^+−^{t}Bu).

En-yne compound (7a). A solution of **7** (195 mg, 0.55 mmol) in MeOH (6 mL) was treated with Potassium carbonate (76 mg, 0.55 mmol) at room temperature for 2 h. The solvent was evaporated and the residue was taken up with a mixture of 14% diethyl ether in hexane, filtered to remove precipitate, the filtrate was concentrated. Purification of the residue by column chromatography on silica gel (14% diethyl ether in hexane) afforded **8** (171 mg, 100%) as a colorless oil. $[\alpha]_D^{25}$=+12.1 (c 0.55, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (6H, s, Me_2Si), 0.90 (9H, s, Me_3CSi), 1.35–1.45 (1H, m, H-3a), 1.63–1.70 (2H, m, H-2×2), 1.77 (1H, s, OH), 2.09 (1H, dd, J=12.0, 3.0 Hz, H-3b), 2.26 (1H, dd, J=14.0, 8.0 Hz, H-6a), 2.69 (1H, dd, J=14.0, 1.0 Hz, H-6b), 3.28–3.40 (3H, m, H-1a, H-4, H-5), 3.87 (1H, dt, J=11.0, 2.0 Hz, H-1b), 4.41 (2H, s, H-10×2), 5.32 (1H, s, C=CH_2), 5.40 (1H, s, C=CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.1, 18.3, 25.6, 25.9, 33.0, 40.0, 52.2, 67.7, 70.2, 80.5, 85.2, 88.0, 123.6, 127.9. MS-EI (*m*/*z*): 253 (M^+−^{t}Bu). IR (KBr): 3422, 2932, 2858, 1734, 1718, 1473, 1363, 1258, 1097, 837 cm^{-1}. Anal. Calcd for $C_{17}H_{30}O_3Si$: C, 65.76; H, 9.74. Found: C, 65.64; H, 9.96.

Acetylene–biscobalthexacarbonyl complex (8). To a solution of **7a** (70 mg, 89 μmol) in degassed CH_2Cl_2 (1 mL) was added dropwise a solution of biscobaltoctacarbonyl (160 mg, 0.18 mmol) in degassed CH_2Cl_2 (2 mL) at 0°C under argon atmosphere, the mixture was stirred at room temperature for 2 h. The solvent was evaporated and the residue was directly subjected to column chromatography on silica gel (20% diethyl ether in hexane) to afford the cobalt complex **8** (53 mg, 100%) as a dark-red oil. $[\alpha]_D^{25}$=−8.0 (c 0.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.13 (6H, s, Me_2Si), 0.94 (9H, s, Me_3CSi) 1.35–1.49 (1H, m, H-3a), 1.61–1.74 (4H, m, H-2×2, H-12×2), 1.80–1.98 (2H, m, H-11×2), 2.14 (1H, br d, J=11.0 Hz, H-3b), 2.43 (1H, dd, J=14.5, 8.5 Hz, H-6a), 2.91 (1H, dd, J=14.5, 2.5 Hz, H-6b), 3.24–3.44 (3H, m, H-1a, H-4, H-5), 3.88 (1H, br d, J=11.0 Hz, H-1b), 4.87 (2H, s, H-10×2), 5.48 (1H, s, C=CH_2), 5.56 (1H, d, J=1.0 Hz, C=CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.7, 22.6, 25.5, 25.8, 33.2, 39.6, 64.2, 67.4, 70.5, 81.6, 119.6, 143.1. MS-EI (*m*/*z*): 596 (M^+), 568 (M^+−CO), 540 (M^+−2CO), 512 (M^+−3CO), 484 (M^+−4CO), 456 (M^+−5CO), 428 (M^+−6CO). HRMS-EI (*m*/*z*): [M−2CO]$^+$ calcd for $C_{21}H_{30}Co_2O_7Si$, 540.0424; found, 540.0426.

Bicyclic acetylene–biscobalthexacarbonyl complex (9). A solution of **8** (96 mg, 0.16 mmol) in degassed CH_2Cl_2 (40 mL) was cooled to 0°C, and treated with a solution of boron trifluoride etherate (0.03 mL, 0.16 mmol) in degassed CH_2Cl_2 (40 mL) for 20 min under argon atmosphere. The resulting mixture was washed with cold saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (11% diethyl ether in hexane, R_f=0.22) to afford **9** (65.0 mg, 87%) as a dark-red oil. $[\alpha]_D^{27}$=−71.3 (c 0.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45–1.54 (1H, m, H-3a), 1.58–1.70 (2H, m, H-2×2), 2.10–2.13 (1H, m, H-3b), 2.64 (1H, dd, J=14.0, 2.0 Hz, H-6a), 2.79 (1H, dd, J=14.0, 4.0 Hz, H-6b), 3.11 (1H, td, J=10.0, 4.5 Hz, H-4), 3.31–3.38 (2H, m, H-1a, H-5), 3.90 (1H, dd, J=12.0, 4.0 Hz, H-1b), 4.88 (1H, d, J=16.0 Hz, H-10a), 5.11 (1H, d, J=16.0 Hz, H-10b), 5.46 (1H, s, C=CH_2), 5.56 (1H, s, C=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 30.5, 40.5, 68.1, 74.0, 77.4, 80.7, 122.1, 141.0. MS-EI (*m*/*z*): 464 (M^+), 436 (M^+−CO), 408 (M^+−2CO), 380 (M^+−3CO), 352 (M^+−4CO), 324 (M^+−5CO), 296 (M^+−6CO). HRMS-EI (*m*/*z*): M^+ calcd for $C_{17}H_{14}O_8Co_2$, 463.9352; found, 463.9325.

Protected 1,4-butanediol (10a). A solution of 1,4-butanediol (3.28 g, 36.4 mmol) in anhydrous THF (60 mL) was cooled to 0°C, and treated with Sodium hydride (60% dispersion in mineral oil, 1.46 g, 36.4 mmol) for 40 min under nitrogen atmosphere, white precipitate formed during this period. A solution of *tert*-butylchlorodiphenylsilane (10.0 g, 36.4 mmol) in THF (40 mL) was added to the above solution over 1 h, the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was poured into saturated aqueous NH_4Cl (100 mL), extracted with diethyl ether (×3), dried over Na_2SO_4 and concentrated. Purification the residue by column chromatography silica gel (50% diethyl ether in hexane, R_f=0.32) afforded alcohol **10a** (10.72 g, 90%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (9H, s, SiBu^t), 1.60–1.74 (4H, m, CH_2×2), 1.99 (1H, t, J=5.0 Hz, OH), 3.64–3.72 (4H, m, OCH_2×2), 7.34–7.69 (10H, m, Ph×2).

Protected butanaldehyde (10b). To a slurry of the alcohol **10a** (10.70 g, 32.6 mmol) in CH_2Cl_2 (250 mL) containing potassium acetate (0.96 g, 9.78 mmol) was added pyridinium chlorochromate (10.55 g, 48.9 mmol) in one portion, the mixture was stirred at room temperature for 2 h. The resulting mixture was diluted with diethyl ether, filtered through a pad of silica gel, washed thoroughly with diethyl ether. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (20%

diethyl ether in hexane, R_f=0.30) to afford the aldehyde **10b** (8.55 g, 80%) as a colorless oil. R_f=0.59 (silica gel, 1:1, ether–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s, SiBu^t), 1.89 (2H, m, CH_2), 2.55 (2H, td, J=7.0, 2.0 Hz, CH_2CHO), 3.69 (2H, t, J=6.0 Hz, OCH_2, 7.34–7.69 (10H, m, Ph×2), 9.79 (1H, t, J=2.0 Hz, CHO).

Propargyl alcohol (10c). A solution of trimethylsilylacetylene (5.2 mL, 36.7 mmol) in THF (150 mL) was treated dropwise with *n*-butyllithium (1.6 M in hexane, 24.6 mL, 39.4 mmol) at −78°C under nitrogen atmosphere, the mixture was stirred at 0°C for 30 min. A solution of **10b** (8.55 g, 26.2 mmol) in THF (50 mL) was added to the above solution, and the resulting mixture was stirred at 0°C for 15 min. The reaction mixture was poured into saturated aqueous NH_4Cl solution, extracted with diethyl ether (×3), dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (14% diethyl ether in hexane, R_f=0.21) to afford **10c** (10.98 g, 92%) as a colorless oil. R_f=0.25 (silica gel, 1:4, ether–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.20 (9H, s, Me_3Si), 0.90 (9H, s, SiBu^t), 1.68–1.92 (4H, m, CH_2×2), 2.78 (total 1H, two d, J=2.0 Hz, OH), 3.68–3.78 (2H, m, OCH_2), 4.45 (total 1H, two t, J=6.0 Hz, *CH*OH), 7.38–7.76 (10H, m, Ph×2).

Hex-5-yn-1,4-diol (10). A solution of **10c** (10.96 g, 25.8 mmol) in DMF (200 mL) was treated with sodium hydride (60% dispersion in mineral oil, 1.24 g, 31.0 mmol) at 0°C for 30 min. Benzyl bromide (4.0 mL, 33.6 mmol) was added to the above solution, and the resulting mixture was stirred at room temperature for 2 h. The reaction solution was poured into cold saturated aqueous NH_4Cl solution, extracted with diethyl ether (×3). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (3% diethyl ether in hexane, R_f=0.18) to afford **10** (9.71 g, 85%) as a colorless oil. R_f=0.66 (silica gel, 1:4, ether–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (9H, s, SiBu^t), 1.70–1.94 (4H, m, CH_2×2), 2.46 (1H, s, C≡CH), 3.67 (2H, t, J=6.0 Hz, OCH_2), 4.11 (total 1H, two t, J=6.0 Hz, OCHC≡C), 4.48 (1H, d, J=11.0 Hz, OCH_2Ph), 4.79 (1H, d, J=11.0 Hz, OCH_2Ph), 7.33–7.69 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 26.8, 28.2, 32.1, 63.4, 68.3, 70.4, 73.9, 82.8, 127.7, 128.0, 128.4, 129.6, 134.0, 135.6, 137.9.

En-yne compound (11). A slurry of palladium(II) acetate (232 mg, 1.0 mmol) and copper(I) iodide (185 mg, 0.1 mmol) in benzene (50 mL) was treated with triphenylphosphine (535 mg, 2.0 mmol), and the mixture was stirred at room temperature for 20 min. To the resulting solution was added a solution of **10** (4.90 g, 11.1 mmol) and **6** (3.17 g, 10.2 mmol) in benzene (20 mL), the mixture was degassed twice with argon line, and then treated with *n*-butylamine (0.10 mL, 1.1 mmol), stirred over night under argon atmosphere. The color of the solution changed from brown to orange during this period. The reaction mixture was poured into saturated aqueous NH_4Cl solution, extracted with diethyl ether (×3). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (25% diethyl ether in hexane, R_f=0.24) to afford **11** (4.44 g, 89%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s, SiBu^t), 1.37–1.50 (1H, m, H-3a), 1.64–1.84 (4H, m, H-2×2, H-12×2), 1.87–1.97 (2H, m, H-11×2), 2.02 (3H, s, CH_3CO), 2.15 (1H, br d, J=12 Hz, H-3b), 2.26 (1H, dd, J=14.0, 9.0 Hz, H-6a), 2.48 (1H, dt, J=14.0, 2.0 Hz, H-6b), 3.33 (1H, dt, J=12.0, 3.0 Hz, H-1a), 3.59 (1H, td, J=9.5, 3.2 Hz, H-5), 3.69 (1H, t, J=6.5 Hz, H-13×2), 3.92 (1H, ddd, J=12.0, 4.0, 1.5 Hz, H-1b), 4.26 (1H, t, J=6.5 Hz, H-10), 4.53–4.60 (1H, td, J=9.5, 5.0 Hz, H-4), 4.51 (1H, dd, J=12.0, 2.0 Hz, OCH_2Ph), 4.81 (1H, d, J=12.0 Hz, CH_2Ph), 5.30 (1H, s, C=CH_2), 5.43 (1H, s, C=CH_2), 7.28–7.68 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 21.1, 25.0, 26.8, 28.4, 29.4, 32.2, 40.1, 63.5, 67.8, 68.9, 70.4, 71.9, 85.7, 88.5, 123.5, 127.5, 127.7, 128.0, 128.4, 129.6, 134.0, 138.1. IR (KBr): 2931, 2858, 1739, 1239, 1101, 702 cm^{-1}. HRMS-EI (*m*/*z*): M^+ calcd for $C_{39}H_{48}O_5Si$, 624.3271; found, 624.3257. Anal. Calcd for $C_{39}H_{48}O_5Si$: C, 74.96; H, 7.74. Found, C, 74.97; H, 7.80.

Alcohol (12a). A solution of **11** (5.67 g, 9.07 mmol) in MeOH (50 mL) was treated with potassium carbonate (750 mg, 5.43 mmol) at room temperature for 2 h. The resulting mixture was evaporated to dryness, the residue was taken up with CH_2Cl_2 (400 mL), washed with saturated aqueous NH_4Cl, brine, and water, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography silica gel (50% diethyl ether in hexane, R_f=0.20) to afford **12a** (5.08 g, 96%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (9H, s, SiBu^t), 1.23–1.45 (1H, m,H-3a), 1.43–1.78 (4H, m, H-2×2, H-12×2), 1.86–1.93 (2H, m, H-11×2), 2.00–2.10 (1H, m, H-3b), 2.36 (1H, dd, J=15.0, 8.2 Hz, H-6a), 2.93 (1H, br d, J=15.0 Hz, H-6b), 3.20–3.32 (3H, m, H-1a, H-4, H-5), 3.60–3.72 (2H, m, H-13×2), 3.86 (1H, br d, J=11.0 Hz, H-1b), 4.68 (total 1H, two t, J=3.0 Hz, H-10), 4.52 (1H, d, J=11.0 Hz, OCH_2Ph), 4.81 (1H, dd, J=11.0 Hz, OCH_2Ph), 5.48 (1H, s, C=CH_2), 5.50 (1H, s, C=CH_2), 7.26–7.70 (15H, m, Ph×3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 19.1, 25.5, 26.8, 28.4, 32.2, 32.9, 40.1, 63.5, 67.8, 70.2, 70.4, 80.6, 86.2, 88.5, 123.7, 127.7, 128.0, 128.4, 129.6, 134.0, 135.6, 138.2.

Cobalt complex (12). A solution of **12a** (3.14 g, 5.40 mmol) in degassed CH_2Cl_2 (140 mL) was treated with a solution of biscobaltoctacarbonyl (3.32 g, 9.72 mmol) in degassed CH_2Cl_2 (60 mL) at 0°C under argon atmosphere, the mixture was stirred at room temperature for 2 h. The solvent was evaporated, and the residue was purified by column chromatography on silica gel (33% diethyl ether in hexane, R_f=0.25) to afford cobalt complex **12** (4.37 g, 87%) as a dark-red oil. R_f=0.36 (silica gel, 1:1, ether–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (9H, s, ^{t}Bu), 1.22–1.42 (1H, m, H-3a), 1.54–1.80 (4H, m, H-11a, H-12a, H-2×2), 1.80–2.07 (3H, m, H-11b, H-12b, H-3b), 2.36 (1H, dd, J=15.0, 8.0 Hz, H-6a), 2.93 (1H, d, J=15.0 Hz, H-6b), 3.20–3.30 (3H, m, H-1a, H-4, H-5), 3.68 (2H, m, H-13×2), 3.85 (1H, m, H-1b), 4.28 (2H, t, J=3.0 Hz, H-13×2), 4.57 (1H, d, J=11.5 Hz, $PhCH_2O$), 4.67 (1H, two dt, J=4.0, 3.0 Hz, H-10), 4.82 (1H, dd, J=11.5, 2.0 Hz, $PhCH_2$), 5.48 (1H, d, J=1.0 Hz, C=CH_2), 5.51 (1H, d, J=1.0 Hz, C=CH_2), 7.28–7.67 (15H, m, Ph×3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 25.6, 26.9, 29.5, 33.2, 35.0, 35.1, 39.6, 63.6, 67.3, 70.4, 72.6, 79.9, 81.8, 118.3, 127.5, 127.6, 127.9, 128.3, 129.5, 134.0, 135.6, 135.9, 136.1, 138.2, 199.9.

Bicyclic cobalt complex (13). A solution of **12** (4.37 g, 4.73 mmol) in degassed CH_2Cl_2 (1120 mL) was cooled to 0°C. To this solution was added dropwise a solution of boron trifluoride etherate (0.59 mL, 4.73 mmol) in degassed CH_2Cl_2 (118 mL), the mixture was stirred at 0°C for 40 min under argon atmosphere. The reaction mixture was washed with cold saturated aqueous $NaHCO_3$ (400 mL), brine and water, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (20% diethyl ether in hexane, R_f=0.31) to afford **13** (3.62 g, 94%) as a dark-red oil. R_f=0.59 (silica gel, 1:1, ether–hexane). $[\alpha]_D^{27}=-23.6$ (c 0.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (9H, s, Bu^t), 1.40–1.51 (1H, m, H-3a), 1.50–1.62 (H, m, H-2×2), 1.65–1.78 (2H, m, H-11a, H-12a), 1.89–94 (1H, m, H-12b), 2.00–2.04 (1H, m, H-3b), 2.07–2.16 (1H, m, H-11b), 2.63 (1H, dd, J=14.0, 2.0 Hz, H-6a), 2.75 (1H, dd, J=14.0, 4.0 Hz, H-6b), 3.14 (1H, td, J=10.0, 4.0 Hz, H-4), 3.30–3.36 (2H, m, H-1a, H-5), 3.69–3.80 (2H, m, H-13×2), 3.90 (1H, dd, J=12.0, 4.0 Hz, H-1b), 4.61 (1H, dd, J=10.0, 3.0 Hz, H-10), 5.42 (1H, s, C=CH_2), 5.55 (1H, s, C=CH_2), 7.34–7.68 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 26.0, 26.7, 29.6, 30.4, 40.4, 63.4, 68.0, 77.3, 80.7, 82.5, 96.6, 102.4, 121.3, 127.7, 129.6, 133.9, 134.0, 135.6, 141.4, 199.6. EIMS (m/z): 760 (M^+), 676 (M^+-3CO), 592 (M^+-6CO). HRMS-EI (m/z): $[M-3CO]^+$ calcd for $C_{33}H_{38}Co_2O_6Si$, 676.1101; found, 676.1084.

Bicyclic cobalt complex (13a). A solution of **12** (29 mg, 31 μmol) in degassed CH_2Cl_2 (25 mL) was cooled to 0°C. To this solution was added dropwise a solution of boron trifluoride etherate (4 μL, 1 mM) in degassed CH_2Cl_2 (5 mL). After stirring 1 min, the reaction was quenched with cold saturated aqueous $NaHCO_3$ (10 mL), the mixture was extracted with dichloromethane (×2), washed with brine and water, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (20% diethyl ether in hexane, R_f=0.31) to afford a mixture of **13a** and **13** (15 mg, 60%, calcd **13a**:**13**=1:3 on the base of ^{1}H NMR) as a dark-red oil. **13a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (9H, s, Bu^t), 1.40–1.51 (1H, m, H-3a), 1.50–1.62 (H, m, H-2×2), 1.65–1.78 (2H, m, H-11a, H-12a), 1.89–94 (1H, m, H-12b), 2.00–2.04 (1H, m, H-3b), 2.07–2.16 (1H, m, H-11b), 2.63 (1H, dd, J=14.0, 2.0 Hz, H-6a), 2.76 (1H, dd, J=14.0, 4.0 Hz, H-6b), 3.14 (1H, td, J=10.0, 4.0 Hz, H-4), 3.30–3.36 (2H, m, H-1a, H-5), 3.69–3.80 (2H, m, H-13×2), 3.90 (1H, dd, J=12.0, 4.0 Hz, H-1b), 5.00 (1H, dd, J=11.0, 2.0 Hz, H-10), 5.49 (1H, s, C=CH_2), 5.59 (1H, s, C=CH_2), 7.34–7.68 (10H, m, Ph×2).

Bicyclic acetylene–biscobalthexacarbonyl complex (14a, 14b). A solution of **13** (1.79 g, 2.36 mmol) and 2,4,6-triisopropylbenzenesulfonylhydrazide (10 g, 33.5 mmol) in MeOH (15 mL) was treated with triethylamine (1.23 mL, 16.8 mmol). After stirring at room temperature for 2 days, the mixture was filtered through a pad of silica gel, washed thoroughly with diethyl ether. The filtrate was concentrated to give a dark-red residue, which was separated with flash chromatography on silica gel (2% diethyl ether in hexane) to afford the major product **14a** (1.12 g, 63%), and the minor product **14b** (433 mg, 24%). **14a**: R_f=0.44 (silica gel, 1:10, ether–hexane, repeat three time). $[\alpha]_D^{26}=+29.3$ (c 0.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (9H, s, SiBu^t), 1.38 (3H, d, J=7.0 Hz, CH_3), 1.42–1.50 (1H, m, H-3a), 1.57–1.66 (3H, m, H-2×2, H-11a), 1.75–1.90 (3H, m, H-6a, H-12×2), 1.98 (1H, br d, J=14.0 Hz, H-6b), 2.00–2.10 (2H, m, H-11b, H-3b), 3.04–3.14 (2H, m, H-7, H-4), 3.17 (1H, dt, J=8.5, 2.0 Hz, H-5), 3.26 (1H, td, J=11.0, 3.0 Hz, H-1a), 3.68–3.79 (2H, m, H-13×2), 3.85 (1H, dt, J=11.0, 2.0 Hz, H-1b), 4.52 (1H, dd, J=10.5, 2.8 Hz, H-10), 7.33–7.70 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 25.1, 25.7, 26.7, 29.5, 31.7, 35.3, 36.8, 45.1, 63.5, 67.6, 83.1, 83.2, 84.3, 100.0, 107.9, 127.7, 129.6, 134.0, 135.6, 200.0. EIMS (m/z): 678 (M^+-3CO), 594 (M^+-6CO). HRMS-EI (m/z): calcd for $C_{33}H_{40}Co_2O_6Si$ $[M-3CO]^+$, 678.1258; found, 678.1238. **14b** (the minor product): R_f=0.43 (silica gel, 1:10, ether–hexane, repeated three times). $[\alpha]_D^{25}=-81.0$ (c 0.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (9H, s, SiBu^t), 1.35 (3H, d, J=7.0 Hz, CH_3), 1.42–1.49 (1H, m, H-3a), 1.55–1.72 (3H, m, H-2×2, H-11a), 1.69–1.71 (1H, m, H-12a), 1.96–2.09 (3H, m, H-3b, H-6a, H-11b), 3.17 (1H, m, H-7), 3.32–3.36 (3H, m, H-1a, H-4, H-5), 3.75 (2H, m, H-13×2), 3.88 (1H, dd J=11.0, 4.0 Hz, H-1b), 4.64 (1H, dd, J=10.0, 2.5 Hz, H-10), 7.34–7.67 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 24.7, 26.1, 26.7, 29.6, 30.4, 31.8, 34.7, 40.7, 63.4, 68.0, 76.9, 80.1, 82.6, 101.1, 108.9, 127.7, 129.6, 133.9, 134.0, 135.6, 200.2. EIMS (m/z): 678 (M^+-3CO), 594 (M^+-6CO). HRMS-EI (m/z): $[M-3CO]^+$ calcd for $C_{33}H_{40}Co_2O_6Si$, 678.1258; found, 678.1235.

α-Methyl bicyclic olefin (15a). A solution of **14a** (840 mg, 1.03 mmol) and n-butyltin hydride (1.41 mL, 5.15 mmol) in benzene (20 mL) was heated at 50°C for 5 h. The color of the solution changed from dark-red to yellow during this period. The solvent was evaporated in vacuo, and the residue was directly subjected to column chromatography (11% diethyl ether in hexane) to afford olefin **15a** (813 mg, 96%) as a colorless oil. R_f=0.58 (silica gel, 1:3, ether–hexane). $[\alpha]_D^{25}=-38.4$ (c 0.40, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s, SiBu^t), 1.40–1.5 (1H, m, H-3a), 1.50–1.65 (4H, m, H-12a, H-11a, H-2×2), 1.65–1.80 (3H, H-6, H-11b, H-12b), 1.99 (1H, br d, J=12 Hz, H-3b), 3.05 (1H, br quart, J=7.0 Hz, H-7), 3.16–3.26 (2H, m, H-4, H-5), 2.29 (1H, dd, J=11.0, 3.0, H-1a), 3.68 (2H, t, J=5.5 Hz, H-13×2), 3.82 (1H, dt, J=11.0, 3.0 Hz, H-1b), 3.94 (1H, m, H-10), 5.18 (1H, ddd, J=11.0, 3.5, 1.0 Hz, H-9), 5.31 (1H, ddd, J=11.0, 7.0, 1.0 Hz, H-8), 7.75–7.33 (10H, m, Ph×2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 24.5, 25.5, 26.8, 27.1, 28.8, 30.7, 32.0, 43.0, 63.7, 67.3, 76.6, 79.4, 79.6, 127.6, 128.9, 129.5, 134.1, 135.6, 137.9.

Alcohol (16a). A solution of **15a** (450 mg, 0.94 mmol) in THF (12 mL) was treated with tetrabutylammonium fluoride (1.0 M in THF, 0.94 mL, 0.94 mmol) at room temperature for 3 h. The resulting mixture was diluted with diethyl ether (100 mL), washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (67% diethyl ether in hexane, R_f=0.25) to afford alcohol **16a** (193 mg, 85%) as a colorless oil. $[\alpha]_D^{25}=-46.5$ (c 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (3H, d, J=7.0 Hz, CH_3), 1.34–1.46 (2H, m, H-3a, H-6a), 1.46–1.60 (2H, m, H-11×2), 1.62–1.71 (4H, m, H-2×2, H-12×2), 1.74 (1H, dd, J=14.0, 5.6 Hz, H-6b), 2.08 (1H, br d, J=12.0 Hz, H-3), 2.20 (1H, br s, OH), 3.07 (1H, m, H-7), 3.18–3.35

(3H, m, H-1a, H-4, H-5), 3.63 (2H, d, J=2.5 Hz, H-13×2), 3.80 (1H, dt, J=11.0, 2.0 Hz, H-1b), 3.98 (1H, m, H-10), 5.17 (1H, ddd, J=11.5, 4.0, 1.5 Hz, H-9), 5.31 (1H, ddd, J=11.5, 7.5, 1.0 Hz, H-8). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 25.4, 27.1, 29.3, 30.7, 32.3, 42.9, 62.8, 67.3, 76.8, 79.4, 79.6, 128.4, 138.2. IR (KBr): 342, 2932, 2857, 1457.4, 1338, 1097, 952, 730.2 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.94; H, 10.30.

β-Methyl bicyclic olefin (15b). A solution of **14b** (100 mg, 0.12 mmol) and *n*-butyltin hydride (0.40 mL, 1.44 mmol) in benzene (6 mL) was heated at 50°C for 3 h. The color of solution change from dark-red to yellow during this period. The solvent was evaporated in vacuo, and the residue was purified by column chromatography on silica gel (hexane→11% diethyl ether in hexane, R_f=0.24) to afford **15b** (50 mg, 86%) as a colorless oil. R_f=0.58 (silica gel, 1:3, ether–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s, SiBu^t), 1.16 (3H, d, J=7.0 Hz, CH_3), 1.20–1.50 (2H, m, H-6a, H-3a), 1.51–1.68 (4H, m, H-12×2, H-2×2), 1.69–1.82 (2H, m, H-11×2), 1.93 (1H, dd, J=8.5, 3.5 Hz, H-6b), 2.01 (1H, m, H-3b), 2.63 (1H, br quart, J=7.0 Hz, H-7), 3.18–3.31 (2H, m, H-4, H-5), 3.34 (1H, dd, J=10.5, 3.5 Hz, H-1a), 3.64–3.70 (2H, m, H-13×2), 3.84 (1H, m, H-1b), 4.06 (1H, m, H-10), 5.24 (1H, ddd, J=12.0, 4.5, 2.0 Hz, CH=CH), 5.57 (1H, ddd, J=12.0, 8.0, 2.0 Hz, CH=CH), 7.68 (10H, m, Ph×2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 22.1, 25.1, 26.8, 28.8, 29.6, 30.5, 32.9, 40.1, 63.7, 67.3, 77.4, 77.6, 79.0, 127.6, 129.6, 131.1, 134.1, 135.6, 136.4.

Alcohol (16b). A solution of **15b** (60 mg, 0.13 mmol) in THF (1.5 mL) was treated with tetrabutylammonium fluoride (1.0 M in THF, 0.13 mL, 0.13 mmol). After stirring at room temperature for 3 h, the reaction mixture was diluted with diethyl ether (10 mL), washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (67% diethyl ether in hexane, R_f=0.25) to afford alcohol **16b** (28 mg, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (3H, d, J=7.0 Hz, CH_3), 1.35–1.46 (2H, m, H-3a, H-6a), 1.53–1.46 (6H, m, H-2×2, H-11×2, H-12×2), 1.73 (1H, ddd, J=14.0, 6.0, 2.0 Hz, H-6b), 1.94 (1H, ddd, J=12.0, 9.0, 4.0 Hz, H-3b), 2.04 (1H, m, OH), 2.61 (1H, br quart, J=7.0 Hz, H-7), 3.20–3.36 (3H, m, H-1a, H-4, H-5), 3.63 (2H, m, H-13×2), 3.81 (1H, dt, J=10.0, 4.0 Hz, H-1b), 4.12 (1H, m, H-10), 5.22 (1H, ddd, J=13.0, 4.0, 1.5 Hz, H-9), 5.56 (1H, ddd, J=13.0, 6.0, 1.5 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 25.1, 29.3, 29.6, 30.4, 33.2, 40.0, 62.8, 67.3, 77.5, 77.8, 79.0, 130.5, 136.6.

8-Chloromercurric-9,10-*cis*-tricyclic compound (17). A solution of **16a** (15 mg, 0.063 mmol) and mercury(II) acetate (96 mg, 0.32 mmol) in CH_2Cl_2 (0.8 mL) was stirred at room temperature for 20 h. The reaction mixture was diluted with CH_2Cl_2, washed with brine. The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (50% diethyl ether in hexane) to afford **17** as a white foam (15 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (3H, d, J=7.0 Hz, CH_3), 1.36–1.46 (1H, m, H-12), 1.58–1.73 (2H, m, H-6a, H-3a), 1.73–1.96 (3H, m, H-6b, H-11, H-12), 2.05 (1H, br d, J=12 Hz, H-3), 2.54 (1H, m, H-7), 3.02–3.11 (1H, td, J=9.5, 4.0 Hz, H-4), 3.17 (1H, br t, J=9.5 Hz, H-5), 3.24–3.32 (1H, m, H-1a), 3.43 (1H, dd, J=11.0, 3.0 Hz, H-13a), 3.50 (1H, dd, J=10.5, 3.5 Hz, H-8), 3.67 (1H, dd, J=5.0, 2.0 Hz, H-10), 3.77 (1H, dd, J=10.5, 2.0 Hz, H-9), 3.81–3.94 (2H, m, H-13b, H-1b). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 21.1, 22.6, 24.9, 26.0, 28.9, 31.6, 32.5, 62.6, 67.1, 68.0, 75.3, 80.6, 81.5.

9,10-*cis*-Tricyclic compound (18). To a solution of **17** (14 mg, 0.03 mmol) in toluene (1.0 mL) was added *n*-butyltin hydride (0.09 mL, 0.09 mmol) and AIBN (1 mg), the mixture was heated at 55°C for 2 h. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane→20% diethyl ether in hexane) to afford **18** (6.1 mg, 85%) as a colorless oil. R_f=0.47 (silica gel, 1:1, ether–hexane). $[\alpha]_D^{25}$=+56.3 (c 0.11, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (3H, d, J=7 Hz, CH_3), 1.35–1.44 (1H, m, H-3a), 1.52 (1H, ddd, J=12, 10, 4 Hz, H-6a), 1.58–1.64 (1H, m, H-11a), 1.61–1.71 (2H, m, H-2×2), 1.84–1.92 (2H, m, H-12×2), 2.00–2.09 (2H, m, H-3b, H-11b), 2.11–2.22 (1H, m, H-7), 3.07 (1H, td, J=10, 5 Hz, H-4), 3.16 (1H, td, J=10, 2 Hz, H-5), 3.28 (1H, ddd, J=11, 9, 5 Hz, H-1a), 3.45 (1H, td, J=11, 3 Hz, H-13a), 3.59 (H, dd, J=5, 2 Hz, H-9), 3.62 (1H, dd, J=4, 2 Hz, H-10), 3.84 (1H, ddd, J=11, 5, 2 Hz, H-1b), 3.92 (1H, ddd, J=11, 5, 2 Hz, H-13b). ^{13}C NMR (125 MHz) δ 18.1, 21.2, 23.7, 26.2, 26.3, 29.6, 32.1, 43.0, 66.7, 67.8, 75.5, 75.9, 81.0, 82.1. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.85; H, 10.18. HRMS-EI (m/z): M^+ calcd for $C_{14}H_{24}O_3$, 240.1725; found, 240.1718.

8-Iodo-9,10-*trans*-tricyclic compound (19). A solution of **16a** (16 mg, 0.067 mmol) in CH_3CN (0.5 mL) was treated with iodine (88 mg, 0.23 mmol) at 0°C. After stirring at room temperature for 1 h, the reaction was quenched with cold saturated aqueous Na_2SO_3 (1 mL), the mixture was stirred until the yellow color disappeared, extracted with diethyl ether (×3), dried over Na_2SO_4, concentrated. The residue was purified by column chromatography on silica gel (25% diethyl ether in hexane, R_f=0.22) to afford **19** (13.7 mg, 56%) as a colorless oil. R_f=0.45 (silica gel, 1:1, ether–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (3H, d, J=6.5 Hz, CH_3), 1.29–1.41 (1H, m, H-6a), 1.50 (1H, m, H-3a), 1.62–1.74 (2H, m, H-2×2), 1.72–1.93 (4H, m, H-7, H-12×2, H-11a), 1.93–2.04 (2H, m, H-6b, H-3b), 2.29 (1H, td, J=6.5, 2.0 Hz, H-11b), 2.51 (1H, dd, J=9.0, 1.5 Hz, H-8), 3.03 (1H, ddd, J=10.5, 8.5, 4.0 Hz, H-5), 3.16 (1H, ddd, J=10.5, 8.5, 4.0 Hz, H-4), 3.36–3.49 (1H, m, H-1a), 3.84–3.93 (3H, m, H-1b, H-13×2), 4.04 (1H, dd, J=9.0, 1.5 Hz, H-9), 4.24 (1H, dt, J=9.0, 6.5 Hz, H-10). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.6, 25.6, 25.8, 29.2, 33.9, 36.3, 37.7, 42.6, 67.8, 68.9, 77.8, 78.0, 79.6, 80.4. HRMS-EI (m/z): $[M-I]^+$ calcd for $C_{14}H_{23}O_3$, 239.1637; found, 239.1645.

9,10-*trans*-Tricyclic compound (20). A solution of **19** (10.0 mg, 0.027 mmol), *n*-butyltin hydride (0.14 mL, 0.14 mmol) and AIBN (1 mg) in toluene (0.5 mL) was heated at 55°C for 2 h. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane→33% diethyl ether in hexane) to afford **20** (4.7 mg, 72%) as a colorless oil. R_f=0.38 (silica gel, 1:1, ether–hexane). $[\alpha]_D^{25}$=+35.8 (c 0.17, $CHCl_3$). ^{1}H NMR

(300 MHz, $CDCl_3$) δ 0.89 (3H, d, J=7 Hz, CH_3), 1.20 (1H, ddd, J=12, 9. 4 Hz, H-6a), 1.26 (1H, ddd, J=12, 6, 2 Hz, H-8a), 1.36 (1H, dd, J=13, 6 Hz, H-3a), 1.40–1.49 (2H, m, H-8b, H-11a), 1.46–1.52 (1H, m, H-7), 1.66–1.73 (2H, m, H-2×2), 1.80 (1H, ddd, J=12, 7, 2 Hz, H-11b), 1.86–1.92 (2H, m, H-12×2), 1.96 (1H, dt, J=12, 5 Hz, H-6b), 2.02 (1H, ddd, J=13, 9, 2 Hz, H-3b), 2.98 (1H, td, J=9, 4 Hz, H-5), 3.02 (1H, td, J=9, 6 Hz, H-4), 3.19 (1H, td, J=9.5, 2 Hz, H-9), 3.40 (1H, ddd, J=12, 10, 5 Hz, H-1a), 3.74 (1H, dd, J=13, 7 Hz, H-13a), 3.84 (1H, dd, J=13, 7 Hz, H-13b), 3.86–3.93 (1H, m, H-1b), 4.08 (1H, td, J=9.5, 7 Hz, H-10). ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 25.6, 25.7, 29.4,31.9, 36.0, 38.6, 39.1, 67.5, 67.8, 75.8, 77.8, 78.4, 80.6. HRMS-EI (m/z): M^+ calcd for $C_{14}H_{24}O_3$, 240.1725; found, 240.1719. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.91; H, 10.15.

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References

1. (a) Murata, M.; Legrand, A. M.; Ishibashi, Y.; Yasumoto, T. *J. Am. Chem. Soc.* **1989**, *111*, 8929. (b) Murata, M.; Legrand, A. M.; Ishibashi, Y.; Fukui, Y.; Yasumoto, T. *J. Am. Chem. Soc.* **1990**, *112*, 4380. (c) Yasumoto, T.; Murata, M. *Chem. Rev.* **1993**, *93*, 1897. (d) Scheuer, P. J. *Tetrahedron* **1994**, *50*, 3. (e) Gillespie, N. C.; Lewis, R. J.; Pearn, J.; Bourke, A. T. C.; Helms, M. J.; Bourke, J. B.; Shields, W. J. *Med. J. Aust.* **1986**, *145*, 584–590. (f) Satake, M.; Morohashi, A.; Oguri, H.; Oishi, T.; Hirama, M.; Harada, N.; Yasumoto, T. *J. Am. Chem. Soc.* **1997**, *119*, 11325–11326.

2. (a) Connor, R. E.; Nicholas, K. M. *J. Organomet. Chem.* **1977**, *125*, C45–C48. (b) Nicholas, K. M.; Pettit, R. *J. Organomet. Chem.* **1972**, *44*, C21. (c) Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1977**, 3472.

3. (a) Schreiber, S. L.; Sammakia, T.; Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *108*, 3128–3133. (b) Krafft, M. E.; Cheung, Y. Y.; Wright, C.; Cali, R. *J. Org. Chem.* **1996**, *61*, 3912–3915.

4. (a) Isobe, M.; Yenjai, C.; Tanaka, S. *Synlett* **1994**, *11*, 916–918. (b) Hosokawa, S.; Isobe, M. *J. Org. Chem.* **1999**, *64* (1), 37–48. (c) Saeeng, R.; Isobe, M. *Tetrahedron Lett.* **1999**, *40*, 1911–1914. (d) Isobe, M.; Hosokawa, S.; Kira, K. *Chem. Lett.* **1996**, 473. (e) Hoskawa, S.; Isobe, M. *Tetrahedron Lett.* **1998**, *39*, 2609–2612. (f) Yenjai, C.; Isobe, M. *Tetrahedron* **1998**, *54*, 2509–2520.

5. Isobe, M.; Nishizawa, R.; Hosokawa, S.; Nishikawa, T. *J. Chem. Soc. Chem. Commun.* **1998**, 2665–2676.

6. Alvarez, E.; Mercedes, D.; Delgado, M.; Liu, H.; Perez, R.; Martin, J. D. *Tetrahedron Lett.* **1996**, *37*, 2865–2868.

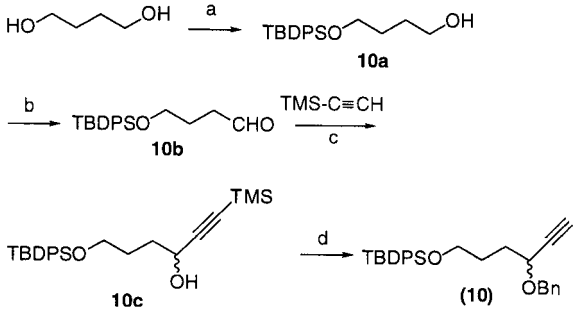
7. (a) Sommer, L. H.; Bailey, D. L.; Goldberg, G. M.; Buck, C. E.; Bye, T. S.; Evans, F. J.; Whitmore, F. C. *J. Am. Chem. Soc.* **1954**, *76*, 1613. (b) Ottolenghi, A.; Fridkin, M.; Ziliha, A. *Can. J. Chem.* **1963**, *41*, 2977–2982.

8. (a) Nunomoto, S. *J. Org. Chem.* **1983**, *48*, 1912–1914. (b) Derguini-Boumechal, F.; Linstrumelle, G. *Tetrohedron Lett.* **1976**, *36*, 3225–3226. (c) Huynh, C.; Linstrumelle, G. *Tetrahedron Lett.* **1979**, *12*, 1073–1075. (d) Fouquet, G.; Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 82. (e) Shea, K. J.; Pham, P. Q. *Tetrahedron Lett.* **1983**, *24*, 1463.

9. (a) Chan, T. H.; Lau, P. W. K.; Mychajlowskij, W. *Tetrahedron Lett.* **1977**, *38*, 3317–3320. (b) Barluenga, J.; Alvarez-Garcia, J.; Gonzalez, J. M. *Tetrahedron Lett.* **1995**, *36*, 2153–2156. (c) Chan, T. H.; Koumaglo, K. *Tetrahedron Lett.* **1986**, *27*, 883–886. Miller, R. B.; Reichenbach, T. *Tetrahedron Lett.* **1974**, *6*, 543–546.

10. (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467–4470. (b) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. (c) Ratovelomanana, V.; Hammoud, A.; Linstrumelle, G. *Tetrahedron Lett.* **1987**, *28*, 1649.

11. Preparation of the protected form of Hex-5-yn-1,4-diol (**10**).



a) NaH, TBDPSCl, THF, 0 °C-rt, 90%. b) PCC, KOAc, CH_2Cl_2, 80%. c) *n*-BuLi, THF, -78-0 °C, 92%. d) BnBr, NaH, DMF, 0 °C, 85%.

12. (a) Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1971**, *37*, 3475–3478. (b) Cusack, N. J.; Reese, C. B.; Roozpeikar, B. *J. Chem. Soc. Chem. Commun.* **1972**, 1132–1133. (c) Cusack, N. J.; Reese, C. B.; Roozpeikar, B. *Tetrahedron* **1976**, *32*, 2157–2162.

13. (a) Chamblin, A. R.; Mulholand, Jr. R. L. *Tetrahedron* **1984**, *40*, 2297–2302. (b) Danishefsky, S. J.; Larson, E.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1274–1280. (c) Giese, B.; Bartman, D. *Tetrahedron Lett.* **1985**, *26*, 1197–1200. (d) Chamblin, A. R.; Dezube, M.; Dussault, P.; McMills, M. *J. Am. Chem. Soc.* **1983**, *105*, 5819–5825. (e) Still, W. C.; Barirish, J. *J. Am. Chem. Soc.* **1983**, *105*, 2487–2489. (f) Midland, M. M.; Halterman, R. L. *J. Org. Chem.* **1981**, *46*, 1227–1229.

14. (a) Kahn, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650–663. (b) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 666–671. (c) Chamberlin, A. R.; Mulhollend, Jr., R. L. *J. Am. Chem. Soc.* **1987**, *109*, 672–677. (d) Houk, K. N.; Rondan, N. G.; Yun-Dong, W.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257–2274. (e) Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162–7166.

15. Pasto, D. J.; Gontar, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 6902–6908.

16. (a) Whitesides, G. M.; San Filippo, Jr. J. *J. Am. Chem. Soc.* **1970**, *92*, 6611–6624. (b) Evans, D. V.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506–2526.

17. (a) Rychosky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. (b) Bartlett, P. A.; Richardsin, D. P.; Myerson, J. *Tetrahedron* **1984**, *40*, 2317–2327. (c) Bartlett, P. A.; Ting, P. C. *J. Org. Chem.* **1986**, *51*, 2230–2240.

18. (a) Kuivila, H. G.; Menapace, L. W. *J. Org. Chem.* **1963**, *28*, 2165–2167. (b) Grady, G. L.; Kuivila, H. G. *J. Org. Chem.* **1969**, *34*, 2014–2016. (c) Kuivila, H. G. *Synthesis* **1970**, 449; Kupchik, E. J. *Organotin Compounds*; Marcel Dekker: New York, 1971; Vol. 1, Chapter 2.